


# Epilepsy in Rett Syndrome

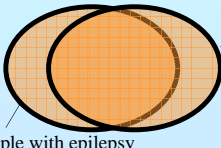


**Professor Mike Kerr**  
WALES

Cardiff University, Wales

## Aim

- To discuss what epilepsy is, how it effects people, treatment options and special issues related to Rett syndrome.



People with Rett

All people with epilepsy

## Overview

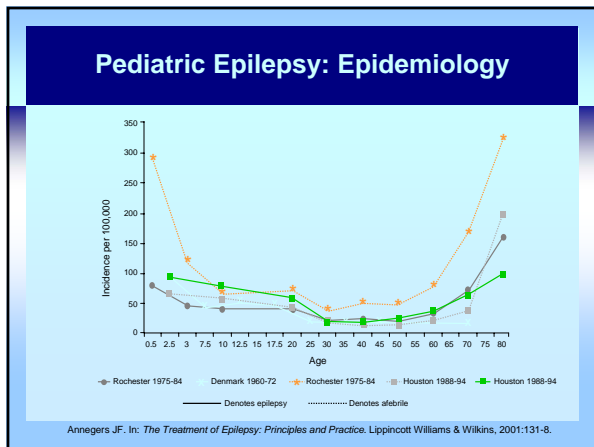
A bit about epilepsy

Impact & Treatment

Special issues In Rett syndrome

## Epilepsy

How common?  
Diagnosis  
Misdiagnosis



### Comparison within people with Intellectual Disability

General population	Range <b>0.4-1.0%</b> depending on age
Mild Intellectual Disability	Range <b>5-15%</b> depending on comorbidity
Severe Intellectual Disability	Range <b>30-75%</b> depending on comorbidity
Downs syndrome	Range <b>8-10%</b>

## Diagnosis & Misdiagnosis

### How do we diagnose epilepsy?

- 1. The history - with witness
- 2. EEG -
- 3 Brain scans- CAT MRI SPECT PET

### What sort of seizures are there?

And why do we need to know about them?

- Generalised
- Generalised tonic clonic,
- Tonic
- Myoclonic
- Atonic
- Absence
- Partial
- Simple partial
- Complex partial
- Secondarily generalised tonic clonic
- Unclassified

### Standards - who should you see?

- The diagnosis of epilepsy should be established by a specialist medical practitioner with training and expertise in epilepsy (NICE-draft)
- The diagnosis of epilepsy should be made by a neurologist or other epilepsy specialist (S.I.G.N)

### History – Possible seizure related symptoms (adapted from Duncan)

Have there been any spontaneous and otherwise unexplained paroxysmal symptoms?	<p><b>In Particular:</b></p> <p>Sudden falls</p> <p>Involuntary jerky movements of limbs while awake</p> <p>Blank spells</p> <p>Unexplained incontinence of urine with loss of awareness, or in sleep</p> <p>Odd events occurring in sleep, e.g. fall from bed, jerky movements, automatisms</p> <p>Episodes of confused behaviour with impaired awareness, recollection</p>	<p><b>Possible simple partial seizures:</b></p> <p>Epigastric rising sensation</p> <p>Déjà vu</p> <p>Premonition</p> <p>Fear</p> <p>Elation, Depression</p> <p>De-personalisation, derealisation</p> <p>Inability to understand or express language (written or spoken)</p> <p>Loss of memory, disorientation</p> <p>Olfactory, gustatory, visual, auditory hallucination</p> <p>Focal motor or somatosensory deficit, or positive symptoms (jerking, tingling)</p>
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### History – to classify

- Recognise questions on all seizure types
- Especially myoclonic jerks, focal and lateralising features

### History – related to differential diagnosis

Syncope/Cardiac	Posture, Colour, Position.
Neurological	Reflux-Sandifers Reflex –Noise, emotion Visual phenomena
Behavioural/psychiatric	Mental state examination Functional analysis of behaviour
Parasomnias	Timing, age

### Recording

- Prospective recording of events, including video recording and written descriptions, can be helpful in reaching a diagnosis

### Investigations – EEG EEGs can cause a lot of trouble!

- An EEG should be used to support a diagnosis of epilepsy in adults in whom the clinical history suggests the seizure is likely to be epileptic in origin.
- Not in cases of probable syncope
- Does not exclude epilepsy
- Cannot be used in isolation
- It should occur within four weeks of request

### EEG sensitivity and specificity How accurate are they?

Results of interictal EEG	Epilepsy (n=764)	Not epilepsy (n=948)
Epileptiform activity	397	<b>38</b>
Normal	<b>367</b>	910

### EEG - syndrome

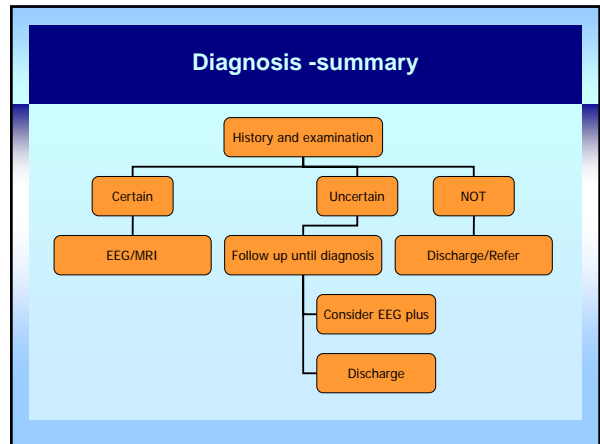
- An EEG can be used to help determine seizure type and epilepsy syndrome prognosis in individuals suspected of having a diagnosis of epilepsy. This enables individuals to be given the correct prognosis

### EEG - Plus

- Sleep EEG should be performed where standard EEG has not contributed to diagnosis or classification
- No advantage in repeated standard EEGs
- Long term video-EEG and Ambulatory have important role in individuals who present diagnostic difficulties following standard EEGs

### Neuroimaging

- Neuroimaging should be used to identify structural abnormalities
- MRI is imaging investigation of choice
- CT can be used to identify gross pathology when MRI not available



### Misdiagnosis

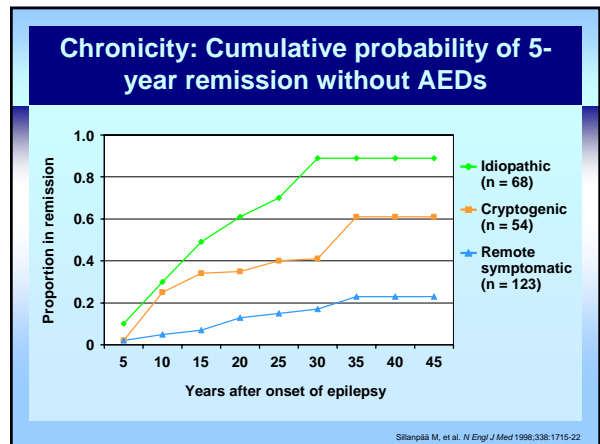
Smith et al. 1999 Community population	Misdiagnosis 46/184 26.1%
Scheepers et al. 1998 Population study	Misdiagnosis 49/214 22.9%

## Treatment

Why treat?  
What to treat with?

### Why treat: the impact of epilepsy

Chronicity	Mortality
Mental/Behavioural health	Cognitive deterioration
Injury hospitalisation	Social inclusion



## Mental health problems in children with epilepsy

Group (N)	Percentage with psychiatric disorder				
	Any	Emotional	Conduct	ADHD	PDD
Complicated EP (25)	56	16	24	12	16
Uncomplicated Ep (42)	26.2	16.7	16.7	0	0
Diabetes (47)	10.6	6.4	8.5	2.1	0
All other (10,202)	9.3	4.2	4.7	2.2	0.2

Davies et al. Dev Med & Child Neurol 2003, 45: 292-295

## Treatment GOALS

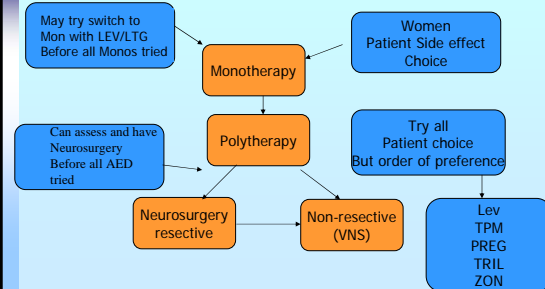
- Seizure freedom
- No side effects
- No injury
- No sudden death
- Or best possible balance

## Therapy

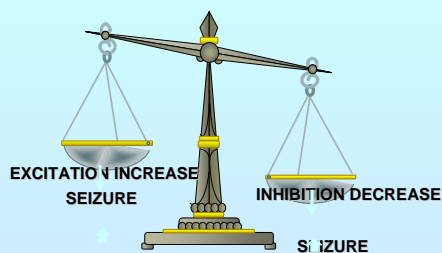
Drugs  
Operations



## Treatment pathway




## What do the drugs do?



## Ideal drug characteristics

- Efficacy
- Broad range of seizure type
- Ease of use including varied preparations / taste / blood levels
- Low side effect profile
- Known action
- Cost effective

### Have there been many good studies?



- This gave a total of 13 studies to be evaluated for inclusion in this review with a total of 829 participants comparing 9 different pharmacological agents: Lamotrigine, carbamazepine, gabapentin, topiramate, vigabatrin, felbamate, clobazam, cinromide and flunarizine.
- Four of these trials were cross-over trials (Battaglia, Eriksson, Kaski, Siegel),
- Six were parallel studies (Crumrine, Kerr, Motte, Ritter, Sachdeo, Yamatogi),
- One was an open label parallel study (Crawford)
- In two studies the design was unclear (Luna, Schlumberger).

### Surgery

- Surgery: lesional, gamma knife, callosotomy, hemispherotomy and VNS

### Non pharmacological studies





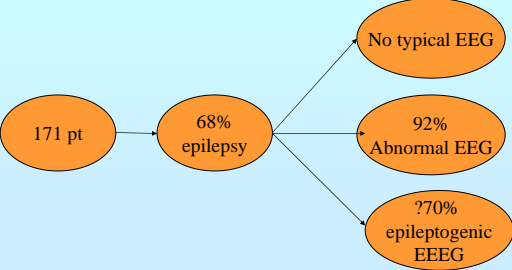

### Special issues in Rett syndrome

- Overview
- Diagnosis
- Management issues

### Epilepsy in Rett Overview 1

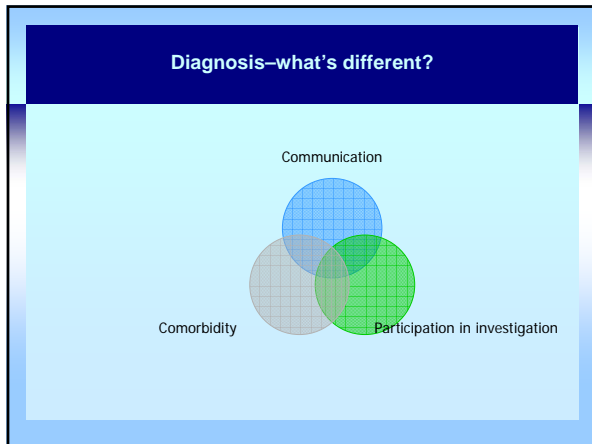
How Common?	81% More likely if early developmental delay
Treatment	Ketogenic diet vagal Nerve stimulator Topiramate? <b>NOT GOOD STUDIES</b>

### Epilepsy in Rett Overview 2



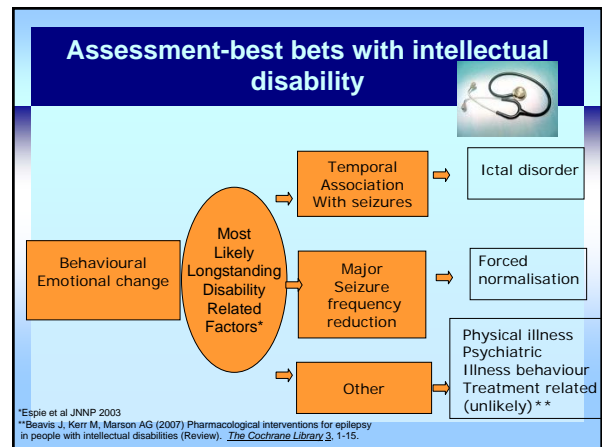
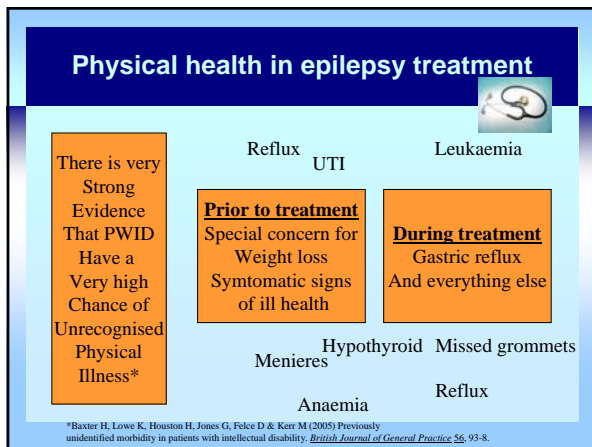
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graph LR
    A(171 pt) --> B(68% epilepsy)
    B --> C(92% Abnormal EEG)
    B --> D(70% epileptogenic EEG)
    B --> E(No typical EEG)
  
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### Management issues

Understanding change associated with treatment?



### Conclusion

- Epilepsy provides a major co-morbidity to the lives of people with Rett and their families
- Always demand the best diagnostic process, always demand the best treatment and always demand the best assessment of the epilepsy.