ID histo prep. ID structures A,B.
• **Leptomeninges**
• (A) arachnoid and (B) pia mater
• mild edema present which allows for better visualization of the two layers
• dura mater is not present but would be a thick fibrous band overlying the arachnoid.
Describe.
Perivascular Cuffing

• expansion of Virchow-Robin’s space by mononuclear cells (lymphocytes, plasma cells and macrophages).
• type of inflammation observed in these cuffs may indicate a particular type of infectious agent or insult.
• For example, swine with salt toxicity often have prominent perivascular cuffs composed of eosinophils.
• Describe ID structure.
• Parenchyma
• Gray matter (Neuropil)
• Neurons and associated processes
• Glial cells
• A neuron cell body (black arrow) is identified in a photomicrograph of the gray matter of the spinal cord.
• Describe ID structure.
• White matter
• – Axons
• – Axon sheaths
• – Glial cells
• An axon surrounded by an axon sheath
Describe.
• The image depicts 3 normal neurons with obvious Nissel substance and one (lower left with central chromatolysis. In this neuron the nucleus is eccentrically placed and the cytoplasm has a pale eosinophilic “ground glass” appearance.
• Neuronophagic nodule
  – Neurophagia rarely seen
  – Assoc w/ viral infection
Describe. ID structures.
• Necrosis

• Necrotic neurons
  – Very eosinophilic, angular, shrunken
  – Pyknotic, karyorrhectic, karyolytic nuclei
ID intracellular accumulation.
• Lipofuscin
ID intracellular accumulation.
• Lysosomal Storage Disease
  – Ex: Sphingolipidoses, Glycoproteinoses, Mucopolysaccharidoses, Glycogenoses, Mucolipidoses
  – Compounds accumulate w/I lysosomes
  – Lysosomes fill cell and displace cellular components
What changes do you see?
• Enlarged gyri & shallow sulci with white (inflammatory) infiltrate
• **Glial Cells**
  • • Neuroectoderm
  • – Astrocytes (CNS)
  • • Satellite cells (PNS)
  • – Oligodendrocytes (CNS)
  • • Schwann cells (PNS)
  • – Ependyma
  • • Bone marrow derived
  • – Microglial cells
ID structures.
• Arrow heads – oligodendrocytes
• Solid arrows – astrocytes
• Dashed arrows – microglia
ID structures (be specific)
Microglia

• Tissue macrophage system of the CNS
  – Extensive cell processes
• Primary immune effector cells
  – MHC, cytokines, phagocytosis
• Response to injury
  – Proliferation (microglial nodules)
  – Activation to macrophages
    • Phagocytosis (Gitter cells, neuronophagia)
ID. Location, function.
Epindymal and Choroid Plexus

- Line the ventricular system and central canal
  - Cuboidal to columnar, ciliated

- Function is the formation (choroid plexus) and circulation (ependyma) of cerebrospinal fluid (CSF)
  - Scavenging and detoxifying compounds in the CSF
Describe the flow of CSF?
• CSF flow
  - Lateral ➤ 3\textsuperscript{rd} ➤ Mesencephalic aqueduct ➤ 4\textsuperscript{th}
    ➤ Subarachnoid space ➤ Absorbed by arachnoid villi
  - The central canal is open to the 4\textsuperscript{th} ventricle but little circulation occurs
Describe. ID structures.
Wallerian Degeneration

This is from the spinal cord of a cow with lymphoma. The arrows highlight swollen axon sheaths (swollen myelin) which are numerous in the image. Myelin is lipid and washes out of the section in processing leaving a clear space. Also in the image are numerous spheroids or swollen axons (circles).
Higher magnification from the same slide. Note in addition to spheroids, several digestion chambers can be visualized. Digestion chambers (circles) are composed of myelin and axon debris intermingled with foamy macrophages or Gitter cells (arrows).
Peripheral Nerve
This image depicts how the peripheral nerves are bundled within a fibrous sheath (perinurium) which is in turn transected by thin fibrovascular septae (endoneurium) forming small nerve bundles.
Describe presentation.
Peripheral Nerve Injury

• Loss of proprioception d/t hit by car
Peripheral Nerve injury - Sweeney

- Suprascapular nerve
- Poorly fitting collar
- Trauma from collision
Brachial Plexus Avulsion

• Caudal plexus avulsion
  – C7/8 to T2 (1/3 of cases)
• Complete (most common)
• Sensory, motor deficits
  – Horner’s syndrome
    • When T1-T2 involved
    • Preganglionic sympathetic to eye
Consequence of peripheral n. damage

• Pic 1- atrophy of cells
• Pic 2- myofiber clumping

• Denervation Atrophy
  – Loss of neuronal input results in rapid muscle atrophy.
    • > ½ of muscle mass lost in a few weeks
  – Not a feature of neuromuscular junction disorders

• Renervation results in fiber-type grouping
Conseq. Of peripheral n. damage

• Acral mutilation
• Dx. CS. Etiol.
Peripheral n. injury

• Roaring
  – Laryngeal paralysis
  – Left recurrent laryngeal nerve
    • Guttural pouch infection
    • Lead
    • Trauma
    • Idiopathic
  – Denervation atrophy
    • Cricoarytenoid dorsalis
• Dx. CS. Etiol.
Peripheral nerve injury

• Stringhalt
  – Pelvic limb neuropathy
    • Exaggerated flexion
  – Trauma
  – Hypochoeris radicata
    • Flatweed, false dandelion
• Dx. Describe.
Peripheral nerve injury

- Calving paralysis
  - Damage to the 6th lumbar (L6) nerve root
    - Obturator
    - Sciatic
  - Muscle trauma
  - Hypocalcemia
• Dx.
• Describe
• Pathogenesis
Peripheral nerve sheath tumor

• Sarcoma assoc w/ surrounded nerve
• Tumor surrounds/compresses nerves => Wollarian degeneration
Peripheral nerve sheath tumor

- Image depicts a MPNST surrounding CN5 as it exits the brain stem
Tumor adjacent to the parenchyma compressing on the brain is called what? Species commonly affected?
Meningioma

• Peripheral nerve sheath tumor surrounding CN 5 as it exits the brain stem, cut section
• cats
Top differential for a cat/ horse? What if it was a dog?
Top ddx:

- Horse/ cat- lymphoma with probably bilateral paraparesis here

- Dog- MPNST

- Nerve root sheaths are thickened by pale tan tissue here
Cat: major ddx? C/S?
• Lymphoma is more common on the spinal cord and meningioma on the brain.
• monoparesis
Chicken: what are the clinical signs/disease?
Marek’s Disease

• Range paralysis, Unilateral paralysis
Chicken: ID lesion
• The right side nerve is thicker. Tumor likes to hit the sciatic nerve. Probably caused by viral infection
Maerk’s Disease

- Tumor infiltrates the eye and causes the eye to grey out

- Range paralysis
- Gallid herpesvirus-2, serotype 1
  - Alphaherpesvirus
- T cell lymphoma
  - Neurolymphomatosis
    - Sciatic nerve but others too
  - Acute Marek’s
  - Ocular lymphomatosis
    - Gray eye
    - Cutaneous form
Dorsal view of the spinal canal. Dx. Pathogenesis.
• IVDD Hansen Type I
• Pathogenesis:
  – Chondrodystrophic breeds
  – Nucleus pulposis degenerates early
  – Cartilaginous metaplasia (mineralization) of NP
  – Extrusion into canal
  – Wallerian degeneration
Describe. Dx
IVDD

- Hemorrhage with disc compressing the spinal cord
Dx. Describe
IVDD Hansen Type II

• Chronic region here and periosteum has proliferated causing joint ankylosis
• Annulosis fibrosis weakened, protrudes upward into spinal cord
What does this slide represent?
Consequence of IVDD

- Macrophages eating up the axons
What would the presentation of this disease be?
Fibrocartilagenous Emboli (FCE)

- Present with acute onset paraparesis
- Get ischemic necrosis and infarction of the spinal cord. Often ventral areas of spinal cord affected. Areas of hemorrhage and malacia will end up as cavitation.

Most common vascular spinal cord disease of dogs
- Large breeds (Great Danes) 3 to 7 years old

Nucleus pulposis gains access to vasculature
- Herniation into vertebral body or sinuses
  - Venous emboli
- Retrograde propulsion? Arteriovenous anastomoses?
  - Direct penetration of arteries of annular fibrosis?
  - Arterial emboli

Ischemic necrosis (infarct)
Dx. ID A, B, C
FCE

- A = fibrin in wall of vessel, inflamm cells
- B = cartilage
- C = cartilage (in vessel) stained w/ alcian blue
Dx. Describe. Species affected. Etiologies. Significance?
Diskospondylitis

- Infection of IVisc (lumbosacral spine)
- Large male dogs, pigs
- Bacterial most common
- Etiol:
  - Dogs: staph intermedius/aureus**, strep, Ecoli, brucella**
  - Pigs: erysipleothrix**, arcanaobacterium, staph aur**, brucella**
- **significance: ZOOONOTIC
Dx. ID A,B
• Diskospondylitis
• A= periosteum proliferation/attempt to stabilize
• B= infection, inflamm, proliferation
Disease Name and major clinical sign?
Cauda Equina Neuritis

• Major Clinical Finding- Flaccid tail paralysis, urinary incontinence
• Immune- mediated cause is postulate

  • Idiopathic granulomatous inflammation
    – Perhaps immune mediated
  • Progressive
  • Thickened nerve roots with hemorrhage and fibrosis
  • Axonal degeneration
Aortic Thromboembolism

- myopathy d/t ischemia as opposed to a neuropathy

- Cardiomyopathy in cats
- Hypothyroidism in dogs

- Clinical signs
  - Pain, Paresis, Pulseless, Poikilothermic, Pallor
  - Mimic spinal disease, but spinal cord is rarely affected
Aortic Thromboembolus- how would you determine this is antemortem thrombus, NOT postmortem clot? (3 ways)
• Thrombus would be attached to vessel wall
• Currant jelly/chicken fat clot = postmortem
ID: A,B,C,D. Dx.
• A= aorta
• B= elastin (black)
• C= subintimal space
• D= internal elastic lamina
  – Fragmented (should go all the way across)
Name & describe the anomaly
Kyphosis

• Dorsal deviation of the vertebral bodies
Describe and name the anomaly.
Spina Bifidum

Neurotube Closure Defects

- Meningomyelocele
- Spina bifidum
Name the spinal cord anomalies:
• Syringomyelia
  – Tubular cavitation
  – Does not communicate with the central canal

• Hydromyelia
  – Dilatation of the central canal

A congenital and inherited myelodysplastic (dysraphism) syndrome in Weimaraner dogs exists. Affected dogs move the pelvic limbs together in a “bunny hopping” or “kangaroo-gait” fashion.
Describe lesions.
What C/S would you see if this was a cervical/C6-T2/T3-L3/L4-S3 lesion?
• Vertebral fractures and hemorrhage d/t trauma

• Cervical: UMN signs to all 4 limbs
• C6-T2: LMN forelimbs; UMN hindlimbs
• Thoracic region: UMN hindlimbs
• L4-S3: LMN hindlimbs
Describe lesions.
• Hemorrhagic spinal cord and subdural hemorrhage causing cord compression
• Note: top looks blue b/c dura is still there
Describe lesions. Dx? Etiologies?
Lesions

Note the hemorrhage within the central canal (left) and hemorrhage within the right ventral horn (right) that extends over both segments.

Dx= Hematomyelgia

- Warfarin toxicities and other coagulopathies can cause this leading to central bleeding and sudden death.
- Nothing prevents (no fibrous connective tissue) it from dissecting up the spinal cord.
Discolored photo of goat spine: Describe lesions. Dx? What are some risk factors for various species?
Caseous abscess dorsal to vertebral bodies caused by bacterial infection

Dx = Epidural Abscess

**ROI:**

- Tail docking in dogs/ goats
- Tail fractures in cats
- Tail biting in pigs
- Migrating plant awns= seeds that move through tissues b/c of seed shape & body mvmt
- Animal bites
- Iatrogenic- contaminated needle
List and give examples of pathogen routes of entry into the CNS
• Hematogenous
  - Meninges, neuropil
  - Choroid plexus, CSF

• Direct extension
  - Penetrating trauma (dehorning cattle)
  - Ear infection
  - Nasal cavity/sinuses (via cribiform plate)

• Retrograde axonal transport: Rabies, Listeria

• Leukocyte trafficking (a subset of hematogenous): FIP in MP
Small dog brainstem: Describe lesion. Ddx? What is the specific tissue to which this Dx is restricted?
Lesion

Note the pale yellow tan discoloration of the dorsal left portion of the brainstem. This area also seems expanded by a poorly defined mass effect. This is due to the infiltrating inflammatory cells.

Ddx = neoplasia (though typically will not blend into surrounding tissue as well); inflammation

Dx = Granulomatous Meningioencephalomyelitis (GME)

- Sporadic disease of dogs
  - Middle aged, small breeds
- No infectious agent has been identified
- Lesions confined to white matter
  - Spinal cord
  - Brain stem
  - Cerebrum
GME: What cell types account for the multifocal basophilic pattern & what is their arrangement?
How is GME different from NME?
N(necrotizing)ME: Affects grey matter (not white). Affects meninges & brain but not spinal cord.
Section of spine: Describe normal anatomy & lesion present. Ddx?
Spinal cord showing Wallerian degeneration

Dx = **Extradural Lymphoma** marked by basophilic proliferation (round cells on higher mag)

Extradural tumor Ddx: #1=HSA; OSA; Chondrosarc; Fibrosarc; LSA; Multiple myeloma
Describe lesions. Dx? Which animals (spp & breeds) are at risk?
Lesions

Note the cone shaped vertebral canal on the left and lower right (normal is top right). The stenotic opening is an example of a static compressive lesion.

Dx

Caudal Cervical Stenotic Myelopathy (Wobblers)

- Thoroughbreds, Quarter Horses, Warmbloods
- 8-18 months
- C3-C5
- Lesions due to cervical instability are difficult to assess on necropsy
- Articular facets of vertebrae
  - Osteophytes

Dogs: large/giant breeds (Dobermans & GD’s)

Multiple lesions present
- Stenosis of canal
- Vertebral instability
- Ligamentous hypertrophy
- Joint capsule proliferation
- Osteophyte formation
- Disk herniation
Yorkie presents with neck pain, but still ambulatory (not tetraparetic) Rads above. Dx? Pathogenesis? Other spp/breed affected?
Atlanto Axial Subluxation

- Miniature toy dog breeds
  - Failure of fusion of the odontoid process (dens)
  - Compression of cervical cord by dens
- Arabian foals
- Traumatic AA subluxation can occur
Describe & Dx. What is the mechanism and where does it act?
Tetanus

Note the spastic paralysis of these animals which are affected with tetanus. The horse has an example of the “pump handle” tail that animals with tetanus often exhibit.

- *Clostridium tetani*
- Spastic paralysis
  - Targets inhibitory upper motor neurons
    - Renshaw cells
  - Pre-synaptic inhibition of glycine release
- Extensor spasms
- Hyperesthesia
What are the functions of the vestibular system? Vestibular signs?
• Functions:
  – Posture
  – Eye mvmt
  – Head position

• Synergized with:
  – Vision
  – Sensory input (proprioception)

• Signs:
  – Ataxia (falling, rolling, circling)
  – Head tilt
  – Strabismus
  – nygastagmus
Compare central vs. peripheral vestibular signs (lesion location, presence of paresis/prop def/consciousness)
<table>
<thead>
<tr>
<th></th>
<th>CENTRAL</th>
<th>PERIPHERAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>LESION</td>
<td>Vestibular sensing apparatus (inner ear)</td>
<td>Vestibular nucleus (brain stem)</td>
</tr>
<tr>
<td>PARESIS</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>PROP DEF</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>CONSCIOUSNESS</td>
<td>ALTERED</td>
<td>NORMAL</td>
</tr>
</tbody>
</table>
Dx. Pathogenesis. Etiologies (calf, pig, lamb, cat, dog)
• Periph vest dz: (Otitis Media-Interna)

• Pathogenesis: inflamm/bacteria erode through tympanic membrane and damage vest apparatus

• Etio:
  – Toxins: aminoglycoside antibiotics, iodophor/chlorhexidine antiseptics
  – Extension of otitis externa (usually 2’ to allergies: food/flea/env)
    • Calves (via eustachian tube): mycoplasma, Pmultocida, histophilus
    • Pigs: strep zooepidemicus, actinobacillus pl pneum, mycoplasma
    • Lambs: mannheimia heamolytica (pneumonia)
    • Cats: cryptococcus
    • Dogs: staph intermed, pseudomonas, proteus, strep
Cat. Dx. Describe. Histo findings.
• Feline Middle Ear Polyps → PVD
• fibrovascular polyps covered by oropharyngeal epithelium
• Originate in auditory tube
• Histo:
  – Characteristic loose conn tiss core containing numerous small vessels/scattered aggregates of mononuclear leukocytes
  – Ciliated epith covering mass is prerequisite for confirmation
Ddx for central vestibular disease.
• Encephalitis
  – Rickettsial dz
  – GME
  – FIP
  – Listeria monocytogenes

• Neoplasia

• Vascular accident (stroke)

• Toxic
  – metronidazole
Dx. Describe (CS, non-neuro signs)
• Listeriosis
  – CS: (encephalitis)
    • mental confusion
    • Depression
    • head pressing
    • Circling
  – Non-neuro signs:
    • Abortion
    • Sepsis
    • Purulent endophthalmitis
Dx. Pathogenesis.
• Listeriosis

• Pathogenesis:
  – Organism multiplies in spoiled, incompletely fermented, nearly frozen silage
  – Indoor animals feed on silage during winter
  – Organism breaches oral mucosa/invaded CN V
  – RETROGRADE AXONAL TRANSPORT
  – Access to CNS
  – Brain stem lesions most common
Dx. Describe gross/histo.
• Listeriosis
• LEFT:
  – multifocal to coalescing red-tan areas, extending from brain stem to thalamus
• RIGHT: microabscess w/I neutrophil
  – Central aggregate of degen neuts surrounded by swollen axons/sheath, necrotic debris
Function of cerebellum? CS assoc w/ cerebellar dz?

(whisper) “It’s right here” -LB
• FUNCTION:
  – Controls unconscious proprioception
  – Coordination of movement

• CLINICAL SIGNS:
  – Broad based stance
  – Hypermetria/hypometria
  – Intensino tremor
  – **Weakness is NOT a feature**
Dx. Most common causes.
• Cerebellar hypoplasia
• Common causes:
  – Genetic: foals, calves, puppies
• In utero viral infection (destruction of mitotically active neuron cells of external granular layer)
  – Feline panleukopenia virus (parvovirus)
  – BVDV (pestivirus)
  – Border disease virus (pestivirus)
  – Classical swine fever virus (pestivirus)
Breed identification. How is the dz affecting this breed different from cerebellar hypoplasia?
• Kerry Blue terrier
• Hereditary striatonigral and cerebello-olivary degeneration
  – Atrophy/abiotrophy of Purkinje cells
    • Premature/accelerated degeneration of formed elements
    • Often caused by metabolic defect
    • Cerebellum formed normally but degenerated
• Cerebellar hypoplasia
  – Destruction/interference w/ external granular layer prevents cerebellum from developing normally
Dx. Describe gross lesions.
• Hereditary Striatonigral and Cerebello-olivary Degeneration

• LEFT: cerebellar folia are thinned/collapsed (atrophied)

• RIGHT: caudate nuclei (arrows) and putamen (arrow heads) are dark yellow-brown and cavitated d/t cellular loss (atrophy)
CS assoc w/ forebrain lesions.
• SEIZURES

• Behavioral changes

• Altered mentation
  – Obtundation
  – Stupor
  – Coma
  – Dementia
  – Delirium

• If lesion in hypothalamic region:
  – Endocrine dz signs:
    • PU/PD (provide 25 Ddx!!!!! –DJM ), polyphagia/anorexia, poor temp reg, altered sleep pattern
Describe seizures [causes, classification]
• **CAUSES:**
  
  – Intracranial
    • Tumors, inflamm, congenital anomalies, epilepsy
  
  – Extracranial
    • Metabolic disorders, toxicities

• **CLASSIFICATION:**

  – Generalized:
    • Tonic-clonic (grand mal)
    • Absence (petit mal)
  
  – Focal
Describe the 4 observable components (phase/period) of a seizure.
• PRODROMAL PHASE:
  – Hiding, attention seeking, altered behavior
• AURA:
  – Difficult to discern from prodromal phase
• ICTUS PERIOD:
  – Period of convulsions and altered consciousness
• POSTICTAL PERIOD:
  – Lingering period of weakness or behavioral changes
ZOIT!!! NARF!!!
Describe condition (cause, 2 forms)
• HYDROCEPHALUS
  – Accumulation of CSF w/ l ventricular syst causing compression of the brain, degeneration and atrophy

• FORMS:
  – Obstructive:
    • d/t congenital or acquired blockage of normal CSF flow @ interventricular foraminae, mesencephalic aqueduct, or lateral apertures of 4th ventricle (less common)
  – Non-obstructive:
    • Previous meningitis or congenital defect results in dec absorption of CSF from arachnoid granulations
Congenital vs. acquired hydrocephalus.
• CONGENITAL:
  – Small, toy and brachycephalic breeds
    • Persistent fontanelles allow for expansion of calveria
    • Once sutures form, progression can be rapid
  – Sporadically in domestic livestock
    • Can be d/t plant/viral teratogens

• ACQUIRED:
  – Inflammation: encephalitis, meningitis
  – neoplasia
Dx?
Describe the lesion?
Species/etiology?
• Hydrancephaly
• Porancephaly (small cavitations) in white matter that progress to thin rim of remaining cortex covered by the leptomeninges
• Cattle- teratogenic viruses
  – Akabane virus
  – Bluetongue
  – Rift Valley fever
  – Wesselbron virus
  – BVDV
  – Border disease virus
• Sheep- Cu deficiency
  – Swayback
  – Enzootic ataxia
Dx? Describe the abnormality?
Congenital or acquired?
Predisposed breeds?
• Dx- lissencephally/agyria
• Congenital abnormality of forebrain
  – Telencephalon has primitive appearance, sulci and gyri are absent
• Lhaso Apso predisposed but can occur in other breeds
Describe the two major metabolic causes of forebrain signs. Describe gross lesions of each.
• HEPATIC ENCEPHALOPATHY
  – Congenital/acquired shunt
  – Acute liver failure
  – Congenital deficiency of urea cycle enzymes

• HYPOGLYCEMIA
  – Insulinoma
  – Leiomyoma/sarcoma
  – Sepsis
  – End-state hepatic dz
  – Neonatal
  – Xylitol toxicosis
  – Congenital glycogen storage disorders

• NO GROSS CNS LESIONS PRESENT (dx w/ clinical chemistry, other ancillary testing)
Cat. Describe lesion. Dx. Etiol.
• Cerebral infarction (stroke)= focal ischemic necrosis in forebrain
• Dx= feline ischemic encephalopathy
  – Usually unilateral
  – Middle cerebral artery
• Etiol= migrating Cuterebra larvae and toxin-induced vasospasm (debated)
What are common causes of multifocal CNS disease?
• Infectious agents
• Inflammatory
• Toxic
• Neoplasia
• Edema (herniation)
• Trauma
Viral diseases of CNS: routes of invasion?
• Retrograde transport
  – Centripetal spread
  – Olfactory, trigeminal nerves

• Hematogenous
  – Infect endothelial cells
  – Infect glial cells
Describe host response to viral CNS infection.
• Inflammation: mononuclear infiltrates
  – Lymphocytes, plasma cells, histiocytes
    • Usually confined to perivascular space (Virchow-Robin’s space)
  – Pattern referred to as PERIVASCULAR CUFFING
  – Satellitosis: oligodendrocytes increase in number and surround neuron cell body
  – Astrocytosis: increase in number/size of astrocytes making large prominent cells (gemistocytic astrocytes)
  – Neuronophagic nodules: small nodules around neurons formed by proliferative microglial cells
• Demyelination: disintegration of myelin sheaths w/ I white matter (esp canine distemper, lentivirus of goats)
  – Direct infection of oligodendroglia (K9 distemper)
  – d/t bystander injury secondary to production of inflammatory cytokines

• NOT specific for viral infection (similar toxins can cause similar lesions)
Describe rabies:
- virus family,
- pathogenesis,
- clinical signs,
- susceptible species,
- dx test
• Lyssavirus of the Rhabdoviridae

• Pathogenesis:
  – Bite of rabid animal => replication of virus in myocytes => invades neuromuscular j(x) => ascend to CNS, replicate => descend to salivary glands (virus secreted in saliva for a few days prior to clinical signs)

• CS:
  – Hypersalivation, multifocal neuro signs (furious form, paralytic/dumb form), photophobia, hydrophobia, behavior changes

• ALL mammals susceptible

• Collection of brain for flourescent Ab testing @ state agency is gold standard
Etiology?
CNS clinical signs?
In addition to CNS signs describe the other manifestations of the disease
How would the disease present in a 5 yr old dog vs 10 yr old dog?
• Canine Distemper Virus
• Circling, swaying, head pressing
  – 1/3 focal neurologic signs
  – 2/3 multifocal neurologic signs
• Respiratory, GI, ocular, hyperkeratotic lesions, dental defects, abortion
• 5 yr old dog: multifocal distemper encephalitis
  – Not preceded by GI or respiratory signs
• 10 yr old dog: old dog encephalitis
  – Persistent infection
Dx?
Where does this virus replicate?
What tissues would be good to sample to isolate the virus/what would virus look like?
• Canine Distemper
• Virus replicates in epithelium
• Tissues: stomach, pancreas, urothelium of renal pelvis, urinary bladder
• Intranuclear and Intracytoplasmic eosinophilic inclusions
Describe lesion
How can this lesion vary?
Where is this lesion most frequently observed?
DDx
• Perivascular cuffs of mononuclear inflammatory infiltrates in conjunction with intracytoplasmic eosinophilic viral inclusion bodies
  – Negri bodies
• Can vary greatly in size
• Carnivores- hippocampus
  herbivores- Purkingie cells
• Ddx-
  – Rabies: Babes’ nodules (nodular accumulations of microglial cells)
  – Other CNS dz causing inflammation can cause perivascular cuffing
Pig: Describe lesions. Dx? Pathogenesis? Likely organisms?
• Inflammatory mass on the left between the cerebellum and brain stem.

• The purulent material directly extended from a middle/inner ear infection.

• Dx= Otitis media-interna

• Etiologies in pig: Strep zoo, Mycoplasma hyorhinus
• Ecchymoses of kidneys (turkey-egg)

• Ddx=bacterial septicemia; viral (herpes)

• Dx= Canine Herpesvirus 1 (CHV-1)

• Canine herpesvirus 1 infects and replicates within the vascular endothelium. As such multiple tissues are affected including the CNS.

• CNS: Mononuclear encephalitis
Cat: Describe lesions. Ddx? Pathogenesis? Dx tests? CNS signs?
• Lesion: Hydrocephalus


• CNS signs can result from vasculitis with subsequent edema, mass occupying lesions or obstruction of the CSF flow leading to acquired hydrocephalus.

• Dx tests results on CSF: High cell count (neutrophils); Increased protein (>200mg/dl)

Note the pygranulomatous vasculitis and perivasculitis. The image on the right is of a immunohistochemical stain for FIP coronavirus.
Swine herd showing signs: abortion; incoordination; paralysis; tremors; convulsions. Histopath above. Describe lesions. Dx?
• Lesions:

• Dx= Pseudorabies.

• Swine signs are highly variable, with incoordinated pigs rapidly progressing to paralyzed.

• Animals other than pigs have intense itching as major CS
List & describe 2 other viral CNS diseases of pigs.
Viral Diseases of the CNS (PIG)

- Porcine Reproductive and Respiratory Syndrome virus
  - Arterivirus
    - Abortion mummification
    - Pneumonia
    - Nonsuppurative encephalomyelitis

- Porcine Circovirus 2
  - Granulomatous inflammation
  - Multiple systems affected

PRRS and circovirus type 2 can infect the central nervous system. Perivascular mononuclear infiltrates are the commonly observed histologic lesion. Interestingly, PCV2 causes granulomatous inflammation complete with multinucleated giant cells with intracytoplasmic inclusions in multiple organ systems.
See Borst lec slide 57 & 58 for WNV, V/E/W-EE
• A
Horse: Describe lesions. Ddx? CS?
• Multifocal hemorrhagic necrotizing lesions due to vasculitis (viral replication in endothelium)

• Ddx= EHV-1 > EHV-4.

• CS: Fever and rhinitis often precede neurologic signs, which include ataxia, paresis and paralysis. Predominantly occurs in pregnant mares & nursing foals
Goat carpal joint. Describe lesions. Dx/etiology? What are the expected CNS signs & lesions and how do they relate to the above photo? Other CS?
• Marked proliferative synovitis & cartilage erosion

• Dx/etiology= Caprine Arthritis and Encephalitis Virus (CAE) [Lentivirus]

• Affects (2-4mo) kids & is frequently fatal. Early lesions include hind limb weakness and ataxia with paresis that progresses over several weeks to paralysis.

• Arthritis develops in those that develop inapparent nervous dz.

• Mastitis (hard bag) and interstitial pneumonia (ovine progressive pneumonia, maedi) and arthritis are also manifestations of this disease.
Sheep: Describe lesions. Ddx? CNS lesions & CS? Age group affected?
• Interstitial pneumonia (with consolidation of carinoventral lung lobe?)

• Dx/etiology= Maedi-Visna virus [lentivirus]

• Early signs including slight lip tremors and subtle caudal ataxia. Eventually signs progress to extensor paralysis and death. CSF evaluation in sheep with visna reveals markedly increased numbers of lymphocytes which persists until death.
  • Histologically there is both mononuclear infiltration and demyelination principally involving the white matter.

• Affects sheep older than 2 (insidious)
Describe lesions. Ddx? Pathogenesis of CNS lesions?
• L: uveitis & conjunctivitis (hyperemia apparent)
• R: Catarrhal d/c of mucosa

• Ddx for oral lesions = IBR, BVD, MCF
• Dx = Malignant Catarrhal Fever

• MCF: Fatal multisystemic lymphoproliferative (hyperplastic lymphoid tissue) & inflammatory dz, with marked vasculitis & enlarged LN’s present. GI signs mimic BVD.

• CNS signs d/t vasculitis

• Vasculitis
  – Corneal edema and uveitis
  – Skin lesions – hoof/horn sloughing
  – Petechial or ecchymotic hemorrhage
  – Necrotizing vasculitis in CNS
List and describe teratogenic viral infections in the CNS per species.
Teratogenic Viral Infections of the CNS

- Ruminants
  - Bovine viral diarrhea virus (pestivirus)
  - Akbanе virus (bunyavirus)
  - Border disease virus (pestivirus)
- Cats
  - Panleukopenia virus (parvovirus)
- Pigs
  - Parvovirus
  - Classical swine fever (pestivirus)

Hydrocephalus and cerebellar hypoplasia are the most common congenital defects caused by viral infection of the CNS.
List and describe bacterial disease routes of invasion to the CNS.
Bacterial Disease of the CNS

- Routes of invasion
  - Retrograde transport
    - *Listeria monocytogenes*
  - Hematogenous
    - Most others
  - Direct Extension
    - Otitis media
    - Nose rings
    - Foreign body

Bacterial invasion into the CNS is usually through the hematogenous route; however, extension from the nasal cavity through the cribriform plate, from an inner ear infection, from migrating foreign bodies occurs fairly commonly. *Listeriosis* was covered above and will not be discussed again in this section.
Describe lesions. Ddx/Etiologies?
• Diffuse haziness of the meninges which is most apparent in the sulci. Also the vasculature is diffusely hyperemic.

• Suppurative meningitis

• Sepsis likely to be cause
  • Etiologies: *E.coli*, *Klebsiella* spp.; *Streptococcus* spp: *Streptococcus suis* types 1 and 2, *Streptococcus zooepidemicus*, *Streptococcus canis*; *Pasteurella* spp.: *Pasteurella multocida*, *Mannheimia haemolytica*; *Heamphilus parasuis*, *Arcanobacterium pyogenes*, *Psuedomonas aeruginosa* and *Erysipelothrix rhusiopathiae* (hopefully you can remember more of these than I can)
Ruminant: Describe lesions. Ddx? Why in this location? Risk factor in cattle?
• Pituitary abscess

• In ruminants, the pituitary gland is a favored site for abscess formation due to it’s ventral location.

• Ascending infections along the embryologic route of Rathke’s pouch can occur following nose ringing in bulls.

• Ddx include many aforementioned bacteria
Ox: Describe lesions. Ddx/etiology? What part of the CNS is infected? Other (non-CNS) lesions & signs? Pathogenesis?
• Microthrombi lodged in CNS vasculature causing cerebral hemorrhage.

• Dx = Thrombotic Meningioencephalitis (TME)
• Etioogy = Histophilus sommni (formerly Haemophilus somnus)

• CNS is NOT actually infected, nor does it contain bacterial emboli.

• Other signs/lesions: pneumonia, laryngitis and otitis media in cattle.

• Causes CNS damage by creating a hypercoaguuble state via endothelial damage by the virulence factor lipo-oligosaccharide (LOS). This endothelial damage, which the small vessels of the CNS are particularly sensitive to, results in the formation of multiple microthrombi in the CNS.
Describe lesions. Ddx? Etiology? Pathogenesis? What are the other sites predisposed?
• Large cerebral abscess (I know, I know, it’s hard to see)

• Dx = Bastard strangles (Dx by culture)
• Etiology = Streptococcus equi ssp equi

• Pathogenesis: Strangles starts as an upper respiratory lymphadenitis, followed by metastatic abscessation at distant sites.

• Other tissue sites: thoracic/abdominal LN’s; lungs; liver; spleen; kidney
Pig (post-weaning) GI: Describe lesions. Dx? Etiology? Pathogenesis? Other sites where this lesion is found? CNS lesions/signs?
- Mesocolonic edema.

- Dx= Edema disease  
- Etiology= Shiga toxin producing E. coli (STEC)

- Shiga toxin targets endothelial cells causing them to swell/round up & become leaky \(\rightarrow\) vasogenic edema

- Other sites: eyelid; pericardium; gastric submusoca; ventral abdomen; brain

- CNS: edema builds up within parenchyma of CNS \(\rightarrow\) neurologic signs vary & will progress severly
Pig: Dx?
• Edema Dz
Cat: Describe lesions. Dx? Etiology? Why is there no visible immune response?
• L: Multifocal pale gelatinous areas of cerebrum & cerebellum
• R: (cerebellum) the meninges are expanded by a pale soapy-appearing material which consists of numerous yeast organisms surrounded by a thick mucinous capsule.

• Dx=Cryptococcosis
• Etiology= Cryptococcus neoformans (thermodimorphic fungus – mycelium @ RT, yeast @ BT)

• Thick capsule of crypto inhibits phagocytosis & immune response → no inflammation
Dog: Describe lesions. Dx? Explain lack/presence of inflammatory response. Other sites of infection?
• Cerebral pyogranulomatous inflammation in both photos

• Dx = Blastomycosis
• Etiology = Blastomyces dermatitidis (thermodimorphic fungus – mycelium @ RT, yeast @ BT)

• In contrast to Cryptococcus, Blastomyces dermatitidis does not have a thick capsule and is highly immunoreactive → MP’s & Neut’s present.

• Other sites: lungs (right), eyes, skin bone
CNS Histo: Describe lesions. Ddx? How would you separate the Ddx for a Dx? Life cycle and precautions?
• Tachyzoites (& intracellular bradyzoites?) present in tissue

• Ddx= Toxoplasma gondii, Neospora caninum
• Neospora caninum lifecycle involves dogs & cattle → can prob rule out if this section is not from a fetal bovine
• Dx=Toxoplasmosis

• Cats are the definitive host and can also serve as intermediate hosts. Usually severe clinical signs are seen in those animals that are immunosuppresed (e.g. coinfection with canine distemper virus).

• This is an important zoonosis and cat feces should be removed before sporulation (1 to 5 days) to prevent fetal infection in pregnant women (abortion).

• Can cause abortion in small ruminants
Calf: Describe lesions. Ddx? Hosts?
• Neospora caninum is responsible for cattle abortion due to infection of the fetal CNS where the protozoa causes multifocal necrotizing encephalitis

• Hosts: dogs & cattle
Horse presents with ataxia, limb weakness, & lameness, progressing to tetraparesis. Ddx? Tests? How did horse become infected?
• Ddx= Rabies, EHV, EPM (Sarcocystic neurona)

• This horse was diagnosed with EPM

• Tests: CSF to test for antigen to confirm exposure to Sarcocystis neurona (not necessarily disease)

• Opossum is definitive host. Raccoons, skunks, cats = intermediate hosts. Horse is dead-end host

• Horse ingested sporocysts in opossum feces
Describe lesions. Dx? Pathogenesis? Public health concerns?
• Head tilt (Ddx=vestibular) in a dwarf rabbit
• Multifocal white lesions of kidneys due to granulomatous vasculitis

• Dx= Encephalitozoon cuniculi (microsporidian parasite) infection

• Pathogenesis: obligate intracellular parasite which targets endothelial cells. Brain and kidney are most commonly affected and granulomatous vasculitis in the CNS and lymphoplasmacytic to granulomatous interstitial nephritis are commonly observed. The organism is excreted in the urine.

• Can infect many spp (foxes, minks, dogs, etc.) & IS ZOONOTIC
Describe lesions: Ddx?
• Cysts of Teania causing degeneration & expansion of cavities in brain

In sheep, Coenurus cerebralis, the larval stage of Taenia multiceps causes Gid.

40% of pigs harboring Cysticercus cellulosae the larval stage of the human tapeworm Taenia solium have cysts.
Horse: Describe lesions. Dx? How did the horse present?
• Multifocal malacia of brainstem & spinal cord

• Dx = Equine Protozoal Myeloencephalitis
• Etiology = Sarcocystis neurona

• Presentation: progressive lameness, ataxia, paresis, & muscle atrophy. Rarely can cause seizures
Alpaca: Describe lesions. Dx?
• Lesions: dissecting tract in meninges from worm

• Dx= Meningeal worm = Parelophastrongylus tenuis

• White-tailed deer are subclinical

• Can infect camelids, red deer, elk, moose
Describe lesions. Dx? Name in sheep, cattle, cervids, cats, mink, humans? Risk factors?
• Disruption of normal protein arrangement causing “holes” in brain

• Dx= Transmissible Spongiform Encephalomyelopathy (TSE)
• Caused by prions (beta-pleated sheet forms of proteins), that induces misfolding of more proteins

• Cattle=BSE; Sheep=Scrapie; Cervids=Chronic wasting disease; Mink=TME; Cats=FSE; Humans=variant Creutzfeld-Jacob disease

• Risk factor: refeeding same species protein – Britain’s BSE outbreak d/t feeding ruminant protein to ruminants
• Widespread meningeal hemorrhage which is due to vasculitis

• Dx=Beagle Pain Syndrome = Polyarteritis of beagles

Pathogenesis: presumably immune mediated disease targets the small to medium sized arteries of the meninges and myocardium.

CS: fever, hyperesthesia, severe pain on manipulation, cervical rigidity and anorexia.

Breeds: reported in Boxers, German Shorthaired Pointer, Nova Scotia Duck-tolling Retrievers and rarely in other breeds. Affected dogs have

Histo: The vasculitis is mostly mononuclear with variable amounts of neutrophilic infiltration.
Describe lesions. Dx? Etiologies in ox, pig, & other spp?
• Laminar cortical necrosis
• Dx = Polioencephalomalacia (PEM)

Etiologies
• Ox = Lead, Sulfur, Thiamine deficiency, Salt tox/water depo
• Pig = Salt poisoning
• Any spp = Cyanide
Describe lesions. Dx?
• Lesions: shrunken, hypereosinophilic (necrotic) neurons that are characteristic of PEM

• Dx = PEM
Describe lesions. Dx? Etiology? CS? Hx?
• Decreased and cavitated white matter of brain

• Dx = Leukoencephalomalacia

Etiology in horse
• Moldy corn → Fusarium growth → Fumonisin B1 toxin production → necrosis of cerebral white matter

• CS: sudden in onset and consist of drowsiness, impaired vision, partial or complete pharyngeal paralysis, weakness, staggering and circling

• Hx: horse fed moldy corn >1mo
List the primary neoplasms for the following locations: Brainstem-cerebellum; Optic nerve; Spinal cord
Neoplasia (primary)

- Brainstem-cerebellum
  - Choroid plexus papilloma
  - Meningioma
- Optic nerve
  - Meningioma
  - Pituitary tumors
- Spinal cord
  - Lymphoma
  - Nephroblastoma
  - Glial tumors
Describe lesion. Dx? Diagnostic tests to confirm?
• Unilateral, dullgrey/white mass that seems to blend into surrounding tissue

• Dx = Astrocytoma

• Tests: IHC stain for glial fibrillary acidic protein (GFAP). Tumors of astrocytic origin stain for GFAP
Dog: Describe lesion. Dx? What breeds might this be associated with
• Mass: glistening or mucoid in appearance, with small scattered areas of hemorrhage (and are very soft almost fluctuant to the touch)

• Dx=Oligodendroglioma

• Often found in brachycephalic breeds
Cat: Describe lesion. Dx? Biologic behavior?
• Large textured raised mass on ventral aspect of brain

• Dx = Meningioma

• These tumors arise from the meningeal stroma and compress, but do not invade the adjacent parenchyma
Describe lesions. Dx?
Ependymomas are neuroglial tumors that arise from the lining epithelium of the ventricles and central canal of the spinal cord.
Describe lesions. Dx?
• Mass of ventrolateral aspect of cerebellum & brainstem

• Dx= Choroid plexus papilloma
Horse: Describe lesion. Dx? Specific site of origin? How will the patient present? What is a potential sequela from mass this large?
• Pituitary mass → Dx=Pituitary adenoma

• Arises from pars intermedia

• Failure to shed the winter coat (hirsutism), laminitis and obesity are seen

• Enlargement of the pituitary can cause pressure necrosis of the optic chiasm and visual deficits
Dog Describe lesion. Dx? CS? Specific site of origin?
• Pituitary mass

• Adrenal glands have been dissected out to show cortical atrophy → nonproductive tumor

• polyuria, polydipsia, alopecia and abdominal distension are some of the characteristic clinical signs

• Dx = pituitary adenoma

• Arises from pars distalis or intermedia
Horse: neuro lesion?
• Pituitary adenoma
What are your differentials and where are the most likely lesions locations
• You should be able to do this on your own by now
Neoplastic Ddx? What percent of brain neoplasms are primary?
• Metastatic neoplasia (accounts for 17-30% of brain tumors) → >70% are primary

• Sarcomas
  – Hemangiosarcoma
  – Melanoma
  – Fibrosarcoma

• Carcinomas
  – Nasal
  – Pulmonary
  – Mammary
  – Renal