

Pediatric Epileptic Syndrome

Common neonatal seizure patterns

- Clonic
- Subtle: abnormal eye movements; mild posturing; oral lingual movements; pedaling and rowing movements; tremors, apneas
- Tonic
- Myoclonic
- Ictal apnea
- Absence-like
- Oculomotor
- Further ictal manifestations: finger contractions; alternating 'warding off' arm movements; sudden awakening w crying; eye opening; paroxysmal blinking; nystagmus; chewing, 'swimming, rowing and pedaling'; abrupt changes in respiration, skin color, salivation

	BFNC (benign familial neonatal convulsions)	BINC (benign idiopathic neonatal convulsion)
FH	constant; (EBN1) 20q13.3 BFNC (EBN2) 8q - code for novel potassium channels*	rare (2%)
Age of Occurrence	day 2, 3--abate by 6 mos of age	day 4, 5
Persistence of Sz	longer	
Sz	partial or G clonic szs, occ. apnea	
Occurrence of Epilepsy	14%	0.5%

* Science 1998;279:403-406 and Nat Genet 1998;18:25-29

Febrile Convulsions

- 3% to 4% of all children, age-dependent, benign and outgrown.
- Only 25% to 30% of children who have a single FS will have a second, and half of those who have two will have a third.
- Less than 9% of children with FS will have more than three.
- The first prolonged FS does not increase the chance of recurrent FS.

Risk factors of later epilepsy:

1. Prolonged or unilateral
2. Prior neurological deficit or suspected neurological deficit
3. Family history of epilepsy

Significant Predictors of Recurrent Febrile Convulsions

- Duration of fever
- Temperature
- Family history of FS
- Age <18 mo

Nonsignificant Predictors

- Family history of epilepsy
- Neurodevelopmental abnl
- Complex febrile seizure
- Male sex
- Race or ethnic group (Black, Hispanic)

Berg et al, 1992

What is the best medicine for febrile seizures?

NOT necessarily to prescribe medication, BUT rather to sit with the family and talk.

Hippocampal malformation as a cause of familial febrile convulsions and subsequent hippocampal sclerosis (*Neurol* 1998;50:909-917)

Infantile spasms (West syndrome)

- Prevalence: 1.3% of all patients with epilepsy
- Incidence: one per 4000-6000 live birth
- Onset: between 3 and 12 months of age with a peak at 5 months (onset of spasms before one year of age is the rule in 90% of patients with IS)
- Spasms: flexor, extensor, mixed
- Mental retardation presents in about 95% of cases
- Etiology: idiopathic or cryptogenic (10-15%)
- Hypsarrhythmia
- Treatment: ACTH, Prednisone, AEDS i.e. Vigabatrin, VPA, nitrazepam, surgery

Lennox-Gaustaut syndrome

- Epileptic seizures: atypical absences and atonic or myoclonic
- EEG: slow spike and wave discharges or multifocal spikes
- Slow mental development
- 60% of the patients with this syndrome are children already suffering from previous encephalopathy
- Prognosis: unfavourable in most cases, as regards both the seizures and the patients' neuropsychic condition

Rasmussen's Syndrome (Chronic Encephalitis and Epilepsy)

- Rare disease with onset 2-11 years
- Insidious onset and gradual progression of unilateral brain dysfunction
- Intractable focal seizures (epilepsia partialis continua: EPC), hemiparesis, and dementia
- Path: perivascular lymphocytic cuffing, microglial nodule, neuronal loss; little affinity for white matter and cerebral commissures; high incidence of frontocentral resections---centrifugal spread from an initial focus

The search for viral antigens

- No viral inclusions by light and electron microscopy
- Immunocytochemical studies for herpes simplex, measles, influenza, mumps, and parainfluenza-negative (Mizuno et al 1985)
- In situ hybridization using cDNA probes of herpes simplex virus and JC strains of papovavirus-negative (Aksamit)
- In situ hybridization for human cytomegalovirus- 7/10 of Rasmussen's encephalitis [other neurologic diseases- 2/42, fulminant liver transplant- 10/27] (Poland et al, 1991)
- The search for scrapie-associated fibril antibodies-unsuccessful (Gray et al 1987)

Etiologic consideration

- immunoglobulins and HLA in 7 patients
- with 13 of their first-degree relatives (Andermann et al, 1991)
- immune-mediated mechanism
- lymphocyte-macrophage infiltration, associated with the progressive tissue destruction presence immunoreactivity against glutamate receptor (GluR)2 or GluR3 fusion proteins and "native" GluR3 in 3 RS patients (DUMC, *Science* 1994;265:648-651) and more cases including MCG cases (2 cases)
- possible interactions between the host's immune system and viruses likely to cause persistent infections of the CNS.
- Anti-GluR3 antibodies promote destruction of cortical cells in vitro by a complement-dependent mechanism (*Neuron* 1998;20:153-163)

Surgical treatment

- Cortical resection
- Functional hemispherectomy
- Multiple subpial transection
- Lindsay et al. (1987) and Verity et al. (1982) : hemispherectomy prevents the continued intellectual deterioration and results in stabilization or improvement in function.

- Timing of surgery? It is difficult to define "early"
- Prior to surgery, seizures must be both intractable and interfering with function
- Then progressive and unilateral nature of the condition must be obvious to the physician, the family, and to the child.
- The inevitability of the hemiplegia with and without surgery must be understood by all and be acceptable to all.
- When the risks and benefits to the patient of the surgery outweigh the risks and benefits of waiting.
- There is no benefit to waiting for a complete hemiplegia to occur spontaneously.

Medical treatment:

- High-dose steroids or immunoglobulins (Hart et al, 1994)
- Ten of 17 p'ts receiving steroids
- Eight of 9 p'ts receiving immunoglobulins
- Some reduction of sz frequency in the short term
- Slight improvement in hemiparesis
- Immunoglobulin treatment
 - IVIG at a dose of 400 mg/kg/d on 3 successive days
 - If no improvement within 1 month, start steroid treatment
 - If improvement, monthly IVIG at a dose of 400mg/kg/d for 1 day until further improvement fails to occur.
 - If further treatment is necessary, high-dose steroid
- High-dose steroid treatment
 - IV methylprednisolone (400 mg/m² of BS) for 3 consecutive infusions, one every other day.
 - At monthly for the first year, at 2-month intervals for the second year, and 3-month interval for the third year.
 - Accompanied by oral prednisolone (2 mg/kg/d) for 1 to 2 years.

Childhood Absence

- Autosomal dominant (8q24)
- A form of primary generalized epilepsy occurring in normal children (peak: 6-7 years)
- Very frequent absences of any kind
- EEG: 2.5-3.5 c/s spike-waves
- Evolution:
 - remission
 - rare persistence of absences only
 - tonic-clonic seizures during adolescence or later

Mistaking absence seizures for complex partial seizures is a serious diagnostic error leading to inappropriate therapy

Juvenile Absence Epilepsy

- Age of onset: 12-15 years
- Simple absences - more common
- >grand mal
- >absence status
- EEG: 4-6 c/s spike wave

Benign Partial Epilepsy with Centro-Temporal Spikes of Childhood, Benign Rolandic Epilepsy (BRE)

- The most frequent and the best known of the benign partial epilepsies
- Onset between 3 and 13 years (peak: 9-10 years)
- Recovery before 15-16 years
- Seizures: brief, hemifacial motor, with frequent associated somatosensory symptoms, usually nocturnal
- EEG: blunt, high voltage centro-temporal spikes, often followed by slow-waves, activated by sleep and tending to spread and/or to shift from side to side
- Complex-variable penetrance more than one gene \pm acquired factors -15q14 (Neurol 51:1608-12, 1998)

Landau-Kleffner syndrome (acquired aphasia of childhood with epilepsy)

- Associated symptoms: epileptic seizures (72%), behavioural and psychomotor disturbances (72%)
- Verbal auditory agnosia with rapid reduction of spontaneous oral expression
- Epileptic seizures are generally rare and varied. disappear before the age of 15

Epilepsy with continuous spikes and waves during slow sleep (CSWS) - otherwise described as ESES (epilepsy with electrical status epilepticus during slow sleep)

Progressive Myoclonus Epilepsies

- Heterogenous-debilitating-fatal
- Segmental ---> massive myoclonus
- GTCS or Clonic seizures
- Dementia
- Progressive Neurologic deficits
- Cerebellar dysfunction
- Unverricht-Lundborg: 21q22.3; onset 6-15 yrs of age; stimulus-sensitive myoclonus

Baltic-Mediterranean PME

- Lafora's Disease: onset early adolescence; progressive to constant myoclonus; demetis, dyspraxia, visual loss, vegetative state, fatal; 6q24 EPM2A-protein

tyrosine phosphatase (Laforin); AR (*Nature Genetics* 1998;20:171-174); How this mutation leads to Lafora neuronal inclusion bodies and the clinical phenotype of Lafora's disease is unknown.

- Neuronal ceroid-lipofuscinoses
- Gaucher's disease
- Sialidosis type 1
- MERRF

Juvenile Myoclonic Epilepsy (JME)

(Impulsive Petit Mal of Janz)

- Appears around puberty
- Sz with bilateral, single or repetitive, arrhythmic, irregular myoclonic jerks
- No disturbance of consciousness
- Awakening myoclonus
- Often precipitated by SD, ETOH, fatigue, stress
- Associated with often GTC and, less often, infrequent absences
- Interictal and ictal EEG: rapid, generalized 3.5-6Hz, often irregular spike-wave and polyspike-waves
- Response to valproic acid is good
- Chromosome 6 (dominant gene on 6p, unidentified recessive gene)