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 the participant prepare for certification exams.

Session Objectives
Upon completion of this presentation, the participant will be able to:
▪ discuss embryology, physiology and pathophysiology of common neurologic conditions in the newborn;
▪ discuss 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
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
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
- Ballottable
- 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

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
  - Ineffective 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 plexis 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

Shoulder Dystocia
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

- Metopic
- Coronal
- Sagittal
- Lambdoidal

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**

- 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

**Spina Bifida Cystica**

- Meningocele (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 (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
Congenital Anomalies of the Brain
- Fairly common due to complex neural embryology
- 3:1000

Cranial Meningocele
- Contains only the meninges

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

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

- 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

- Usually die early in infancy
- No cognitive development

Holoprosencephaly

- Affects 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

Microcephaly

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

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

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

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
- Non-communicating
  - Obstruction occurs along the passages connecting the ventricles

Aqueductal Stenosis

- Diagnosis
  - Head circumference
  - Transillumination
  - Ultrasound
  - CT or MRI
- Treatment – VP shunt
  - Drains CSF from ventricles into peritoneum
- Complications
  - Infection
  - Disconnection

Etiology
- Aqueductal stenosis
- Arnold-chiari malformation
- IVH – most common
- Tumor
- Infection

Hydrocephalus

Diagnosis
- Head circumference
- Transillumination
- Ultrasound
- CT or MRI
- Treatment – VP shunt
  - Drains CSF from ventricles into peritoneum
- Complications
  - Infection
  - Disconnection
Periventricular/Intraventricular Hemorrhage

- Incidence
  - 50% < 750 grams
  - 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
Germinal Matrix

- Bleeding into germinal matrix
- Hematoma forms
- Blood is released into ventricular system if the hematoma ruptures

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

GERMINAL 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 capillary walls
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

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%

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

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 + chorion = highest incidence

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
Prognosis

- Cerebral palsy
- Lower limbs
- Developmental delays

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

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
  - Cellular 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>
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</thead>
<tbody>
<tr>
<td>Level of consciousness</td>
<td>alert</td>
<td>lethargy</td>
<td>coma</td>
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<tr>
<td>Muscle 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>
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<tr>
<td>Moro</td>
<td>exaggerated</td>
<td>exaggerated</td>
<td>absent</td>
</tr>
<tr>
<td>Doll eye</td>
<td>normal</td>
<td>overactive</td>
<td>reduced/absent</td>
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<tr>
<td>Abdominal function</td>
<td>aliased, reactive</td>
<td>constuctive, reactive</td>
<td>variable or fixed</td>
</tr>
<tr>
<td>Respiration</td>
<td>regular</td>
<td>changes in rate, rhythm</td>
<td>variable or fixed</td>
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<td>Heart rate</td>
<td>normal</td>
<td>bradycardia</td>
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<tr>
<td>ECG</td>
<td>normal</td>
<td>low voltage, periodic</td>
<td>periodic/periodic</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

### Clinical Manifestations

- Liver
  - Impaired liver function
  - Clotting disorders
- GI
  - Changes in GI motility
  - Mucosal damage
  - NEC
- Heme
  - DIC
  - Decreased clotting factors
  - Thrombocytopenia

### Brain Imaging

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

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**Hypothermia**

![Hypothermia Diagram](image)

[Insult] \[\rightarrow\] Primary Neuronal Death

\[\rightarrow\] Opportunity for Neuronal Rescue

\[\rightarrow\] Delayed Neuronal Death

**Management**

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

- 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

Types 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

Diagnosis

- HISTORY, HISTORY, HISTORY
- Electrolytes
- Sepsis workup including LP
- Ultrasound/CT
- EEG
  - Electrical seizures may not correlate with clinical seizures
- Video EEG
- aEEG

Treatment

- Treat underlying etiology
- Medications
  - Phenobarbital
  - Phenytoin
  - 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

The End

Questions?