Infantile Spasms

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Epidemiology of Epilepsy

- Epilepsy is a very common disorder.
- Each year, **150,000** children and adolescents in the USA will have a single unprovoked seizure.
- 30–45% of these children will go on to develop epilepsy.
- 1.0% prevalence of epilepsy in the general population. Bimodal distribution.
- **1 in 5** people will have a single seizure in their lifetime.
Infantile Spasms

- First described in 1841 by Dr. West:
  - At 4 months of age: “Slight bobbings of the head forward. . . These bobbings increased in frequency and strength.”
  - At 1 year of age: “. . . He neither possesses the intellectual vivacity or the power of moving his limbs of a child his age. . .”

Infantile Spasms

- Relatively common (1,200–2,500 per year)
- Onset at 3–8 months of life
- Characterized by clusters of flexor, extensor, or mixed myoclonic jerks
- May have associated autonomic or focal features
- Hypsarrhythmia pattern on electroencephalogram (EEG)
- Associated with a poor developmental outcome
- Non-standard antiepileptic therapies
Video 1-Infantile Spasms
Video 2-Infantile Spasms
Infantile Spasms—Hypsarrhythmia
Infantile Spasms—Ictal
Infantile Spasms—Ictal
Etiologies of Infantile Spasms

- Malformations of cortical development
- Neurocutaneous disorders (e.g., tuberous sclerosis)
- Genetic syndromes, including Trisomy 21
- Inborn errors of metabolism
- Hypoxic-ischemic encephalopathy
- Meningitis/encephalitis
- Stroke
- Trauma
What Causes Infantile Spasms?

- Brain development requires excitatory pathways for active neurogenesis, synaptogenesis, and programmed apoptosis.

- Subcortical pathways are initially better developed than the cortical pathways, resulting in subcortically mediated volleys of epileptogenic discharges.
Age-Dependent Epileptic Encephalopathies

- Evolution of seizure semiology
- Evolution of EEG characteristics
- Directly correlated with the increasing, programmed synaptogenesis and reorganization of the developing brain
- Results in increased synchronization of EEG and changing seizure phenotype
Outcome of Infantile Spasms

- In children who are not controlled, the spasms generally evolve to other seizure types, including tonic seizures by 1–2 years of age.
- Most develop Lennox-Gastaut syndrome, with associated tonic, atonic, generalized tonic clonic, myoclonic, and atypical absence seizures.
- If seizures persist, 70–90% have persistent intellectual impairments.
Treatment of Infantile Spasms

- Adrenocorticotropic hormone (ACTH)—Treatment of choice
- Vigabatrin—Treatment of choice for patients with tuberous sclerosis
- Prednisone—Not as effective
- No standard antiepileptic medications have proven efficacy
- A small subset of patients with infantile spasms may be candidates for epilepsy surgery
Infantile Spasms: What is Effective Treatment?

- In the American Academy of Neurology (AAN) and Child Neurology Society (CNS) practice parameter, a “responder” is defined as:
  - Complete cessation of infantile spasms, as confirmed by video EEG monitoring
  - Elimination of hypsarrhythmia pattern on prolonged EEG

- The goal of therapy is to treat the infantile spasms and the ongoing epileptic encephalopathy as seen on the EEG (i.e., hypsarrhythmia pattern)

Early Recognition and Treatment Can Affect Outcome

- In a study of 37 children with cryptogenic infantile spasms, treatment started within one month of onset of spasms, using ACTH, followed by prednisone in decreasing doses, produced 100% normal outcome in 22/22 patients.

- If treatment was initiated after one month, normal outcomes occurred in 6/15 patients (i.e., only 40%).

Early Treatment Affects Developmental Outcomes

- In patients with tuberous sclerosis, only 18/50 patients (36%) had an IQ over 70.

- Three factors are associated with poor developmental outcomes:
  - Increased time from infantile spasms onset to cessation
  - Increased time from treatment to cessation
  - Poor control of other seizures after infantile spasms

Infantile Spasms is a Medical Emergency

- Immediate referral to a pediatric neurologist
- These infants are often admitted to the hospital for quick confirmation of the diagnosis and initiation of treatment
- The data now clearly supports the conclusion that early treatment, started within one month of onset of spasms, has a positive impact on developmental outcome and decreased risk of other seizures
- The goal: No spasms; no hypsarrhythmia
Infantile Spasms

- **ACTH**: The “Gold Standard”
  - FDA approved for infantile spasms
  - AAN/CNS practice parameter: ACTH is probably effective for the short term in infantile spasms treatment
  - Expensive
  - Side effects need monitoring

- **Vigabatrin**: Best for some patients (i.e., tuberous sclerosis)
  - FDA approved for infantile spasms
  - Requires specialty pharmacy
  - Side effects need monitoring
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