Idiopathic epilepsy syndromes

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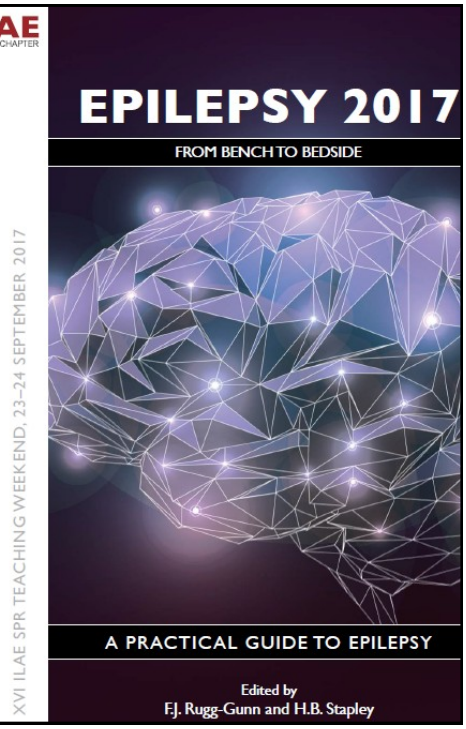
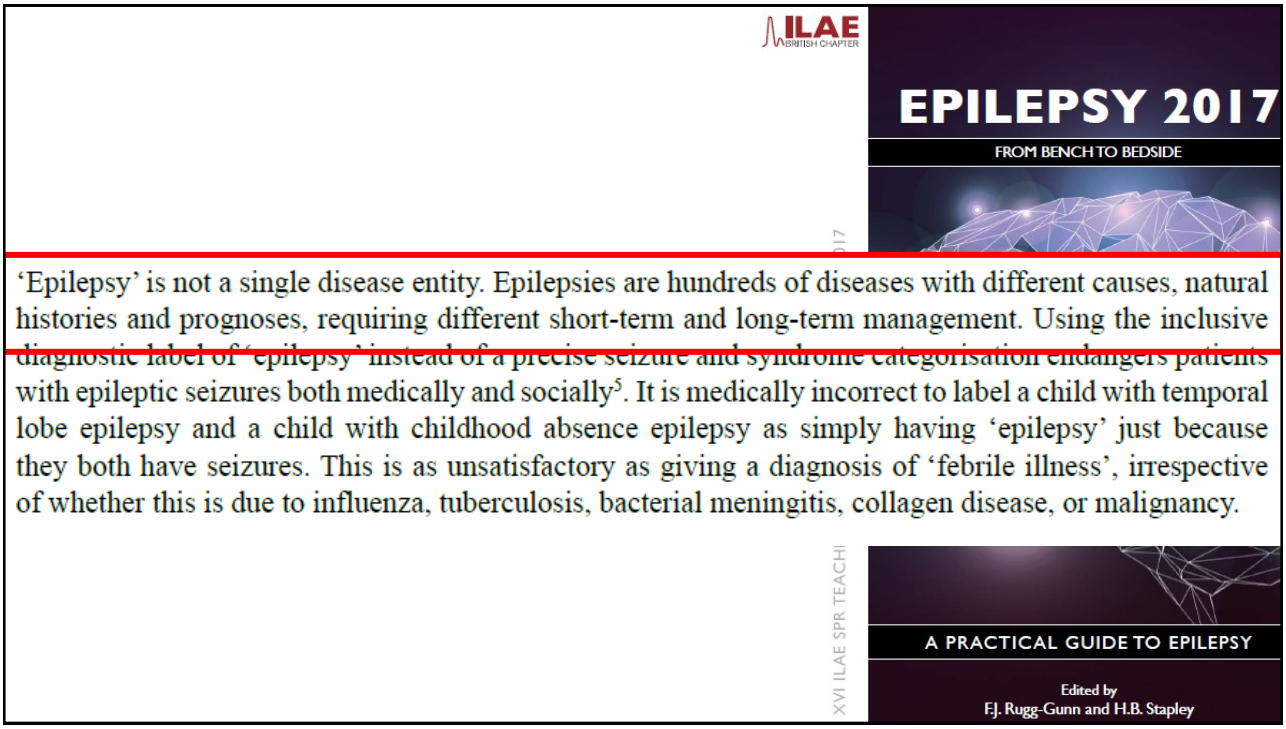
Outline of topic

- Definition
- Idiopathic generalized epilepsies
- Idiopathic focal epilepsies

https://www.epilepsydiagnosis.org





Idiopathic epilepsy syndromes

- A syndromic that is only epilepsy, with no underlying structural brain lesion or other neurological signs or symptoms. These are presumed to be genetic and are usually age-dependent.

Idiopathic Epilepsy Syndromes

LUMPER

SPITTER

- Idiopathic ~~(Genetic)~~ Generalized Epilepsy
- Idiopathic (Self-Limited) Focal Epilepsy

The Commission on Classification of the ILAE[3] defined IGE as follows:

Idiopathic generalised epilepsies are forms of generalised epilepsies in which all seizures are initially generalised (absences, myoclonic jerks and generalised tonic-clonic seizures), with an EEG expression that is a generalised bilateral, synchronous, symmetrical discharge (such as is described in the seizure classification of the corresponding type). The patient usually has a normal inter-ictal state, without neurological or neuroradiologic signs. In general, inter-ictal EEGs show normal background activity and generalised discharges, such as spikes, polyspike spike-wave, and polyspike-waves ≥3 Hz. The discharges are increased by slow sleep. The various syndromes of idiopathic generalised epilepsies differ mainly in age of onset. No aetiology can be found other than a genetic predisposition towards these disorders.

IGE Definition

Table 1. Idiopathic generalised epilepsies as perceived by the relevant Committees of the ILAE.

Commission of the ILAE (1989)

Idiopathic generalised epilepsies

Benign neonatal familial convulsions
Rare, dominantly inherited disorders manifesting mostly on the second and third days of life, with clonic or apnoeic seizures and no specific EEG criteria. History and investigations reveal no aetiological factors. About 14% of patients develop epilepsy later.

Benign neonatal convulsions
Very frequently repeated clonic or apnoeic seizures occurring about the fifth day of life, without known aetiology or concomitant metabolic disturbance. Inter-ictal EEG often shows alternating sharp theta waves. No recurrence of seizures. Psychomotor development not affected.

Benign myoclonic epilepsy in infancy
Characterised by brief bursts of generalised myoclonus associated with generalised spike-waves occurring during the first or second year of life in otherwise normal children who often have a family history of convulsions or epilepsy. Generalised tonic-clonic seizures may occur during adolescence.

Childhood absence epilepsy (pyknolepsy)

Juvenile absence epilepsy

Juvenile myoclonic epilepsy (impulsive petit mal)

Epilepsy with generalized tonic-clonic seizures on awakening
Epilepsies with seizures precipitated by specific modes of activation
Most of the photosensitive epilepsies belong to the group of idiopathic generalised epilepsies.

Other generalised epilepsies not defined above

ILAE Task Force on Classification (2001)

Idiopathic generalised epilepsies

Benign myoclonic epilepsy in infancy

Epilepsy with myoclonic astatic seizures

Childhood absence epilepsy

Epilepsy with myoclonic absences

Idiopathic generalised epilepsies with variable phenotypes
- *Juvenile absence epilepsy*
- *Juvenile myoclonic epilepsy*
- *Epilepsy with generalized tonic-clonic seizures only*

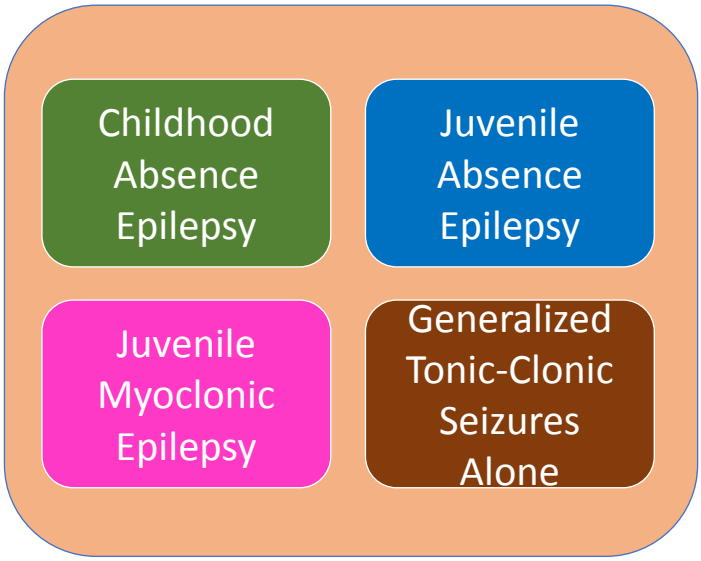
Generalised epilepsies with febrile seizures plus (to consider)

IGE-Subclass syndromes

The IGE syndromes currently recognised by the ILAE are shown in Table 1. Benign neonatal familial convulsions, benign neonatal convulsions and benign myoclonic epilepsy in infancy are not dealt with here.

IGE syndromes not yet recognised by the Commission of the ILAE include eyelid myoclonia with absences (EMA), perioral myoclonia with absences (PMA), idiopathic generalised epilepsy with phantom absences, and stimulus-sensitive absence epilepsies.

'Idiopathic Generalized Epilepsies'



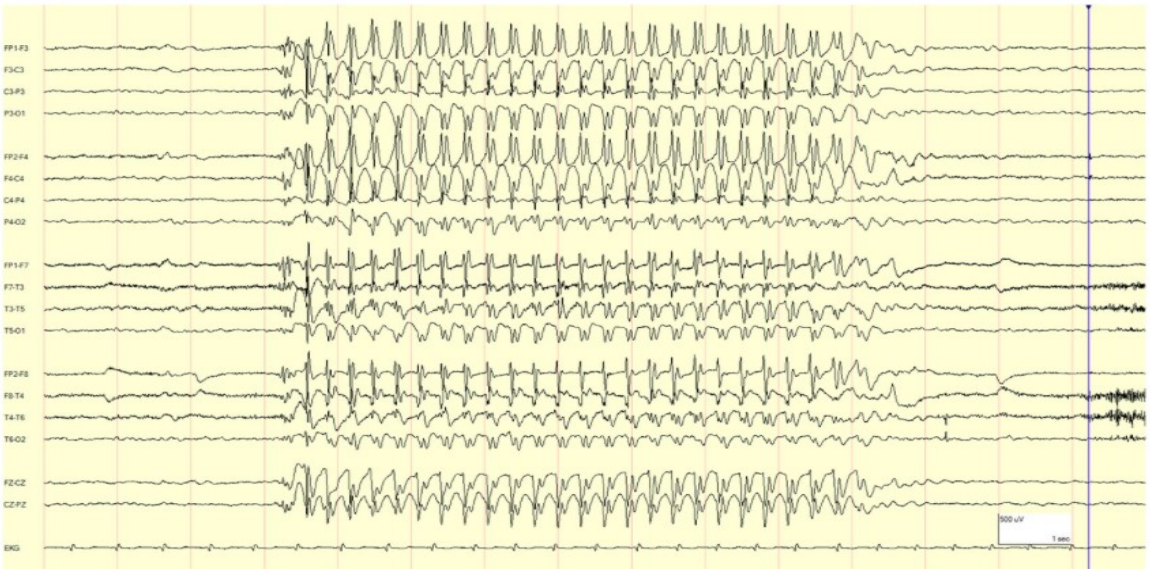
Other syndromes:

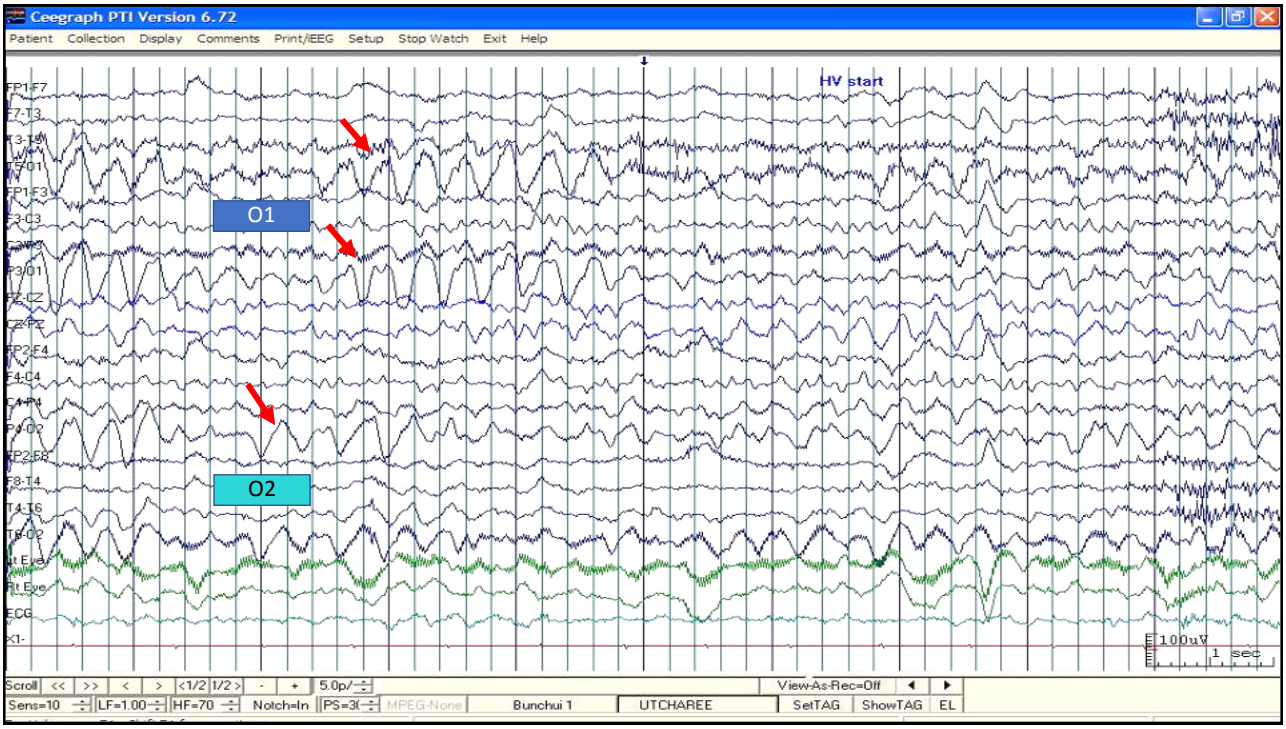
- **Myoclonic Absence epilepsy (MAE)**
- **Eyelid Myoclonia with Absence (EMA)**
- **Perimyoclonia with Absence (PMA)**
- **Absence with specific mode of precipitation (photic pattern, video-games, emotional upset, intense thinking and reading)**

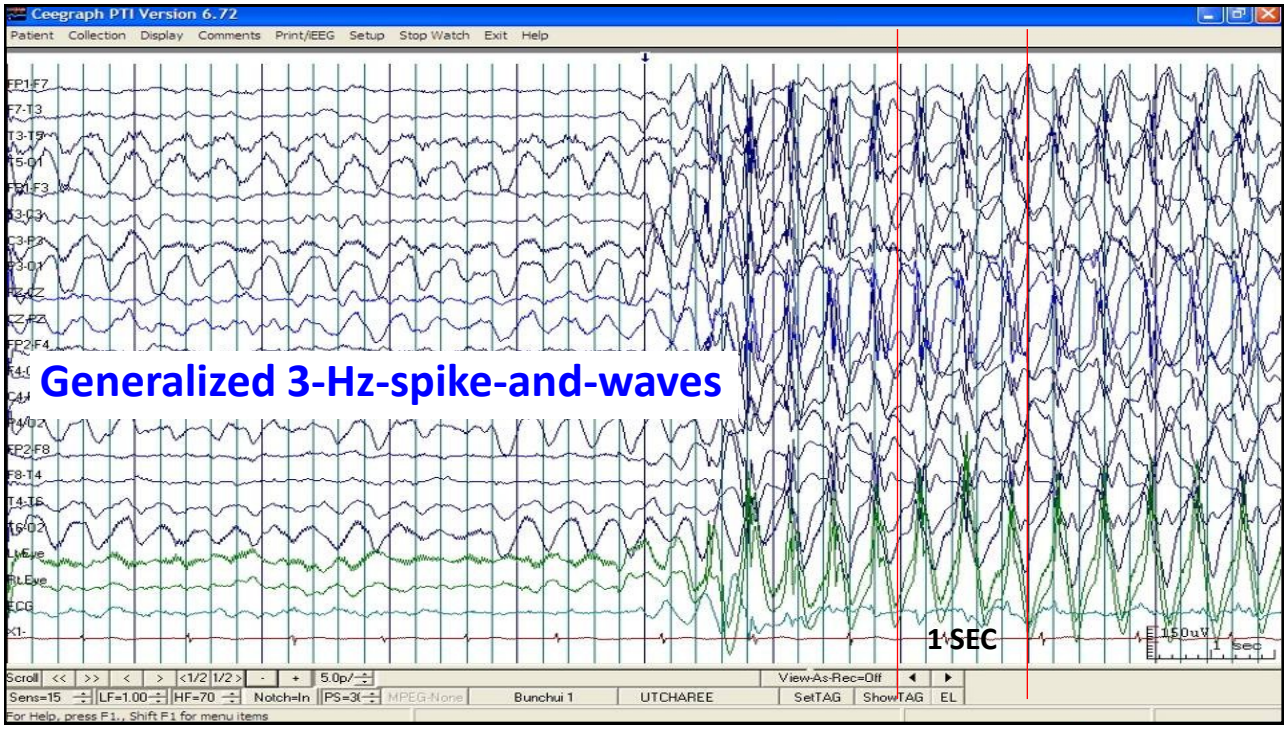
1 Childhood absence epilepsy

Age of onset	2-12 years (peak 5-6 years)
Seizure type	Absence only (multiple daily 10-100/d, brief 4-30 s, LOA)
EEG	IEDS: 3 Hz Generalized spikes and waves; Normal background, OIRDA
Prognosis	Self-limited age of 12, evolved to other

Childhood absence epilepsy



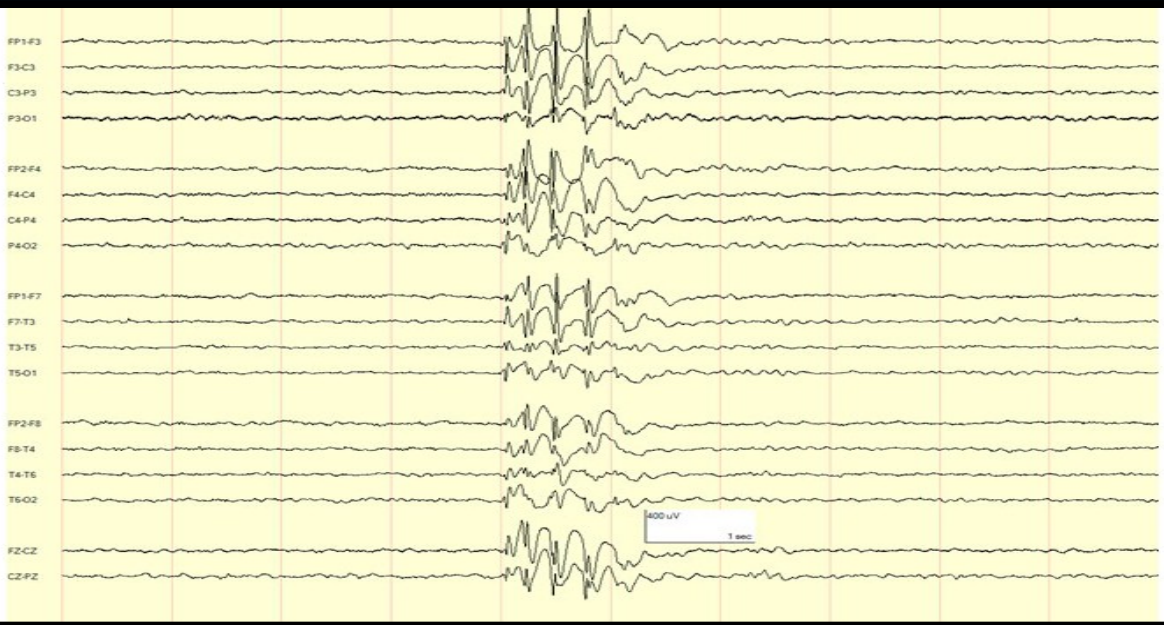




2 Juvenile absence epilepsy

Age of onset	8-20 years (peak 9-13 years)
Seizure type	Absence (not frequent, not severe, awareness, mild LOA) with automatisms (6-10 s after onset) GTC at onset-> Absence in adolescent, 1/5 ASE GCs (80% of cases, upon awakening, infrequent)
EEG	IEDS: **3-6 Hz** Generalized spikes/polyspikes and waves, normal background, OIRDA(may), as CAE but brief Ictal: Absence: Regular 3-6 Hz GSW or PSW, brief (<4 s) GCs : EEG obscure by artifact, generalized fast rhythmic spikes-tonic phase, spike and slow waves and postictal period slowing
Prognosis	Life long disorder, 80% response to tx, risk:relapse sz

Juvenile absence epilepsy



3 Juvenile myoclonic epilepsy (Janz)

Age of onset	8-25 years (peak 9-13 years) **5% of cases from CAE**
Seizure type	Myoclonic (mandatory), especially on awakening (within 30min-1hr), precipitate: sleep deprive, fatigue, alcohol GTCs (>90%) preceded by series of myoclonic Absence (1/3 of cases, briefer<3 seconds) ;40%Photosens
EEG	IEDS: **3.5-6 Hz** GSW/P SW,normal background, fragments hyperventilation may provoked absence, <10% sz induced by visual stimuli Ictal: single generalized PSW correlates with myoclonic seizures
Prognosis	Life long disorder, sz improved after 4th decade

4 Epilepsy with GTCs alone(on awakening)

Age of onset	5-40 years (peak 11-23 years)
Seizure type	GCs especially on awakening (within 1-2 hr of wakening) infrequent, typically provoked by sleep deprivation, PH of childhood absence epilepsy
EEG	IEDS: GSW/PSW (½ of cases seen only during sleep) fragmented, intermittent photoparoxysmal response, normal BG (no slowing) Ictal: GCs: Ictal EEG patterns
Prognosis	GTCS increase with age, may unpredictable in both sleep and awake. Avoidance of precipitating factors and adjustment of lifestyle are essential.

DDx: MTLS & TA

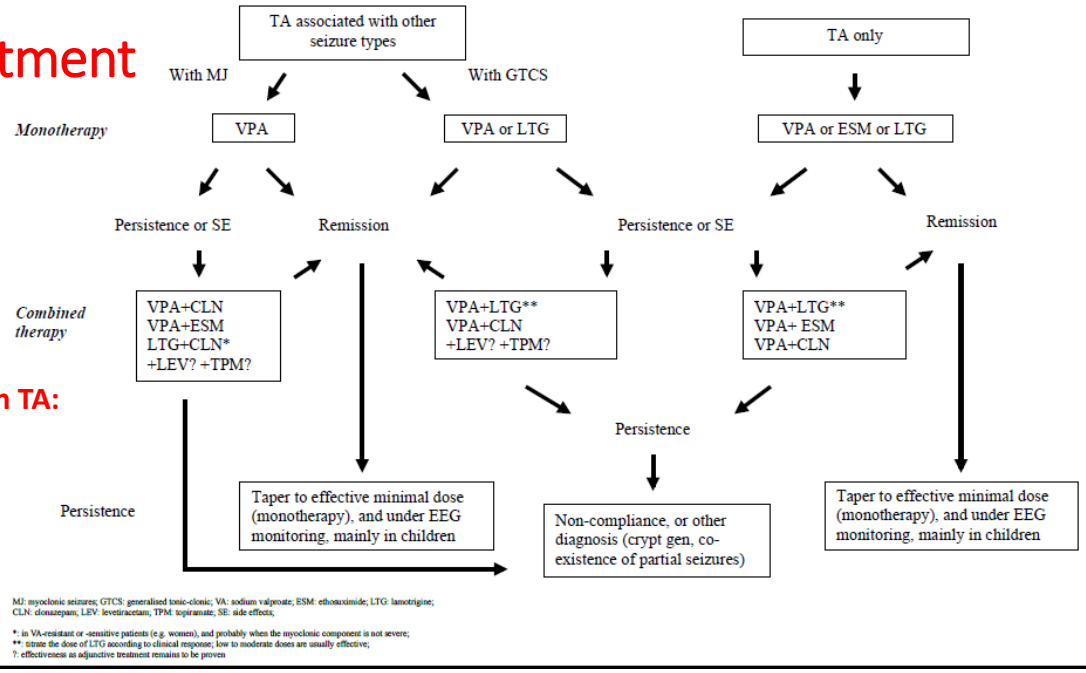
Table 2. Differential diagnosis between typical absences and limbic temporal lobe seizures.

History	Limbic CPS (mesial TLE)	Typical absences (IGE)
Febrile convulsions	Frequent; usually multiple, prolonged or complicated	Frequent but rarely prolonged or complicated
Family history	Usually of febrile convulsions; rarely of partial seizures (familial TLE)	Positive in up to 40% of patients
Onset	Usually within the second half of the first decade	Usually syndrome-related
Course (natural history)	Often bi-phasic	Continuous*
Diurnal variation	Non-specific	Usually in the morning/after awakening
Ictal clinical features		
Aura	Frequent	Never
Precipitation by HV	Exceptional	As a rule
Precipitation by IPS	Exceptional	Typical (but usually syndrome-related, as in JME and EMA)
Lapse of awareness	Usually profound	Varies (often syndrome-related)
Automatisms	Almost invariably, often involving trunk and legs. Ipsilateral to the focus automatisms associated with contralateral dystonic posture may occur in 40% of patients late in the seizure	Up to about 2/3 of seizures, rarely involving trunk or legs
Clonic components	Rare; unilateral – if present – and late in the ictal sequence	Frequent, bilateral, mainly restricted to the eyelids or mouth
Reactive automatisms	Frequent	Only during absence status
>1 min duration	As a rule	Exceptional
Non-convulsive status	Exceptional	Well recognised feature
Post-ictal symptoms/signs	Invariably confusion, recent memory deficit, dysphasia if onset from the dominant side. Relatively rapid clearing may occasionally occur	Never
Inter-ictal EEG (scalp)	Unilateral or bilateral independent temporal spikes, or regional slow activity. Brief bilateral and synchronous bursts of spike-wave may occur in the context of obvious or occult secondary bilateral synchrony	Generalised spike and wave discharges at 4–2.5 Hz. Focal spikes may occur in up to 30–40% of traces but they show frontal topography, and do not disturb background activity
Ictal EEG (scalp)	Focal onset	Generalised onset
Neurological examination	Normal (a degree of facial asymmetry may be present)	Normal
Neuropsychology	Often discrepancy between Verbal IQ and Performance IQ, material specific memory deficits	Normal
Brain MRI	Usually mesial temporal atrophy	Normal

HV: hyperventilation; IPS: intermittent photic stimulation;
*: in CAE GTCS may occur in up to 1/3 of patients after the remittance of the typical absences

Treatment

Table 3. Tree diagram of the treatment of TA according to syndrome-related co-existence of other seizure types.



MJ: myoclonic seizures; GTCS: generalised tonic-clonic; VA: sodium valproate; ESM: ethosuximide; LTG: lamotrigine; CLN: clonazepam; LEV: levetiracetam; TPM: topiramate; SE: side effects;

*: in VA-resistant or -sensitive patients (e.g. women), and probably when the myoclonic component is not severe;
**: titrate the dose of LTG according to clinical response; low to moderate doses are usually effective;
?: effectiveness as adjunctive treatment remains to be proven

CI AEDs in TA:

- **-CBZ**
- **-VGB**
- **-TGB**
- **-GB**

Summary of IGE

IGE	CAE	JAE	JME	GTCSA
Age onset	Childhood 2-12 (5-6) yrs	Juvenile 8-20 (9-13) yrs	Juvenile 8-25 (9-13) yrs	Juvenile 5-40 (11-23) yrs
Seizure type	Absence	Absence GTCs	Myoclonic GTCs, Absence	GTCs
EEG	3 Hz GSW	3-6 Hz GSW	3.5-6 Hz GSW	GSW/PSW

'Idiopathic (Self-Limited) Focal Epilepsies'

The term idiopathic focal epilepsies of childhood (IFE) is not formally recognised by the ILAE in its 2010 revision (Berg *et al.*, 2010), nor are its members and boundaries precisely delineated. The IFEs are amongst the most commonly encountered epilepsy syndromes affecting children.

Clinical semiologies and electrographic features that highlight the focal origin of seizures characterise the idiopathic focal epilepsies (IFEs) of childhood. They describe a spectrum of syndromes with no underlying structural brain lesion or attendant neurological signs or symptoms. They are presumed to be genetic and are usually age dependent. Their characteristics imply not just the absence of obvious causative factors, but also specific clinical and EEG findings (Berg *et al.*, 2010).

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'Idiopathic (Self-Limited) Focal Epilepsies'

- Benign Epilepsy with CentroTemporal Spikes (BECTS)
- Self-Limited Occipital Epilepsy of Childhood: Panayiotopoulos type (early-onset):PS
- COE-G Gastaut type (late onset)

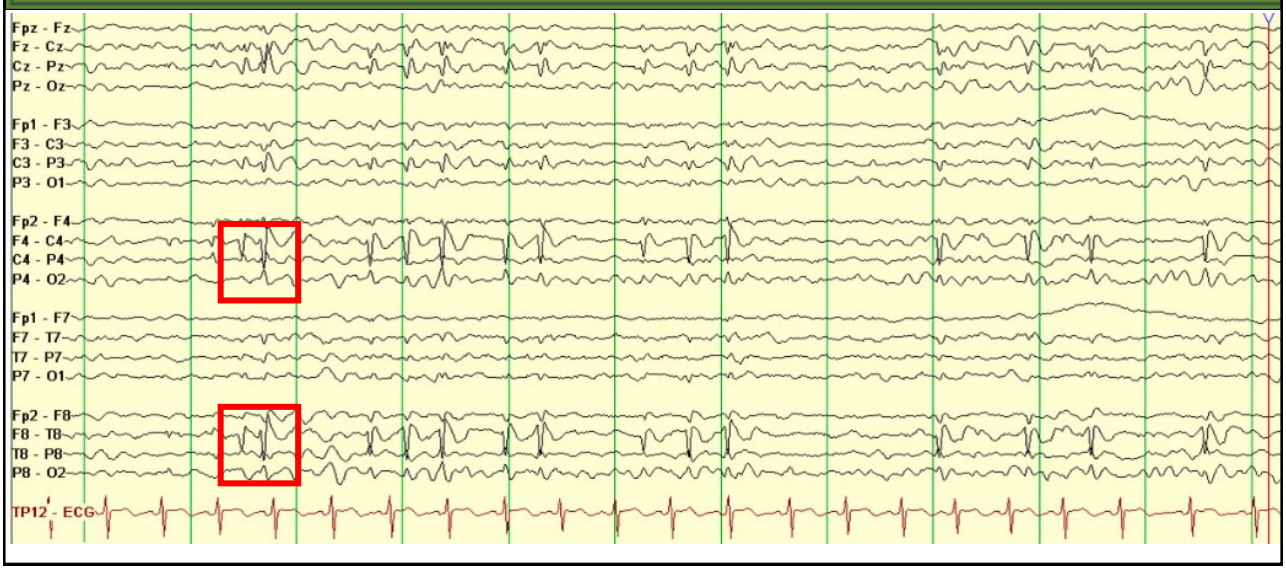
Other syndromes:

- **Benign familial and non-familial infantile szs**
- **Benign focal seizures in adolescents**
- **Benign childhood seizures with affective symptoms**
- **Benign childhood epilepsy with parietal spikes**
- **Benign childhood seizures with frontal or midline spikes**
- **Benign focal seizures of adolescence**
- **Atypical Benign Focal Epilepsy of Childhood (ABFEC)**
- **Landau-Kleffner syndrome (LKS)**
- **The related (idiopathic) epilepsy with continuous spikes and waves in sleep (CSWS or ESES)**

Benign Childhood Epilepsy with Centrotemporal Spikes (BECTS) / Rolandic Epilepsy (RE) 1	
Age of onset	3-14 years (peak 8-9 years)
Seizure type	**Fronto-parietal opercular features** –hemifacial (lip,mouth and tongue),clonic movements (with may be unilateral), laryngeal symptoms, articular difficulty (aphasia), swallowing or chewing movements and hypersalivation, brief (<5 minutes), Few, (may) secondarily generalize (typically nocturnal events) (not GTC during awake) SPS face

Benign Childhood Epilepsy with Centrotemporal Spikes	
EEG	IEDs: High amp. Centrotemporal Spikes or SSWC max. negativity in CT (C3/C4 and T3/T4) and max. positivity F, increased during drowsiness and sleep, unilat or bilat, (may) SPK outside CT region (midline, parietal, frontal and occipital), (may) photoresponsive (age.10 yrs), 10-20%-by sensory stimuli of fingers or toes Ictal: rare to obtained ictal recording
Prognosis	Excellent, **Self-limited** usually resolved by age 13 years (occasionally occur up to age 18 years)

Benign Childhood Epilepsy with Centrotemporal Spikes



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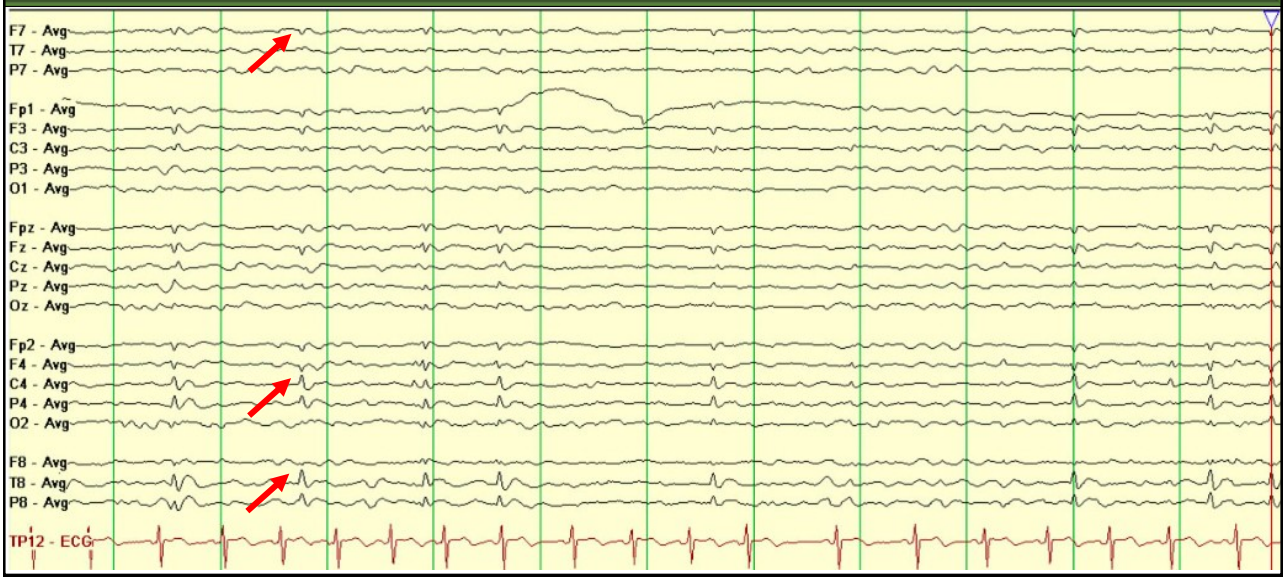

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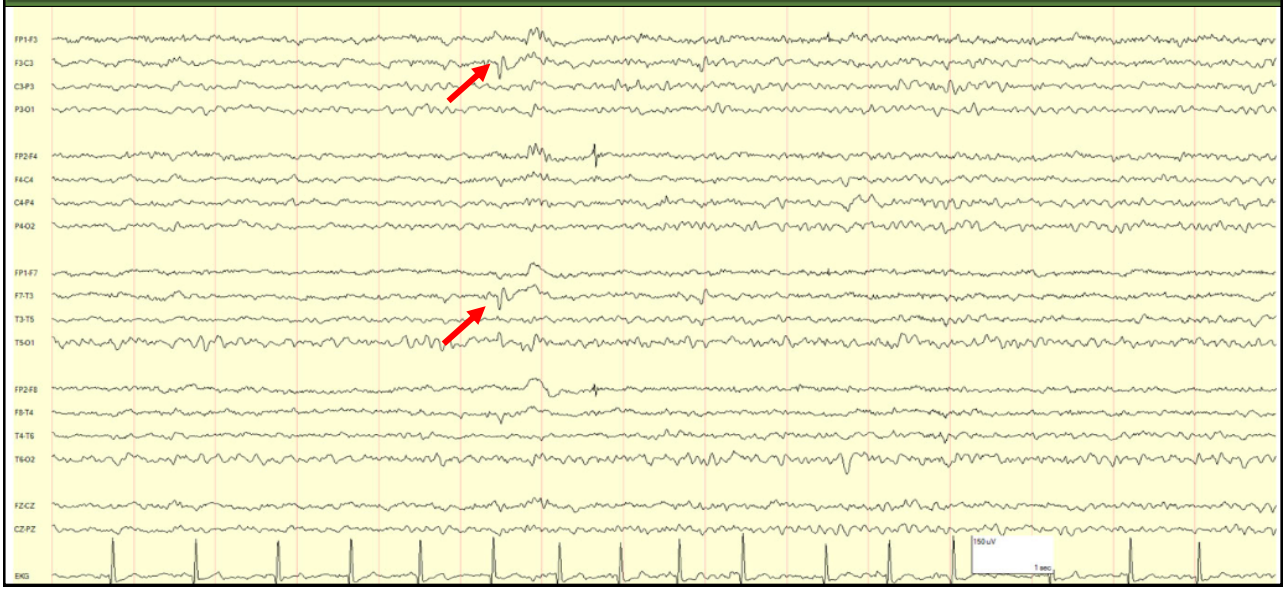
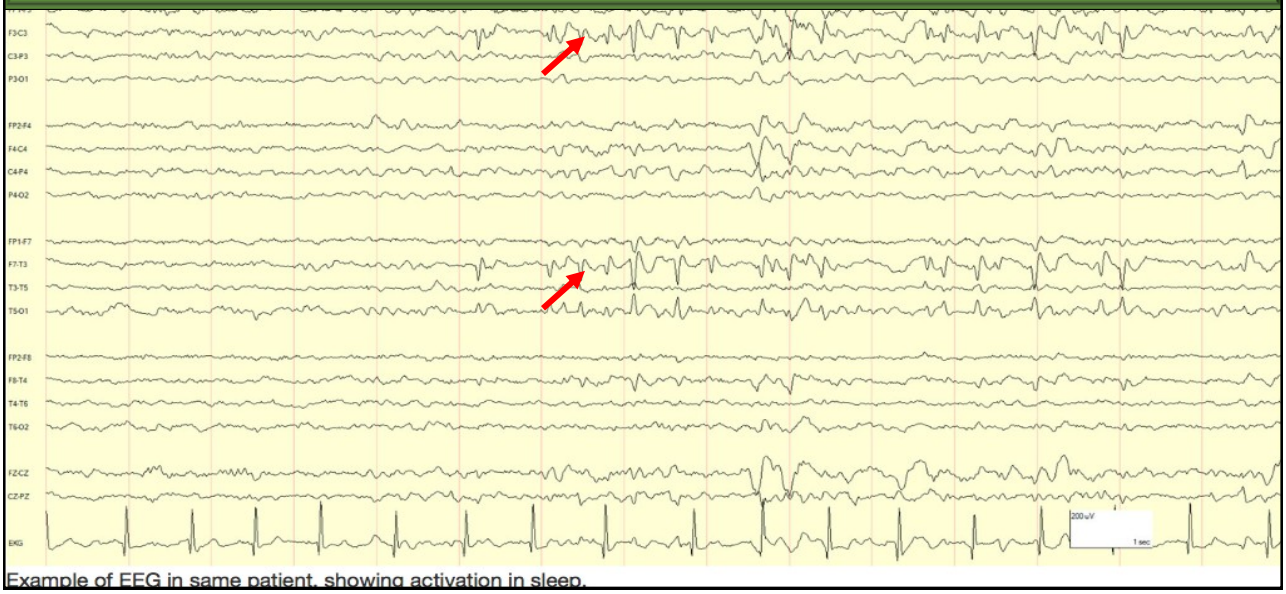


Benign Childhood Epilepsy with Centrotemporal Spikes



Example of EEG in same patient, showing activation in sleep.

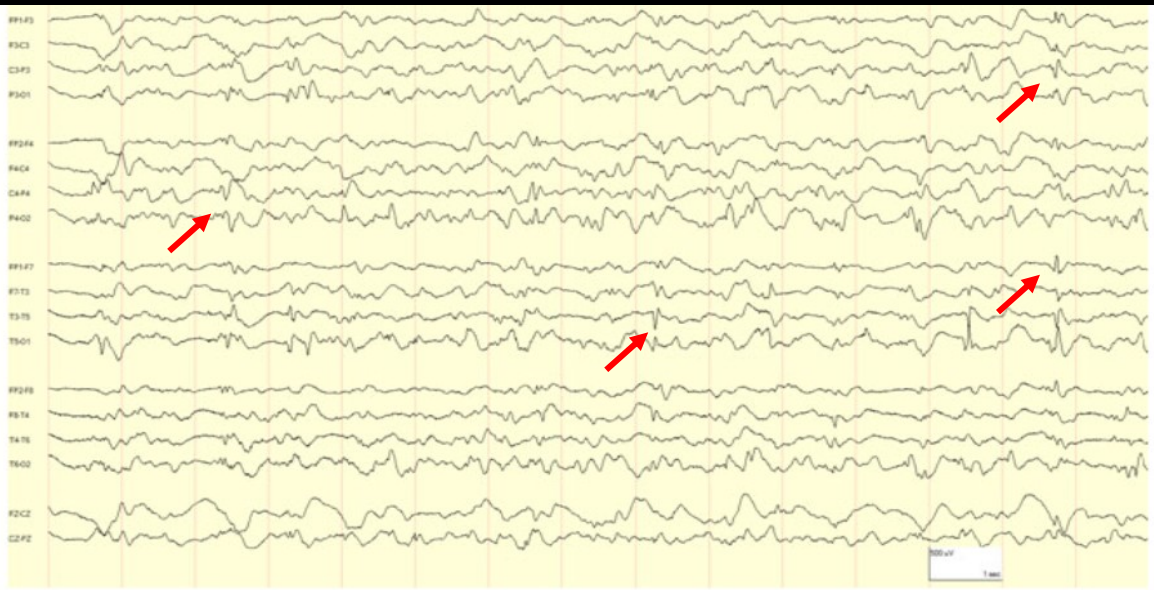
2 Panayiotopoulos syndrome

Age of onset	1-14 years (peak 3-6 years) **Self-limiting, resolve by age 11-13 years**
Seizure type	**Autonomic features** mainly emetic (nausea, retching, vomiting); other: pupillary (mydriasis), circulatory (pallor, cyanosis), heart and respiratory change, syncope -like. Apnea and asystole can occur (severe case). **Prolong duration**, but without residual neuro deficit, some of case- fronto-parietal opercular (25%may autonomic SE), infrequent, at night, shortly after falls asleep, last a few minutes. A common clinical pattern is one of vomiting and gazing toward one side, often evolving to rhythmic muscle contractions on one or both sides of the body

Panayiotopoulos syndrome

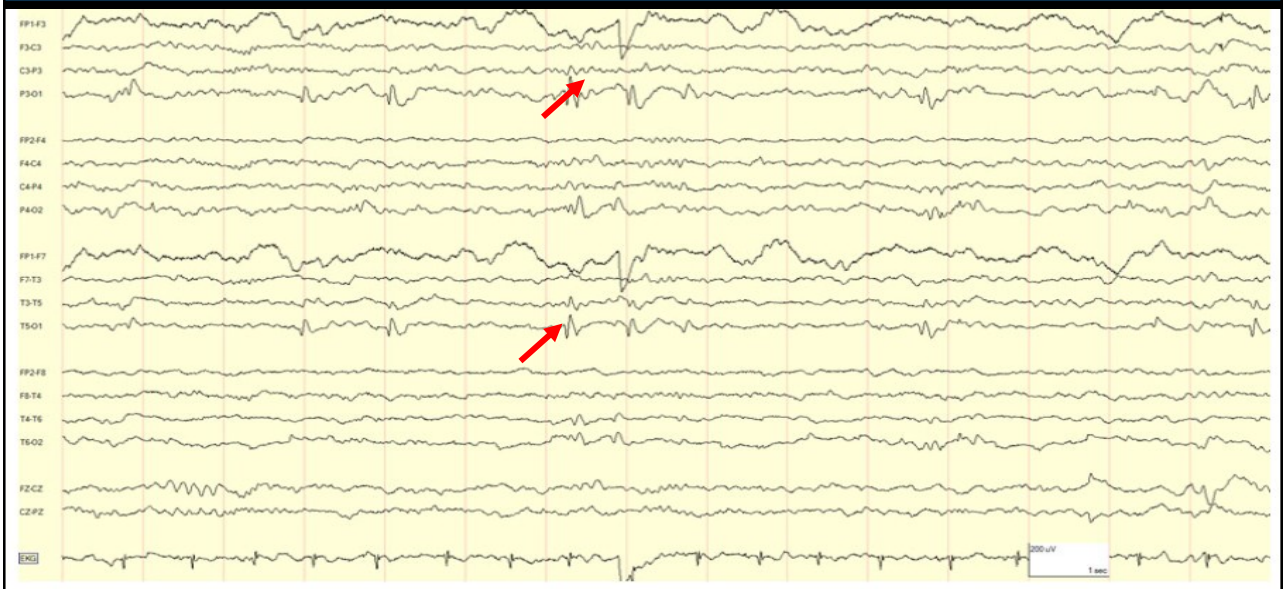
EEG	**IEDs: Multifocal SPK/SW 90%** **Normal single EEG 10%** **Occipital spikes 60% of patients** **Low voltage SPK and Gen d/c minority of cases.** **Activation: Eye closure (elimination of central vision and fixation off sensitivity) may activate occipital spikes. EEG abnormality is enhanced by sleep deprivation and by sleep** **Ictal: Unilateral, often posterior onset, with rhythmic slow (theta or delta) activity intermixed with small spikes**

Panayiotopoulos syndrome



Example of multifocal spikes in Panayiotopoulos syndrome.

Panayiotopoulos syndrome



Example of occipital (left) spikes of high amplitude in Panayiotopoulos syndrome.

Late onset childhood occipital epilepsy (Gastaut type)

Age of onset	5 months-19 years (peak 8-9 years)
3 **Seizure type**	Seizures with **visual aura** occur from awake states, brief (typical seconds, most < 3 minutes, rarely up to 20minutes Visual aura; multi-colored circles in peripheral vision increased involved and moving horizontally to the other side, these may be followed by deviation of eyes or head turning (ipsilateral) May Other occipital features; ictal blindness, complex visual hallucinations, visual illusions, orbital pain, eyelid fluttering or repetitive eye closure, ictal headache or N/V May spread outside the occipital lobe resulting in hemiparesthesia, dyscognitive features, hemiclonic

Late onset childhood occipital epilepsy(Gastaut type)

EEG	**IEDs: Occipital spikes or SW (may) only during sleep, 20% of cases may co-exist with CT, frontal or GSW, BG normal** **Activation by sleep deprivation and by sleep, 20-90% of cases –induced by fixation-off sensitivity (elimination of central vision** **Ictal: during oculo-clonic seizure or ictal blindness : BG activity reduction and then occipital faster rhythms with spikes of low amplitude, these may be slower SW**
Tests: Genetic	**Unknown**
Prognosis	**Self-limiting** Easily controlled (50-60% remission in 2-4 years after onset) 90% dramatic response to carbamazepine

Summary of SFE

SFE	PS	BECTS	COE-G
Age onset	Infantile Childhood 1-14 (3-6) yrs	Childhood 3-14 (4-9)yrs	Childhood 5 mo-19 yrs (8-9 yrs)
Seizure type	Autonomic (Emetic)	Perisylvian	Occipital (visual aura, ictal blindness)
EEG	Multifocal 90% Occipital 60% Normal 10%	Centrotemporal Dipole	Occipital