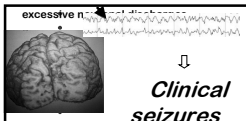
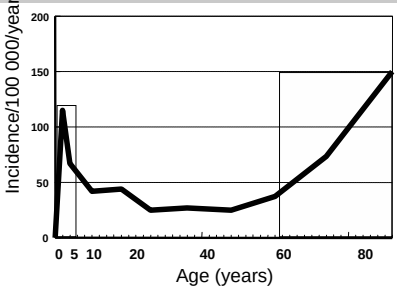


Pediatrics Primary Generalized

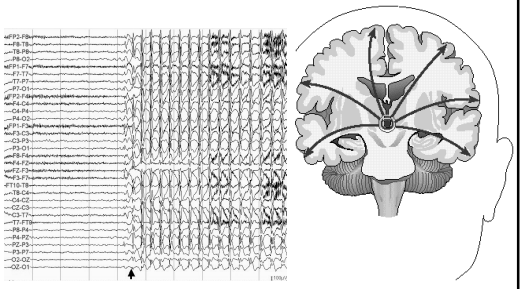
Epileptic Syndromes

ทายาท ดีสุดจิต
คณะแพทยศาสตร์
จุฬาลงกรณ์มหาวิทยาลัย

Incidence of epilepsy



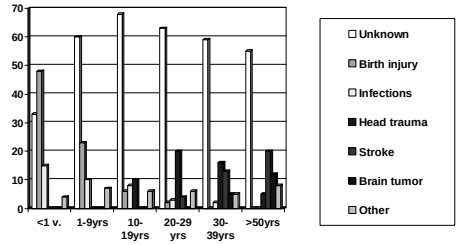
Generalized seizure



Syndrome Type Def:

- Idiopathic epilepsy syndrome: A syndrome that is only epilepsy, with no underlying structural brain lesion or other neurological signs or symptoms. Etiology presumed to be genetic. Usually age-dependent
- Symptomatic epilepsy syndrome: Epileptic seizures are result of an identifiable structural lesion
- Probably symptomatic epilepsy syndrome: Epileptic seizures are believed to be symptomatic, but no aetiology has been identified
- Benign epilepsy syndrome: Epileptic seizures are easily treated or need no treatment and remit without sequelae

Etiology of epilepsy



Age at onset

PROPOSED **DIAGNOSTIC SCHEME** FOR PEOPLE WITH EPILEPTIC SEIZURES AND WITH EPILEPSY

Engel et al. *Epilepsia* 2001;42(6):796-803

Axis 1 **Ictal phenomenology**
- detailed description of symtoms during the seizure

Axis 2 **Seizure type or types**
- according to ictal phenomenology and EEG

Axis 3 **Syndrome**
- list of syndromes, syndromic diagnosing is not always possible

Axis 4 **Etiology**
- genetic defects, or specific pathological substrates for symptomatic focal epilepsies

Axis 5 **Impairment**
- disability caused by epilepsy

ILAE Classification of Epilepsy

	Localization-Related (named by location)	***Generalized (named by disease)***
Idiopathic	Benign Rolandic epilepsy (Benign childhood epilepsy with centro-temporal spikes) Benign occipital epilepsy of childhood Autosomal dominant nocturnal frontal lobe epilepsy Primary Reading Epilepsy	Benign Neonatal Convulsions (+/- familial) Benign myoclonic epilepsy in infancy Childhood absence epilepsy Juvenile absence epilepsy Juvenile myoclonic epilepsy Epilepsy with GTCs on awakening Some reflex epilepsies
Symptomatic	Temporal lobe Frontal lobe Parietal lobe Occipital lobe (Rasmussen's encephalitis) (Most Reflex epilepsies)	Early myoclonic encephalopathy Early infantile epileptic encephalopathy with suppression- burst (Ohtahara's syndrome) Cortical abnormalities -malformations -dysplasias Metabolic abnormalities - amino acidurias - organic acidurias - mitochondrial diseases - progressive encephalopathies of childhood West's Syndrome Lennox-Gastaut Syndrome
Cryptogenic	(Any occurrence of partial seizures without obvious pathology.)	Epilepsy with myoclonic-astatic seizures Epilepsy with myoclonic absence

Diagnostic Features of Idiopathic Generalized Epilepsy

- age of onset-late childhood to early adult life
- seizure type - absence, myoclonus, tonic-clonic
- lack of underlying structural etiology although microscopical/QMRI changes may be present
- specific EEG finding (3 Hz spike and wave/photosensitivity)
- genetic basis and positive family history
- diurnal pattern of seizure occurence (awakening)
- excellent response to "valproate"-like AEDs

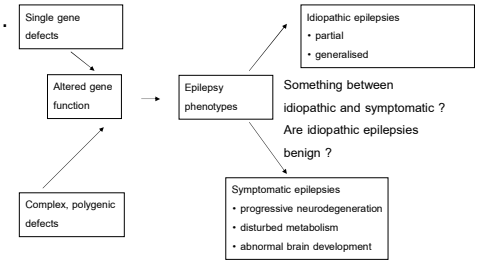
Diagnostic Features of Focal Epilepsies

- age of onset -throughout lifetime
- seizure type – simple/complex partial and/or secondarily generalized tonic-clonic
- underlying structural etiology may be found and MRI should be performed
- focal EEG finding may be present, but interictal EEG may be also normal
- response to "carbamazepine"-like AEDs

Idiopathic vs Symptomatic Generalized Epilepsies

	Idiopathic	**Symptomatic**
1. Etiology	**Genetic**	**Acquired/Genetic**
2. Seizure types	**Absence** **Myoclonic** **Tonic-clonic**	**Atypical absences** **Tonic, atonic** **Tonic-clonic**
3. Exam	**Normal**	**Intellectual disability**
4. EEG	**Normal background, Spike-wave 3 Hz**	**Background Slowing, Spike-wave 2,5Hz**
5. Imaging	**Normal (cortical abnormality)**	**Often focal or diffuse lesions**
6. Prognosis	**Good**	**Poor**

From gene defect to epilepsy phenotype



Genetically defined epileptic syndromes and specific diseases

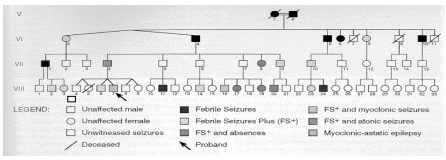
– epilepsies in inborn errors of metabolism
– progressive myoclonic epilepsies (PME)
– epilepsies and chromosomal disorders
– epilepsy and malformations of the cerebral cortex
– new epilepsy syndromes or subsyndromes with single gene inheritance
– Rasmussen´s syndrome
– the mesio-temporal lobe epilepsy syndrome

Epilepsy syndromes

Generalized Epilepsy with Febrile Seizures plus (GEFS+).
A genetic disorder with heterogeneous clinical phenotypes.

Scheffer IE, Berkovic SF. *Brain 1997 Mar;120 (Pt 3):479-90.*

- family with members with generalised epilepsies of various types and FS
- FS + febrile seizures lasting over age of 6 years
- FS+ absences or myoclonic sz's or atonic sz's, myoclonic-astatic epilepsy



GEFS+

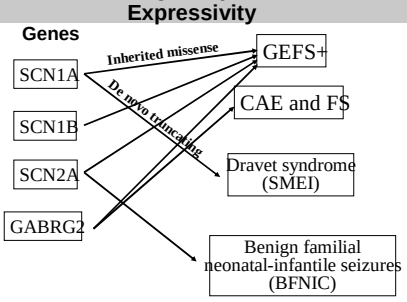
GENE LOCUS	GENE	GENE PRODUCT
19q13	SCN1B (missense)	Voltage-gated Na channel – beta 1 subunit
2q24	SCN1A (missense)	Voltage-gated Na channel – alpha 1 subunit
2q24	SCN2A (missense)	Voltage-gated Na channel – alpha 2 subunit
5q34	GABRG2 (missense)	GABAa receptor – gamma 2 subunit

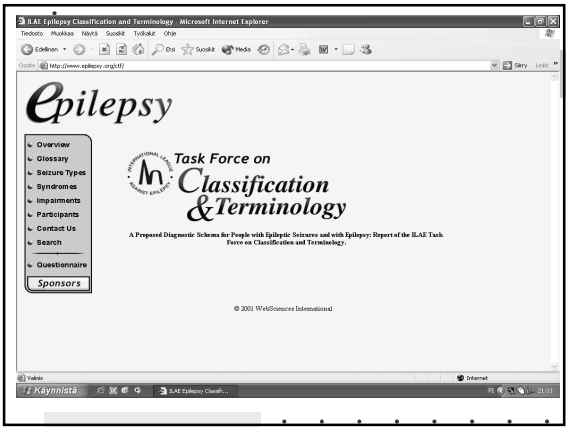
Known idiopathic epilepsy genes

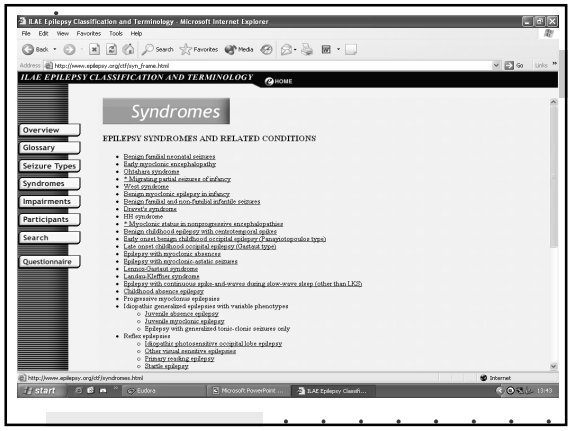
Guerrini et al., TRENDS in Molecular Medicine Vol.9 No.7 July 2003

Gene	Function	Locus	Inheritance/ MIM	Type of mutations	Epilepsy syndrome	Seizure types
GABRA1 $GABA_A$ α1 receptor subunit	Partial inhibition of GABA-activated currents	5q34	AD/606904	Missense	ADJME	Tonic–clonic, myoclonic, absence
GABRG2 $GABA_A$ receptor γ2 subunit	Rapid inhibition of GABAergic neurons	5q31	AD/604233	Missense, truncation	FS, CAE, GEFS$^+$	Febrile, absence, tonic–clonic, myoclonic, clonic, partial
SCN2A sodium channel α2 subunit	Initiation of fast sodium influx and propagation of action potential	2q24	AD/604233	Missense	GEFS$^+$, BFNIC	Febrile, afebrile generalized tonic, tonic–clonic
SCN1A sodium channel α1subunit	Somatodendritic sodium influx	2q24	AD/604233	Missense	GEFS$^+$, SMEI	Febrile, absence, myoclonic, tonic–clonic, partial
SCN1B sodium channel β1 subunit	Coadjuvate and modulate α subunit	19q13	AD/604233	Missense	GEFS$^+$	Febrile, absence, tonic–clonic, myoclonic
KCNQ2 potassium channel	M current interacts with KCNQ3	20q13	AD/602235	Missense	BFNC	Neonatal convulsions
KCNQ3 potassium channel	M current interacts with KCNQ2	8q24	AD/121201	Missense	BFNC	Neonatal convulsions
CHRNA4 acetylcholine receptor α4 subunit	Pre-synaptic; nicotinic current modulation; interacts with β2 subunit	20q13	AD/600513	Missense	ADNFLE	Sleep-related focal seizures
CHRNB2 acetylcholine receptor β2 subunit	Pre-synaptic; nicotinic current modulation; interacts with α4 subunit	1p21	AD/605375	Missense	ADNFLE	Sleep-related focal seizures
LGI1 leucine-rich, glioma activated	Dysregulates homeostasis; interactions between neurons and glia?	10q24	AD/600512	Missense	ADPEAF	Partial seizures with auditory or visual hallucinations
CLCN2 voltage-gated chloride channel	Neuronal chloride efflux	3q26	AD	Stop codon, splicing, missense	IGEs	Tonic–clonic, myoclonic, absence

Locus Heterogeneity and Variable Expressivity







EPILEPSY SYNDROMES AND RELATED CONDITIONS

- **Benign familial neonatal seizures**
- **Early myoclonic encephalopathy**
- **Ohtahara syndrome**
- **Migrating partial seizures of infancy**
- **West syndrome/ Infantile Spasms**
- **Benign myoclonic epilepsy in infancy**
- **Benign familial infantile seizures**
- **Benign infantile seizures (non-familial)**
- **Dravet's syndrome (SMEI)**
- **Hemiconvulsion Hemiparesis syndrome**
- **Myoclonic status in nonprogressive encephalopathies**
- **Benign childhood epilepsy with centrotemporal spikes (BECTS)**
- **Early onset benign childhood occipital epilepsy (Panayiotopoulos type)**
- **Late onset childhood occipital epilepsy (Gastaut type)**
- **Epilepsy with myoclonic absences**
- **Epilepsy with myoclonic-astatic seizures**
- **Lennox-Gastaut syndrome**
- **Landau-Kleffner syndrome**
- **Epilepsy with CSWS (other than LKS)**
- **Childhood absence epilepsy**
- **Progressive myoclonus epilepsies**
- **Idiopathic generalized epilepsies**
  - **Juvenile absence epilepsy**
  - **Juvenile myoclonic epilepsy**
  - **Epilepsy with generalized t-c seizures only**
- **Reflex epilepsies**
  - **Idiopathic photosensitive occipital lobe epilepsy**
  - **Other visual sensitive epilepsies**
  - **Primary reading epilepsy**
  - **Startle epilepsy**
- **Autosomal dominant nocturnal frontal lobe epilepsy**
- **Familial temporal lobe epilepsies**
- **Generalized epilepsies with febrile seizures plus**
- **Familial focal epilepsy with variable foci**
- **Symptomatic (or probably symptomatic) focal epilepsies**
  - **Limbic epilepsies**
    - **Mesial temporal lobe epilepsy with HS**
    - **Mesial temporal lobe epilepsy defined by specific etiologies**
    - **Other types defined by location and etiology**
  - **Neocortical epilepsies**
    - **Rasmussen syndrome**
    - **Other types defined by location and etiology**

Neonatal Epileptic Syndromes : Idiopathic

Benign familial neonatal seizures*	Onset day 2-3, up to 10-20 Sz/day, Autosomal. Dominant Chr. 20->Fam Hx(+), Stop in 1-6 m/o. 10% turn epielptic
Benign idiopathic neonatal seizures (fifth-day fits)*	Common up to 5% of FT Sz. Multifocal clonic, can have apnea, status epielpticus.Sz stop in 1 to max. 15 days. Poss. Zn def as etiology.
Benign neonatal sleep myoclonus	Myoclonic Sz in sleep, NI EEG. Onset 1st wk, resolved in 2 months.
Benign myoclonus of early infancy (benign nonepileptic Infantile spasms)	Myoclonic sz during wakefulness, Onset 3-9 months,can continue up to 1-2 year.

Benign Familial Neonatal Seizures (BFNS)

Insidence:	1.4/10 000 live births
Age of onset:	80% D2-3 (rest up to1-3 mth, usually premature)
Etiology:	EBN1 locus 20q13.3 gene KCNQ2 EBN2 locus 8q24 gene KCNQ3
Seizures:	start with a diffuse tonic component, followed by various autonomic and motor (clonic)changes
EEG:	interictal normal ictal: flattening of background, focalized or generalized spikes or slow waves
Therapy:	short-term PB or VPA up to 6 months
Prognosis:	favourable , risk of febrile seizures 5%, subsequent epilepsy 11%, especially BECTS, no mental retardation, no neurological abn.,no severe epilepsy

Benign Idiopathic Neonatal Seizures (BINS)

Prevalence:	2-7 % of all neonatal seizures
Age of onset:	97% D3-D7
Etiology:	idiopathic
Seizures:	clonic partial, and/or apneic, never tonic
EEG:	interictal: normal or bursts of theta rhythms on Rolandic areas ictal: rhytmic spikes and spike waves
Therapy:	no treatment or short-term AEDs
Prognosis:	favorable, however, probably up to 50% have some abnormalities as child; febrile seizures, other seizures, BECTS, minor neurological impairment

Early infantile epileptic encephalopathy with suppression-bursts (EIEE, Ohtahara´s syndrome)

Insidence:	no data
Age of onset:	within first 3 months
Etiology:	cerebral dysgenesis, anoxia, cryptogenic
Seizures:	tonic spasm, focal motor, hemiconvulsions, generalized seizures
Background EEG:	suppression-burst ** in both awake and sleep
Ictal EEG:	diffuse synchronization, cluster of fast activity
Therapy:	ACTH, B6-vit., VPA, other AEDs, surgery
Prognosis:	static impairment to severe mental retardation, quadraplegia and bed-ridden, evolution to West and Lennox Gastaut syndrome, high incidence of death

Otahara : Dx criteria

- Aicardiand Ohtahara 2002:

(1) Onset in early infancy, within the first 3 months, mainly within the first 10 days of life
(2) Main seizure pattern: tonic spasms
(3) Other seizures: partial seizures, rare myoclonic seizures
(4) Suppression bursts in EEG, during both waking and sleeping states
(5) Poor prognosis: severe psychomotor retardation and frequent death during infancy
(6) Intractable seizures and frequent progression to West syndrome
(7) Polyetiology, but majority of cases are associated with structural brain damage

Early (neonatal) myoclonic encephalopathy (EME)

Insidence:	no data
Age of onset:	neonatal
Etiology: cryptogenic	inborn errors of metabolism, familial,
Seizures:	erratic or fragmentary myoclonus, massive myoclonus, simple partial seizures, infantile spasms, tonic
EEG:	suppression-burst in sleep, discharges of slow waves/spikes and fast activity in awake
Therapy:	ACTH ineffectíve, pyridoxine may be tried
Prognosis:	progressive impairment to vegetative state, infantile spasms, high mortality in infancy

IEM & EME

- inborn error of metabolism, can produce the clinical and EEG picture typical of early myoclonic encephalopathy.
- nonketotic hyperglycinemia (Several authors)
- DB glyceric acidemia (Grandgeorge et al 1980),
- propionic acidemia (Vigevano et al 1982; Lombroso 1990)
- molybdenum cofactor deficiency (Aukett et al 1988)
- **methylmalonic acidemia (Lombroso 1990).
- "Abnormal oligosaccharide in" 3/10 (Schlumberger et al 1992).

- **PyridoxineB dependency
- Wang and colleagues reported a patient with a clinical picture of early myoclonic encephalopathy and an atypical suppressionBburst pattern, with full recovery after administration of pyridoxine (Wang et al 1998).
- CNS malformation ->early myoclonic encephalopathy (Martin et al 1981), but more often they produce Ohtahara syndrome.

severe neonatal epilepsies with suppression-burts pattern

NEONATAL EPILEPTIC SYNDROMES CHARACTERIZED BY PERSISTENCE (OR APPEARANCE) OF BURSTSUPPRESSION BEYOND 1-2 WEEKS OF AGE

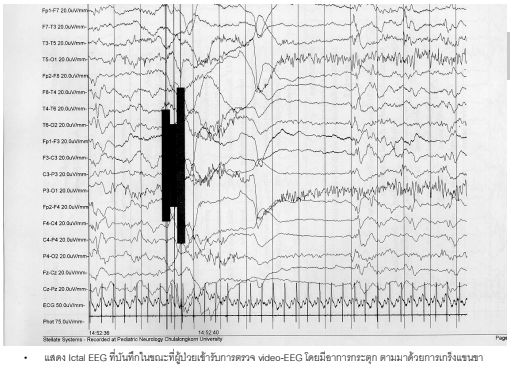
CLINICAL FEATURES	EARLY ENCEPHA-LOPATHY(EME)	MYOCLONIC EPILEPTIC ENCEPHA-LOPATHY (EIEE)	EARLY INFANTILE
Major clinical Seizure types at Onset	Myoclonic and clonic seizures "tonic spasms"	"Tonic spasms"	
Most common Etiology	Inborn error of metabolism	Bilateral structural cerebral lesions- malformative or destructive	
Outcome	Variable, usually Poor	Poor	

Otahara syndrome

ตัวอย่างผู้ป่วย

- ผู้ป่วยเด็กหญิงไทยอายุ 21 วันได้รับการส่งตัวจากโรงพยาบาลในจังหวัดชลบุรี ประวัติการตั้งครรภ์และการคลอด ปกติ
- สองชั่วโมงหลังการคลอดผู้ป่วยเริ่มมีอาการกระตุกที่แขนขาและลำตัวเป็นระยะ ได้รับการรักษาด้วยยากันชัก phonobarbital, phenytoin และ diazepam แต่อาการชักไม่หยุด
- ผู้ป่วยได้รับการตรวจ cranial ultrasound & MRI of the brain และ serum amino acid ผลปกติ

- EEG พบ Burst suppression generalized สลับกับ EEG seizure, Lt. occipital. Right temporal และ multiregional sharp waves
- อาการชักของผู้ป่วยทุเลาชั่วคราวเมื่อได้รับ Vitamin B6 จำนวน 100 mg เข้าหลอดเลือดดำแล้วกลับมาชักอีกในวันที่สอง
- ผู้ป่วยได้รับ vigabatrin 150 mg/kg ทำให้อาการชักลดลง แต่ผู้ป่วยยังคงมีอาการชักทุกวัน
- ผู้ป่วยยังไม่จ้องหน้า ยังไม่มองตาม คว่ำหรือคว้าของที่อายุสองปี



- แสดง Ictal EEG ที่บันทึกในขณะที่ผู้ป่วยเข้ารับการตรวจ video-EEG โดยมีอาการกระตุก ตามมาด้วยการเกร็งแขนขา พร้อมกับ EEG seizure แสดง EEG electrodecrement และ focal repetitive spiking Lt. occipital head area

Epileptic syndromes starting in infancy and early childhood

- infantile spasms and West syndrome
- migrating partial seizures in infancy
- benign myoclonic epilepsy in infancy
- severe myoclonic epilepsy in infancy (Dravet syndrome)
- myoclonic astatic epilepsy
- Lennox-Gastaut epilepsy
- myoclonic status in non-progressive encephalopathies
- febrile seizures
- idiopathic and/or benign localization-related epilepsies
- non-idiopathic localization-related epilepsies

Myoclonic astatic epilepsy (MAE, Doose)

Prevalence:	2% of childhood epilepsies
Age of onset:	between 18 and 60 months (94% under 5 yrs)
Etiology:	idiopathic, found also in GEFS+-families
Seizures:	generalized epilepsy syndrome with multiple seizure types including myoclonic-astatic, absences, tonic-clonic, eventually tonic seizures
EEG:	background normal or 4-7 Hz theta activity, interictally and with myoclonic jerks and atonic component: bursts of 2-3 Hz generalized (poly)spike-and-wave discharges, tonic component: 10-15 Hz polyspike discharges
Therapy:	VPA, VPA+LTG, +ESM, +BZD, TPM,LEV
Prognosis:	Favourable with seizure control in 3 yrs and normal cognitive outcome or unfavourable with resistant epilepsy and cognitive deterioration (if tonic seizures, myoclonic status)

Severe myoclonic epilepsy in infancy (SMEI, Dravet syndrome)

Prevalence:	7% of pts whose seizures start before age f 3 yrs
Age of onset:	before age of 1 year (peak 5 months)
Etiology:	genetic, GEFS+ spectrum (SCN1A-mutation), others
Seizures:	prolonged, generalized or unilateral clonic seizures triggered by fever, focal myoclonic jerking may precede, later: multiple seizure types: GTCSs,GCSs, myoclonic, atypical absences, complex focal seizures, tonic seizures
EEG:	paroxysms of generalised polyspikes and slow waves, 2 Hz spike- wave or both, elicited by photic stimulation and facilitated by sleep, background deteriorates progressively
Therapy:	VPA, BZDs, PB, ESM, TPM, LEV
Prognosis:	epilepsy resistant, psychomotor retardation, progressive ataxia and pyramidal symptoms appear within a year from onset (as the result of severe seizures), mortality high (15%)

Epileptic syndromes starting in childhood

- epilepsy with centro-temporal spikes
- idiopathic childhood occipital epilepsies
- non idiopathic focal epilepsies of childhood
- the HHE syndrome (hemiconvulsions, hemiplegia, epilepsy)
- electrical status epilepticus druing slow sleep (ESES or CSWS) including acquired epilepticus aphasia (Landau-Kleffner)
- childhood absence epilepsy and related syndromes
- the syndrome of myoclonic absences

Benign epilepsy with centrotemporal spikes (BECTS, Rolandic epilepsy)

Prevalence:	15% of children with seizures (1-15 years)
Age of onset:	1 to 14 years, peak at 8-9 years
Etiology:	idiopathic
Seizures:	unilateral facial sensorimotor symptoms, oropharyngolaryngeal manifestations, speech arrest and hypersalivation, 1/3-2/3 have nocturnal sGTCSs
EEG:	interictal EEG shows centrotemporal spikes maybe unilateral, but often are bilateral
Therapy:	not necessarily, AEDs for frequent seizures
Prognosis:	remission in 2-4 years and before 16 years of age, some have linguistic problems, < 2% epilepsy adults, < 1% evolution to CSWS or Landau Kleffner

Early onset benign childhood occipital epilepsy (Panayiotopoulos type)

Prevalence:	at least 6% of pts with seizures below the age of 13 yrs
Age of onset:	3-6 yrs (80%), peak 5 yrs, range 1-13 yrs
Etiology:	idiopathic
Seizures:	infrequent autonomic and behavioural disturbances, ictal emesis, ictal syncope, deviation of the eyes, rare visual hallucinations, autonomic status epilepticus, convulsions
EEG:	variable, occipital/frontal/multifocal spikes, generalized discharges, spikes similar to BECTS
Therapy:	not necessarily needed, AEDs for frequent seizures
Prognosis:	remission in 1-2 yrs after onset, 20% may develop other type of infrequent seizures, 13% BECTS, atypical rare cognitive evolutions like in BECTS have been described

Late onset childhood occipital epilepsies (Gastaut type)

Prevalence:	0.2-0.9% of all epilepsies
Age of onset:	3-16 years, mean 8 years
Etiology:	idiopathic
Seizures:	frequent visual seizures manifested with elementary visual hallucinations or ictal blindness or both, ocular pain, eye deviation, eyelid fluttering may progress to hemiconvulsions or sGTCs
EEG:	interictal: occipital paroxysms eyes closed (fixation-off sensitivity), random occipital spikes, ictal:occipital rapid spikes or discharges
Therapy:	CBZ (response 90%), other AEDs
Prognosis:	remission in 50-60 % in 2-4 years, others continue to have seizures, atypical evolution to CSWS has been described

Electrical status epilepticus during slow sleep (ESES or CSWS)

Insidence:	rare, excact numbers not available
Age of onset:	seizures before ESES start at 2mths-12 yrs (peak 4-5 yrs)
Etiology:	30% have preceding encephalopathy, pre-perinatal problems, congenital hemiparesis, rest cryptogenic
Seizures:	1) motor 2) unilateral partial motor seizures or GTCs, absences 3) atypical absences with atonic or tonic szs
EEG:	ESES develops 1-2 yrs after seizures: during non-REM sleep continuous bilateral and diffuse slow wave SWs mainly at 1.5-2 Hz perisisting through all slow sleep stages
Therapy:	seizures VPA, BZDs, ESM, electrographic abnormalities respond poorly to treatment
Prognosis:	neuropsychological impairment during ESES, afterwards seizures disappear, EEG improves, 50% cognitively impaire

Acquired epileptic aphasia (Landau-Kleffner)

Insidence:	rare, exact numbers not available
Age of onset:	2-8 years (peak 5-7 years)
Etiology:	epileptogenic functional lesion in the speech cortex
Seizures:	sz's present in 70-80%: atypical absences, myoclonic sz, focal sz's w/ 2° generalization, variable prognosis
Clinical :	verbal auditory agnosia → aquired aphasia → behavioural and psychiatric problems
EEG:	bilateral symmetrical/asymmetrical multifocal spikes and SW in temporal and parieto-occipital regions, sleep enhances spiking up to CSWS (85% of slow wave sleep)
Therapy:	VPA, BZDs, ESM, TPM,(steroids, surgery, immunoglobulin)
Prognosis:	aphasia usually improves wtih EEG normalization before adulthood, 10-20 % may achieve complete normalization, others are left with permanent sequalae

The syndrome of myoclonic absences (EMA, Tassinari syndrome)

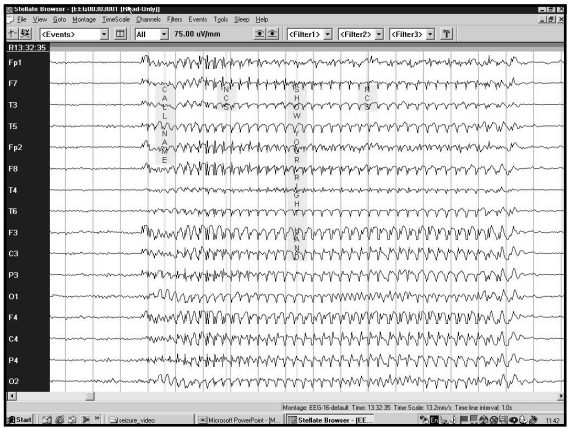
Prevalence:	1% of the epilepsies
Age of onset:	11mths-12 yrs
Clinical:	45% mentally retarded before diagnosis, imaging abnormal 17%
Seizures:	impairment of consciousness variable from mild to complete loss (absence) and bilateral myoclonias (shoulder,arms,legs)
EEG:	GSWDs 3/s
Therapy:	VPA, ETS, LTG, BZD, LEV
Prognosis:	70% mentally retarded, 50% seizures perist over the age of 20 yrs

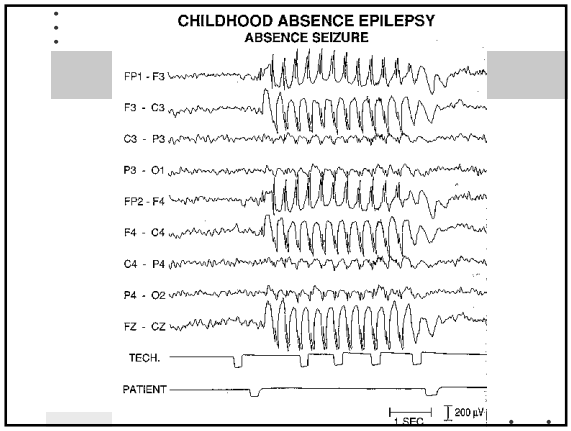
Childhood absence epilepsy (CAE)

Prevalence:	10-12% of children with epilepsy
Age of onset:	between 4 and 10 years, peak at 5-7 years
Etiology:	idiopathic (normal neurological state and development)
Seizures:	brief (4-20 s) and frequent (tens per day) absence seizures with abrupt and severe impaiment (loss) of consciousness. Automatisms are frequent but have no significance in the diagnosis
EEG:	ictal discharges of generalized high-amplitude spike and double (maximum occasional three spikes are allowed) spike- and slow-wave complexes, rhytmic at around 3 Hz, duration 4-20 s
Therapy:	ESM,VPA,LTG,BZDs, TPM ?,LEV?
Prognosis:	remission in 33-78% at age of 3-19 yrs, risk for later GTCs 36-60%, psychosocial problems in 30%

Childhood Absence Epilepsy

- Onset 4-8 Y(3-12 Y range)
- Clinical: Brief blank staring / impairment in school performance
- Up to 50 % has one GTC,
- EEG : 3 Hz SWC on Normal BG
- DOC : Ethosuximide / VPA
  - Use VPA if the patient has other type of seizure
  - Can be followed by EEG with Hyperventilation





Epileptic syndromes starting in older children and adolescence

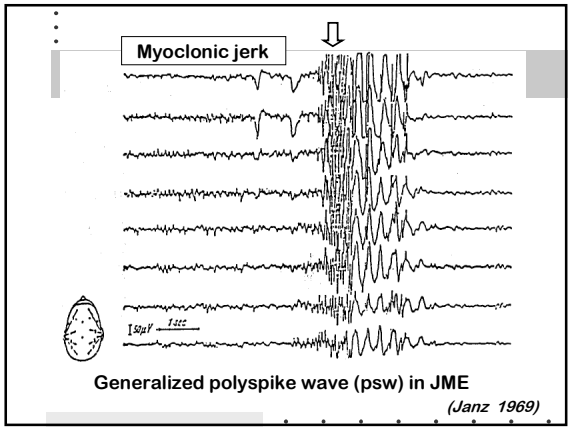
- complex reflex epilepsies: reading epilepsy and praxis induction
- isolated focal seizures of adolescence
- juvenile absence epilepsy
- juvenile myoclonic epilepsy
- epilepsy with generalized tonic-clonic seizures only

Juvenile absence epilepsy (JAE)

Prevalence:	2-3 % of adults with epilepsy
Age of onset:	7-17 years, peak at 10-12 years
Etiology:	Idiopathic
Seizures:	Frequency of absence seizures lower and impairment of consciousness less severe than in CAE, manifests in most patients also with infrequent tonic-clonic seizures and sporadic, infrequent myoclonic jerks
EEG:	background normal, generalized symmetric SW discharges with frontal accentuation, faster than 3 Hz (3-4.5 Hz)
Therapy:	VPA,LTG,BZDs,TPM?,LEV?
Prognosis:	Life long disorder, although seizures can be controlled in 70-80%

Juvenile myoclonus epilepsy (JME,Janz)

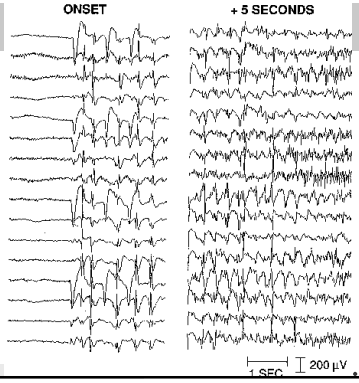
Insidence:	5-10 % of all epilepsies
Age of onset:	between 8 to 26 years, mostly between 12 to 18 years
Etiology:	idiopathic
Seizures:	1) myoclonic jerks (characteristic spontaneous, brief, involuntary, sudden, synchronous and symmetric) 2) typical absence seizures (in one third) 3) tonic-clonic seizures (in majority)
EEG:	bilateral polyspike-wave discharges, synchronous and symmetric, include 5-20 spikes, 12 to 16 Hz. Interval between apex of spike and myoclonic jerk in EMG is short 20-50 ms indicating cortical myoclonia
Therapy:	VPA,LTG,TPM,LEV,BZDs
Prognosis:	life-long, 15% resistant with increased risk of SUDEP, 30% has psychological or subtle frontal lobe dysfunctions

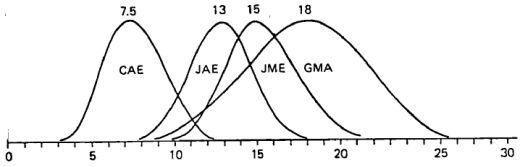


Generalized polyspike wave (psw) in JME

(Janz 1969)

JUVENILE MYOCLONIC EPILEPSY
CLUSTER OF MYOCLONIC JERKS



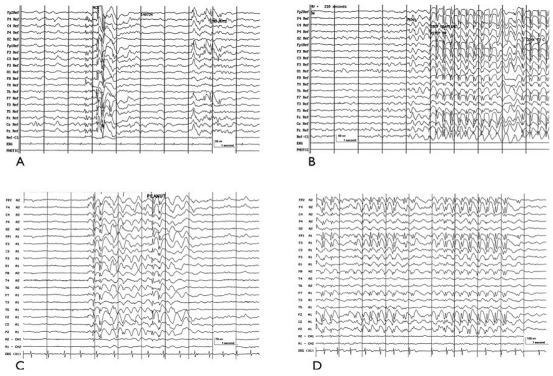


Continuum of 4 epileptic syndromes

EEG features of absence seizures in idiopathic generalized epilepsy: Impact of syndrome, age, and state

*Lynette Grant Sadleir, †Ingrid E. Scheffer, ‡Sherry Smith, §Bendix Carstensen, ‡Kevin Farrell, and ‡Mary B. Connolly

Discussion: **The EEG features of absence seizures are influenced by a complex interaction of age, epilepsy syndrome, level of arousal, provoking factors, and other intrinsic factors. Epilepsy syndrome alone cannot predict specific features of GSW; however, JME is more frequently associated with polyspikes and disorganization of the paroxysm.**



Circadian Rhythm and Personality Profile in Juvenile Myoclonic Epilepsy

*Tamara Pung and †Bettina Schmitz

We studied 20 patients with JME and a matched comparison group with temporal lobe epilepsy (TLE) using standardized questionnaires with respect to the sleep-wake rhythm and with respect to personality profiles. We confirmed the characteristic circadian rhythm in JME with the tendency to go to bed later at night, to get up later in the morning, and to feel fit at a later time during the day compared to patients with TLE. With the exception of some subanalyses we did not find evidence for a specific personality profile in JME. **Key Words:** Circadian rhythm—Personality profile—Juvenile myoclonic epilepsy.

Epilepsy with GTCS only

Prevalence:	not available
Age of onset:	between 6 to 47 years, peak at 16-17 years
Etiology:	idiopathic, high incidence of other IGEs
Seizures:	includes GTCSs occuring on awakening, diffusely while awake or during sleep or randomly
EEG:	generalized discharges of spike/multiple spike slow waves
Therapy:	VPA, LTG,TPM,LEV,BZDs, (sodium-channel-blockers)
Prognosis:	life-long disease with a high (83%) insidence of relapse on withdrawal

Primary reading epilepsy

Insidence:	not available
Age of onset:	between 12-25 years
Etiology:	idiopathic localization-related epilepsy, frequently hereditary
Seizures:	perioral reflex myocloni precipiated by reading>> talking>> other language related activities, rare: visual/oculomotr, dyslexic aura, high risk of sGTC
EEG:	interictal EEG often normal, reading provocation results in sharp waves or SW discharges (parieto-temporal/frontal)
Therapy:	VPA, CLN
Prognosis:	drug response good, complete remission rare

Ring chromosome 20 syndrome (r20S)

Insidence:	unknown (especially the silent forms)
Age of onset:	seizures usually begin in childhood
Etiology:	the formation of the ring is associated with loss of telometric material on both arms of chromosome 20, the severity of mental retadation correlates with the precentage of the abnormal lymphocytes while epilepsy does not
Seizures:	atypical absences (long periods of loss of contact, non-convulsive status) myoclonia, focal seizure types
EEG:	during non-convulsive status: high-amplitude rhytmic slow activity (2-3 Hz) with spikes or SW, predominatly frontal
Therapy:	VPA,LTG (TPM,LEV,BZDs)
Prognosis:	drug-resistant epilepsy, life-long

Progressive myoclonus epilepsies(PME)

- Neuronal ceroidlipofuscinoses
- MERFF
- Gaucher type III
- Lafora's disease
- Unverricht-Lundborg's disease (EPM1)
- Dentato(rubro)pallidoluysian atrophy

Progressive myoclonus epilepsy (EPM1,ULD)

Prevalence:	about 200 patients in Finland
Age of onset:	between 7-18 years, 86% starts between 9-13 years
Etiology:	mutations in the gene (EPM1) mapped to 21q22.3 encoding cystatin B (CSTB), a cysteine protease inhibitor
Seizures:	begins with action myoclonus, which is most prominent in the morning upon wakening, or with nocturnal clonic, or tonic-clonic seizures, myoclonus becomes invalidating
EEG:	spontaneous spike-wave discharges, photosensitivity and polyspike discharges during REM sleep, the almost continuous, small amplitude jerks are often not time-locked to EEG discharges, only the large-amplitude ones often are
Therapy:	VPA, LTG,TPM,LEV, piracetam,CLN,CLB,PB
Prognosis:	variable, but progressive,many patients need wheelchair at least occasionally, no major cognitive decline

Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE)

- มีการถ่ายทอดแบบ autosomal dominant โดยมี gene ที่ผิดปกติอยู่บน chromosome 20q (CHRNA4 gene)
- onset ตั้งแต่ 2 เดือน ถึง 52 ปี โดยเฉลี่ย 11.7 ปี โดยมากเริ่มเกิดก่อนอายุ 20 ปี
- ผู้ป่วย ADNFLE มักมีสติปัญญาดี ตรวจร่างกายปกติ และ MRI ปกติ

Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE)

- อาการชักมักเป็นตอนหลับเท่านั้น
- การเคลื่อนไหวที่รุนแรงของลำตัวและขา (thrashing hyperkinetic activity) hypermotor หรืออาจมีอาการเกร็ง หรือกระตุก ขณะชักมักไม่สูญเสียความรู้สึกตัว แต่มักตอบสนองไม่ได้ อาจมี secondary GTC ตามมาได้ (59%)
- อาการชักมักเกิดติด ๆ กันเป็นcluster อาจเกิดบ่อยถึง 10 ครั้งต่อคืน แล้วเว้นช่วงไปเป็นสัปดาห์หรือเดือน

Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE)

- อาการเหล่านี้เหมือนกับอาการของ nocturnal paroxysmal dyskinesia ซึ่งในปัจจุบันเชื่อว่าเป็นโรคลมชัก
- DOC ยากันชักกลุ่ม focal เช่น carbamazepine และ phenytoin แต่มักหยุดยาไม่ได้เนื่องจากอาการชักมักกลับเป็นขึ้นใหม่
- EEG interictal discharge บริเวณ frontal ได้ประมาณ 16 % ขณะชักพบ ictal discharge เป็น rhythmic sharp and slow wave ทั้งสองข้าง บริเวณด้านหน้า หรืออาจ ไม่พบ discharge ใดๆ เลย