Saving the Day - the Medical Mission

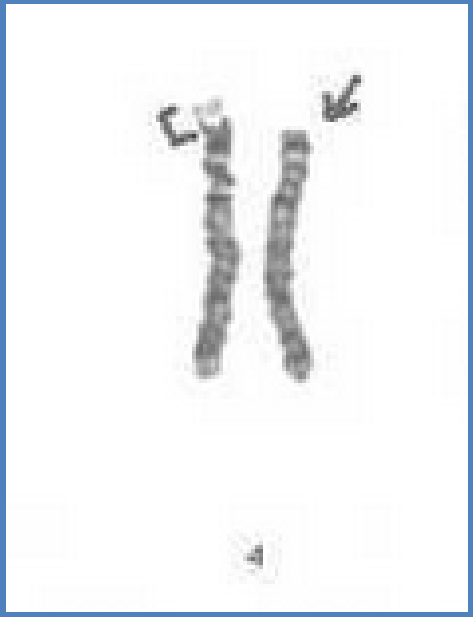
Dr Sukhvir Wright

Honorary Consultant Neurologist, Birmingham Children's Hospital

Research Fellow, Aston University

My mission today…

- Introduction
- Epilepsy
- Epilepsy in WH syndrome
- First aid for seizures at home
- New drugs on the block



- Questions

My background

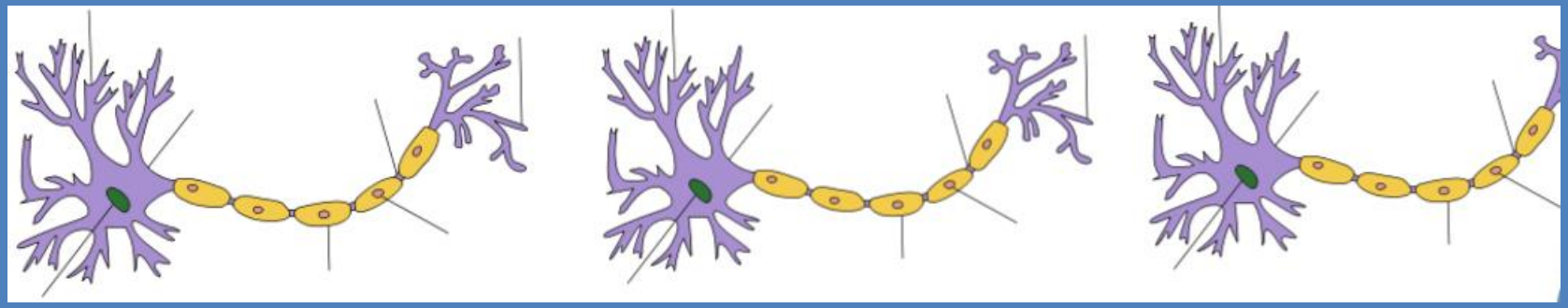
Epilepsy- affects the brain

The brain controls everything we do

If our bodies were cars the brain would be the driver behind the wheel!

The brain has lots of parts and each part controls a different part of what we do

It works by sending electrical signals to the rest of the body on paths called nerves

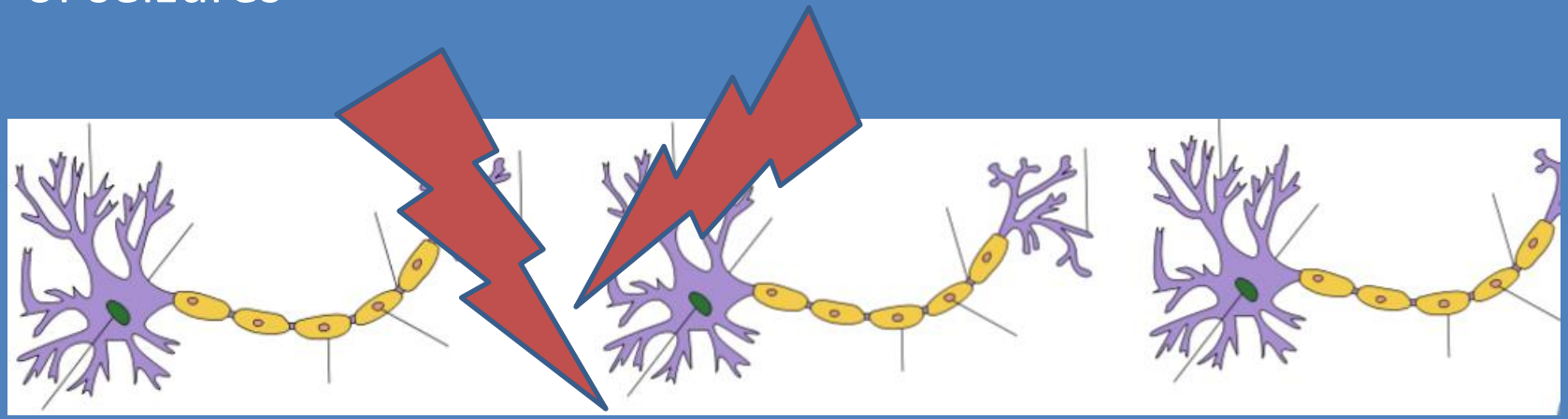


Epilepsy – disruption of normal brain activity

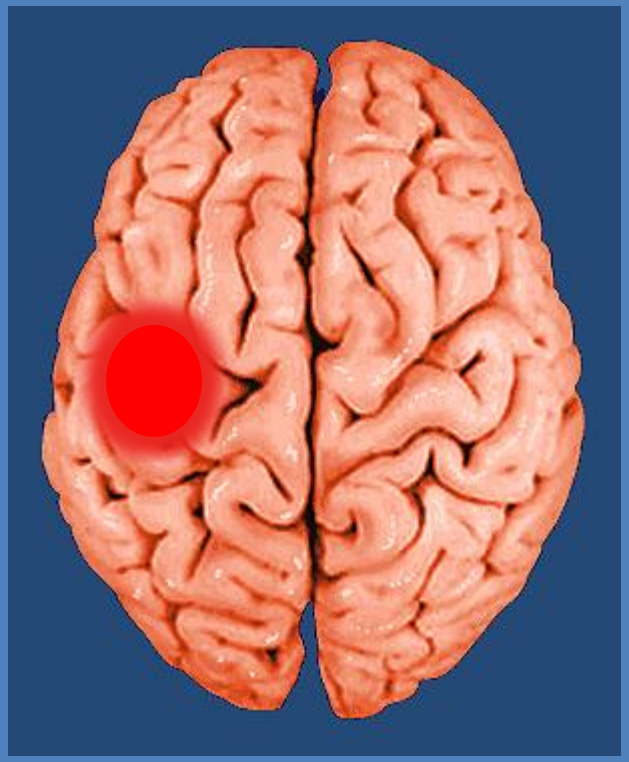
A seizure happens when there is a sudden burst of intense electrical activity in the brain

This causes a temporary disruption to the way the brain normally works and the result is an epileptic seizure

The type of disruption and area affected results in different types of seizures

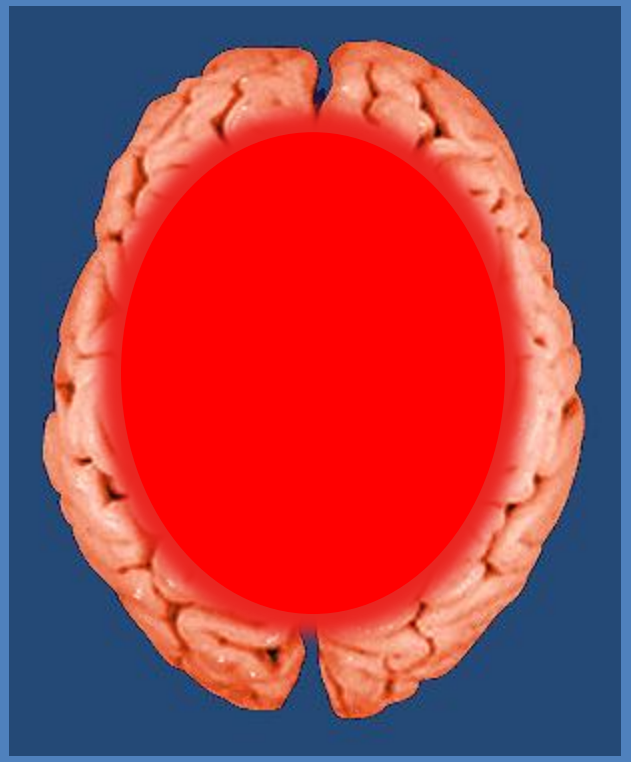


Epilepsy – types of seizures



Focal Onset

epileptic activity starts in one part of the person's brain

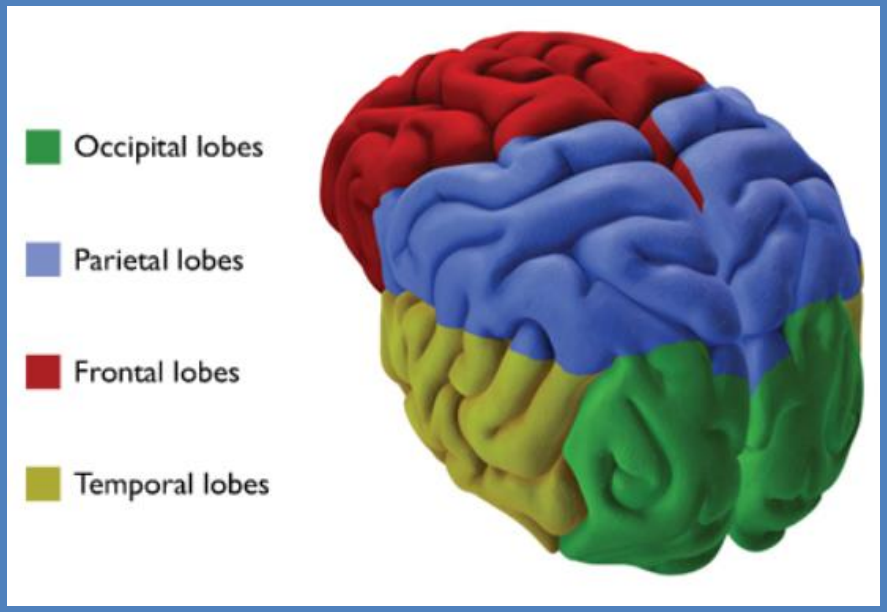


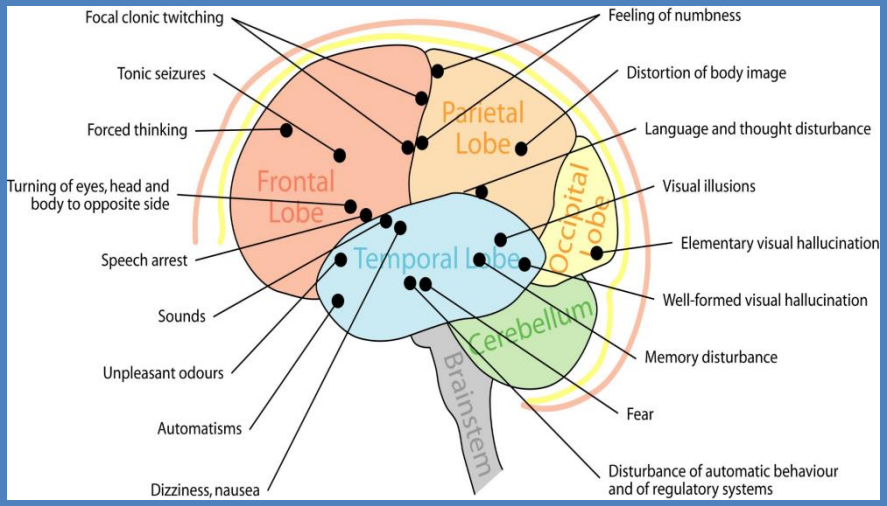
Generalised onset

epileptic activity in both halves of the brain

Epilepsy – types of seizures

Focal onset





General onset

- Tonic-clonic
- Tonic
- Spasms
- Atonic
- Myoclonic
- Absence

Epilepsy – types of seizures

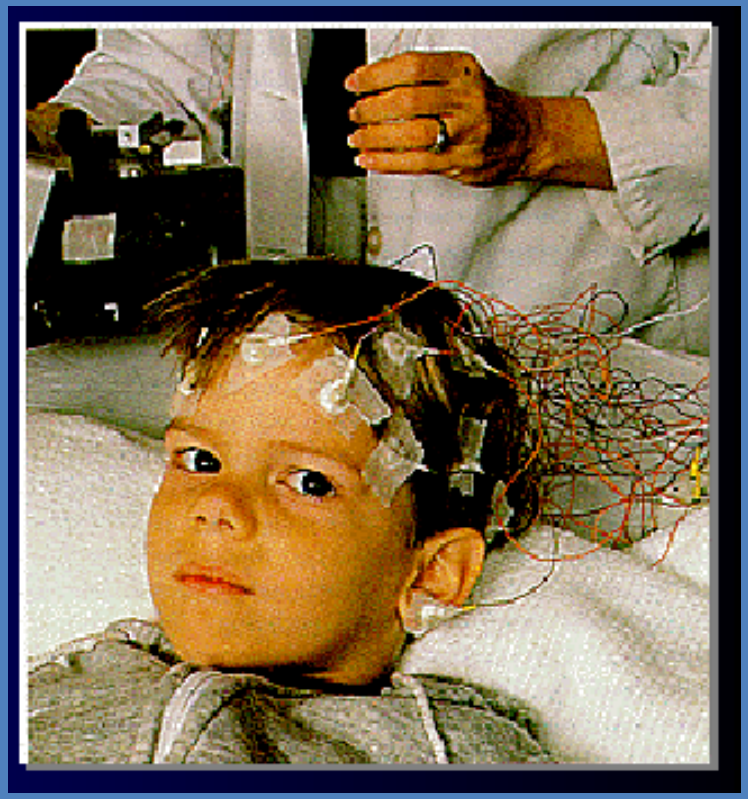
- Status epilepticus
  - Prolonged tonic clonic seizure > 30 minutes
- Febrile seizures
  - Seizure associated with fever/febrile illness
  - Usually tonic clonic
  - Common

How is a diagnosis of epilepsy made?

- NICE guidelines
- Children with suspected seizure/epilepsy should be seen within 2 weeks of event
- Eyewitness account most valuable (written descriptions, video)
- Questions that may be asked by specialist
  - How often
  - When (time of day)
  - Warnings beforehand
  - Colour change
  - Alteration in conscious level
  - Movements
  - Duration of attack
  - Recovery and behaviour after attack
- EEG and MRI can be useful additional investigations

The Role of the EEG

EEGs should be used as in addition to good clinical history and should be reported by experienced specialists with paediatric EEG experience

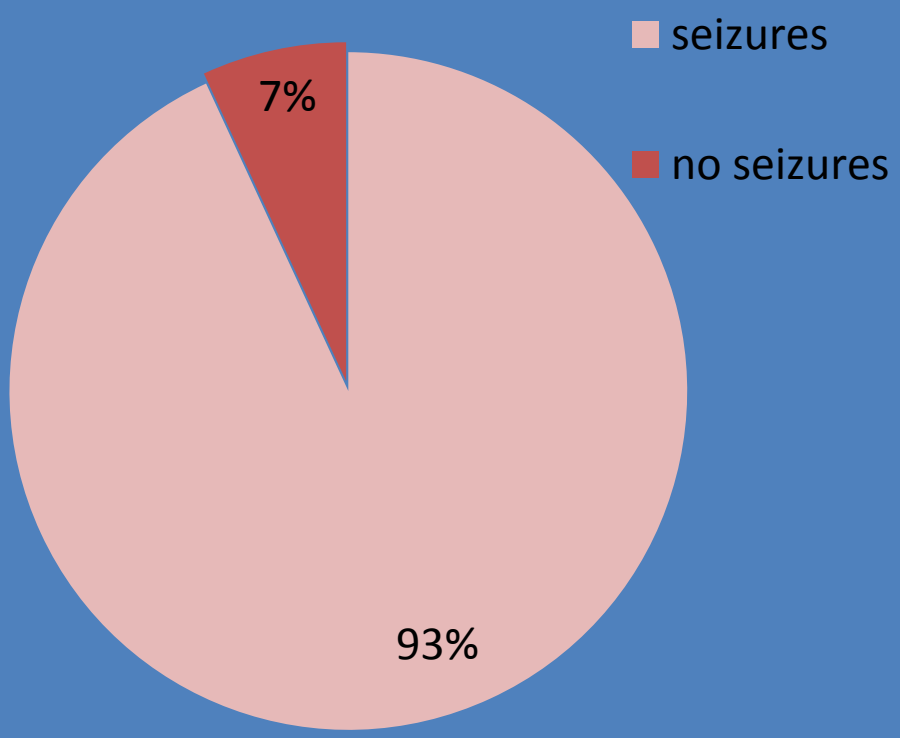


Epilepsy in chromosomal disorders

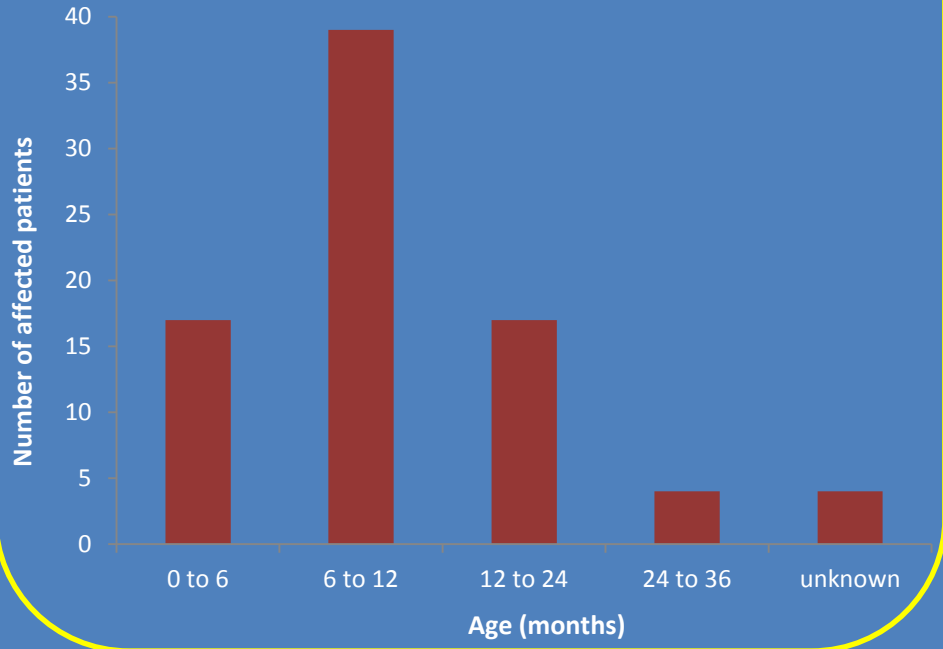
- Epilepsy is a frequent feature in chromosomal disorders
- Usually challenging as there is pre-existing disability
- Important to identify and treat for long and short-term cognitive outcome
- Other examples include Angelman's syndrome and ring chromosome 20 syndrome

Wolf Hirschhorn Syndrome (WHS) and epilepsy

- Epilepsy is a major medical challenge during first few years of life
- Occurs in majority of patients with WHS
- Series published in 2009 (Battaglia et al)
- Characterised epilepsy in 87 patients



Most patients develop epilepsy in the first 3 years of life



Tonic clonic seizures most common (74%)

Half of patients suffered SE

Fever most common trigger (73%)

Atypical absences may be misdiagnosed

Epilespy well controlled in 81%

One drug 21%

Two or more 60%

Epilepsy improved with age in all patients

32/58 still seizure free

Seizures stopped at mean age of 4.5yrs (1y 9m to 13 years)

What to do if your child is having a tonic-clonic seizure

WELFARE

- Assess the situation – are they in danger of injuring themselves?
- Remove nearby objects that could cause injury
- Cushion their head

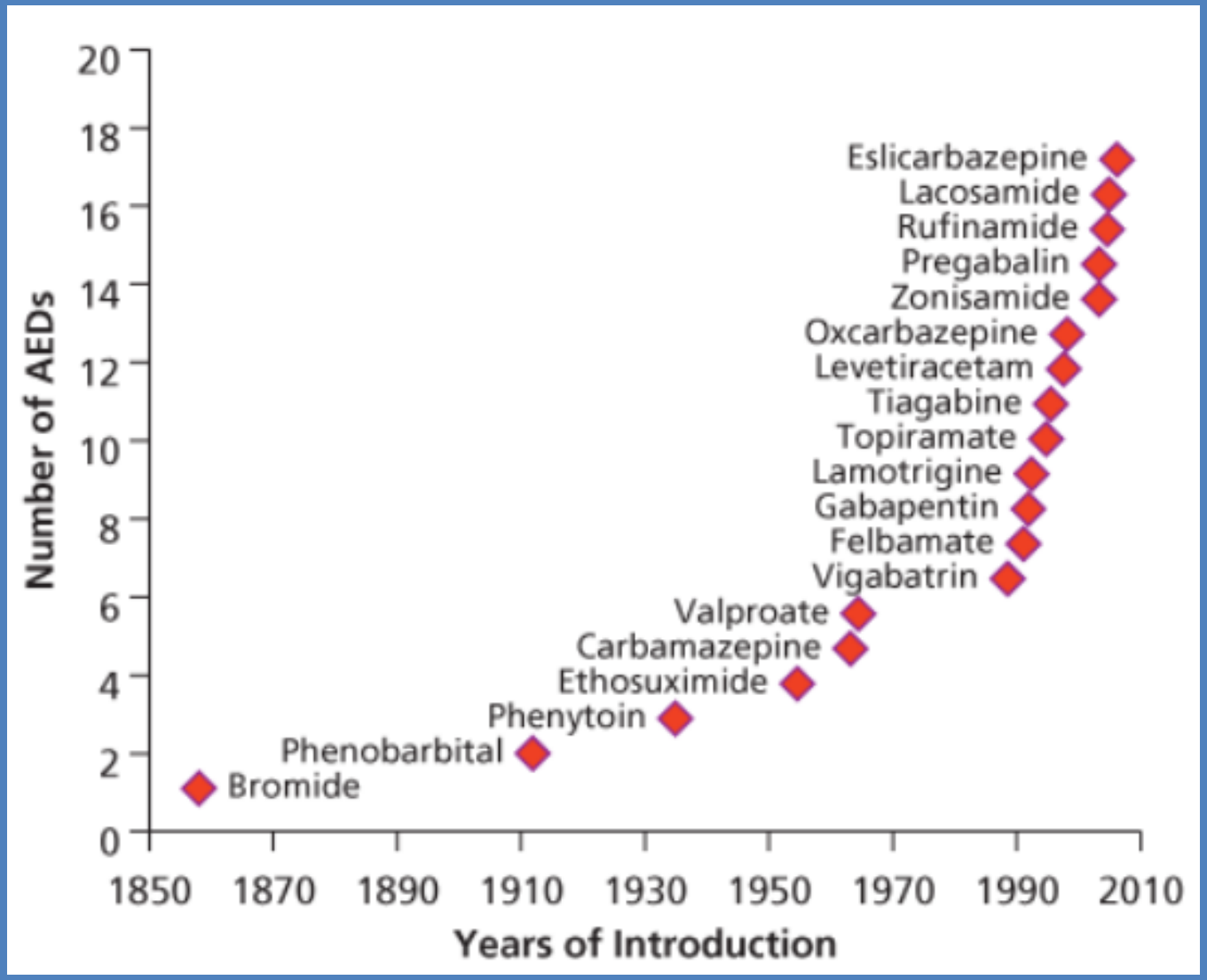
HELP

- Check the time – if the jerking lasting longer than 5 minutes call 999
- If you are concerned at any time call 999

SEIZURE RECOVERY

- Once the jerking has stopped, put them on their side
- Reassure

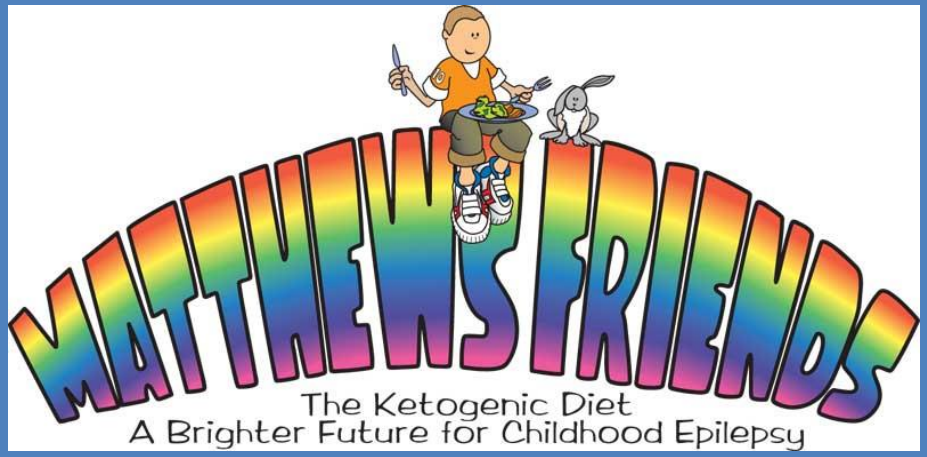
Anti-epileptic medication



Brodie 2010

When the drugs don't work…

- Ketogenic diet
  - Mimics starvation in the diet
  - Can be more effective that adding 2nd/3rd AED
  - Requires commitment and support of a dedicated team (neurologist, dietician, epilepsy nurse)



Our experience

"…..had infantile spasms and numerous other problems including irritability and spasticity. [Patient] responded very well to nitrazepam and then VPA"

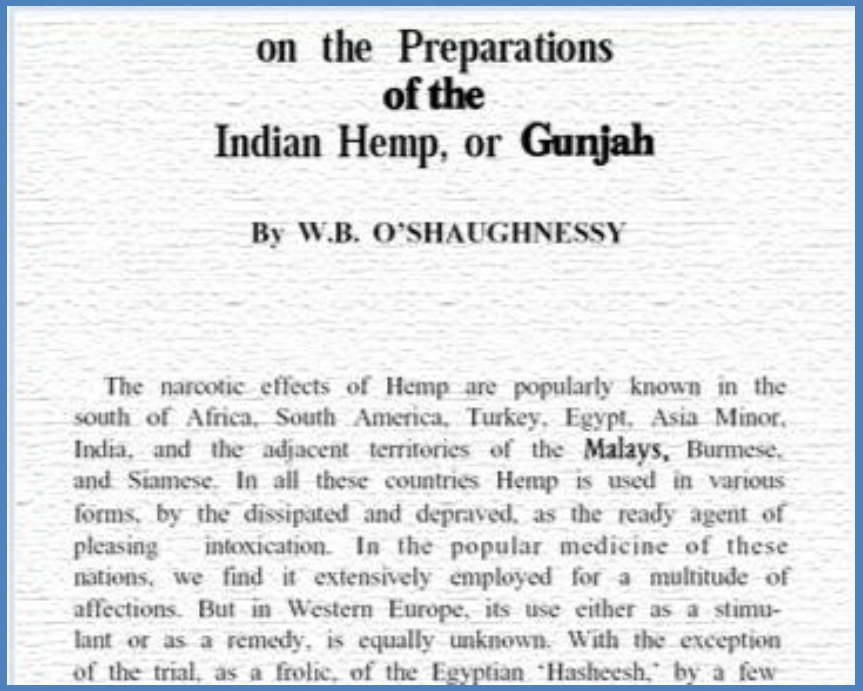
"….. presented with frequent seizures. Eventually has responded to combination of LVT PHB and TPM. The PHB seems to have made the biggest difference. Each time I have tried weaning the PHB [patient] seizes again"

The new drug on the block

- Cannabinoids
  - Cannabis sativa and C.indica
  - Two components that act on the brain – THC and cannabidiol (non-psychoactive)

- ***2600 BC*** *– Chinese emperor Huang Ti advised taking Cannabis for relief of cramps, and rheumatic and menstrual pain*

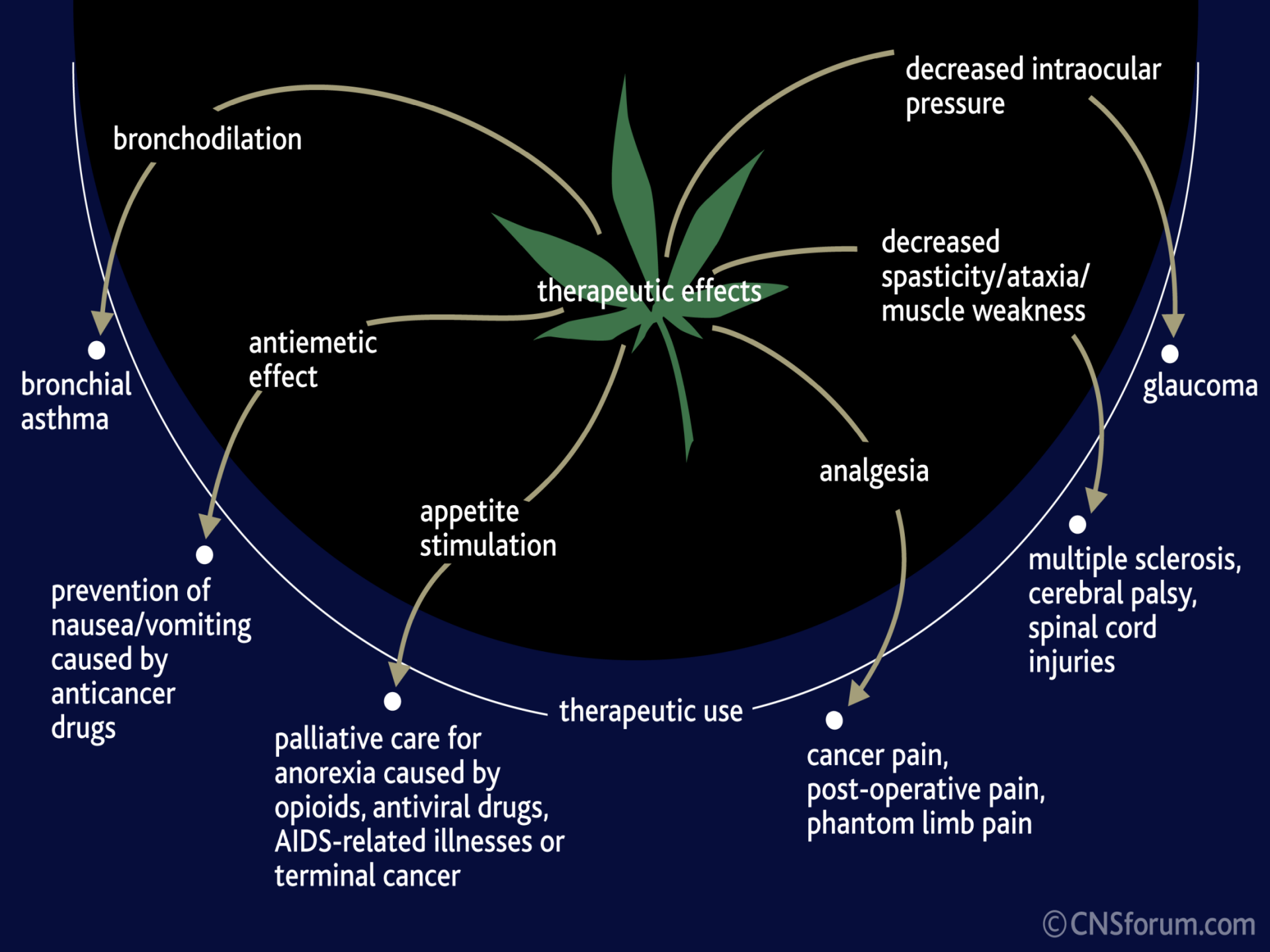
- ***1839*** *– Publication by British physician O'Shaughnessy publicizes therapeutic potential of Cannabis to Western world*



on the Preparations
of the
Indian Hemp, or **Gunjah**

By W.B. O'SHAUGHNESSY

The narcotic effects of Hemp are popularly known in the south of Africa, South America, Turkey, Egypt, Asia Minor, India, and the adjacent territories of the **Malays,** Burmese, and Siamese. In all these countries Hemp is used in various forms, by the dissipated and depraved, as the ready agent of pleasing intoxication. In the popular medicine of these nations, we find it extensively employed for a multitude of affections. But in Western Europe, its use either as a stimulant or as a remedy, is equally unknown. With the exception of the trial, as a frolic, of the Egyptian 'Hasheesh,' by a few


bronchodilation
decreased intraocular pressure
therapeutic effects
decreased spasticity/ataxia/ muscle weakness
antiemetic effect
bronchial asthma
glaucoma
appetite stimulation
analgesia
multiple sclerosis, cerebral palsy, spinal cord injuries
prevention of nausea/vomiting caused by anticancer drugs
therapeutic use
palliative care for anorexia caused by opioids, antiviral drugs, AIDS-related illnesses or terminal cancer
cancer pain, post-operative pain, phantom limb pain
©CNSforum.com

CBD and epilepsy

- Add-on therapy for the treatment of the potentially devastating epileptic encephalopathies
- Several publications of parental reports on the efficacy of cannabidiol-enriched cannabis extracts
- Overall responder rate of 85 %
- These studies, however, are small, and are prone to bias
- Randomized clinical trials are required to evaluate efficacy of CBD in children with epilepsy as well as to assess safety and appropriate dosing.

CBD and epilepsy

- Open-label trial in US (11 centres)
- Pts aged 1-30 years with paediatric onset medically refractory epilepsy
- 214 patients enrolled
- Adverse events reported in 79%
- Most common were somnolence, decreased appetite, diarrhoea, fatigue and convulsion
- Median reduction in seizures was 36.5%

Could this drug be used in WHS?

- Main patients used in have Dravet syndrome
- Patients carry mutation in SCN1A gene
- Potential mechanistic link between WHS and Dravet
- Both have complex pattern of seizures, they can be prolonged, intractable to treatment in some, brought on by febrile episodes, cognitive, motor and behavioural impairment
- Both show similar responses to AEDs

Has this drug been used in WHS?

- Markham et al
  - Online survey of parents from 4p-support-group
  - Roughly 5% indicated use of such alternative agents (?under-reporting)
  - 80% reported reduction of seizure frequency >50% and related benefits in terms of reduced side effects from lowered AED therapy

Notes of caution

- Beware of unlicensed products
- **Only trust appropriately standardized and tested pharmaceutical formulations of cannabidiol**
- Randomised controlled trials are on-going
- Not yet available routinely in UK unless part of a clinical trial
- Orphan drug designation in LGS, Dravet
- Very promising results hot off the press for LGS
- Real science is underway ….including in my own lab!

Future research

- Precision medicine is coming…
- Recent studies correlate deletion size with seizure severity
- Early genetic studies could pre-empt EEG changes/ epilepsy

Summary

- Epilepsy is common in WHS and is one of the major concerns for parents and professionals caring for children with WHS
- However, although frequent and sometimes hard to control in the early years, seizures usually brought under good control
- For best outcome, recognise seizures and treat early
- New research and treatments hold some promise

Acknowledgements and thanks

WOLF HIRSCHHORN SYNDROME TRUST