Stopping seizures

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Disclosures

Honoraria from Eisai, GW Pharma, Sanofi, UCB Pharma and Zogenix. Meeting support from LivaNova, Bial, Novartis.
Stopping Seizures

Seizures, epilepsy, and why this is important

Status epilepticus

Acute management of seizures

Management of epilepsy
Epilepsy is different

Chronic disorder
- Intermittent
- Collection of symptoms
- Likely at any age

Neurological disorder
- Common and treatable
- Not progressive
- Tests may be unhelpful
Definitions

A disorder of the brain characterised by an enduring predisposition to generate epileptic seizures

“An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain”

Practically - two unprovoked seizures >24 h apart

But also - one unprovoked seizure and a recurrence risk of at least 60%; diagnosis of an epilepsy syndrome
Seizures

“Not a fundamental change but allows greater flexibility and transparency in naming seizure types”
Seizures – At a glance

Partial -> Focal

“Awareness”
Dyscognitive, simple/complex partial, psychic are all lost

“Focal to bilateral tonic clonic seizure”
Secondarily generalised is lost
Age-related incidence of epilepsy in industrialised countries. Banergee & Hauser (2007)
Epilepsy Treatment
# Classification

<table>
<thead>
<tr>
<th>Genetic</th>
<th>Focal</th>
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<tbody>
<tr>
<td>Idiopathic</td>
<td>Partial</td>
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<tr>
<td>Presumed genetic</td>
<td>Presumed acquired</td>
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<td>Onset in childhood</td>
<td>Onset in adulthood</td>
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<tr>
<td>Photosensitive</td>
<td>Seizures may be bizarre</td>
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<tr>
<td>Sleep sensitive</td>
<td>Surgery is possible</td>
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<td>May remit</td>
<td>Likely lifelong</td>
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<tr>
<td>Valproate</td>
<td>Lamotrigine</td>
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<tr>
<td>Levetiracetam</td>
<td>Carbamazepine</td>
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<tr>
<td>Clobazam</td>
<td>Levetiracetam</td>
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</table>
Genetic generalised epilepsy

Marson AG et al.

The SANAD study of effectiveness of valproate, lamotrigine, or topiramate for generalised and unclassifiable epilepsy: an unblinded randomised controlled trial.

Lancet 2007;369(9566):1016-26
Valproate

Indication
   Generalised epilepsy, migraine, bipolar disorder

Side effects
   Weight gain
   Ataxia, hair loss, parkinsonism, PCOS

Secondary benefits
   Mood
   Many formulations
I am taking valproate* and planning to become pregnant

What does this mean for me?

If you are planning a baby, first talk to your GP or specialist but:

- Keep taking valproate
- Keep using contraception until you have talked with your doctor.

It is important that you do not become pregnant until you have discussed your options with your specialist.

- Your specialist may need to change your medicine a long time before you become pregnant – this is to make sure your condition is stable.
- Valproate can harm babies even in early pregnancy. It is therefore important that you do not delay seeing your GP or specialist if you think you may be pregnant.

Information on the risks of valproate (Epilim, Depakote, Convulex, Episenta, Epival, Kentlim, Orlept, Sodium Valproate, Syonell & Valpal) use in girls (of any age) and women of childbearing potential.

*prevent valproate pregnancy prevention programme

Read this booklet carefully before prescribing valproate to girls (of any age) and women of childbearing potential.

This Guido is a risk minimisation measure part of prevent – the valproate pregnancy prevention programme, aimed at minimising pregnancy exposure during treatment with valproate.

This guide also contains information on switching pregnant women from valproate.

It is recommended that pregnant women taking anticonvulsant drugs in general, and valproate in particular, are enrolled in the UK Epilepsy and Pregnancy Register (http://www.epilepsyandpregnancy.co.uk). This should be done as early as possible in the pregnancy, before the outcome is known.

The information in this Guide has been approved by the MHRA.
Do I have to treat this?

• Treat
  Two or more seizures
  Scan or EEG abnormal
  Spontaneous seizures
  Part of a syndrome
  Harm of seizures outweighs harm of drugs
  Patient wants full control - driving

• Leave it be
  One seizure
  Normal tests
  Provoked seizures
  Part of a syndrome
  Harm of drugs outweighs harm of seizures
  Patient wants no drug side effects

Sudden Unexpected Death in Epilepsy - SUDEP
Why treatment is important

Deaths associated with neurological conditions in England 2001 to 2014

Data analysis report
Sudden Unexpected Death in Epilepsy

Kills more than house fires
Kills more than AIDS
Kills as many as asthma

1,000 epilepsy-related deaths in UK per year – predominantly young adults

Women with epilepsy have a 10 times higher risk of death in pregnancy
Status Epilepticus
Status Epilepticus

Time sensitive medical emergency

Convulsive SE – 5 minutes
Or two without regaining consciousness within 5 mins
Algorithms

Stage one
Loraz iv 4mg

Stage two
Lev or PHT

Stage three
ITU
LEV or PHT?

Consider 30-60mg/kg LEV
80kg man = 2.4g iv loading
(Max 4.5g iv)
Causes of SE

Acute symptomatic causes are most common (48–63%)

Stroke is the leading cause (14–22%)
Acute seizure management
Seizure has stopped – now what?

- Eye witness history
- Examine the patient
- Temperature
- Senior review – particularly if LD
- Think alcohol, drugs

Is there a patient safety issue here?
Seizures in established epilepsy

Presume medication nonadherence / malabsorption / under-prescription – and check for cryptic sepsis

AED drug levels please
Tox screen
Lactate

If they are not typical – treat as ‘first seizure’ and reinvestigate

Be aware of injury – including dislocations and fractures
### Table 1  Non-pill formulations of antiepileptic drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Solution</th>
<th>Suspension</th>
<th>Elixir</th>
<th>Sprinkle</th>
<th>Chewable tablet</th>
<th>Dispersible/disintegrating tablet</th>
<th>Capsule that can be opened</th>
<th>Crushable</th>
<th>Intravenous</th>
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<tbody>
<tr>
<td>Acetazolamide</td>
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<td>Brivaracetam</td>
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<td>Carbamazepine</td>
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<td>Clemazepam</td>
<td>2.5 mg/1 mL</td>
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<td>Clonazepam</td>
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<td>Eslicarbazepine</td>
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<td>Ethosuximide</td>
<td>250 mg/5 mL</td>
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<td>Felbamatine</td>
<td>600 mg/5 mL</td>
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<td>Gabapentin</td>
<td>250 mg/5 mL</td>
<td>25 mg/1 mL</td>
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<td>Lacosamide</td>
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<td>Lamotrigine</td>
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<td>Levetiracetam</td>
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<td>Oxcarbazepine</td>
<td>300 mg/5 mL</td>
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<td>Perampanel</td>
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<td>Phenobarbital</td>
<td>20 mg/5 mL</td>
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<td>Phenytoin</td>
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<td>Pregabalin</td>
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<td>Retigabine (ezogabine)</td>
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<td>Rufinamide</td>
<td>40 mg/1 mL</td>
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<td>Topiramate</td>
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<td>Valproate</td>
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<td>Vigabatrin</td>
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<td>Zonisamide</td>
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- *Only immediate-release formulation is crushable.
- †Not available in the USA.

Three short-term strategies

1. Oral to iv
2. Benzo bridge Loraz or clonaz
3. Replace with iv AED Lev (Lac)
Review of 53 published and 20 unpublished cases using 1:1 dose of Lev
- Normal dosing range
One sterile abscess after 25 days of use

Start at 500mg to 1000mg/24hrs
Epilepsy Management
Epilepsy Management

Refer, refer, refer

Patient safety
  Driving
  Employment
  Lifestyle
  Epilepsy meds
  Pregnancy

bmj open

Referral patterns after a seizure admission in an English region: an opportunity for effective intervention? An observational study of routine hospital data

Ruth Grainger,1,2 Michael Pearson,3 Peter Dixon,2 Elizabeth Devonport,2 Michelle Timoney,3 Keith Bodger,4,5 Jamie Kirkham,6 Anthony Marson2

Results: 1.4% of all emergency medical admissions are as a result of seizure. In the following 12 months 35% were readmitted and experienced a mean of 2.3 emergency department visits. Only 27% (48% of those already known to specialists and 13% of those not known) were offered appointments. Subsequent attendance at a specialist clinic is more likely if already known to a clinic, if aged <35 years, if female, or required a longer spell in hospital. Extrapolation from other work suggests 100 000 bed days per annum could be saved.

Conclusions: Most seizure admissions are not being referred for the help that could prevent future admissions. The majority of those that are referred are not seen within an appropriate time frame. Our service structures are not providing an optimum service for people with epilepsy.
Hints and tips

Levetiracetam may not always be right but it is rarely wrong

Adults may be ‘absent’ but they are not having absences – likely focal seizures – check for CNS pathology if new

Use narrative descriptions and resist the temptation to leap to a classification
Hints and tips

In status, treat first – ask questions later – could these be non-epileptic?

Ensure regular meds are prescribed and taken at the right time – 100% of the time

If in doubt – refer; If you are not in doubt – refer
Thanks a lot