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Pathology of the Nervous System
Unit 1 - Normal Form and Function

The nervous system coordinates all activities of an animal. The nervous system consists of the brain and the spinal cord, as well as all the nerves throughout the body. We call the brain and spinal cord the Central Nervous System (CNS) and all of the nerves throughout the body are referred to as the Peripheral Nervous System (PNS).

The CNS is a very complicated system. The brain is composed of multiple parts, each with its own distinct function. Every part of the brain is made up of similar types of cells, but their organization and their function differs considerably.

IN GENERAL,
- Cerebrum is responsible for consciousness, “thinking”, and many motor and sensory functions.
- Thalamus is the connection point between the cerebrum and the brainstem, so it processes many impulses.
- Cerebellum functions in balance and locomotor activity.
- Brainstem keeps the basic physiology of the body working – heartbeat, respiration, etc.
Let’s look at a cross-section of brain:

The gray matter contains primarily neurons, whereas the white matter consists of the axons of those neurons (you will see a typical cell below).

Also, as you look at the surface of the brain, there are many folds, each raised part is called a “gyrus”, and plural is “gyri.” The parts that are folded in are called “sulcus”, plural is “sulci”.

The spinal cord is less diverse in its anatomy and function. Every part of the spinal cord is basically similar, there is a central area composed of neurons, and peripheral areas composed of the axons of those neurons. Then coming off of every segment of the spinal cord is a spinal nerve that reaches out to the body, sending impulses, and receiving input.
There are several cell types in the nervous system. The primary cell type is the NEURON.

Each neuron RECEIVES impulses through its dendrites, and then SENDS impulses out through its axon. A neuron has only one axon but it can have many dendrites.
The axons are surrounded by a sheath, which helps to insulate the electrical impulse. This sheath is composed of MYELIN.

There are other cells in the CNS and PNS in addition to the main cell type, the neuron. These cells include:

- **Astrocytes** – These cells are found wherever neurons are present, they are supportive cells and help to maintain the neurons
- **Oligodendroglia or Schwann cells** – these cells make the myelin which the neuron needs in order to shield its axons
- **Microglia** – these are the macrophages of the nervous system, they are present in order to phagocytose anything that comes into the nervous system that shouldn’t be there.

These supporting cells outnumber neurons 10 to 1.

The brain is bathed in cerebrospinal fluid (CSF). This CSF is made by the choroid plexus, and circulates within the ventricles and up and over the brain, within the meninges.

The brain is covered by 3 layers of connective tissue, called the MENINGES. These are vascular and fibrous tissues that help to supply blood and cushion the brain. The inner two layers are very thin and vascular (called the pia and arachnoid layers). The outermost later is more fibrous and is called the dura mater.
Pathology of the Nervous System
Unit 2 - Response to injury

Cells in the CNS vary in their response to injury. Neurons are the most sensitive. They have a very high metabolic rate and need a constant supply of oxygen or they will die. Depriving a neuron of blood flow for even as short a period of time as 6-8 minutes will cause the neuron to die. Neurons do not regenerate.

Healing in the brain is different from the rest of the body. There are no fibroblasts in the brain and so when there is necrosis, there is no scarring, no fibroplasia as we see in the other body systems. Instead, the part of the brain that has undergone necrosis just gets soft and is eventually consumed and cleaned up by the microglia, leaving a hole in the brain.

There is a special term for necrosis in the brain: malacia. It appears as a big soft spot within the brain.

There is very little area for the brain to expand. Consequently if there is inflammation, or edema, or hemorrhage, or a tumor, the brain becomes slightly bigger than normal, and it presses against the dura mater and the cranium. This pressure compromises the blood flow and neurons may die because they do not get the oxygen they need because the blood vessels are compressed.

Here are some examples of malacia:

This animal had a tumor growing on the inside of the cranium, probably a chondroma or chondrosarcoma. The tumor pressed on the brain and caused necrosis (malacia) of much of the cerebrum on one side.
This animal was infected with Toxoplasma. It went to the brain and caused focal inflammation, creating focal malacia and focal encephalitis in the thalamus.

This animal had a vertebral fracture, and the spinal column compressed the spinal cord. If the location was in the cervical area of the spinal cord, the animal would not be able to walk (could not use any of its legs). It is happened further back (thoraco-lumbar area), the dog would be able to use its front legs but not the hind legs.

This sheep had a bacterial infection that went to the brain, where it caused severe and focal inflammation and necrosis of brain matter. This is malacia. Another term would be: purulent encephalitis.

The areas of malacia never recover. Even if the insult is removed, the brain cannot regenerate.
The brain is a dense structure closely bounded by bone. There is NO room for the brain to expand. As a result when there is swelling of the brain, and edema is the most common reason for swelling, there is no place for the brain to go. It enlarges, and presses against the cranium. The pressure causes a decrease in blood flow, and hypoxia of the neurons then occurs.

As neurons become hypoxic and die, the functions they are responsible for also stop. So, when the center of the brain responsible for heartbeat or respiration gets compromised, life gets compromised also.

What are the reasons for edema in the brain?
- Inflammation can always generate edema.
- A space-occupying mass such as a hematoma or a tumor will cause edema to form.
- Hypoxia will cause the cells to function poorly, they develop cell swelling, and there is resulting edema.
- Hydrocephalus, which happens when the drainage of CSF is blocked, will lead to more fluid and pressure.

As the brain swells, the cerebellum gets pushed backwards and can protrude out through the foramen magnum.

Below are sagittal sections of two brains. The one on the left is normal. The brain on the left has had some edema, there was so much pressure that the cerebellum got pushed out through the foramen magnum and it has a kind of “tail” now. We call this “coning” of the cerebellum, it is a very dangerous sequela to pulmonary edema. Because when the cerebellum pushes through and compresses the brain stem, it can compromise the cardiovascular centers there and, uh oh, the heart stops.

Some of the most sensitive areas to hypoxia are the neurons in the cerebral cortex. As these become compromised, animals will often exhibit seizures.

Any kind of trauma to the brain can cause hemorrhage. Because the brain is soft, the blood tends to continue flowing from a damaged vessel, and can create a space-occupying problem in the brain.
Because this blood build-up occurs quickly, it can cause acute brain swelling and death. A common place to bleed is the leptomeninges, a hematoma forms within the leptomeninges (below the dura). The dura is tough collagen, it can’t stretch, and so the brain gets compressed. These lesions are called subdural hematomas, and they are a common cause of death in any kind of head trauma.

In humans, a common cause of brain problems is STROKE. This happens when an embolus (usually from atherosclerosis) breaks off of the aorta and travels up the carotid artery. It gets stopped in the smaller vessels of the brain, and creates an infarct. The endothelium breaks down in this zone and then there is hemorrhage. We don’t see stroke in domestic animals because they do not get atherosclerosis.
BACTERIA

Bacteria tend to reach the brain primarily by traveling there through the bloodstream. They often do not penetrate into the brain, but they will cause a purulent inflammation in the meninges, which affects function. So most bacterial infections of the central nervous system are MENINGITIS.

Bacterial meningitis is most common in young farm animals, especially calves and lambs, and can include a variety of organisms. Most common route of infection into the animal is through the open umbilicus. There is a septicemia, and organisms settle in the meninges.

An animal with meningitis is likely to appear very “dull”, and might even be in a stupor. This animal will probably also have fever because meningitis is usually due to bacteria, and most bacteria will stimulate fever.
This is the brain of a calf that never did well, was not alert, was basically a “dummy” from birth. A bacteria got in through the umbilicus, and traveled to the brain, to live in the meninges, where it caused a purulent meningitis. Can you see the white fluid within the meninges overlying the sulci?

Here is more severe meningitis, in a lamb. Similar pathogenesis to that described above. Bacteria got in through the umbilicus, went around in the blood stream and settled in the meninges. Here it is creating an accumulation of purulent material in the meninges overlying the ventral aspect of the brainstem.
And, occasionally bacteria will actually be able to get INTO the brain from the meninges, and if not controlled properly, can create a BRAIN ABSCESS:

There are some other ways that bacteria can reach the brain:
  - Extension from otitis (inflammation of the ear)
  - Traveling up the cranial nerves from the oral cavity, this is how Listeria gets to the brain

Most bacteria that cause problems in the brain are not specific brain infections, that is, the bacteria are not specifically “looking” for brain.

A notable exception is LISTERIOSIS. When there is Listeria in the feed, and any oral erosion, the Listeria bacteria will get into the submucosal tissue of the oral cavity, find the cranial nerves, and move up the nerves to infect the brainstem. Once in the brainstem, they grow as microabscesses.

This sheep died of listeriosis. Lesions are not always visible grossly, but in this case they are. There are multiple areas of hemorrhage and necrosis in the brainstem. Microscopically these would appear as microabscesses.
VIRUSES

There are several viruses that have neurons or other nervous system cells as their specific target.

Rabies
The disease is spread to humans from another animal, commonly by a bite or scratch. Infected saliva that comes into contact with any mucous membrane is also a risk. Globally almost all cases are the result of a dog bite. The rabies virus grows in the brain and the salivary gland of infected animals. So, when an infected animal bites another animal (including a human), the rabies virus is inoculated. The virus moves into the nerves, and then moves UP the nerves, toward the spinal cord, at a very slow rate, only about 3mm per day.

Once in the brain, it will infect various neurons, causing disease that differs according to the species. In cattle, sheep, goats, and horses, it is usually “dumb” rabies, with animals being very slow and almost stuporous. In dogs and wildlife, the virus is more likely to cause the “furious” rabies, with animals becoming very aggressive, and more likely to spread the virus through biting. It moves to the salivary glands about the same time as it is in the brain.
The diagnosis of rabies requires fluorescent antibody testing or histopathology. Using an antibody specific for rabies, and impression smear of brain from an animal infected by rabies will have fluorescence. By histopathology, Negri bodies may be visible in brain sections:

![Image of rabies diagnosis]

There are several other viruses that will cause encephalitis in animals. Many are hard to distinguish from one another. Most will create lymphocytic inflammation in the brain, leading you to think that it is probably a viral infection (by contrast, bacterial infections of brain and meninges will have mostly neutrophils in the inflammation).

Some examples of viral diseases that might cause an animal to display neurologic signs because brain tissue is infected:

- Bovine herpes encephalitis, cattle
- West Nile encephalitis, horses
- Louping ill, sheep
- Tick-borne encephalitis, dogs and horses
- Caprine arthritis-encephalitis, goats

**FUNGUS**

There are several fungi from the environment that, once they gain access to the body, may settle out in brain. There are almost always lesions in other organs as well, there are no fungi that are specific for brain.

*Aspergillus* might be the most common fungal infection among domestic animals.

**PARASITES**

*Toxoplasma* is a common infection among all mammalian species. The cat is the definitive host and it is shed in cat feces. The organism will encyst in tissues of other mammals. The organism usually lies
quietly in tissue, causing no problems. However, sometimes the cysts in the brain will rupture and create necrosis and inflammation, especially in young animals.

The dog tapeworm, *Echinococcus granulosus*, can cause serious problems in sheep (and also humans). The intermediate form is cystic and can occur in many body tissues, including brain, although liver and lung are affected far more frequently.
Thiamin deficiency
Thiamin is also known as B1. It is essential for metabolism in many organs, including brain. Ruminants are especially sensitive to a deficiency of thiamin. If there is not sufficient thiamin in the diet, the neurons in the cerebral cortex will die. The lesion is often called polioencephalomalacia.

Here is a brain from a calf with thiamine deficiency. This is a very severe case. The outer part of the cerebral cortex (the gray matter) is all soft and malacic.

Lead poisoning
Animals that have access to old batteries or fuel can develop lead poisoning. This is seen most commonly in cattle. It is directly toxic to neurons and astrocytes, so the damage is primarily in the cerebral cortex.

Copper deficiency
- Pregnant sheep that do not have enough copper in their diet (or, too much molybdenum, which keeps copper from being absorbed), may give birth to lambs that have severe incoordination. Lack of sufficient copper during gestation will cause inadequate development of the white matter (axons and myelin) throughout the brain. Animals cannot walk, have very poor balance, and eventually die.
• If a growing animal does not receive enough copper in the diet, there will also be damage to the white matter, and this shows up in goat kids and lambs as ataxia. There is severe axonal degeneration and lack of re-myelination.

**Hepatic encephalopathy**
When the liver fails to function adequately, there is excess ammonia in the circulation, and this is toxic to astrocytes. The astrocytes degenerate, and brain edema develops.

**Botulism**
Clostridium botulinum produces one of the most powerful toxins known. Even a very small amount of ingested toxin will cause paralysis. This is considered an intoxication, not an infection. The toxin acts by preventing the release of acetylcholine from the end of the axon onto the motor endplate.

As a result, the muscle does not get the signal, and does not contract. This is a FLACCID paralysis. It occurs most commonly in waterfowl, affecting large groups of birds all drinking the same contaminated water, and in these birds, is called “limber neck”.

![Image of a bird with FLACCID paralysis](image-url)