Neuro Anatomy, Physiology and Common Pathology

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Neuro Anatomy, Physiology and Common Pathology

• Objectives
• Upon completion of this course the nurse will be able to:
  – Describe the grading system for intraventricular hemorrhage
  – List the pathway of CSF flow through the ventricular system
  – Compare and contrast HIE from PVL in the preterm and term neonate
Neurologic Development

- *Dorsal induction*
- *Ventral induction*
- Proliferation
- Migration
- Organization
- Myelination
Germ Layer Derivatives

Ectoderm derivatives

Surface ectoderm
- epidermis, hair, nails, sweat glands, sebaceous glands, mammary glands, lens of eye, inner ear, enamel of teeth and anterior pituitary

Neuroectoderm
- Neural tube
  - central nervous system, retina, pineal body and posterior pituitary
- Neural crest
  - cranial and spinal sensory nerves and ganglia, adrenal medulla, pigment cells, head mesoderm, branchial arch cartilages, sympathetic ganglia and nerves, Schwann cells

Endoderm derivatives

Epithelial parts of the tonsils, pharynx, thyroid, parathyroids, pharyngotympanic tube, tympanic cavity, trachea, bronchi and lungs

Mesoderm derivatives

Head
- skull, dentine, muscles and connective tissue

Paraxial
craniocaudal skeleton except skull, muscles of trunk, dermis of skin and connective tissue

Intermediate
trochlear system (gonads, ducts and accessory glands)

Lateral plate
cardiovascular system, blood cells, lymphatic system and cells of lymph, spleen, adrenal cortex, visceral and limb muscles, visceral connective tissue, serous membranes of pericardium, pleura and peritoneum

A. Herring XX (Day 40-42).
The arms curve over the heart bulge and the toe rays are present on the foot. 20 mm CR (+3.5)
Figure 4-4. Photographs of an infant with a large sacrococcygeal teratoma, probably of primitive streak origin. These tumors are more common in females than in males, and they often become malignant during infancy. (Courtesy of Dr. Jan Hoogstraten, Children’s Centre, Winnipeg, Canada.)
6 stages of embryonic development

- *Dorsal induction*
- *Ventral induction*
- *Neuralation*
- Proliferation
- Migration
- Organization
- Myelination
FIGURE 1-3: Anencephaly. A, Face-on and B, dorsal views. (Courtesy of Dr. Ronald Lemire.)
**Figure 1-5:** Encephalocele. A. Newborn with a large occipital encephalocele. B. Newborn with both an occipital encephalocele and a thoracolumbar myelomeningocele. (Courtesy of Dr. Marvin Fishman.)
Arnold Chiari Malformation

1. Inferior displacement of the medulla and the 4th ventricle into the upper cervical canal
2. Elongation and thinning of the medulla and pons
3. Inferior displacement of the cerebellum through the foramen magnum into the upper cervical region.

A variety of boney defects of the foramen magnum, occiput +/- upper cervical canal
FIGURE 1-16: Holoprosencephaly, CT scan. Note crescent-shaped, single lateral ventricle and fused thalami (A). In B, note cystic expansion of ventricular system in posterior cranium (detectable clinically by transillumination). In semilobar holoprosencephaly (C), sagittal cleavage with formation of parieto-occipital lobes is apparent.
Figure 1-15: Newborn with holoprosencephaly. Note ocular hypotelorism, flat, single-nostril nose, and severe median cleft lip and palate. (Courtesy of Dr. Marvin Fishman.)
Hydrocephalus

3 Critical Events

- Choroid plexus secretes CSF
- Roof of the 4th ventricle perforates
- The subarachnoid villi are able to absorb
Etiology of hydrocephalus

- Aqueduct stenosis 33%
- Arnold Chiari defect 28%
- Communicating hydrocephalus 22%
- Dandy Walker malformation 7%
- Other 10%
Hydrocephalus
Dandy Walker Malformation

- Cystic dilation of the 4th ventricle
- Abnormal migration and absence of the corpus collosum
- Failure of the 4th ventricle to open
FIGURE 1-28: Dandy-Walker malformation, CT scan from a 5-day-old infant. A, Note dilated fourth ventricle, expanding into a posterior fossa cyst, with an agenetic vermis. B, Note ventriculomegaly consistent with hydrocephalus, and agenesis of the corpus callosum, manifested in this slice by superiorly displaced, midline third ventricle.
Dandy Walker Malformation
Neuronal proliferation

- Ventricular and subventricular zones are the sites of proliferation (subependymal)
- Neuronal proliferation (2-4 months)
- Glial multiplication - migration (>5 months)
6 Stages of Embryonic Development

- Dorsal induction
- Ventral induction
- Proliferation
- Migration
- Organization
- Myelination
Disorders of Migration
FIGURE 9-19: Coronal ultrasound scans of periventricular leukomalacia in a premature infant on postnatal days 5 (A) and 24 (B). Note in A the periventricular echodensities (arrowheads) and in B the small echoluent foci, consistent with cysts, in the same areas (arrow).
Membranes surrounding the brain

[Diagram showing the layers of the brain and its membranes, including the scalp, skin, fat, periosteum, skull, dura mater, arachnoid villus, superior sagittal suture and sinus, epidural space, subdural space, subarachnoid space, endosteal dura, meningeal dura, cerebral cortex, white matter, and falx cerebri.]
Caput Succedaneum
Caput succedaneum
Cephalohematoma
Cephalhematoma
Subgaleal Hemorrhage
Subdural Hemorrhage
Subdural hematoma
Subarachnoid Hemorrhage
Pathway of CSF
Bones and Sutures
Brachycephaly
Brachycephaly
Plagiocephaly

Diagram showing the differences between the back and front of the head.
Plagiocephaly
Scaphocephaly
Dolichocephaly
Periventricular/Intraventricular Hemorrhage

• Primary lesion is bleeding from small vessels
• in the supependymal germinal matrix

1970’s incidence was as much as 50%

• Incidence
  - 751 to 1000 grams  12%
  - 501 to 750 grams  26%
Periventricular Intraventricular Hemorrhage

- <34 weeks gestation
- Low apgar scores
- Asphyxia
- Low birth weight
- Acidosis
- Anemia

- Mechanical ventilation
- Hyperosmolar solutions
- Coagulopathy
- Pneumothorax
- PDA ligation
IVH incidence

- <1500 grams
- 20-30% - first few hours after birth
- 50% - 24 hours of age
- 80% - 72 hours of age
Signs & Symptoms of IVH

- Sudden deterioration
- Desaturation spells
- Bradycardia
- Anemia
- Shock

- Hyperglycemia
- Change in fontanelles
- Metabolic Acidosis
- Hypotonia
Grade I IVH: Subependymal hemorrhage in the Periventricular Germinal Matrix. Often localized at the Foramen of Monro.

Grade 2 IVH: Partial filling of lateral ventricles without ventricular dilatation.

Grade 3 IVH: Intraventricular hemorrhage with ventricular dilatation.

Grade 4 IVH (small and large): Parenchymal involvement or extension of blood into the cerebral tissue itself. Can be present to a lesser degree.

Correlation between the severity or extent of involvement and subsequent impairment is not absolute. Because outcomes are so varied, assessment of early symptoms and the practice of purposeful interventions are extremely important.
Grade I Periventricular Hemorrhage (PVH) Subependymal Germinal Matrix Hemorrhage

- Subependymal is a region that lies just under the wall of the lateral ventricle.
- The germinal matrix supports the division of glioblasts and differentiation of glial elements. This highly metabolic area is fragile network of capillaries.
- This is where the hemorrhage occurs.
Grade II PVH

• Grade II - Subependymal hemorrhage with extension into lateral ventricles without ventricular enlargement, as shown below
Grade III PVH

• Grade III - Subependymal hemorrhage with extension into lateral ventricles with ventricular enlargement.
Periventricular Hemorrhagic Infarction (PVHI)
Old Grade IV IVH

• Periventricular Hemorrhagic Infarction (PVHI) previously classified as grade IV IVH
• Compression of the terminal vein by the GMH which can impair venous drainage causing congestion and lead to a hypoxic ischemic event in the periventricular white matter.
• GMH & PVL occur together 75% of the time

QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.
PIVH mechanisms of vulnerability

- Vascular anatomic immaturity
- Hemodynamic factors
- Inflammatory mediators

QuickTime™ and a TIFF (LZW) decompressor are needed to see this picture.
Vascular Anatomic Features

- Venous drainage is through the terminal vein, which empties into the internal cerebral vein; this in turn empties into the vein of Galen. Blood flow changes from an anterior direction to a posterior direction from the terminal vein to the internal cerebral vein causing

- **Venous congestion**

- These are fragile thin walled, immature vessels prone to rupture

QuickTime™ and a TIFF (LZW) decompressor are needed to see this picture.
Hemodynamic Factors
Passive cerebral pressure autoregulation

• Increases in CBF
  - Hypertension
  - Rapid volume expansion
  - Pressor treatment
  - Hypercarbia,

• Decreases in CBF
  - Hypotension
  - Hypocapnia

• Elevated Cerebral Venous pressure
  - Positive pressure ventilation

• Fluctuating CBF
  - unsynchronous ventilation
Cytokines & Inflammatory Mediators

• Many studies have suggested an association between cytokines, inflammatory mediators and the development of PIVH
Can we prevent this PVH?

- Antenatal corticosteriods
- Magnesium
- Paralyetics - NAVA?
- Indomethacin
<table>
<thead>
<tr>
<th>Hypoxia</th>
<th>Ischemia</th>
<th>Encephalopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased Oxygen</td>
<td>Decreased Blood flow</td>
<td>Brain Damage</td>
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Asphyxia

- Hypoxemia
- Hypercapnia
- Acidosis
QuickTime™ and a
TIFF (Uncompressed) decompressor
are needed to see this picture.
HIE

- Not a single event but a progressive injury/lesion
- Necrosis may occur then followed by apoptosis later
Asphyxia - Incidence

- Antepartum 20%
- Intrapartum 30%
- Ante/intrapartum 35%
- Postpartum 10%
- Unknown 5%
Birth Asphyxia

- **First to go**
  - Color
  - Respiration
  - Tone
  - Reflex
  - Heart rate

- **First to come back**
  - Heart rate
  - Reflex
  - Color
  - Respiration
  - Tone
Mild Encephalopathy

- Seen in the first 24 hours and usually improves by 1 week of age
  - Lethargy to hyperalertness
    - Jitteriness to hyper-responsiveness
    - Irritability
  - Hypoglycemia
  - Dilated pupils
Moderate Encephalopathy

- Seen in the first 12 hours
- Lethargy progressing to hypotonia
- Decreased movement and jitteriness
- By 48-72 hours the baby will get better or worse
Severe Encephalopathy

- Initially with decreased LOC
- Progressing to obtunded, stupor and coma
- Seizures are common in the first 12 hours
- Severe hypotonia
- Absent reflexes
- Abnormal EEG
QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.
Therapeutic Hypothermia

- Indications for use for newborns with moderate to severe HIE
  - A. 36 weeks or > with one of the following
    - Apgar score of 5 or less at 10 minutes
    - Continued need for resuscitation at 10 minutes
    - Within 60 minutes of life a pH <7
    - Within 60 minutes of life a Base Deficit ≥16
Therapeutic Hypothermia

• Indications for use for newborns with moderate to severe HIE
  – B. An alter state of consciousness
    • Hyptonia
    • Abnormal reflexes
    • Absent or weak suck
    • Clinical seizures
• Indications for use for newborns with moderate to severe HIE
  – C. For paralyzed newborns, criteria C is an amplitude-integrated electroencephalogram/cerebral function monitor (aEEG/CFM) recording for 20 minutes that is abnormal, or seizures
QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.
New Infant Brain Monitor

*aEEG Cerebral Function Monitor*

- Continuously monitors and records brain activity
- Aids in detecting and treating seizures
- Monitors effects of drugs and other therapies on the brain
- Aids in identifying HIE and predicting long-term outcome
- Improves accuracy of newborn neurological examinations
- Determines need for further neurological examination or transport
Normal Trace
Note the variation in the amplitude indicating sleep-wake cycling. The upper margin of the band of activity is above 10 microvolts (μV). The lower margin is above 5 μV.

Severely Abnormal
This trace is from an infant that suffered a severe asphyxial insult. Note the very narrow, suppressed band of activity with spikes indicating burst suppression.

Severely Suppressed with Seizures
This is an example of a severely asphyxiated infant with suppressed background and frequent seizures.
Periventricular leukomalacia

- HIE in prematures
  - Ischemic injury
  - Coagulation necrosis
  - Phagocytosis of necrotic material
  - Fluid filled cysts
  - Compensatory ventriculomegaly
PVL

- Coagulation necrosis in the cerebral white matter
- Microglial infiltration
- Astrocytic proliferation and repair
- Cyst formation - scarring
Pathways of White Matter Injury

Ischemia

Glutamate

Cytokine release

Oligodendroglial Cell death

Reperfusion

Free radical formation
PVL Vascular Factors

- Watershed or Border zones
- Increased risk of ischemia due to loss of CBF autoregulation with the sick preemie
- Limited ability of the vessels to dilate after ischemic injury during the reperfusion phase
PVL Damage to Oligodendrocytes

- **Free radical injury**
  - Ischemic injury to the periventricular white matter releases free radicals that lead to cell death apoptosis of the oligodendrocytes

- **Cytokines**
  - Ischemia/reperfusion activates microglia, releases cytokines and other inflammatory mediators - toxic to oligodendrocytes
PVL & GMH

- The bleeding into the periventricular white matter results in a coagulation necrosis, resulting in death of the tissues responsible for manufacturing myelin.
Risk factors for PVL

- Prenatal
  - <36 weeks gestation
  - Chorioamnionitis
  - Multiple gestation
Risk factors for PVL

- Intrapartum
  - Perinatal asphyxia
  - Head compression
  - Cord ph <7.1
Risk factors for PVL

- Postnatal
  - Hypotension
  - Hypertension
  - Apnea
  - PDA
  - Intraventricular hemorrhage
Imaging Techniques

- Ultrasound
- CT Scan
- MRI
Areas for Further Research
References

• Flavin, NE. (2001, Apr) Perinatal Asphyxia: A clinical review, including research with brain hypothermia. Neonatal Network
HIE Scale

- Thompson et al. HIE Scale, ACTA Paediatrics – 1997, page 757