Generalized seizures

Dr Magali Gauthey
HISTORY:

comes from “to seize upon”

Has always existed, is very well described

- first by Sakikku 1000 BC, Babylonian scholar: focal seizure, invasion by evil spirit
- Hippocrates, 400 BC: comes from the brain
- 19th century: better understanding, treatments arrivals
Generalized seizures

**EPIDEMIOLOGY:**

- 1% children will experience 1 afebrile seizure (USA)
- 3-5% single febrile seizure
  - 30% additional febrile seizure
  - 3-6% afebrile or epilepsy

Mean number of people with epilepsy per 1000 population in WHO regions and the world

N=105

ATLAS Epilepsy care in the world, 2005, WHO UpToDate
DEFINITION:

Clinical manifestation of abnormal, excessive, synchronous discharges of neurons

- Focal: restricted area
- Generalized: both hemispheres and subcortical regions
- Status Epilepticus: prolonged or immediately recurrent (>30 min, or 5 min?)
CLASSIFICATION: ILAE 2010

Recommendations, not final classification

Based on ictal semiology, and better understanding

- **Generalized**: “originating at some point within, and rapidly engaging, bilaterally distributed networks”
  - Tonic-clonic
  - Tonic
  - Atonic
  - Clonic
  - Myoclonic: myoclonic, myoclonic-atonic, myoclonic-tonic
  - Absences: typical, atypical, special features (myoclonic, eyelid myoclonia)
CLASSIFICATION: ILAE 2010

- **Focal:** “originating within networks limited to one hemisphere, discretely localized or more widely distributed. For each seizure type ictal onset is consistent from one seizure to another, with preferential propagation patterns that can involve the contralateral hemisphere.”
  - With or without impaired consciousness = awareness = dyscongnitive

- **Unknown**
PATHOPHYSIOLOGY:

**Propagating depolarization wave**

Cellular polarization depends on:
- **Entry of**
  - $K^+$ potassium channels
  - $Cl^-$ GABA
- **Exit of**
  - $Na^+$ AMPA, sodium channels
  - $Ca^+$ NMDA, calcium or potassium channels

Balance between
- **Depolarizing currents are excitatory:** glutamatergic pathways
- **Hyperpolarizing currents are inhibitory:** GABA (gamma-aminobutyric acid)ergic pathways.
Generalized seizures

PATHOPHYSIOLOGY:

Glial cells regulate the extracellular ions and neurotransmitters concentration.

Spreading: cortical and subcortical pathways

3 steps:

1. **Initiation**: missing ATP $\rightarrow$ diminished NA/K ATPase activity $\rightarrow$ loss of polarization $\rightarrow$ action potential

2. **Upholding**

3. **Ending**: vasodilatation $\rightarrow$ more O2 available $\rightarrow$ more ATP available

Deficient in status epilepticus

A unifying concept of seizure onset and termination. Doman. Medical Hypothesis. 2004

ETIOLOGY: Epilepsy

**Table 1. Etiologies Identified in the Subjects**

<table>
<thead>
<tr>
<th>Etiological Factors</th>
<th>Frequency (n)</th>
<th>Percentages (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal asphyxia</td>
<td>47</td>
<td>37.3</td>
</tr>
<tr>
<td>CNS infections</td>
<td>28</td>
<td>21.9</td>
</tr>
<tr>
<td>Kernicterus</td>
<td>12</td>
<td>9.5</td>
</tr>
<tr>
<td>Recurrent febrile seizure</td>
<td>10</td>
<td>7.9</td>
</tr>
<tr>
<td>Prematurity</td>
<td>10</td>
<td>7.9</td>
</tr>
<tr>
<td>Neonatal seizures</td>
<td>9</td>
<td>7.1</td>
</tr>
<tr>
<td>Head injury</td>
<td>9</td>
<td>7.1</td>
</tr>
<tr>
<td>Cerebral malaria</td>
<td>5</td>
<td>4.0</td>
</tr>
</tbody>
</table>

**KEY:** Some Subjects had Multiple Aetiologies. CNS – Central Nervous System Infections.

**Table 2. Percentage Distribution of Microbial Causes**

<table>
<thead>
<tr>
<th>Causes</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>323</td>
<td>65</td>
</tr>
<tr>
<td>Worms</td>
<td>49</td>
<td>10</td>
</tr>
<tr>
<td>Virus</td>
<td>74</td>
<td>15</td>
</tr>
<tr>
<td>Cysticercosis</td>
<td>35</td>
<td>7</td>
</tr>
<tr>
<td>Unknown</td>
<td>16</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 1: Pattern of childhood epilepsies in Sagumu, Nigeria, T. Ogunlesi, 2009
Table 2: Clinical Microbiological aspects of epileptic seizures in the tropical countries with specific focus on Nigeria, I. Kanu, The Scientific World, 2005
**ETIOLOGY: Seizures**

* > 2 month
  * Head injury
  * Malnutrition
  * Febrile convulsion (measles)
  * Meningitis, encephalitis (measles), cerebral abscess, tuberculous meningitis (cryptococcal if HIV)
  * Malaria
  * Dysentery
  * Sepsis
  * Typhoid fever
  * Dengue
  * Hypoglycemia (< 3 mmol/l)
  * Poisoning: organophosphorus and carbamate compounds, iron

*Pocket book of Hospital care for children, WHO, 2013*
Generalized seizures

- **Sudden loss of consciousness** (defined by the incapacity to respond normally to an external stimulus)

- Generalized seizures with motor manifestations: tonic, clonic, tonic-clonic or atonic
Generalized seizures

CLINICAL DIAGNOSIS

Tonic seizure

Tonic phase

- The child abruptly immobilizes or falls
- There is an immediate loss of consciousness
- All the muscles are involved
- The jaws tighten
- The eyes roll back
- The extremities are stiff, pronated, with internal rotation
- Respiration stops
- Duration: 10 to 20 sec.

Job Aid, Identifying Adverse Events of Special Interest (AESI), in infants and young children GSK, 2014
Generalized seizures

**CLINICAL DIAGNOSIS**

**Clonic phase**

- Brisk movements of flexion-extension of all extremities
- The face grimaces
- Rapid eye movements (roll back)
- Breathing becomes noisy
- Clonic movements
- Duration: 2 to 3 min. sometimes longer

Job Aid, Identifying Adverse Events of Special Interest (AESI), in infants and young children GSK, 2014
Generalized seizures

**Tonic-clonic seizure**

**Tonic phase**
- The child abruptly immobilizes or falls
- There is an immediate loss of consciousness
- All the muscles are involved
- The jaws tighten
- The eyes roll back
- The extremities are stiff, pronated, with internal rotation
- Respiration stops
- Duration: 10 to 20 sec.

**Clonic phase**
- Brisk movements of flexion-extension of all extremities
- The face grimaces
- Rapid eye movements (roll back)
- Breathing becomes noisy
- Clonic movements
- Duration: 2 to 3 min. sometimes longer

**Resolution phase**
- Clonic movements stop
- The body becomes limp
- Confusion or comatose state

Job Aid, Identifying Adverse Events of Special Interest (AESI), in infants and young children GSK, 2014
Generalized seizures

**Atonic seizure**

**Atonic Phase**

- Sudden loss of muscle tone
- The child goes limp and falls to the ground
- Spasms
- Seizure duration less than 30 seconds
- The child regains consciousness and alertness rapidly after the seizure

Job Aid, Identifying Adverse Events of Special Interest (AESI), in infants and young children GSK, 2014
Generalized seizures

Ask for a **full description**: mime, video

Don’t forget

- The beginning and ending
  - Aura
  - Postictal state (somnolence, hemiparesis: Todd’s paralysis, dysphasia)
- Precipitating circumstances
  - Time of day, activity, medication: herbal supplements, fever, illness, trauma,…
- Eyes opened during the event
- Incontinence, tongue biting (non specific, may be absent)
Generalized seizures

If the seizure is witnessed by the health personal

Level 1 diagnostic certainty
- The highest level of specificity
- Sensitive for the respective AEFI
- Principally applicable in clinical trials, in the setting of active follow up and in settings with more resources.

If the seizure is reported by a close contact

Level 2 diagnostic certainty
- Intermediate specificity level
- Sensitive for the respective AEFI
- Applicable in clinical trials and post marketing surveillance.
Generalized seizures

CLINICAL DIAGNOSIS

Other generalized motor manifestations

- Involuntary movements are well described and nonspecific

Level 3 diagnostic certainty

- Lowest level of specificity
- Very sensitive for the respective AEFI
- Applicable in clinical trials, post marketing surveillance and less resources.
Generalized seizures

MANAGEMENT:

① ABC

② Drugs

③ Complementary examinations
MANAGEMENT:

A. Airway
- Open airways
- Give oxygen

B. Breathing
- If the patient is not able to protect airways: intubation
- Prefer drugs with anti-epileptic action

C. Circulation
- Fluids: 20 ml/kg normal saline solution or Ringer
MANAGEMENT:  Drugs

AEDs: antiepileptic drugs

Reestablish excitatory / inhibitory equilibrium

New drugs regularly discovered
Generalized seizures

DRUGS

① Benzodiazepines transmucosal
   - IR, intranasal, intrabuccal (between gum and cheek)
② Benzodiazepines IV
③ Antiepileptic drugs IV
   - Phenobarbital 15-20 mg/kg
   - Phenytoin
   - Valproic acid
   - Levetiracetam
How to give diazepam rectally

1. Give **diazepam rectally**:
   - Draw up the dose from an ampoule of diazepam into a tuberculin (1-ml) syringe. Base the dose on the weight of the child, when possible. Then remove the needle.
   - Insert the syringe 4–5 cm into the rectum, and inject the diazepam solution.
   - Hold the buttocks together for a few minutes.

### Chart 9. How to give diazepam rectally

<table>
<thead>
<tr>
<th>Age (weight)</th>
<th>Diazepam given rectally 10 mg/2 ml solution</th>
<th>Dose 0.1 ml/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks to 2 months (&lt; 4 kg)</td>
<td></td>
<td>0.3 ml</td>
</tr>
<tr>
<td>2–&lt; 4 months (4–&lt; 6 kg)</td>
<td></td>
<td>0.5 ml</td>
</tr>
<tr>
<td>4–&lt; 12 months (6–&lt; 10 kg)</td>
<td></td>
<td>1.0 ml</td>
</tr>
<tr>
<td>1–&lt; 3 years (10–&lt; 14 kg)</td>
<td></td>
<td>1.25 ml</td>
</tr>
<tr>
<td>3–&lt; 5 years (14–19 kg)</td>
<td></td>
<td>1.5 ml</td>
</tr>
</tbody>
</table>

**Note:** Use **phenobarbital** (200 mg/ml solution) at a dose of 20 mg/kg to control convulsions in infants < 2 weeks of age:
- Weight 2 kg – initial dose, 0.2 ml; repeat 0.1 ml after 30 min
- Weight 3 kg – initial dose, 0.3 ml; repeat 0.15 ml after 30 min

} If convulsions continue
**Generalized seizures**

**DRUGS**

- If convulsions continue after 10 min, give a second dose of diazepam (or give diazepam IV at 0.05 ml/kg = 0.25 mg/kg if IV infusion is running).
- Do not give more than two doses of diazepam.
- If convulsions continue after another 10 min, suspect status epilepticus:
  - Give phenobarbital IM or IV at 15 mg/kg over 15 min;
  - or
  - Phenytoin at 15–18 mg/kg IV (through a different line from diazepam) over 60 min. Ensure a very good IV line, as the drug is caustic and will cause local damage if it extravasates.
- If high fever:
  - Undress the child to reduce the fever.
  - Do not give any oral medication until the convulsion has been controlled (danger of aspiration).
  - After convulsions stop and child is able to take orally, give paracetamol or ibuprofen.

*Warning:* Always have a working bag and mask of appropriate size available in case the patient stops breathing, especially when diazepam is given.
<table>
<thead>
<tr>
<th>Medications to treat status epilepticus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-Line Medications: Benzodiazepines</strong></td>
</tr>
<tr>
<td>Lorazepam</td>
</tr>
</tbody>
</table>
| Diazepam  | IV 0.2–0.3 mg/kg (max: 10 mg per dose)  
PR 0.5–1.0 mg/kg |
| Midazolam | IV 0.05–0.1 mg/kg (max: 6 mg per dose less than 6 y; 10 mg per dose 6 y and older)  
IM 0.1–0.2 mg/kg (max: 5 mg per dose)  
IN 0.2–0.3 mg/kg (max: 7.5 mg per dose)  
Buccal 0.15–0.3 mg/kg (max: 20 mg per dose) |
| **Second-Line Medications** |
| Phenytoin  | IV 15–20 mg/kg (no faster than 1 mg/kg/min) |
| Fosphenytoin | IV/IM 15–20 PE/kg (no faster than 3 PE/kg/min) |
| Phenobarbital | IV 15–20 mg/kg (no faster than 1 mg/kg/min) |
| Valproate  | IV 20–40 mg/kg load; can follow with 3–6 mg/kg/min infusion |
| Levetiracetam | IV 20–30 mg/kg load |
| Dextrose   | IV 2–4 mL/kg of 25% dextrose |
| Pyridoxine | IV 50–100 mg per dose |
| **Infusions for Refractory Status Epilepticus** |
| Midazolam  | IV 0.1–0.3 mg/kg load followed by 0.05–0.4 mg/kg/h |
| Propofol   | IV 2.0–3.5 mg/kg load followed by 125–300 µg/kg/min |
| Pentobarbital | IV 0.5–1.0 mg/kg load followed by 1–6 mg/kg/h |
| Ketamine   | IV 1–2 mg/kg load followed by 5–20 µg/kg/min |
| Lidocaine  | IV 1–2 mg/kg load followed by 4–6 mg/kg/h |

**Abbreviations:** IM, intramuscular; IN, intranasal; IV, intravenous; max, maximum; PE, phenytoin equivalents; PR, rectally.

*Data from* Refs. 10, 22, 111, 138
**GENERALIZED SEIZURES**

**MANAGEMENT:**

**Blood**
- Systematically performed thin and thick smears for parasites

**CSF**
- Lumbar puncture at the slightest doubt of meningitis

Prepare an extra tube of blood for serology
Prepare a CSF sample for possible viral PCR
Generalized seizures

EEG:

Valuable adjunct to the assessment of children with suspected seizures:
  - Awake and sleep EEG
  - Close to the seizure (week)

But:
  - 30-50% of children with epilepsy will be “EEG-negative”
  - 5% of non epileptic children will be “EEG-positive”
  - Can be misleading
  - Not available easily
Generalized seizures

**NEUROIMAGING:**

**CT scan:** emergency
- If not fully recovered (consciousness, neurological exam)

**MRI:** distance
- Help to find structural abnormalities
- Children <2 years necessitate special sequences
Generalized seizures

OUTCOME:

Recurrence after 1st seizure
- 54%, within 2 years
- Increase if abnormal EEG or neurodevelopment

Remission after epilepsy
- **70% remission from seizures**
- 60% discontinue treatment
- 10% intractable epilepsy

Sudden death
- 1/1000 in seizures
- 1/150 in poorly controlled seizures

Pediatric seizures. Maneesha Agarwal, Emerg Med Clin N Am 31 (733-754), 3013
FEBRILE SEIZURES:

2-5% of children, 25-40% + family history

Definition

Fever (> 100.4°F or 38°C) + seizure + 0-5 years of age

Simple 65% of FS

- Primary generalized tonic-clonic seizure
- < 15 min
- Postictal brief

Complex 35% of FS, 5% in SE

- Focality
- > 15 min
- Recurrence within 24h

Pediatric seizures. Maneesha Agarwal, Emerg Med Clin N Am 31 (733-754), 3013
FEBRILE SEIZURES:
Pathophysiology
- Increase of fever versus peak temperature
- Simple: no correlation with severe infection
  - Except status epilepticus (12-18%)
Management
- Same as afebrile seizure, + antipyretics
- Investigate fever as usual but not seizure
- Inform parents
Prognosis: 33% recurrence
- No side effects → no prevention, diazepam IR
- Epilepsy: same as normal population
**Generalized seizures**

**DIFFERENTIAL DIAGNOSIS**

**Jitteriness, newborn tremors**
- Tremor: involuntary, rhythmical oscillatory movement of equal amplitude around a fixed axis
- Jitteriness: recurrent tremor
- Symmetrical, extremities sparing the face
- Can be stopped by gentle restraint

**Cyanotic breath-holding spells**
- Precipitated by crying/upset/trauma
- Brief, self-resolving, without post-ictal change
- 6 months - 5 years, 5% of all children

UpToDate
Pediatric seizures. Maneesha Agarwal, Emerg Med Clin N Am 31 (733-754), 3013
Nonepileptic motor phenomena in the neonate, R. Huntsman, PaedChildHealth, 2008
Generalized seizures

Differential Diagnosis

**Tics, stereotypies**
- Precipitated by engrossment, excitement, stress, fatigue or boredom
- Rhythmic, repetitive, fixed movements, predictable in pattern and location
- Involuntary
- Last seconds to minutes
- 3 years – adolescence

**Simple vasovagal syncope**
- Precipitated by standing position
- Preceded by nausea and dizziness

**Cardiac arrhythmia**
- Anoxic: pale but nor cyanotic

UpToDate
Pediatric seizures. Maneesha Agarwal, Emerg Med Clin N Am 31 (733-754), 3013
Nonepileptic motor phenomena in the neonate, R. Huntsman, PaedChildHealth, 2008
Generalized seizures

DD:

Migraine
  - With nausea and vomiting, headache before the seizure.

Pallid infantile syncope:
  - Sudden transient bradycardia → anoxic seizure (pallor) and spontaneous recovery
  - Precipitate by unexpected blow to the head or upper torso
  - Caused by excessive vagal tone

Attention deficit hyperactivity disorder
  - Staring episodes only in the classroom

UpToDate
Pediatric seizures. Maneesha Agarwal, Emerg Med Clin N Am 31 (733-754), 3013
Nonepileptic motor phenomena in the neonate, R. Huntsman, PaedChildHealth, 2008
Generalized seizures

DD:

Myoclonus

- Brief shock-like movement of a limb caused by muscle contraction
- Localized or generalized
- Single or repetitive
- Irregular and arrhythmic
- Big amplitude
- Can be epileptic: can not be provoked, neither stopped
- Benign or severe
- Conscious

Benign myoclonus of sleep

...
CONCLUSION:

Facts:
- Common problem in Pediatrics
- Lack of knowledge: stigma

Your role:
- **Recognize** a seizure
- **Inform** patient and population
- Right targeted investigation
- Treat fast: **time is neurons**
REFERENCES:

- Shake, rattle, and roll – an update on pediatric seizures. S. Szlam, Pediatric Emergency Care. 2013
Generalized seizures

THANK YOU