The Central Nervous System

Reaction to Injury

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This is the first CNS lecture, so she is going to give some background info.
Unique features of CNS that influence its response to injury:

- Cell types unique to CNS
- Complex neural circuit architecture
- Little internal structural support
- Very limited room to expand
- No typical lymphatic drainage

Brain is like Jello, no internal structure, it can't support itself. Only the skull keeps it together.

A very small lesion can really cause problems when you mess up something in this complicated circuit.
R&C Chapter 28: The CNS

• Cellular Responses to Injury

• Cerebral Edema, Hydrocephalus, Raised Intracranial Pressure & Herniation

• Perinatal Brain Injury

• Trauma

Developing brains respond differently to injury
R&C Chapter 28: The CNS

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The cells of the CNS

**Neuroectodermal origin**
- Neurons
- Glia (astrocytes, oligodendroglia, ependymal/choroid plexus cells)
- Stem/progenitor cells

**Mesodermal origin**
- Resident microglia
- Meningial cells
- Blood vessels and blood cells

*Glia means glue. They are the supporting cells that hold everything together, physically and functionally. They may also modulate neuronal synapses.*

*Act as macrophages.*

*Most cells in the CNS are unique to the CNS. Blood vessels are not unique.*
Up to 150 different kinds of neurons, not just the few kinds we normally learn about.

Purkinje cells have incredibly complex dendrites. Half neurons in the brain are in the cerebellum.
Neuronal reaction (acute)

• "Red neurons" in hypoxia/ischemia
• Selective vulnerability

Neurons are very vulnerable and are some of the first cells to be lost with injury, especially Purkinje cells. Glial cells are much more resilient.
Neuronal reaction (subacute/chronic)

• Apoptosis (in situ and trans-synaptic)

Neuron itself can die from insult or downstream neurons can die due to lack of signalling
Neuronal reaction (subacute/chronic)

• Apoptosis (in situ and trans-synaptic)

• Regeneration: axonal reaction (central chromatolysis)

Neurons labeled C are bad, they are trying to recover from an insult, it is producing a lot of protein. They should normally look like the neuron labelled N.
Neuronal reaction (subacute/chronic)

• Apoptosis (in situ and trans-synaptic)

• Regeneration: axonal reaction
  (central chromatolysis)

• Neuronal inclusions (lipofuscin)

Lipofuscin buildup in normal in aging brains. Sign of wear and tear, accumulates as we age.
Astrocytes

One of the glial cells. Most reactive and most likely to cause problems after an insult. They put their hands on everything. They maintain synapses, nourish neurons, mop up stuff, they form the blood brain barrier on capillaries, they uptake neurotransmitters, etc.

Glial fibrillary acid protein (GFAP)
(Electron microphotograph)
Reactive astrocytes

- **Astrogliosis: hypertrophy and hyperplasia**

  - When astrocytes are insulted, there are a number of changes.
  - Astrocytes with clear nuclei due to changes in metabolism from increased ammonia exposure.

  - Alzheimer type II astrocytes (H&E)

  - Gemistocytes (H&E)

  - Reactive astrocytes (silver stain)

  - Can also become fat and plump due to metabolic changes.

  - Pictures of astrocytes like these just tell you that something bad has been happening.

Astrocytosis is both hypertrophy and hyperplasia of astrocytes.

This is not Alzheimers disease, these are just named after the same guy.
Reactive astrocytes (chronic gliosis)

Glial “scar”

Collections of excretions from astrocytes in areas where there are lots of astrocyte podocytes. Common as we age and in epilepsy.

Brain cant form collagenous scars like other tissues. Brain just leaves holes. Glial scars are collections of reactive astrocytes filling in the holes left by dying neurons.

Abnormal deposit in chronic gliotic states and in some tumors. Consist of heat shock proteins, GFAP. Alexander disease causes lots of GFAP buildup and kills children by age 10.

Corpora amylacea

Rosenthal fibers
Oligodendrocytes

These don't really react much. They just die. When functioning, they insulate the neurons. These are lost in MS
Ependymal cells & choroid plexus

Normal ependyma

Ependymal granulation

Normal choroid plexus

Choroid is specialized ependymal cells that produce CSF in the ventricles

Ependymal cells line the ventricles. They have cilia. Possible stem cells are below this layer. Ependymal granulations occur when it is damages, but it is actually just astrocytes from below this layer reacting.
Microglia are the macrophages of the CNS. They are reactive cells when you have infection or insult. They try to clean up the area. Amoeboid forms (actively cleaning up) and rod cell forms.

H&E stain of a microglial nodule (viral encephalitis)

H&E stain of a microglial nodule in a viral infection, which consists of a bunch of reactive microglia

Neuronophagia in spinal cord (H&E)

Meninges

Arachnoid surface

Mesodermal in origin. 3 layers: Dura, arachnoid and pia mater. Blood vessels usually run in the subarachnoid space.
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Cerebral (brain parenchymal) edema

- **Vasogenic:** blood-brain barrier is compromised (e.g. trauma, tumor)
  - Fluid from blood goes into brain tissue, no lymphatics to drain it
- **Cytotoxic:** cellular injury (e.g. hypoxic or metabolic insult)
  - Cellular injury can also cause edema

CT scan: hemorrhage  
H&E frozen section: glioma

All these wholes are filled with fluid, lots of edema in gliomas
Hydrocephalus
(excess cerebrospinal fluid)

Ventriculomegaly, or enlarged ventricles. This is due to excess cerebral spinal fluid (hydrocephalus).
Cerebrospinal fluid flow

CSF normally produced in choroid plexus (bright pink) in the ventricles and out into the subarachnoid space, where it flows all over the brain. Granulations in subarachnoid space come in contact with venous sinuses, allowing CSF to drain.

Pressure hydrocephalus

• **Communicating (impaired CSF absorption)**
  
  Build up of pressure due to excess CSF, cause compression of the brain

  CSF can flow freely between ventricles, so all of brain is compressed

• **Non-communicating (obstructive)**

  Obstruction between ventricles cause one region to buildup

• **(versus hydrocephalus ex vacuo)**

  Hydrocephalus ex vacuo is enlarged ventricles due to brain atrophy
Initial signs and symptoms of increased intracranial pressure:

- Headache
- Vomiting
- Altered mental status
- Papilledema (engorgement of the optic disk)

Raised intracranial pressure due to:
- Cerebral edema
- Pressure hydrocephalus
- Tumor
- Hemorrhage
- Abscess

Increased pressure starts by shifting the brain tissues, then compression of vasculature, then flattening of sulci and gyri and serious damage.
Endpoint of severe IIP: Herniation

If increased pressure persists, brain squeezes out like jello. It will go wherever it can - around dural flaps, down spinal cord, etc.
Example: herniation following trauma

Contusion leads to edema, leads to diffuse swelling and shifting of midline to the left. This causes herniations around falx cerebri and the tentorium cerebelli. This falcine herniation gets trapped and bleeds, leading to hemorrhagic infarction.
Uncal (transtentorial) herniation

Illustrations of two of the herniations. These are real bad.

Tonsillar herniation
Site-specific consequences of herniation

- can be clinically silent
- ACA compression

- PCA compression (visual field defect)
- CNIII compression (blown pupil)
- Cerebral peduncle compression (paresis)
- Sylvian aqueduct occlusion (hydrocephalus)
- Duret hemorrhages

- compression of the medulla (cardiorespiratory arrest)
Duret (secondary brainstem) hemorrhages

• Sequela of transtentorial (uncal) herniation

• Caused by stretching of the penetrating branches of the basilar artery as the midbrain descends
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Perinatal brain injury

Sites of injury

• Germinal matrix
• Periventricular white matter
• Cortex and underlying white matter
• Deep nuclei

Sequelae

• Static motor deficits (cerebral palsy): spasticity, dystonia, ataxia/athetosis, and paresis
• Cognitive deficits

Only in developing brain, has stem cells

Childrens brains in perinatal period are still developing, have different kinds of injury.
Germinal matrix

Stem or progenitor cells in this region that are active in the developing brain. This region does not exist in the adult brain. This region is very sensitive, especially in premature babies. These neurons are not myelinated, they are easily damaged.

Germinal matrix bleeds are especially common when pressing on the head during resuscitation, this can lead to serious brain damage or may be subclinical.


24-week-postconception neonate
(alkaline phosphatase and cresyl violet)
Germinal matrix

24-week-postconception neonate
(alkaline phosphatase and cresyl violet)

**Germinal matrix**


24-week-postconception neonate
(alkaline phosphatase and cresyl violet)
Periventricular leukomalacia (from white matter damage)

Hypoxia or infection of white matter around the ventricles will lead to hydrocephalus.
Ulegyria
(from cortical hypoxia/ischemia)

Gray matter ribbon has different widths in different places. Due to cortical hypoxia or ischemia.
Multicystic encephalopathy
(from gray and white matter hypoxia/ischemia)

Cystic holes all over the brain due to gray and white matter hypoxia
Status marmoratus
(from hypoxia/ischemia of deep nuclei)

Glial “scar” and aberrant myelinization in basal ganglia
Clinical sequelae include choreoathetosis and related movement disorders
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Trauma

• Skull fractures

• Parenchymal injury
  Direct injury to the brain

• Vascular injury
Trauma: Skull fractures

Diastatic fractures

Different signs on face depending on what bone is fractured

Fractures that span different bones

Emedicine.medscape.com

Displaced fracture

Chunk of bone dives into the brain
Trauma: Skull fractures

Basal skull fractures

CSF leaking out of nose and ears is also bad

Raccoon sign. Blood leaks out of from anterior fossa fracture

Battle sign from postauricular hematoma. Fracture around temporal bone

“Panda bear” or “raccoon” sign due to leakage of blood from anterior fossa into periorbital tissues. Absence of conjunctival injection differentiates fracture from direct eye trauma

Longitudinal (A) and transverse (B) fractures of petrous pyramid of temporal bone, and anterior basal skull fracture (C)

wikipedia.org
Trauma: Parenchymal injury

- lacerations
- contusions
- diffuse axonal injury

Contusions

Coup-contre coup damage. One side hits the skull and is bruised, then the brain rebounds back and hits the opposite side. So you end up with two contusions on opposite sides.

Contusion

remote

acute

yellowish plaque is an old insult that has become a glial scar
Diffuse axonal injury
(traumatic rotation, deep white matter stretching)

High torque on the brain causes stretching of axons, which can lead to damage - tearing, swelling, etc. This can easily be seen on MRI and in histology. Eventually this leads to white matter degeneration.

MRI: hyperintense signal in the corpus callosum, septum pellucidum, and external capsule

Beta amyloid precursor protein (BAPP) stain

Axonal swelling

White matter degeneration
Trauma: Vascular injury

Intra-axial: parenchymal hemorrhage

Extra-axial: subarachnoid hemorrhage
    subdural hemorrhage
    epidural hemorrhage
Parenchymal hemorrhage

-hypertension, vascular malformations, tumors, drugs, amyloid angiopathy

Due to small vessels inside the brain tissue leaking or bursting.

MRI: acute hemorrhage with associated edema

Hemorrhage with edema surrounding it, causing intracranial swelling.

Subarachnoid hemorrhage

- bleeding from corticomeningeal arteries into the CSF space
- rupture of a cerebral aneurysm in most cases
- sudden onset ("thunderclap headache")
- poor prognosis (up to 50% death rate)

CT scan of SAH

Arteries on the outside of the brain run in subarachnoid space. Rupture of vessels leads to bleeding into this space. High pressure bleed, so expands very quickly. Usually caused by ruptured aneurysm around the circle of willis. Not usually from traumatic injury like the epidural and subdural hemorrhages.
Epidural versus subdural hemorrhage

**Epidural Hematoma**
- Dura (peeled off skull)
- Skull fracture
- Arterial blood

**Subdural Hematoma**
- Dura (still attached to skull)
- Venous blood

Subdural space can be filled with venous blood with vein tears. This is a low pressure bleed, so it expands very slowly. Much less deadly.

Epidural bleeds are arterial. Dura is very tightly connected to skull, so it takes a lot of pressure to fill this space.
Review of Meningeal Layers

Meningeal Layers
- Bone
- Superior Sagittal Sinus
- Dura
- Frontal Lobe
- Arachnoid
- Occipital Lobe

Pial and Arachnoid Layers
- Frontal Lobe
- Arachnoid Layer
- Pial Layer
- Parietal Lobe
- Occipital Lobe

http://www.profelis.org
Epidural hematoma

- ruptured dural/meningeal artery
- often associated with intoxication
- period of lucidity following trauma
- mortality rate up to 50% (varies with level of consciousness at surgery)

Often occurs when someone falls down and hits their head. Due to rupture of dural or meningeal artery. Develops quickly. Bleeding is on top of the dura.
Epidural hematoma

- ruptured dural/meningeal artery
- rare in infants and elderly (intracranial)
- often associated with intoxication
- period of lucidity following trauma
- mortality rate up to 50% (varies with level of consciousness at surgery)
Subdural hemorrhage

- bleeding from bridging veins (and accompanying arteries)
- elderly (atrophy) and infants (thin vessel walls and larger space)
- may be subclinical; more rapid development of symptoms if with arteries

This is due to breaks in the bridging vessels between the dura and the arachnoid. Veins are more fragile than the arteries. Most common in older people and children because the brains are smaller and there is more space in this bridging region. Bleeding develops slowly because it is venous. Occasionally an artery can break too, which makes it much more deadly.
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