**Neonatal Seizures - LDP**

**Seizures:**

A neurological event which results from an abnormal electrical discharge from a group of cerebral neurons - usually characterised by an alteration in behaviour, consciousness, movement, posture, sensation and/or autonomic function.

**The Epilepsies:**

A group of disorders in which a person experiences recurrent, unprovoked epileptic seizures.

*NB. single seizures, febrile seizures, neonatal seizures, seizures complicating acute systemic or neurological conditions are not considered epilepsy.*

Neonatal seizures are a neurological emergency, reflecting brain dysfunction or brain damage

Important:

Identifying the etiology – most neonatal seizures are reactive

etiology-specific therapy and may limit central nervous system (CNS) dysfunction

**Physiological background:**

Mielinisation: (best imaged by MRI)

Monkey: CNS fully mielinised at birth - need to perform complex motor tasks from birth for survival

Human: 30 weeks only base of capsula interna mielinised

40 weeks superficial layers of cortex only beginning to mielinise

Newborn brain is not a good substrate for seizures:

* Not mielinated i.e. slow spread of depolarisation
* Fewer synaptic connections
* Neurotransmitter activity: balance towards inhibitory transmitters in newborn

Neonates mostly have partial seizures, compared to adults where there is rapid spread with Jacksonian progression and generalisation.

**Types of seizures in the neonate**

Generally brief and subtle

Predominance of oral and buccal phenomena (smacking, sucking, chewing), gaze abnormalities and apnoea, reflecting the relatively advanced development of the limbic stuctures

Suspicious behaviour can be abnormal, but non epileptic

Studies based on continuous EEG monitoring show higher rates of fitting than thought from clinical evaluation

**Types of seizures:**

**Subtle or fragmentary seizures**

50% of seizures in newborn

May coexist c other seizure types (see below)

* Repetitive facial activity
* Sucking, mouthing, drooling, yawning
* Eyes
* Repetitve blinking or fluttering of eyelids Tonic horizontal deviation, usually c jerking of the eyes
* Momentary fixation of gaze
* Tonic posturing of a limb
* Unusual bicycling or pedalling movements
* Apnoea - seldom only manifestation of seizure
* Autonomic dysfunction (repetitive changes in HR, BP or sats)

Thus: Regard any repetitive stereotypical event as suspicious of seizure

Suspicious behaviour may be inconsistent c coincident EEG documented seizures, suggesting a subcortical focus (i.e. "deep", not reaching surface where depolarisation is measured

Suspicious behaviour can be abnormal, but non epileptic

Studies based on continuous EEG monitoring show higher rates of fitting than thought from clinical evaluation

**Clonic seizures**

* Rhythmical movements of groups of muscles

Gentle flexion of limb does not suppress (tremors are suppressed)

* Rarely true generalised “TCS”
* **Focal**: Most often of metabolic origin, but may be result of focal injury eg cerebral contusion (consider c focal headinjuryeg forceps marks), subarachnoid bleed or infarct - contralateral hemisphere
* Frequently **multifocal:** wandering clonic movements, non-jacksonian
* May involve pharyngeal and diaphragmatic muscles
* **Mostly** a/w **EEG** abnormalities
* May be associated c post ictal weakness - Todd's paresis
* Prognosis generally good

**Tonic seizures**

* Sustained flexion or extension of limb or trunk
* Focal tonic Sz commonly **a/w EEG** abnormalities, but need EEG monitoring to distinguish from tonic **posturing** freq not a/w EEG changes

(eg decorticate/decerebrate posturing)

* Often associated eye deviation
* Can be associated c significant neocortical damage eg prems c IVH, ie prognosis generally poor

**Myoclonic Seizures**

* Myoclonic movements occur normally
* Myoclonus can be divided into
* Normal myoclonus
* Pathological myoclonus (non-epileptic)
* Myoclonic Sz
* Generalised myoclonus more likely to be a/w EEG discharges
* Typical EEG: hypsarythias
* Age-appropriate sleep related myoclonic clusters more likely in pre-term neonates
* Normal benign myoclonus occurs only during sleep
* Myoclonic seizures generally the result of diffuse CNS pathology, prognosis poor

NB focal sz in neonate do not necessarily reflect focal pathology

**Neonatal behaviours that are not seizures**:

**Sleep-wake behaviour**

By 30 weeks, 4 states of arousal:

* **Wakefulness**
* **Active/REM sleep**: - grimacing, rapid horizontal eye movements, sucking, irregular respirations, myoclonic movements, head rolling, squirming
* **Transitional sleep**: - in between
* **Quiet sleep**: - rhythmical sucking, regular respirations, paucity of movement

**Benign neonatal sleep myoclonus**

Predominantly in preterm infants

Brief and sudden movements, can be bilateral and synchronous or asymmetrical and asynchronous

In clusters, suppressed when awake, may be stimulus sensitive

N neuro exam

**Tremulousness/jitteriness**

No adult equivalent

Usually provoked by stimulation, suppressed by holding

Fast periodicity characteristic

Associated c:

Chemically dependent babies, particularly Benzo's

Hypoglycaemia

HypoCa

Post-asphyxia, mild HIE

To distinguish jitters from fits: **Periodicity**

Fits fast - slow, impossible to induce, impossible to stop by eg. touching

Jitters fast - fast, stimulus sensitive

Stop c holding and passive flexing (arms on chest)

No other subtle signs

**Abnormal posturing**

Non epileptic, but sometimes need EEG to know

Decorticate and decerebrate posturing often stimulus sensitive - triggered by painful procedures eg extubation, suctioning

**Decorticate** (flexed, adducted, fisted arms, ext legs) – neurological syndrome at level of diencephalon, midbrain, upper pons

**Decerebrate** posturing (ext adducted pronated fisted arms and extended legs) – lower pontine/ medullary level

**Opisthotonos** – arching of the trunk = abN extensor tone - indicates an acute dysfunction of the neocortex or a chronic condition

**Causes of neonatal seizures**

1. **Asphyxia/Hypoxic ischaemic encephalopathy**

Probably commonest cause of neonatal sz

Mostly asphyxia is suffered before or during delivery, only 10% result of postnatal events

**Definition:**

* requires evidence of neonatal acidosis
* pH <7.2, BE< -10

(some evidence that even with a cord pH <7.0 the incidence of hypoxic ischaemic brain injury is less than 50%)

* Also: low 10, 15 and 20 minute Apgars - 5 minute Apgar not of predictive value
* Intra uterine factors contributing:
* Preeclampsia
* Abruption
* Cord compression
* Placental infarction
* Chorioamnionitis and passing meconium - causes vasoconstriction
* Postnatal signs of encephalopathy
* Biochemically: often metabolic acidosis, hypoCa, hypoglycaemia, hypoMg, hypoNa
* Clinically: altered tone (usu profound hypotonia) , altered consciousness (lethargy to coma), brain stem abnormalities, loss of primitive reflexes, other organ failure
* Seizures are part of the syndrome of Hypoxic-Ischaemic Encephalopathy - usually start in first 2 - 3 days - if within first hours: implies antepartum component

1. **Cerebrovascular lesions**
2. **IVH/PVH** (Intra ventricular or peri ventricular haemorrhage)

* Most common intracranial bleed in preterms, uncommon in full-term infants
* usually occurs in first 72 hours in pre-term infant

1. **Subdural Haemorrhage** - associated c traumatic delivery
2. **Cerebral infarction**

* Event can be ante, intra or postpartum
* Postnatal: associated c asphyxia, polycythaemia, dehydration, coagulopathy, infection
* Seizure is the most common presentation of a unilateral cerebral arterial occlusion (mostly middle cerebral a) - motor abnormalities often not evident

1. **Infection**

CNS infections, including **TORCH**, HIV and enterovirus can cause severe encephalopathic damage resulting in seizures and brain injury

Commonly non-specific manifestations – microcephaly, jaundice, rash, hepatosplenomegaly, chorioretinitis

Neonatal **herpes**:

usually acquired at birth

usually not the cause of seizures in first few days

rather: collapse end of first week

Perinatally acquired **bacterial** infections:

* E. Coli, GBS, listeria monocytogenes – bimodal
* Early: Septicaemia rather than neurological Sx
* Late: More typically meningitis

Lethargy, poor feeding, apnoea

* Other G+ and G- organisms

Investigations:

CSF

Maternal blood – serology (Toxo, Parvo, Rubella, CMV)

Urine and saliva (CMV IF and culture)

Throat swab and other relevant (skin/eye) swabs and CSF PCR for Herpes

±syphilis serology

1. **Metabolic**

**Hypoglycaemia**: risk of longterm disability from symptomatic hypoglycaemia: 10 - 20% - up to 50% quoted in literature

**Hypocalcaemia**

**Hypomagnesaemia**

**Hyponatremia**

1. **Structural Abnormalities of the Brain**:

Lissencephaly - neuronal migration defect - severe intractable seizures, poor prognosis

Holoprosencephaly

1. **Inborn Errors of Metabolism**

Think of in neonates with

* Onset of Sz after 1st 24 hours
* Onset of Sz after introduction of enteral or parenteral nutrition
* Sz are intractable and not responding to medication

**Hypoglycaemia**: risk of longterm disability from symptomatic hypoglycaemia: 10 - 20% - up to 50% quoted in literature

Ix:

**Blood glucose, ammonia, pH, lactate**

**FBE** (Neutropenia/throbocytopenia a/w organic acidaemias)

**CSF** Lactate, pyruvate, glycine and glucose in addition to MC+S and biochemsitry

1. **Drug withdrawal and intoxication**

Tremors, irritability, abN muscle tone and signs of withdrawal for up to 6 weeks c barbiturates, alcohol, marijuhana, methadone, cocaine

C cocaine seizures can be directly from withdrawal or because of placental insufficiency/infarction/abruption antenatally

Methadone: 10% seizures

SSRI's: jittery, irritable, poor feeding, fever = serotonin syndrome rather than withdrawal - benign prognosis

1. **Benign familial neonatal seizures**

Onset on d2-3 of generalised seizures with seizures occuring up to 20 times a day

Seizures cease by 1-6/12

A history of affected family members can usually be elicited (autosomal dominant)

**Physical examination:**

* All **vital signs**
* **Gestation**al age - Dubovitz or Ballard - invalid if severely depressed
* **Growth** parameters - relative head sparing?
* **Skin** lesions: rashes, macules, hemangiomas, hyper or hypopigmented lesions Woods lamp - ? congenital infection or neurocutaneous Sx (eg tuberous sclerosis)
* **Fontanelles** and sutures - ?raised intracranial pressure
* **Neuro**:
* Level of **arousal**
* **Fundi:** haemorrhages, papilloedoema
* **Cranial nerves:**
* Extraoccular movements, pupil response to light, equality of pupils, corneal responses
* Sucking, swallowing, phonation
* **Motor**: muscle tone, reflexes
* **Primitive reflexes**
* **Temporal profile**:
* Joint contractures/hypertonicity suggest chronic neurological compromise
* Hypertonia and unresponsiveness related to intrapartum or postpartum asphyxia are expected to last 4 - 5 days.
* Depressed arousal and hypotonia at birth suggest encephalopathy that began well before labour

**Treatment of neonatal Sz**:

* **Consider and treat sepsis**
* **Correct electrolyte imbalance**:

Glucose - 2ml/kg of 10% dextrose followed by infusion 4-6mg/kg/min

* **Anticonvulsants**
  + **Phenobarbitone:**

IV/IM or oral

Loading dose 20mg/kg - IV over 20 minutes

* + **Phenytoin:**

Most effective, but potent negative inotrope

Loading dose of 10mg/kg IV over 30 minutes

* + **Benzo’s:** consider infusion in NICU setting, but not used as first line Rx

**Prophylaxis beyond the newborn period:**

Incidence of epilepsy following neonatal Sz is probably ~20%

(Incidence of epilepsy in general population - 0.5%)

In setting of asphyxia seizures usually resolve after a couple of days, so Rx may be withdrawn after a short period.

Quiet period after first week up to 3 - 6 months - usually not necessary to go home on long term anti convulsants if at discharge

* Seizure free
* Developmentally and neurologically N
* N convalescent EEG
* No major lesion on imaging

Consider ongoing use c ongoing seizures, neurological abnormalities, brain injury or malformation on imaging

Issues:

Anticonvulsants may cause long term changes in brain development

No proof that Rx of neonatal seizures prevents development of epilepsy later

Epilepsy developing after the neonatal period may require different Rx, eg ACTH for infantile spasms

**Prognosis:**

Variable, depending on:

* Post conceptional age
* Aethiology
* Intractable nature

Interictal EEG: Normal interictal EEG in a term infant with early seizures confers a low likelihood of significant neurological impairment.