AED Therapy in Children with Epilepsy
- non-drug treatment issues
- factors influencing choice of AEDs
- general principles of AED therapy in children
- specific AEDs

Treatment of Epilepsy - Overview
- counselling patient and family
e.g. factual information, EFV, emergency Mx of seizures
- treatment of underlying cause
e.g. hyponatraemia, cerebral tumour
- avoid precipitating factors
e.g. sleep deprivation, flashing lights
- lifestyle constraints
e.g. bathing, swimming, heights, alcohol, driving, vocational
- management of comorbidities
e.g. educational, psychological, psychiatric, behavioural
- antiepileptic drug therapy if indicated
  nb. which drug, how long, side effects, goals of Rx
- special treatments for refractory epilepsies
e.g. surgery, ketogenic diet, VNS

Lifestyle Issues with Epilepsy
- safety at home (bathing, hot water, heights etc)
- sports and hobbies (swimming, surfing, boating, climbing)
- school camps
- driving
- alcohol and recreational drugs
- sleep and sleep deprivation
- diet, exercise, smoking
- AED compliance
- school/university, study and exams
- vocational choices and disclosure
- relationships, contraception and pregnancy

Antiepileptic Drugs (AEDs)
- acetazolamide
- ACTH
- brivaracetam
- carbamazepine
- chlordiazepoxide
- clonazepam
- clorazepate
- clonazepam
- clobazam
- diazepam
- ethosuximide
- felbamate
- gabapentin
- ganaxolone
- immunoglobulins
- lacosamide
- lamotrigine
- levetiracetam
- lorazepam
- midazolam
- micronized oxcarbazepine
- midazolam oxcarbazepine
- midazolam oxcarbazepine paraldehyde phenytoin prednisolone pregabalin primidone ranipemide rufinamide stiripentol sulthiame tagabine topiramate valproate vigabatrin zonisamide

Factors Influencing AED Choices
- epileptic seizure & syndrome type - efficacy
  (seizures: GTCS, absence/myoclonic, partial/SGS, spasms, tonic)
  (syndrome: idiopathic vs symptomatic, some specific syndrome issues)
AED Efficacy by Seizure Type

<table>
<thead>
<tr>
<th>Drug</th>
<th>Partial</th>
<th>Tonic-clonic</th>
<th>Absence</th>
<th>Myoclonic</th>
<th>Atonic/Clonic</th>
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<tr>
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<td>Zonisamide</td>
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<td>Oxcarbazepine</td>
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</tbody>
</table>

Relative Efficacy of AEDs (meta-analysis)

- gabapentin
- lamotrigine
- tiagabine
- zonisamide
- oxcarbazepine
- levetiracetam
- vigabatrin
- topiramate

mean number needed to treat to obtain one extra responder over placebo for RCTs of add-on for partial seizures in adults

Factors Influencing AED Choices

- epileptic seizure & syndrome type - efficacy
  (seizures: GTCS, absence/myoclonic, partial/SGS, spasms, tonic)
  (syndrome: idiopathic vs symptomatic, some specific syndrome issues)
- relative/specific tolerability

Side-effects: CNS

- CNS side-effects common to all drugs, especially during introduction and toxicity
  eg. drowsiness, ataxia, tremor, diplopia, vomiting, headache esp. Na+ channel blockers (PHT, CBZ, VPA, TPM, LTG)
Side-effects: CNS

- CNS side-effects common to all drugs, especially during introduction and toxicity eg. drowsiness, ataxia, tremor, diplopia, vomiting, headache esp. Na+ channel blockers (PHT, CBZ, VPA, TPM, LTG)
- adverse behavioural effects relatively specific eg. hyperactivity, aggression, irritability, mood disturbance esp. GABAergic drugs (PB, BZP, VGB, VPA), LEV

Side-effects: Specific / Idiosyncratic

carbamazepine rash, leukopenia, hyponatraemia
valproate weight gain, hair loss, pancreatitis, hepatic failure
phenobarbitone rash
clonazepam increased secretions
phenytoin rash, serum sickness, hirsutism, gum hypertrophy, osteoporosis
lamotrigine rash, SJS, severe hypersensitivity
vigabatrin weight gain, retinopathy, psychosis
topiramate nephrolithiasis, weight loss, acidosis, glaucoma
oxcarbazepine hyponatraemia

AEDs and Weight Changes

- major issue with medication for many patients (up to 40% of patients gain > 5 kg)
- weight gain is common cause of non-compliance
- significant effects on psychological well-being
- implications of obesity for diabetes, HT, IHD etc

<table>
<thead>
<tr>
<th>AEDs</th>
<th>Weight Gain</th>
<th>Weight Loss</th>
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<tbody>
<tr>
<td>Lamotrigine</td>
<td>Carbamazepine</td>
<td>Phenytoin</td>
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<td>Levetiracetam</td>
<td>Gabapentin</td>
<td>Topiramate</td>
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<tr>
<td>Phenytoin</td>
<td>Valproate</td>
<td>Zonisamide</td>
</tr>
<tr>
<td>Vigabatrin</td>
<td>Pregabalin</td>
<td></td>
</tr>
</tbody>
</table>

AEDs, Fractures and Bone Mineral Density

- epilepsy and AED therapy are associated with increased fracture risk and reduced bone mineral density
- fracture risk greater than attributable to reduced BMD, presumably related to trauma eg. TCS, falls, MVA
- AEDs implicated inable, osteomalacia & osteoporosis
  - increased vitamin D catabolism by liver induction
  - decreased absorption of calcium
  - increased catabolism of sex steroids
  - direct AED effect eg. PHT
- epilepsy patients may have co-morbid medical, nutritional, drug and lifestyle reasons for low BMD

Odds ratio (log10) for withdrawal from trial due to adverse events (AED vs placebo) in RCTs of add-on in partial epilepsy in adults.


Relative Tolerability of AEDs (meta-analysis)

AEDs: Teratogenesis

- Increased risk of most types of birth defects with all AEDs (greatest risk with VPA ~10% and polytherapy)
- Small risk increase with epilepsy and no AEDs (1%)
- VPA risk reduced to other AEDs if <900mg/day
- Specific associations reported:
  - Neural tube defects and hypospadias (VPA, CBZ)
  - Congenital heart defects (PHT, VPA, PB)
  - Craniofacial abnormalities (PHT, VPA, PB, PRM)
  - Genitourinary defects (PHT, VPA, PB)
- Effects of AEDs (esp. VPA) in pregnancy on cognition in later childhood? Effects of AEDs on apoptosis and neuroreceptor expression in developing brain (Vinten J, Neurology 2005; Meador KJ, NEJM 2009)

Factors Influencing AED Choices

- Epileptic seizure & syndrome type - efficacy
  (seizures: GTCs, absence/myoclonic, partial/SGS, spasms, tonic)
  (syndrome: idiopathic vs symptomatic, some specific syndrome issues)
- Relative/specific tolerability
- Patient age, gender, ethnicity and comorbidities
  (infant, adolescent girl, developmental disabilities, obesity, metabolic, Asians and AED hypersensitivity)

Factors Influencing AED Choices

- Obesity
- Disabilites
- OCP (potential) pregnancy
- Migraine
- Mood disturbance
- Behavioural problems
- Sleep problems
- Saliva control
- Renal failure
- Liver failure
- Neoproliferation
- Metabolic disease
- Hypertension
- Glaucoma
- Osteoporosis
- Visual impairment
- Hypersensitivity (Asian)
- Psychosis

AED Pharmacokinetics

- Dose
- Elimination
- Metabolism
- Activity & Toxicity
- Effect of concomitant administration of AEDs on the half-life of lamotrigine

Effect of the concomitant administration of AEDs on the half-life of lamotrigine

- Lamotrigine with sodium valproate
- Lamotrigine
- Lamotrigine with carbamazepine or phenytoin

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Lamotrigine</th>
<th>Lamotrigine with sodium valproate</th>
<th>Lamotrigine with carbamazepine or phenytoin</th>
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Plasma concentration (µg/ml) vs. Time (h)
AED Metabolism

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<th>Drug</th>
<th>Metabolism</th>
<th>Active metabolite</th>
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<tbody>
<tr>
<td>CBZ</td>
<td>hepatic oxidation</td>
<td>CBZ-10,11-epoxide</td>
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<tr>
<td>CLB</td>
<td>hepatic demethylation</td>
<td>N-desmethylclobazam</td>
</tr>
<tr>
<td>DZP</td>
<td>hepatic demethylation</td>
<td>N-desmethyldiazepam</td>
</tr>
<tr>
<td>ESM</td>
<td>hepatic oxidation</td>
<td></td>
</tr>
<tr>
<td>PHT</td>
<td>hepatic oxidation</td>
<td></td>
</tr>
<tr>
<td>PB</td>
<td>hepatic oxidation &amp; renal excretion</td>
<td></td>
</tr>
<tr>
<td>VPA</td>
<td>hepatic oxidation &amp; glucuronidation</td>
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</tr>
<tr>
<td>NZP</td>
<td>hepatic reduction</td>
<td></td>
</tr>
<tr>
<td>PRM</td>
<td>hepatic oxidation &amp; renal excretion</td>
<td>phenobarbitone</td>
</tr>
<tr>
<td>LTG</td>
<td>hepatic glucuronidation</td>
<td></td>
</tr>
<tr>
<td>GBP</td>
<td>renal excretion</td>
<td></td>
</tr>
<tr>
<td>VGB</td>
<td>renal excretion</td>
<td></td>
</tr>
<tr>
<td>TPM</td>
<td>renal excretion, some hepatic metabolism</td>
<td></td>
</tr>
<tr>
<td>TGB</td>
<td>hepatic metabolism</td>
<td></td>
</tr>
<tr>
<td>OXC</td>
<td>hepatic metabolism</td>
<td>MHD</td>
</tr>
<tr>
<td>LEV</td>
<td>renal excretion</td>
<td></td>
</tr>
</tbody>
</table>

Co-medication and AEDs

- VPA: avoid CBZ, PHT; consider LTG, ESM
- CBZ/OXC: avoid PHT, PB, VPA, OXC/CBZ, LTG
- BZP: avoid PB, other BZP
- PB: avoid BZP, PHT, CBZ, TPM
- PHT: avoid VPA, CBZ, TPM, LTG, BZP, PB
- TPM: avoid other AEDs if possible, PHT
- LEV: OK
- GBP: OK

- stimulants: ? OK
- SSRIs: ? OK
- antibiotics: caution macrolides
- purgatives: separate dosing

Factors Influencing AED Choices

- epileptic seizure & syndrome type - efficacy
  (seizures: GTCS, absence/myoclonic, partial/SGS, spasms, tonic)
  (syndrome: idiopathic vs symptomatic, some specific syndrome issues)
- relative/specific tolerability
- patient age, gender, ethnicity and comorbidities
  (infant, adolescent girl, developmental disabilities, obesity, metabolic, Asians and AED hypersensitivity)
- concomitant medication
  (adverse and beneficial PK and PD interactions)
- seizure frequency
  (quick fix vs. time to wait)

AED Titration Rates

- Rapid titration
  - benzodiazepines (load)
  - phenytoin (load)
  - phenobarbitone (load)
  - gabapentin (days)
  - levetiracetam (days)
  - valproate (weeks)

- Slow titration
  - carbamazepine (weeks)
  - oxcarbazepine (weeks)
  - lamotrigine (months)
  - topiramate (months)

Factors Influencing AED Choices

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- concomitant medication
  (adverse and beneficial PK and PD interactions)
- seizure frequency
  (quick fix vs. time to wait)
- AED drug mechanisms
  (epileptogenesis and pharmacodynamics, rational polytherapy)

AED Mechanisms of Action

<table>
<thead>
<tr>
<th>Drug</th>
<th>block Na+ channels</th>
<th>enhance GABA effect</th>
<th>increase GABA levels</th>
<th>depress glutamate effect</th>
<th>decrease glutamate release</th>
<th>block Ca2+ channels</th>
<th>carbonic anhydrase inhibition</th>
<th>renal action</th>
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<tbody>
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<td>CBZ</td>
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<td>+</td>
<td>+</td>
<td>+</td>
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<td>+</td>
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</tbody>
</table>
**Other Factors Influencing AED Choices**

- rich knowledge of RCTs (add-on, monotherapy, comparative)
- own comfort or reluctance
- parent wishes, beliefs, internet research
- relative cost to community (GBP, LEV) or patient (CLB)
- hassle (PBS authority, SPX)
- inducements (pens, dinners, travel)

**AED Therapy in Children with Epilepsy**

- non-drug treatment issues
- factors influencing choice of AEDs
- general principles of AED therapy in children
- specific AEDs

**Goals of AED Therapy**

- no seizures, or at least no “major” seizures
- no AED side effects
- no exacerbation (possibly improvement) in comorbidities
- reduce mortality and morbidity
- improved quality of life (patient/family, home/school)
- maximise normal development (cognitive, physical, social)
- reduced health costs
- better QOL for doctor (fewer calls, visits, scripts, forms)

**General Principles of AED Therapy**

- “treat the patient’s seizures, not their EEG”
- “start low and go slow” esp. LTG, TPM, CBZ, VPA, BZP
General Principles of AED Therapy

• “treat the patient’s seizures, not their EEG”
• “start low and go slow” esp. LTG, TPM, CBZ, VPA, BZP
• aim for monotherapy initially

- aim for monotherapy initially
- push AEDs to clinical effect, toxicity or high level
- monitoring AED levels
  - important in PHT, PB
  - useful in CBZ
  - rarely useful in VPA, LTG
  - no value in BZP and new AEDs
- combination therapy where appropriate
  - combine AEDs with different actions
    eg. VPA & LTG/TPM
  - avoid combinations of drugs with similar actions
    eg. CBZ+PHT, BZP+PB
  - avoid AEDs with competing pharmacokinetics
    eg. VPA & CBZ/PHT
• discontinue AEDs slowly
  esp. BZP and PB

AED Level Monitoring

• reasons for doing AED levels
  → check compliance
  → explain inefficacy or side-effects
• may be useful if complicated PK
  - non-linear kinetics
  - self-induction, dose-limited absorption
  - interactions
• problems with AED level monitoring
  - drug-level-response relationship is poor for most drugs
  - reliable therapeutic ranges not available for most drugs
  - wide variability in effects of different levels
  - issue of unmeasured (neuroactive) free compound
• No evidence to support routine AED levels with the aim of optimisation of treatment of patients with newly-diagnosed epilepsy with AED monotherapy (Cochrane database 2007)

Monitoring of AED levels

<table>
<thead>
<tr>
<th>AED</th>
<th>Reasons for High Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>carbamazepine</td>
<td>when at high dose and ? go higher</td>
</tr>
<tr>
<td>valproate</td>
<td>rarely</td>
</tr>
<tr>
<td>barbiturates</td>
<td>often, especially in infants/elderly *</td>
</tr>
<tr>
<td>phenytoin</td>
<td>often, especially in infants/elderly *</td>
</tr>
<tr>
<td>benzodiazepines</td>
<td>never</td>
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<tr>
<td>lamotrigine</td>
<td>never</td>
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<tr>
<td>gabapentin</td>
<td>never</td>
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<tr>
<td>vigabatrin</td>
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<td>oxcarbazepine</td>
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<tr>
<td>topiramate</td>
<td>never</td>
</tr>
<tr>
<td>levetiracetam</td>
<td>never</td>
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</tbody>
</table>

* side effects missed, changing weight and pharmacokinetics

AED Level Monitoring

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  → check compliance
  → explain inefficacy or side-effects
• may be useful if complicated PK
  - non-linear kinetics
  - self-induction, dose-limited absorption
  - interactions
• problems with AED level monitoring
  - drug-level-response relationship is poor for most drugs
  - reliable therapeutic ranges not available for most drugs
  - wide variability in effects of different levels
  - issue of unmeasured (neuroactive) free compound
• clinical or other laboratory evaluation may be more useful
  - history: sedation, insomnia, cognition, paraesthesia
  - exam: tremor, nystagmus, ataxia
  - bloods: WCC, Na+, LFTs, acid-base
General Principles of AED Therapy

• “treat the patient’s seizures, not their EEG”
• “start low and go slow” esp. LTG, TPM, CBZ, VPA, BZP
• aim for monotherapy initially
• push AEDs to clinical effect, toxicity or high level
• monitoring AED levels
  - important in PHT, PB
  - useful in CBZ
  - rarely useful in VPA, LTG
  - no value in BZP and new AEDs
• combination therapy where appropriate

Monotherapy vs Polytherapy

• improved compliance and lower costs with monoRx
• fewer side effects with monoRx
• no drug interaction problems with monoRx
• potential adverse PD effects with some AED combos eg. PHT/CBZ/PB, PB/BZP/VGB, LTG/LEV, LTG/CBZ
• potential adverse PK effects with some AED combos eg. VPA and PHT/CBZ/PB

AED Withdrawal Recommendations

• recognise favourable syndromes (BRE, BOE, CAE) and unfavourable syndromes (TLE, FLE) for withdrawal
• consider after 2 yrs of seizure free therapy in unspecified epilepsy syndromes
• best if patient / parent initiated decision
• easier decision if AED side effects are present
• everyone understands and accept the risks
• modify lifestyle (esp. driving), continue precautions, and ensure school/work environment is safe
• withdraw one drug at a time slowly, very slowly for phenobarbitone and benzodiazepines
• look out for mood and behaviour disturbances

Monotherapy vs Polytherapy

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Predictors of Seizure Recurrence

• seizure onset in second decade
• symptomatic aetiology, intellectual disability, abnormal neurological examination
• myoclonus, especially JME
• strong family history of epilepsy
• abnormal EEG before or during withdrawal
• recurrence after previous attempt to withdraw

General Principles of AED Therapy

• “treat the patient’s seizures, not their EEG”
• “start low and go slow” esp. LTG, TPM, CBZ, VPA, BZP
• aim for monotherapy initially
• push AEDs to clinical effect, toxicity or high level
• monitoring AED levels
  - important in PHT, PB
  - useful in CBZ
  - rarely useful in VPA, LTG
  - no value in BZP and new AEDs
• combination therapy where appropriate

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• combination therapy where appropriate
  - combine AEDs with different actions eg. VPA & LTG/TPM
  - avoid combinations of drugs with similar actions eg. CBZ+PHT, BZP+PB
  - avoid AEDs with competing pharmacokinetics eg. VPA & CBZ/PHT
• discontinue AEDs slowly esp. BZP and PB
AED Therapy in Children with Epilepsy

- non-drug treatment issues
- factors influencing choice of AEDs
- general principles of AED therapy in children
- specific AEDs

Antiepileptic Drugs (AEDs)

- acetazolamide
- ACTH
- brivaracetam
- carbamazepine
- chiorazepate
- clonazepam
- clobazam
- diazepam
- ethosuximide
- felbamate
- gabapentin
- ganaxolone
- immunoglobulins
- lacosamide
- lamotrigine
- levetiracetam
- lorazepam
- midazolam
- oxcarbazepine
- paraldehyde
- phenobarbitalone
- phenytoin
- prednisolone
- pregabalin
- primidone
- remacemide
- rufinamide
- sipradol
- sulthiame
- tiagabine
- topiramate
- valproate
- vigabatr
- zonisamide

Carbamazepine (CBZ)

- Actions: blocks voltage-gated Na+ channels
- Indications: partial epilepsy and generalised TCS
- Efficacy: partial seizures, 1st and 2nd generalised TCS
- Dosing: start 5 mg/kg/day incr. wkly over 2-3 wks to 15-20 mg/kg/day give b.d (CR) or t.i.d. (esp. syrup) +/- levels
- Interactions: liver enzyme induction and lowers AED levels pharmacodynamic interaction with other Na channel blockers (PHT, PB)
- Adverse: rash 3-5%
  CNS side effects + low Na+ & WCC in toxicity exacerbates absence Sz and myoclonus in IGE

Valproate (VPA)

- Actions: blocks Na+ channels +/- GABAergic action
- Indications: partial & generalised epilepsy, inc. absence
- Efficacy: GTCS, absence, myoclonic, tonic + partial Sz drug of choice for idiopathic epilepsies
- Dosing: start 10 mg/kg/day incr. wkly over 2-3 wks to 20-30 mg/kg/day give b.d, no need for levels, take with food
- Interactions: blocks liver enzymes and raises AED levels competes for protein bindings
- Adverse: CNS side effects + tremor in toxicity weight gain, hair loss, GIT disturbance risk of liver failure (infant, multiple AEDs, MR)

Benzodiazepines (BZP)

- Actions: enhance GABA action at synapse
- Indications: partial & generalised epilepsy
- Efficacy: partial, GTCS, myoclonic, tonic +/- absence
- Dosing: depends on drug eg. clonazepam, diazepam, clobazam, nitrazepam, lorazepam generally start very low and go very slow
- Interactions: minimal pharmacokinetic interactions
- Adverse: drowsiness, sedation (esp with PB, other BZPs) increased secretions eg. drooling, respiratory behavioural change, mood disturbance tolerance and tachyphalaxis

Phenobarbitone (PB)

- Actions: blocks Na+ channels, enhances GABA
- Indications: partial seizures, GTCS, neonatal seizures, status epilepticus
- Efficacy: partial and GTCS seizures
- Dosing: load 15-20 mg/kg (higher in SE) maintenance 5mg/kg/day (monitor levels)
- Interactions: VPA, BZP
- Adverse: behaviour and cognitive disturbance, rash
Lamotrigine (LTG)

**Actions:** blocks Na+ channels + ? other actions  
**Indications:** partial and generalised seizures  
**Efficacy:** partial, absence, myoclonic, TCS, tonic  
**Dosing:** start <0.5, max 5-15 mg/kg/day without VPA  
start <0.2, max 1-5 mg/kg/day with VPA  
very slow titration  
**Interactions:** VPA increases levels +++  
beneficial PD effect when used with VPA  
potentiates CBZ side effects  
**Adverse:** rash 3-5%; severe hypersensitivity 0.3-1%  
CNS side effects including tremor in toxicity  
exacerbates seizures in SMEI

Oxcarbazepine (OXC)

**Actions:** converted to MHD, blocks Na+ channels  
**Indications:** partial epilepsy and generalised TCS  
**Efficacy:** partial seizures, 1st and 2nd generalised TCS  
**Dosing:** start 5 mg/kg/day  
increase over 2-3 wks to 15-25 mg/kg/day  
**Interactions:** liver enzyme induction  
**Adverse:** low Na+  
exacerbates absence Sz and myoclonus in IGE

Levetiracetam (LEV)

**Actions:** novel – binds to synaptic vesicle protein  
**Indications:** partial seizures  
**Efficacy:** partial and generalised seizures  
**Dosing:** start 10 mg/kg/day, target 25-50 mg/kg/day  
**Interactions:** nil significant  
**Adverse:** behaviour disorder, psychosis  
sleep disturbance

Topiramate (TPM)

**Actions:** blocks Na+ channels, blocks kainate/AMPA,  
enhances GABA, carbonic anhydrase inhibition  
**Indications:** partial and generalised seizures, LGS  
**Efficacy:** partial, GTCS, tonic, ?spasms, ?absence  
**Dosing:** start 1, max 5-10 mg/kg/day  
slow titration  
**Interactions:** nil significant  
**Adverse:** cognitive, speech  
nephrolithiasis, weight loss

Vigabatrin (VGB)

**Actions:** non-competitive inhibition of GABA transaminase  
**Indications:** partial seizures, infantile spasms  
**Efficacy:** partial and tonic seizures esp. lesional, TS  
**Dosing:** 50-150 mg/kg/day, 0.5-4 g/day  
rapid titration possible  
**Interactions:** nil significant  
**Adverse:** behaviour disorder, psychosis, weight gain  
retinopathy - > 30% adults, ??? children  
exacerbate myoclonic seizures

UKISS Study

- 107 infants with spasms were randomised to hormonal treatment (synacthen or high dose prednisolone) or VGB.  
Control of spasms at Day 14 was achieved in 75% with hormonal treatment and 54% with VGB (p=0.04). More EEG improvement occurred with hormonal treatment.  
- Combined with results from an Italian trial comparing ACTH and VGB, hormonal treatments are superior to VGB in stopping spasms - difference 22% (95%CI 7-38%).  
- The cryptogenic subgroup showed a clinically and statistically significant difference in development:  
  - at age 14 months (mean VABS: hormonal 88 vs VGB 79)  
  - at age 4 yrs (median VABS: hormonal 96 vs VGB 83)  
- ICISS will compare hormonal treatment +/- VGB.  
RCH Protocol for Infantile Spasms

**Prednisolone** is 1st line treatment, except in TS or treatable IEM:
- 10mg QID for 2 wks then wean by one 10mg dose every 5 days
- increase to 20mg tds if spasms continue after 1 week
- twice-weekly monitoring of electrolytes, glucose and BP

**Vigabatrin** is 1st line treatment in TS and 2nd line treatment after 2-4 weeks of no response to prednisolone in non-TS settings:
- 50 mg/kg/day increasing to 150 mg/kg/day (max) over 1 week if spasms do not cease after each dosage step
- treat for 3 months, increasing the dose with increases in weight
- wean over 1 month
- ACTH, other AEDs, ketogenic diet or surgery for refractory cases

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Some Tips

- start VPA for IGE/IPE and CBZ for SPE/IPE
- get comfortable with LTG, OXC and LEV
- avoid high doses of VPA, TPM, CLB/CZP
- use CBZ, LEV, GBP in high dose if working
- tds dosing if using CBZ/OXC liquid (use CBZ-CR tablets)
- plan out path of likely AED changes and additions
- consider low dose VPA+LTG+CLB combination
- more side effects with big doses of one AED than small doses of combinations (+ one drug = polypharmacology)
- remember old AEDs eg. ESM (absence, myoclonic, atypical BRE) PHT (older teenager), PB (infants briefly)
- levels only in PHT and PB (sometimes VPA, CBZ)
- be wary of CBZ/OXC exacerbation of IGEs and BRE/BOE