Neuromuscular Diseases VET 433 A

Disease	Tetanus	Botulism	Tick Paralysis	Polyradiculoneuritis
Presentation	Acute rigid paresis/paralysis May be localized or generalized Reactive to stimuli Limb extension Facial mm contraction Risus Sardonicus Globe retraction Dysphagia Possible autonomic signs	Acute flaccid paresis Signs start in PLs and progress to TLs (can still wag tail) Sever cases may have respiratory paralysis Hyporeflexia and Hypotonia Dysphonia, Mydriasis Sluggish PLRs Poor jaw tone, +/- Megaesophagus, urine retention, constipation Signs begin hours to days after ingestion	Acute flaccid paresis/weakness +/- Gagging, coughing, mydriasis, dysphonia Rapidly progressive 24-48 hours Rarely CN/Respiratory involvement	Acute flaccid paresis/paralysis "Coonhound paralysis" LMN signs in all limbs
Overview	*Clostridium tetani* Spores enter wounds and grow anaerobically Produce tetanospasmin toxin that spreads through the blood	*Clostridium botulinum* Ingestion of preformed botulinum toxin from carrion / improperly canned food Produces botulinum toxin type C (dogs and cats) GIT > Blood > Peripheral nerves Acts on the axon terminals of peripheral nerves. Does NOT go up the axon to the CNS, does NOT cross the BBB	*Dermacentor spp; Ixodes spp* Signs begin 3-9 days after attachment Female tick saliva has a neurotoxin Junctionopathy	Hx of **ANY** antigenic stimulus in the past two weeks, not just raccoon bites! Rapid onset/progression <48 hours
Pathogenesis	Toxin enters motor neuron via end plate Ascends retrograde up the axon to spinal cord and brain Irreversible binding to presynaptic membrane of inhibitory interneurons	Botulinum toxin C breaks down SNARE proteins to Ach vesicles cannot bind and release SNARE proteins allow docking of vesicles to the presynaptic membrane for Ach release No ACh = no muscle excitation	Female tick saliva has a neurotoxin Toxin inhibits Ach release at the neuromuscular junction	Immune-mediated attack of ventral nerve root Loss of myelin and axons Motor function lost, sensory intact True polyneuropathy

	Interneurons are unable to release inhibitory NT such as GABA and Glycine Disinhibition = excessive LMN action			
Diagnosis	Based on clinical signs Titers (rarely needed)	Hx of ingesting carrion ID toxin in serum, or GI contents/feces via mouse inoculation test	Find ticks; signs improve after removal	Clinical signs +/- history Electrodiagnostics
Treatment	Antitoxin Debridement Antibiotics with anaerobic spectrum (metronidazole) Supportive care 4^{+} weeks	Supportive care and time Have to remake SNARE proteins	Remove ticks and apply an antiparasitic	Supportive care (3-4 weeks but can be 4-6 months) Ventilatory support if needed +/- plasmapheresis
Prognosis	Depends on severity of disease Some dogs develop a sleep disorder during/after recovery *black widow envenomation can also cause tetany but less severe than tetanus	Patients that survive typically improve by 24 days *zoonotic risk in a necropsy/lab setting*	Improvement within hours, normal in 3-4 days Good prognosis in the US/Europe Australia has BAD ticks = worse prognosis	Takes weeks to months for full recovery Axons need time to re-myelinate and regrow

Miscellaneous "Junctionopathies"

- Diabetic Polyneuropathy
  - Cats! Femoral nerve is affected leading to a plantigrade stance
  - Reversible with control of diabetes mellitus
- Geriatric onset laryngeal paralysis polyneuropathy (GOLPP)
  - Geriatric Large Breeds
  - Laryngeal paralysis, hind end weakness/paresis, muscle atrophy
- Autoimmune polyneuritis
  - Waxing and waning autoimmune
  - Steroid responsive
  - Dx on nerve biopsy

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Acquired Myasthenia Gravis

Autoimmune attack against Acetylcholine Receptors

Bimodal incidence in dogs (2-4 years and 9-13 years)

- Forms
  - Focal: Esophageal, pharyngeal weakness
  - Generalized: Diffuse weakness (including focal signs)
  - Fulminant: Rare, severe rapidly progressive generalized
- Clinical signs
  - Exercise induced weakness – A decrease in Acetylcholine receptors means that there is less available Ach and the nerves cannot properly stimulate muscles
  - May present as “lame” or “down”
    - Reflexes are often normal by may fatigue
    - Gag often weak
  - Regurgitation/megaesophagus is common
    - HIGH risk of aspiration pneumonia
  - Can occur secondarily to a mediastinal mass such as a thymoma *especially in cats
- Diagnosis
  - Thoracic rads
    - Megaesophagus; thymoma, aspiration pneumonia
  - Gold Standard: Immunological testing
    - Measure AChR antibodies in the serum
    - Stain muscle for IgG
  - Electrodiagnostics
- Treatment
  - Cholinesterase inhibitors
    - Pyridostigmine > adverse effects = SLUDGE-M

        - Immunosuppression *not always done, this can worse aspiration pneumonia etc.
        - Remove thymoma if present
- Supportive care
    - Pressure sores
    - Holding patient vertical while eating and drinking + 15-20 min after
    - Thicken water and food
    - Activity restriction
    - Antibiotics for aspiration pneumonia
- Prognosis
    - HIGH risk of aspiration pneumonia
    - Guarded prognosis
    - If they survive past the first 6 months, there is the chance for spontaneous remission
    - Monitor titers for individual patients

Congenital Myasthenia Gravis

Deficiency / Functional disorder of Acetylcholine Receptors

COLQ mutation in Labs and Goldens

Clinical from birth/few weeks of age

<u>No immunological testing as R is non-functional/missing</u>

- Diagnosis
    - Single fiber EMG
    - Response to treatment
    - Genetic testing *if available
- Treatment
    - Acetylcholinesterase inhibitors
    - Increased risk of aspiration pneumonia
    - Guarded to grave prognosis

- Cannot go into remission since this is a deficiency/functional disorder unlike the autoimmune variant

X-Linked Muscular Dystrophy

*Goldens 8-10 weeks

Cats present older (Sphinx, Devon Rex)

Hereditary deficiency in dystrophin (cytoskeletal protein in myofibers)

- Clinical Signs
  - Progressive weakness, dysphagia, abnormal gait
  - Some mm atrophy, others hypertrophy
- Diagnosis
  - Elevated CK
  - EMG abnormalities
  - Muscle Biopsy (multifocal phagocytosis, regeneration, IHC dystrophin)
- Treatment
  - None
  - Manage secondary complications (aspiration, dysphagia, etc.)

Miscellaneous Non-Inflammatory Myopathies

Myotonia Congenita

Calcium channel disorder leading to persistent muscle contracture

Chow, Min Schnauzer, goats, etc.

Stiff Gait, Hypertrophic mm

- Diagnosis
  - Clinical dx +/- genetic testing
  - "Dive bomber" myotonic potentials
  - Non-specific histopathology
  - CK is normal or mildly increased
- Treatment
  - No treatment available, reasonable quality of life

Hypokalemic polymyopathy

Cats: hyperpolarized muscle = cannot depolarize

Generalized weakness, muscle pain, cervical ventroflexion (no nuchal ligament)

- Diagnosis
  - Elevated CK, Low Potassium
- Prognosis
  - Good if treated early

Malignant Hyperthermia

Mutation in RyR1 gene

Triggered by anesthetic agents

Sustained opening of Ca^{2+} channels = mm contraction

Exertional Rhabdomyolysis

Extreme activity > Myonecrosis

Muscle pain, elevated CK

Myoglobinuria (needs diuresis)

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Inflammatory Myopathies

Masticatory Muscle Myositis

Autoimmune myositis > masticatory mm

Temporalis, masseter, pterygoid, rostral digastricus

- Clinical signs
  - Acute: Pain and swelling
  - Chronic: Atrophy, trismus
  - Unilateral or bilateral
- Pathogenesis
  - Involvement of the mandibular branch of CN V
  - Unique myofibers type 2M
  - Autoimmune antibodies to 2M myofiber protein
  - Can test titers for 2M antibodies
- Diagnosis
  - Antibody test
  - Mildly increased CK
  - EMG
  - Muscle biopsy
  - r/o trigeminal neuropathy

Polymyositis

Autoimmune inflammatory myopathy

- Clinical signs
  - Weakness, stiff, short strided
  - Painful mm +/- atrophy
  - +/- fever, dullness, regurgitation, megaesophagus

- Diagnosis
  - CK MASSIVELY elevated
  - EMG
  - Muscle biopsy

*All autoimmune myositis treatments are the same

Steroid immunosuppression

+/- other immunosuppressants

Treat for 6-8 weeks before a slow taper

Prognosis is fair to good and relapse is possible

Idiopathic Myopathy

Fibrotic myopathy of German Shepherds

Contracture of gracilis +/- semimembranosus