Neigh-ro science: exploring equine degenerative myeloencephalopathy

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ANZCVS

ANZCVS VET SCIENCE WEEK 2025

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Disclosure Statement

Presenter: Sarah F. Colmer, VMD, DACVIM-LAIM

Disclosure:
I do not have any relevant financial or non-financial relationships with industry or commerce to disclose

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Anatomy of today's discussion:

- **Part 1: clinical EDM/eNAD:**
  - What is it? Why do we care?
  - What horses are affected?
  - Why does it happen?
  - What does it look like?
  - Diagnostic procedure, outcomes, prevention (?)

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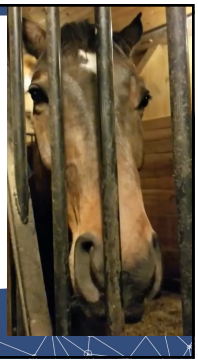
Equine Neuroaxonal Dystrophy and Degenerative Myeloencephalopathy

EDM: what is it?

- Often used interchangeably with neuroaxonal dystrophy (eNAD)
  - Clinically similar, pathologically different
    - Based on location of lesions
      - eNAD - brainstem; EDM – brainstem + spinal cord
- Progressive, symmetric, degenerative disease
  - Ataxia, behavior change
- Possible vitamin E association



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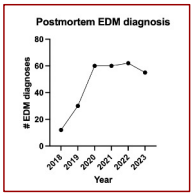
NBC PM neurologic diagnoses

1. EDM/eNAD
2. CVSM
3. EPM



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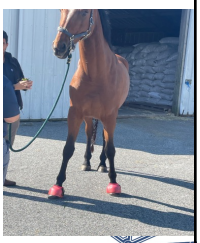
EDM: why does it matter?

- No definitive antemortem diagnostics
- No effective therapeutics
- #1 postmortem neurologic diagnosis at New Bolton Center



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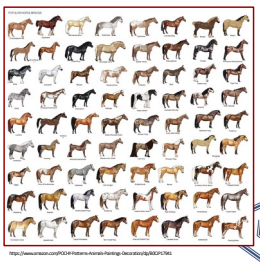
Who is affected?

- No sex predilection
- Huge variety of breeds
- @NBC: Warmbloods >>>>



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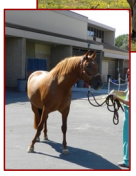
Who is affected?

Equine degenerative myeloencephalopathy: prevalence, impact, and management



- Historically young horses (<1yo)
  - Most 6-12 months
  - Lifelong deficits
  - QH, Appaloosas, Morgans, Lusitanos, Standardbreds
- Genetic susceptibility suspected

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Who is affected?

Clinical and histopathological features in horses with neuroaxonal degeneration: 100 cases (2017–2021)

Signalment	Number of horses
Breed	
Thoroughbred	15
Quarter Horse	5
Warmblood	72
Unspecified	45
Dutch	4
Oldenburg	9
Irish Sport Horse	5
Hanoverian	7
Holsteiner	2
Pony breed	2
Other	6

Sex	
Gelding	80
Mare	18
Stallion	2
Age	
<5 years	7
5-10 years	57
10-15 years	30
≥15 years	6

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EDM/eNAD: why does it happen?

A comparative review of vitamin E and associated equine disorders

- RRR-α-tocopherol
  - Most potent antioxidant
  - When absent, repeated generation of ROS
  - Roles
    - Gene transcription
    - Cell function

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EDM/eNAD: a role for vitamin E

A comparative review of vitamin E and associated equine disorders

- Vitamin E and neuromuscular function
  - Prolonged deficiency: ataxia and muscle dysfunction
    - Muscle degeneration > peripheral nerve degeneration
    - Necrosis of type 1 muscle fibers (highly oxidative)
    - Interruption of active axonal transport

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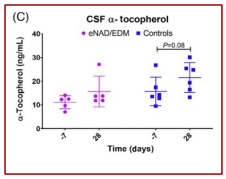
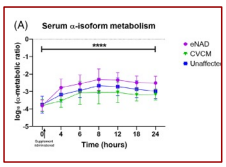
Increased α-tocopherol metabolism in horses with equine neuroaxonal dystrophy





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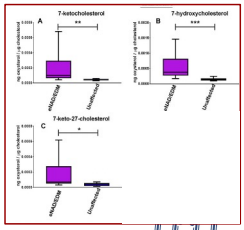
Lipid peroxidation biomarkers for evaluating oxidative stress in equine neuroaxonal dystrophy



- α-tocopherol deficiency → lipid peroxidation
- Lipid peroxidation products
- May interfere with membrane signaling
  - Spinal cord tissue of eNAD/EDM horses
  - Accumulated oxidative stress over time?

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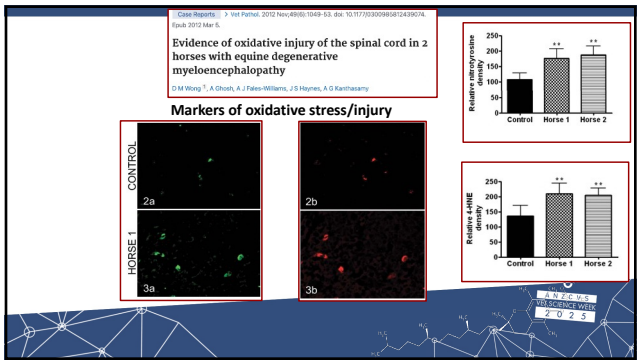
Evidence of oxidative injury of the spinal cord in 2 horses with equine degenerative myeloencephalopathy
Markers of oxidative stress/injury
CONTROL
HORSE 1
2a
3a
2b
3b
Relative nitrotyrosine intensity
Relative 4-HNE intensity
Control
Horse 1
Horse 2
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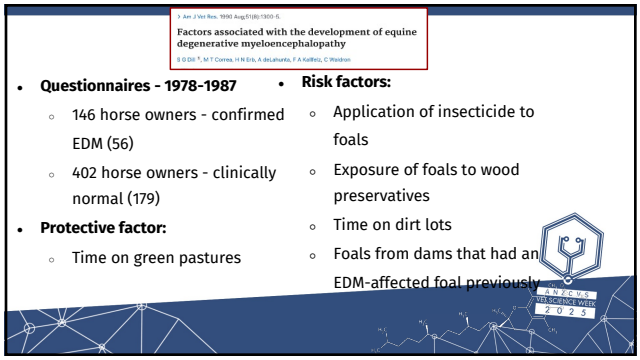
Factors associated with the development of equine degenerative myeloencephalopathy
Questionnaires - 1978-1987
146 horse owners - confirmed EDM (56)
402 horse owners - clinically normal (179)
Protective factor:
Time on green pastures
Risk factors:
Application of insecticide to foals
Exposure of foals to wood preservatives
Time on dirt lots
Foals from dams that had an EDM-affected foal previously
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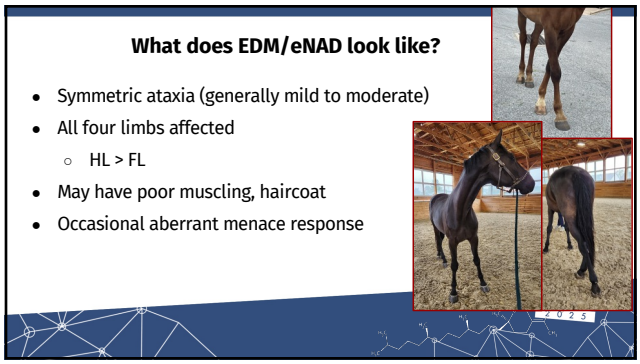
What does EDM/eNAD look like?
Symmetric ataxia (generally mild to moderate)
All four limbs affected
HL > FL
May have poor muscling, haircoat
Occasional aberrant menace response
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What does EDM/eNAD look like?

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What does EDM/eNAD look like?

- Abnormal mentation
  - Dull or anxious demeanor
  - Spookiness
- Abnormal behavior with herdmates
- "Vacant" stare

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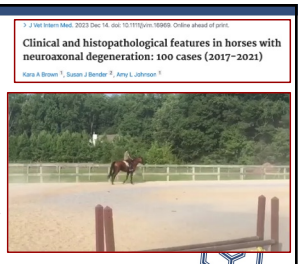
What does EDM/eNAD look like?

- Retrospective at NBC: 100 horses
  - History of ataxia (n=73)
  - History of abnormal behavior (n=69)
    - Under saddle (n=54)
    - On the ground (n=51)
    - *Unpredictable spooking, dangerous or aggressive behavior toward humans or other horses, anxiety, explosivity, abnormal dropping of penis*



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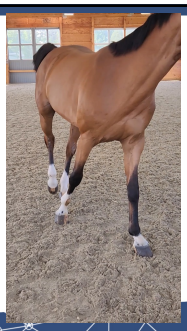
"Penis ataxia"



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Vet Ophthalmol. 2017 Jul;20(4):304-309. doi: 10.1111/vop.12417. Epub 2016 Aug 5.

Pigment retinopathy in warmblood horses with equine degenerative myeloencephalopathy and equine motor neuron disease

Carrie J Finno [1], Heather J Kaese [2], Andrew D Miller [3], Giuliana Gianino [1], Thomas Divers [4], Stephanie J Valberg [5]

- Historically present in EMND horses
- Lipofuscin deposits
- 2/10 horses with EDM/eNAD
- Vitamin E deficiency-associated

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Typical diagnostic procedure

- Neurologic evaluation
  - Mentation
  - Cranial nerve evaluation
  - Gait evaluation
- Grade of ataxia
- Neurolocalization – cervical (to diffuse)

Grade 0	No gait deficits at the walk
Grade 1	No gait deficits identified at the walk and deficits only identified during further testing
Grade 2	Deficits noted at the walk
Grade 3	Marked deficits noted at the walk
Grade 4	Severe deficits noted at the walk and may fall or nearly fall at normal gaits

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Typical diagnostic procedure

- Cervical (to diffuse) neurolocalization
  - Differential diagnoses:
    - 1. CVSM
    - 2. Infectious disease
    - 3. EDM/eNAD

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Typical diagnostic procedure @ NBC

Cervical vertebral imaging (survey radiographs, myelography)

If diagnosis of exclusion: time + progression → (hist)pathology

Neurologic evaluation

CSF/serum analysis: Cytological eval EPM SnSAG 2, 4/3 ELISA

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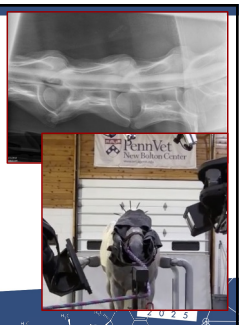
Typical diagnostic procedure

- Cervical imaging
  - Standing lateral radiographs
  - +/- myelography
  - +/- computed tomography



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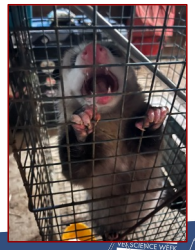
Typical diagnostic procedure

- CSF centesis
  - Cytology
    - Albuminocytologic association
  - EPM - paired samples
    - Sarcocystis neurona
    - Neospora hughesi
  - Lyme - paired samples



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Typical diagnostic procedure

- Serum vitamin E: target = >4 ppm
- Phosphorylated neurofilament heavy?

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Typical diagnostic procedure

Accumulation associated with neurodegeneration

Candidate biomarker for EDM/eNAD

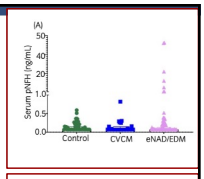
Serum pNFH >1 ng/mL

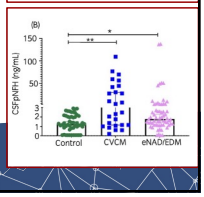
98.8% specific for EDM/eNAD

12% sensitive

CSF pNFH >3 ng/mL

98% sensitive for EDM/eNAD *OR* CVSM





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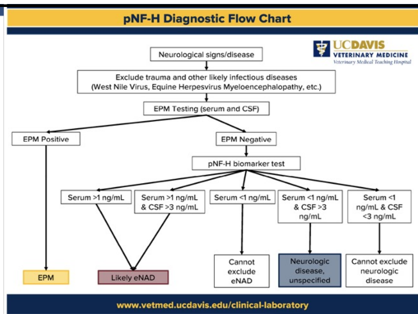

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Diagnosis of exclusion: eNAD/EDM

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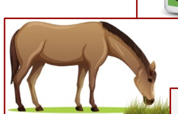
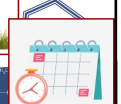
Recommendations

- Vary depending on ataxia and behavior
- Optimize performance
- Physical therapy
- Supportive supplements
  - Vitamin E
  - CoQ10
- Neurologic re-evaluation
- Myopathy investigation





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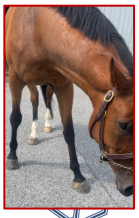
Progression

1. Plateau - less common
2. Worsened ataxia
3. Worsened behavior



Confirmatory diagnosis→ necropsy

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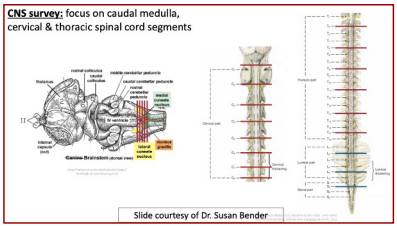
Confirmatory diagnosis: necropsy

CNS survey: focus on caudal medulla, cervical & thoracic spinal cord segments



Slide courtesy of Dr. Susan Bender

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Confirmatory diagnosis: necropsy

- Histological lesions
  - eNAD: Cuneate and gracile nuclei of caudal medulla oblongata
  - EDM: demyelination within ascending tracts
    - Primarily afferent proprioceptive tracts
  - Dystrophic neurons and axons, vacuolization, spheroid formation

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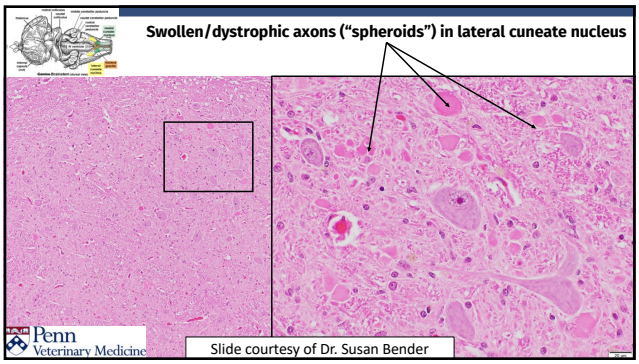
Swollen/dystrophic axons ("spheroids") in lateral cuneate nucleus
Penn Veterinary Medicine
Slide courtesy of Dr. Susan Bender

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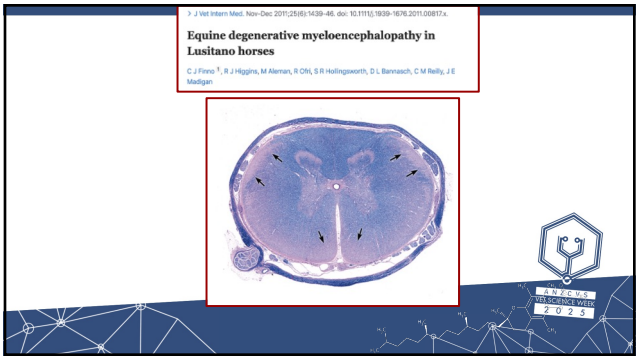
Equine degenerative myeloencephalopathy in Lusitano horses
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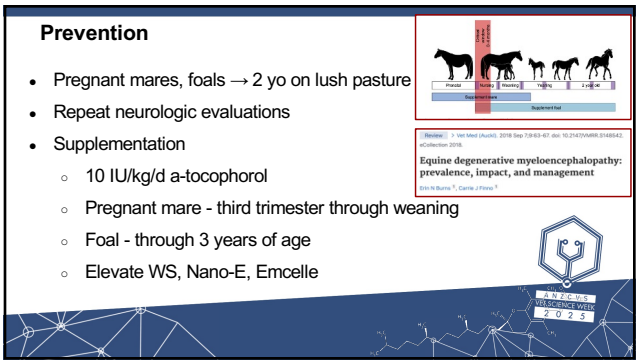
Prevention
Pregnant mares, foals → 2 yo on lush pasture
Repeat neurologic evaluations
Supplementation
10 IU/kg/d a-tocophorol
Pregnant mare - third trimester through weaning
Foal - through 3 years of age
Elevate WS, Nano-E, Emcelle
Equine degenerative myeloencephalopathy: prevalence, impact, and management
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J Am Vet Med Assoc. 2025 Jan 31;263(5):604-611. doi: 10.2460/javma.24.09.0590.
Print 2025 May 1.

Vitamin E concentrations in hospitalized adult horses and foals

Megan G Palmisano [1], Sarah F Colmer [1], Yih Ling Saw [2], Xin Xu [2], Darko Stefanovski [1], Lisa Murphy [2], Amy L Johnson [1]

- Prospective cohort study
- Client-owned horses admitted as patients or companions through the emergency service at a tertiary referral center
- Approximately 1 in 6 horses presented to the emergency service were deficient in vitamin E

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Summary

- EDM is a common neurologic disease
- Unknown pathophysiology – vitamin E?
- Onset of signs can occur in middle age
- Behavior changes are common
- Ataxia is mild
- Diagnosis of exclusion
- Experienced pathologist important for diagnosis

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Questions?
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