Neonatal Neurology Review

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Session Summary

This session will provide a general overview of the diagnosis and management of neurologic diseases and conditions to help attendants prepare for certification exams.

Session Objectives

Upon completion of this presentation, the participant will:

- understand embryology, physiology and pathophysiology of common neurologic conditions in the newborn;
- understand etiology and clinical manifestations of common neurologic conditions in the newborn;
- understand the treatment of common neurologic conditions in the newborn.

Test Questions

1. Which of the following is not true of a subgaleal hemorrhage?
   - a. It occurs in the subaponeurotic space
   - b. It is associated with vacuum extraction deliveries
   - c. It can be life threatening
   - d. Can lead to seizures due to irritation of the nervous system

2. Intraventricular hemorrhages:
   - a. Occur most commonly in the germinal matrix
   - b. Occur most commonly during the birth process
   - c. Often develops after 1 week of age
   - d. Are easily confused with PVL

3. Severe HIE affects which of the following systems:
   - a. Heart
   - b. Liver
   - c. Kidneys
   - d. All of the above
4. Neonatal seizures:
   a. Are always seen on EEG
   b. Are easily diagnosed clinically
   c. Often occur as generalized seizures
   d. Considered a symptom of neurologic dysfunction

5. Which of the following is true of spin bifida occulta?
   a. A defect in the vertebral arch
   b. Often associated with significant spinal cord defects
   c. Associated with protrusion of membranes
   d. Associated with Arnold Chiari syndrome

References


Session Outline

See presentation handout on the following pages.
Neurology Review
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Okay, Let’s Get This Thing Going
- Birth trauma
- Neural tube defects
- Holoprosencephaly
- Hydranencephaly
- Microcephaly/hydrocephaly
- IVH/PVL
- HIE
- Seizures
- Meningitis

Is There Anything Else We Could Possibly Cover??

Birth Trauma

Caput Succedaneum
- Accumulation of serum above the periosteum
- Bruising and petechia
- Due to pressure during labor and delivery
- Crosses the suture lines
- Avoid confusion with subgaleal hemorrhage
- No treatment necessary
- Resolves within 24 to 48 hours
Caput Succedaneum

Cephalohematoma
- Beneath the periosteum
- Develops during the first 24 hours of life
- Does not extend across the suture lines
- Treatment rarely indicated
- Complete recovery occurring by 3 months
- Complications include skull fracture, hyperbilirubinemia and mild anemia

Subgaleal Hemorrhage
- Bleeding into the subaponeurotic space
- Covers the entire cranial vault
- Large enough to hold an infant’s entire blood volume
- Associated with vacuum assisted deliveries
- Mortality rate as high as 22%
Subgaleal Hemorrhage

- Initial symptoms are vague
  - Generalized scalp edema and ecchymosis
  - Ballotable
  - Periorbital and periauricular edema
- May progress to serious symptoms
- Diagnosis
  - Based on clinical symptoms
  - CT or MRI confirms diagnosis
- Treatment
  - Careful monitoring
  - Transfusion of blood products
- Prognosis

Subarachnoid Hemorrhage

- The most common intracranial hemorrhage
- Bleeding into the subarachnoid space from ruptured vessels
- Relatively benign and often asymptomatic
- Transient seizure activity on day 2-3
- Abnormal neurologic examination
- Generally have an excellent prognosis
- Massive hemorrhages occasionally develop
Subdural Hemorrhage

- Hemorrhage between the dura and the arachnoid
- Overstretching of blood vessels during a difficult delivery
- Severity ranges from asymptomatic lesions to massive hemorrhage
- Presents within the first 12 to 72 hours
- Symptoms
  - Seizures and neurologic changes
**Subdural Hemorrhage**

- Diagnosis is either CT or MRI
- Treatment
  - Varies depending upon location, extent, and progression
  - Small hemorrhages require careful assessment
  - Surgery required in 30-50% of cases
- Prognosis
  - Depends on the extent and severity
  - Ranges from complete recovery to rapid deterioration and death

**Facial Nerve Palsy**

- Injury to the facial nerve
- Diagnosis
  - Drooping mouth
  - Perpetually open eye
  - Ineptive suck and swallowing problems
  - Persistent drooling
- Treatment
  - Patching and lubricating eye drops
  - Initial improvement occurs within days
  - Full recovery may take weeks to months
  - Surgical intervention may be necessary

**Brachial Plexus Injury**

- Injury of the upper brachial plexus from C5 to C8 and T1
- Due to lateral traction of the neck
- Erb's palsy
  - Upper cervical nerves (C5-C6)
  - Paralysis of the arm and shoulder
  - Hand muscles remain intact
  - Arm lies adducted, prone and internally rotated
Erbs Palsy

Brachial Plexus Injury
- Klumpke's palsy
  - Injury to nerve roots C6 to T1
  - Normal upper arm and shoulder movement
  - Paralysis of the wrist and hand
- Injury to the entire brachial plexus
  - Paralysis of the entire upper extremity
  - Concurrent sensory loss

Brachial Plexus Injury Treatment
- Conservative treatment
  - Physical therapy
  - 30% of brachial plexus injuries completely recover
- Surgical intervention
- Prognosis
  - Dependent on degree and location of damage
  - Full spontaneous recovery if some improvement within 2 weeks
  - Partial recovery if initial improvement is delayed until 4 to 6 weeks
  - Significant permanent deficit if no improvement by 3 months

Craniosynostosis
- Premature closure of cranial sutures leading to an abnormally shaped head
- Scaphocephaly
  - Premature closure of the sagittal sutures
  - Elongates in the occipitofrontal diameter
- Brachycephaly
  - Premature closure of the coronal sutures
  - Overgrowth of the vertex and lateral aspects of the head

Cranial Sutures

Scaphocephaly
**Brachycephaly**

**Craniocynostosis**
- Diagnosis
  - CT
  - Palpate for sutural ridge
- Treatment
  - Surgery to remove a strip of bone

**Neural Tube Defects**
- Failure of the neural folds to fuse and form the neural tube
- Secondary malformations of the skeletal structure and skin
- Wide spectrum of abnormalities

**Spina Bifida Occulta**
- A defect in the vertebral arch
- Usually presents as a small dimple with a tuft of hair
- Membranes don't externally protrude
- Usually asymptomatic but significant defects of the spinal cord can occur
Spinal Bifida Occulta

- Spina Bifida Cystica
  - Protrusion of the spinal cord and/or meninges through a defect in the arch
  - May occur anywhere along the vertebral column
  - Most common in the lumbar region

Menigocele

- Spina Bifida Cystica
  - Menigocele (25%)
    - Sac contains the meninges
    - Spinal cord in normal position
    - A dermal covering present
    - Defective axial skeleton
    - Prognosis
      - Usually normal
      - Spinal cord abnormalities are possible

Menigomyelocele

- Spina Bifida Cystica
  - Menigomyelocele (75%)
    - Sac contains meninges and neural tissue
    - The spinal cord is a rudimentary neural tube
  - Clinical manifestations
    - Dependent on the level of the defect
      - Functional abnormalities are inferior to the defect
      - 65% in the lumbar region
      - Paralysis
      - Loss of sensation
      - Sphincter paralysis
Types of Spina Bifida

Arnold-Chiari Malformation
- Displacement of the medulla oblongata, the fourth ventricle and some of the cerebellum into the cervical canal
- CSF flow is impaired
- Diagnosed by CT or MRI

Treatment
- Prone position, sterile wrap, antibiotics
- Surgery within 24-48 hours
- Treat hydrocephalus
- Multidisciplinary approach
- Goal: assist each child to develop maximum function and independence
- Family counseling
- Long term prognosis
- Genetic counseling

Prognosis
- Dependent on the level of the lesion
- 14% mortality
- 73% of survivors have IQ >85
- 87% ambulatory
- 90% lack bowel and bladder control
Rachischisis

- Open spinal cord
- Failure of neural folds to fuse
- Often associated with anencephaly

Congenital Anomalies of the Brain

- Fairly common due to complex neural embryology
- 3:1000

Encephalocele

- Affects the meninges and part of the brain
- 60% are occipital
- Can be frontonasal, intranasal, nasopharynx

Diagnosis

- Obvious at birth
- CT to assess for other brain abnormalities

Treatment

- Prognosis

Cranial Menigocele

Contains only the meninges
Anencephaly

- Failure of the rostral neuropore to close
- Missing forebrain
- Remainder of the brain is degenerative
- Absent cranial vault
- 50% open spinal cord
- Stereotypical movements
- Spontaneous/pain induced movements
- Intact reflexes

Anencephaly

- Diagnosis
  - Obvious at birth
  - Increased alpha fetoprotein
  - Prenatal ultrasound
  - Polyhydramnios
  - Post term delivery
  - Supportive treatment

Hydranencephaly

- Complete or nearly complete absence of the cerebral hemispheres
- Intact brain stem

Etiology

- Severe hydrocephaly
- Inutero infection
- Vascular occlusion

Clinical manifestations

- May appear normal at birth
- Irritability/Hyper/hypotonia
- Intact reflexes

Hydranencephaly

Prognosis

- Usually die early in infancy
- No cognitive development
Hydranoecephaly

- Affect the midfacial region and brain
  - Failure of the prosencephalon to cleave
    - Olfactory and optic bulbs
    - Telencephalon and diencephalon

Holoprosencephaly

- Clinical manifestations
  - Wide spectrum
  - Single or divided eye in a single orbit
  - Arhinia (absent nose)
  - Proboscis (fleshy nose-like appendage)
  - Alobar brain
Holoprosencephaly

Microcephaly
- Definition > 2 SD below the mean
- Etiology
  - Small brain = small cranium
  - Chromosomal abnormalities
  - TORCH infections
  - Cerebral atrophy
  - Perinatal infections
  - Metabolic causes

Microcephaly
- Lissencephaly
  - Near-total or total absence of cerebral convolutions (agyria)
- Pachygyria
  - Few broad gyri and shallow sulci

Lissencephaly

Microcephaly
- Clinical manifestations
  - Small or absent anterior fontanel
  - Round head
  - Recessed/sloped forehead
  - Mental retardation
Microcephaly

Hydrocephaly
- Imbalance between CSF production and absorption
- Excessive CSF in the ventricular system
  - Excess formation of CSF (Choroids plexus tumor)
  - Decreased absorption of CSF
  - Obstruction of flow
- Dilated ventricles may compress brain tissue

Hydrocephalus

- Communicating
  - Obstruction occurs after CSF exits the ventricles
- Noncommunicating
  - Obstruction occurs along the passages connecting the ventricles
Hydrocephalus

- **Etiology**
  - Aqueductal stenosis
  - Arnold-Chiari malformation
  - IVH
  - Tumor
  - Infection

**Aquaductal Stenosis**

**Diagnosis**
- Head circumference
- Transillumination
- Ultrasound
- CT or MRI

**Treatment** – VP shunt
- Drains CSF from ventricles into peritoneum
- Complications
  - Infection
  - Disconnection

**Ventricular Access Device**

**Periventricular/Intraventricular Hemorrhage**

- **Incidence**
  - Increasing
  - 25 to 30% of VLBW infants
- Most common in the first 12 hours
  - 50% by 24 hours
  - 90% by 72 hours
**Subependymal Germinal Matrix**
- Most common area of origination
- Beneath the ventricular wall
- Produces glial cells and neurons
- Most prominent between 24-32 weeks
- Primitive and highly vascular
  - Vessels are immature
  - Lack muscle and collagen
  - Susceptible to injury

**Intraventricular Hemorrhage**
- Catastrophic
  - Acute presentation
  - Rapid and severe
  - Neurologic and systemic deterioration
  - High mortality
- Salutatory
  - Evolves over hours to days
  - Changes in neurologic status
- Silent (50%)
  - No overt deterioration

**Classification**
- Papile's classification
  - Grade I – bleeding into the germinal matrix
  - Grade II – rupture into the ventricles without ventricular enlargement
  - Grade III – ventricles are completely filled and at least one lateral ventricle is enlarged
Intraventricular Hemorrhage

- Volpe’s classification
  - Grade I – bleeding into the germinal matrix
  - Grade II – Blood fills less than 50% of the ventricle
  - Grade III – Blood fills over 50% of the ventricle

Grade I

Grade II

Grade III

Grade III With Enlarged Ventricles

Grade IV Hemorrhage

- Hemorrhagic necrosis of the periventricular white matter
- 67% unilateral
- 80% associated with a large IVH
- Hemorrhage due to venous infarction from obstructed blood flow
Grade IV IVH

- Germinatal matrix hemorrhage
- Periventricular venous congestion
- Periventricular ischemia
- Periventricular hemorrhagic infarction

Pathogenesis of IVH

- Fluctuating cerebral blood flow
  - Lack of autoregulation
  - Pressure-passive cerebral circulation
  - Related to prematurity, asphyxia, hypoxia, hypercapnea
- Arterial hypotension
  - Ischemia, injury and subsequent rupture of the capillary wall

Pathogenesis of IVH

- Increased venous pressure impedes cerebral venous return causing venous congestion
  - Heart failure, PPV, high CPAP, labor and delivery
  - Excess fibrinolytic activity
  - Platelet and coagulation disturbances
  - Inflammatory cytokines

Risk Factors for IVH

- Prematurity
- Respiratory distress
- Pneumothorax
- Asphyxia
- Seizures
- Apnea
- Manipulation (tracheal suctioning, positioning, handling)
- Rapid infusion of IV fluids/colloids
- Clotting disorders
- Breathing out of sync with the ventilator

Diagnosis

- Clinical
  - Decreased hematocrit
  - Bulging fontanelle
  - Change in level of consciousness
- Ultrasound
### Prognosis

- **Grade I + II**
  - Similar to infants with no IVH
  - Increased risk for learning problems
- **Grade III**
  - 40% have major disabilities
  - 50% have school difficulties
- **Grade IV**
  - Mortality is 40%
  - 75% risk of neurologic impairment
    - CP
    - Low cognitive scores
    - Seizures
    - Visual disturbances

### Posthemorrhagic Hydrocephalus

- **Pathogenesis**
  - Blood clot obstruction
  - Obstructive inflammation and scarring
- **Incidence**
  - 50% transient ventriculomegaly
  - 50% require treatment
- **Occurs within 4 weeks**
- **Monitoring**
  - Weekly cranial ultrasound
  - Serial head circumferences

### Posthemorrhagic Hydrocephalus Treatment

- **Goals**
  - Maintain normal ICP
  - Prevent compression of the periventricular white matter
  - Sustain cerebral perfusion
  - Serial LPs
  - VP shunts
  - 50% resolve with no treatment

### Prenatal Prevention of IVH

- **Prevention of prematurity**
  - Good luck with this one!
- **Prenatal transport**
- **Antenatal corticosteroids**
  - Matures blood vessels in the germinal matrix
  - Decreases incidence by 50%

### Periventricular Leukomalasia

- **Occurs only in premature infants**
- **Incidence**
  - 4-26% of infants < 1500 grams
  - 27-30 weeks have highest incidence
- **Risk factors**
  - Often associated with an IVH
  - Evidence of infective component
    - PROM > 12 hours
    - Intra-uterine infection
    - PROM + chorio = highest incidence

### Postnatal Prevention of IVH

- **Appropriate neonatal resuscitation**
- **Correction/prevention of hemodynamic disturbances**
- **Avoidance of shifts in CBF**
- **Correction of coagulation**
- **Indomethacin and Ibuprophen**
  - Decreases CBF and CBF fluctuations by inhibiting prostaglandin synthesis
  - Prostaglandin is important in control of CBF control
Pathogenesis of PVL

- Ischemic lesion
- Periventricular white matter necrosis
  - Watershed blood supply
  - High metabolic rate
- Small cysts in white matter
- Diagnosis
  - Periventricular echodensities on ultrasound
  - Ultrasound only detects 40-60%
  - MRI
- Treatment

Hypoxic Ischemic Encephalopathy

- Major cause of acute mortality and chronic neurologic disability
- Occurs in both term and preterm infants
- 10-15% mortality
- 40% of survivors have permanent handicaps
- Mental retardation
- Cerebral palsy
- Learning disabilities
- Epilepsy

Prognosis

- Cerebral palsy
- Lower limbs
- Developmental delays

Etiology

- Placental, fetal or maternal
- 50% predicted by antenatal/perinatal history
  - Decreased fetal movement
  - Abnormal NST
  - Abnormal biophysical profile
  - Scalp pH
  - Abnormal FHR
  - MSF
  - Decreased amniotic fluid
Effects of HIE
- Conversion to anaerobic metabolism
- Rapid depletion of ATP
- Accumulation of lactic acid
- Failure of normal metabolic activity
- Intracellular pump function failure
  - Accumulation of sodium, calcium and water in brain cells
  - Cell death
- Accumulation of fatty acids and free radicals
- Excess release of neurotoxic excitatory neurotransmitters
- Cell apoptosis

Phases of HIE
- Early phase
  - Decreased brain temperature
  - Local release of the neurotransmitter GABA
  - Temporarily decrease cerebral oxygen demand and limit impact
- Latent phase
  - Intervention may be effective
  - Secondary phase of Injury
  - Apoptosis – programmed cell death

Sarnat Stages
- A clinical staging tool for HIE
- Developed for use in full term infants
- Provides information for optimal medical management
- Predicts neurologic prognosis

Sarnat Stages

<table>
<thead>
<tr>
<th>FACTOR</th>
<th>STAGE I</th>
<th>STAGE II</th>
<th>STAGE III</th>
</tr>
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<tbody>
<tr>
<td>Level of consciousness</td>
<td>alert</td>
<td>lethargy</td>
<td>coma</td>
</tr>
<tr>
<td>Morbidity tone</td>
<td>normal</td>
<td>hypotonia</td>
<td>flaccid</td>
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<tr>
<td>Tendon reflexes</td>
<td>increased</td>
<td>increased</td>
<td>depressed/absent</td>
</tr>
<tr>
<td>Reflexes</td>
<td>active</td>
<td>weak</td>
<td>absent</td>
</tr>
<tr>
<td>Grasp</td>
<td>normal</td>
<td>weak</td>
<td>absent</td>
</tr>
<tr>
<td>Skull eye</td>
<td>normal</td>
<td>reactive</td>
<td>miadunsreact</td>
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<td>Abdominal extensor</td>
<td>flaccid, extensor</td>
<td>neurologic, extensor</td>
<td>variable or fixed</td>
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<tr>
<td>Respiration</td>
<td>regular</td>
<td>changes in auscultatory sounds</td>
<td>absent</td>
</tr>
<tr>
<td>ECG</td>
<td>normal</td>
<td>low voltage, periodic</td>
<td>periodic/absent</td>
</tr>
</tbody>
</table>

Clinical Manifestations
- Depends on severity, timing and duration
- Seizures
  - 50-70%
  - First 24 hours
  - Earlier the seizure = more severe disease
  - May be refractory
- Abnormal respiration
- Abnormal positioning/tone
- Irritability

Clinical Manifestations
- Impaired glucose delivery and metabolism
- Anaerobic metabolism
- Renal failure
- Myocardial dysfunction
- Decreased cardiac output
Clinical Manifestations

- Pulmonary involvement
  - PPHN
  - Pulmonary edema
  - Respiratory depression
  - Pulmonary hemorrhage
  - Surfactant inactivation

Brain Imaging

- Early (2-4 days)
  - Cerebral edema
  - Decreased tissue attenuation
- Late (2-4 weeks)
  - Encephalomalacia
  - Cerebral atrophy

Early CT

Encephalomalacia

Management

- Delivery room resuscitation
- Maintain ventilation
- Maintain oxygenation
- Maintain perfusion
- Correction of acidosis
  - Inhibits surfactant production
  - Increases pulmonary vascular resistance
  - Reduces myocardial contractility
Management

- Monitor for renal impairment
- Treat DIC
- Monitor electrolytes
- Maintain normal metabolic state
  - May require 9-15 meq/kg/min glucose
  - Increased calcium requirements

Management

- Control seizures
- Control cerebral edema
  - Fluid restriction
  - Hyperventilation
  - Diuretics
- Withdrawal of treatment

Hypothermia

Insult → Primary Neuronal Death

Opportunity for Neuronal Rescue

Delayed Neuronal Death

Hypothermia

- Evidence is compelling
- Effective in mild to moderate HIE
- Decreases rate of cellular death
- Decreases cellular metabolism
- Conserves ATP stores
- Limits free radical release

Hypothermia

- Criteria vary among institutions
- Initiate less than 6 hours after insult
- Continue for 48-72 hours
- Cool to approximately 34-35 degrees
- Rewarm over 12-24 hours
- Complications
  - Decreased heart rate, cardiac output and stroke volume
  - Renal impairment
  - Acid-base and electrolyte abnormalities
  - Coagulation abnormalities

Prognosis

- Indicators of poor outcome
  - Apgars less than 3 at 10 minutes
  - Early onset and/or refractory seizures
  - Abnormal neurologic signs at discharge
  - Persistently abnormal CT
  - Markedly abnormal EEG or an abnormal EEG after 3 days
- Indicators of normal outcome
  - Normal neuro exam within the first week
  - Normal EEG within 3 days
Neonatal Seizures
- Symptom of neurologic dysfunction
- Excessive simultaneous electrical discharge or depolarization
  - Excessive excitatory amino acid release
  - Deficient inhibitory neurotransmitters (ie GABA)
- Critical to recognize, determine etiology and treat
  - May represent significant illness needing treatment
  - Interference with supportive measures
  - Can cause brain injury

Etiology of Seizures
- HIE
  - Most common cause
  - Subtle, multifocal clonic or focal clonic
- Intracranial/intraventricular hemorrhage
- Subarachnoid hemorrhage
- Subdural hemorrhage
- Arterial or venous stroke

Etiology of Seizures
- Metabolic disturbance
  - Hypoglycemia
  - Hypocalcemia
  - Hyponatremia
  - Hypernatremia
  - Inborn errors of metabolism

Etiology of Seizures
- Intracranial Infection
  - Bacterial
  - Toxoplasmosis
  - CMV
  - Herpes
- Developmental Defects
  - Migrational abnormalities
  - Cerebral cortical dysgenesis
  - Drug withdrawal

Etiology of Seizures
- Benign familial neonatal seizures
  - First 48-72 hours
  - Positive family history
  - Normal development
- Benign idiopathic neonatal seizures
  - Fifth-day fits
  - Day 4-6
  - Normal development
Classification of Seizures

- Subtle
  - Ocular phenomena
  - Horizontal deviation
  - +/- jerking of eyes
  - Sustained eye opening with ocular fixation
  - Oral-buccal-lingual movements
  - Rowing of arms or pedaling
  - Autonomic changes

Classification of Seizures

- Multifocal clonic
  - Several body parts in a migrating fashion
  - Seen in term infants
- Classic Generalized clonic seizures
  - Bilateral symmetric and synchronous movements
  - Rare in neonate

Diagnosis

- HISTORY, HISTORY, HISTORY
- Electrolytes
- Sepsis workup including LP
- Ultrasound/CT
- EEG
  - 80% of neonatal seizures are not seen on EEG
  - Electrical seizures may not correlate with clinical seizures
- Video EEG
- aEEG

Treatment

- Treat underlying etiology
- Medications
  - Phenobarbital
  - Phosphonytoid
  - Benzodiazepines

Prognosis

- Prognosis and etiology are interdependent
- Controlling seizures improves outcome
- Sequelae include
  - Developmental delays
  - Motor deficits
  - Persistent seizures

Meningitis

- Inflammation of the membranes lining the brain and the spinal column
  - Dura mater, pia mater, arachnoid
- Purulent exudate covering the meninges and ventricles
Clinical Presentation

- Nonspecific symptoms of infection
- Irritability
- Lethargy
- Increased ICP (bulging fontanelle, HTN, tremors)
- Persistent and severe vomiting
- Seizures (20-50%)

Diagnosis

- Who do we tap? – controversial
- Abnormal CSF findings
  - >30 wbc (>60% PMNs)
  - Glucose (50% serum)
  - Protein >100 mg/dl
  - Positive culture/gram stain

Treatment and Prognosis

- 2-3 weeks of antibiotics
- Repeat CSF studies until sterile
- Prognosis
  - 20-50% have permanent sequelae
  - Hearing/speech difficulties
  - Hydrocephaly
  - Blindness
  - Seizures
  - Mental retardation
  - Cerebral palsy