
Equine Gastric Ulcer Syndrome:
Glandular Disease & Performance Focus
Jamie Pribyl, DVM
Boehringer Ingelheim

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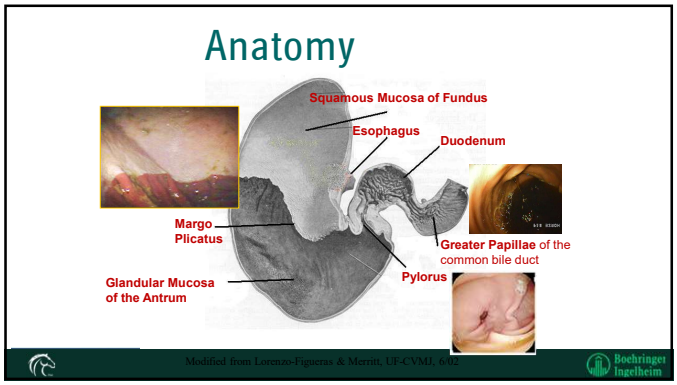
Anatomy
Squamous Mucosa of Fundus
Esophagus
Duodenum
Margo Plicatus
Greater Papillae of the common bile duct
Glandular Mucosa of the Antrum
Pylorus
Modified from Lorenzo-Figueras & Merritt, UF-CVMJ, 6'02
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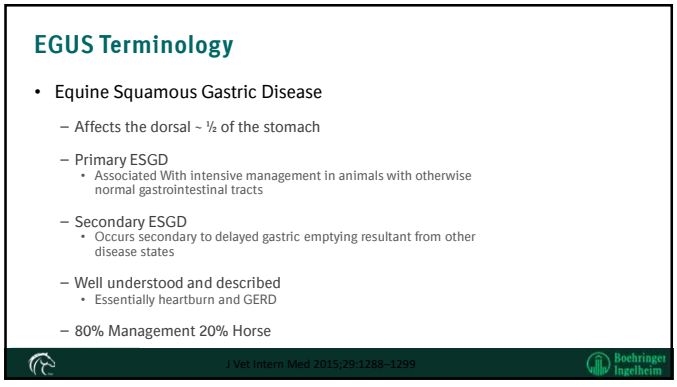
EGUS Terminology
• Equine Squamous Gastric Disease
– Affects the dorsal ~ ½ of the stomach
– Primary ESGD
• Associated With intensive management in animals with otherwise normal gastrointestinal tracts
– Secondary ESGD
• Occurs secondary to delayed gastric emptying resultant from other disease states
– Well understood and described
• Essentially heartburn and GERD
– 80% Management 20% Horse
J Vet Intern Med 2015;29:1288–1299
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EGUS Terminology

- Equine Glandular Gastric Disease
  - Affects the ventral ~ ½ of the stomach
    - Particularly the outflow – Antrum and Pylorus
  - Anatomically
    - Cardia, Fundus, Antrum, Pylorus
  - Less well understood and described
  - 20% Management, 80% Horse

J Vet Intern Med 2015;29:1288–1299

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EGUS Terminology

Journal of Veterinary Internal Medicine

ECEIM Consensus Statement

European College of Equine Internal Medicine Consensus Statement—Equine Gastric Ulcer Syndrome in Adult Horses

Equine Gastric Ulcer Syndrome (EGUS)

Equine Squamous Gastric Disease (ESGD)

Equine Glandular Gastric Disease (EGGD)

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Reported EGUS Risks Factors

- Stomach anatomy physiology
- Low forage diets
- High concentrate diets
- Intense/increasing exercise
- Transportation
- Stress
- Interval feeding
- Management housing changes
- Water deprivation
- Weaning
- Prolonged stabling
- NSAID administration

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Pathogenesis of ESGD

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Factors Associated with ESGD

- **What and how we feed horses**
  - Meal feeding
  - Poor roughage ball integrity
  - High carbohydrate diets
- **When and how long we exercise**
  - Before roughage meal, right after grain
  - Length > 40 minutes per day at trot or higher
- Abnormal gastric acidity in the stomach
  - Acid where it doesn't belong (partially empty stomach)
  - Hyperacidity (too much acid)
- Decreased protective factors
  - ↓ Saliva, roughage presence, quick gastric emptying

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Pathogenesis of EGGD ???

- Acid injury? Not primary cause
- Bacteria? Not primary cause, secondary??
- **Cortisol role**
- NSAIDs
- Very little data to support disease of diet

- **Compromise of mucosal defense mechanisms**
  - Defect in protective barrier → erosion and gastritis/inflammation?
  - Gastritis/Inflammation leads to barrier dysfunction and erosion?

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Factors Associated with EGGD

Journal of Veterinary Internal Medicine ACVIM

STANDARD ARTICLE

Management factors and clinical implications of glandular and squamous gastric disease in horses

Benjamin W. Sykes[1,2] | Mark Bowen[3] | Jocelyn L. Habershon-Butcher[3] | Martin Green[3] | Gayle D. Hallowell[3]

Equine Veterinary Journal

Risk factors for equine glandular and squamous gastric disease in show jumping Warmbloods

S. K. PEDERSEN[1], A. E. CRIBB[1], M. C. WINDEYER[1], E. K. READ[1], D. FRENCH[2] and H. E. BANSE[1]

Journal of Veterinary Internal Medicine

Risk Factors for Equine Gastric Glandular Disease: A Case-Control Study in a Finnish Referral Hospital Population

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Factors associated with EGGD

- **Race horses**
- Exercising ≥ 5 days per week had a 10.4 times increased risk of EGGD – racehorses
- Trainer was also identified as an EGGD risk factor

- **Show horses**
- Exercising ≥ 6 days per week – show horses
- Currently Showing, except international level
- Increased number of caretakers
- Increased number of riders
- Warmbloods

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EGGD and Cortisol

Increased adrenocortical response to adrenocorticotropic hormone (ACTH) in sport horses with equine glandular gastric disease (EGGD)

M.D. Scheidegger[a,*], V. Gerber[a], R.M. Bruckmaier[b], J.H. van der Kolk[a], D. Burger[a], A. Ramseyer[a]

[a] Swiss Institute of Equine Medicine ISME, Vetsuisse Faculty, Agroscope and University of Berne, Länggassstrasse 124, Postfach 8466, 3001 Bern, Switzerland
[b] Veterinary Physiology, Vetsuisse Faculty, University of Berne, Bremgartenstrasse 109a, 3001 Bern, Switzerland

ESGD was diagnosed in 8/11 (73%; 95% confidence intervals [95%CI], 43–92%) endurance horses and 5/15 (33%; 95% CI, 14–58%) eventing horses. EGGD was observed in 9/11 (82%; 95% CI, 53–96%) endurance horses and 9/15 (60%; 95% CI, 35–81%) eventing horses. The presence or severity of EGGD was unrelated to the presence or severity of EGGD. ACTH stimulation induced a larger increase in cortisol concentration in horses with moderate EGGD than in horses with mild EGGD. Cortisol concentration during the entire sampling period (total increase in cortisol concentration during the entire sampling period [dAUC], 31.1 ± 6.4 ng/mL) and the highest measured concentration at a single time point (maximal increase in cortisol concentration [dMAX], 10.3 ± 2.3 ng/mL) were increased ($P = 0.005$ and $P = 0.038$, respectively), indicating that horses with glandular gastric disease exhibited increased adrenocortical responses to ACTH stimulation. These results suggest that EGGD might be associated with an enhanced adrenocortical sensitivity. Further investigations are warranted to confirm the association between adrenocortical sensitivity and EGGD and to elucidate the pathophysiological mechanisms involved.

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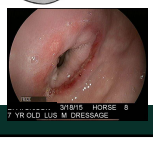
Equine NSAID Evidence

- Experimental overdose (Meschter 1990)
  - Overdose PBZ 4-13.5 mg/kg/d
  - Pyloric ring erosions
  - Neutrophilic eosinophilic fibrinous exudate
  - Foci of necrosis, microvascular thrombosis
- 4 mg/kg/d 42 days (Kunkle 2010)
  - 88% increase in glandular ulcer lesions compared to baseline
  - controls and 0.5 mg/kg/d firocoxib showed an 11% increase, 0.1 and 0.3 mg/kg/day showed no increase



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Boehringer Data

- **2008-2020**
  - 7105 horses
- **2015-2020**
  - 1552 evaluable cases
  - 1433 included glandular evaluation
  - 1221 had complete gastric evaluation
    - Squamous fundus
    - Glandular cardia
    - Glandular fundus (excluding ventral surface)
    - Pyloric antrum
    - Pylorus

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Overall Prevalence 2015-2020

- **Total prevalence of EGUS: 86.3% (1236/1433)***
  - 75.4% had squamous disease (1081/1433)
  - 55.8% had glandular pathology (800/1433)
  - 57.7% had glandular disease when all glandular locations evaluated (705/1221)
  - Squamous disease only: 30.4% (436/1433)
  - Glandular disease only: 10.8% (155/1433)
  - Both: 45.0% (645/1433)

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Overall Prevalence 2015-2020

- **Total prevalence of EGUS: 86.3% (1236/1433)***
  - 73.1% had squamous disease (1134/1522)
  - 75.4% had squamous disease (1081/1433)
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  - Squamous disease only: 30.4% (436/1433)
  - Glandular disease only: 10.8% (155/1433)
  - Both: 45.0% (645/1433)
  - 59.7% of horses with ESGD also had EGGD (645/1081)

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Risk Factors Evaluated

- Discipline
- Active Training - Y/N, level
- # rides/week, workload level
- Housing
  - stall/paddock/pasture/dry lot
  - pasture/dry lot – alone/with others
- Diet
  - Concentrate Y/N, type, meals/day
  - Roughage type and form
- Events over time - <2 weeks, 2-4 weeks, 4-8 weeks, >8 weeks, never
  - Competition single day
  - Competition multi day
  - Trailered <4 hours
  - Trailered >4 hours
  - Increase workload
  - New trainer/location
  - Change in herd dynamics
  - Change in feeding
  - Illness/injury

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Disciplines and EGUS

Endurance	**93.1%**
Cutting	**90.3%**
Western Pleasure	**90.2%**
All others	**between 80 & 90%**
Eventing	**79.5%**
Pleasure	**77.88**
Lessons	**73.3**

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EGUS Prevalence and Housing/Social

- **Stall**
  - Horses never in stall 87% (129/148)
  - Horses in stall 12 hours 86.6% (103/119)
  - Horses always in stall (except working) 85.8% (97/113)
- **Turnout**
  - Pasture alone 75.4%
  - Pasture with others 80.5%
  - Dry lot alone 75.8%
  - Dry lot with others 78.7%

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Clinical Signs

Clinical Sign		% of horses w/ ESGD	% of horses w/ EGGD
Off Feed		7.9%	6.6%
Colic		10.1%	8.9%
Unwilling to Work		13.5%	12.3%
Poor Coat		13.9%	12.6%
Decreased Performance		13.9%	13.8%
Picky Eater		14.9%	14.3%
Wt Loss		15.8%	15.2%
Not Gaining		20.5%	17.4%
Cinchy/Girthy		31.1%	31.4%
Bad Attitude		35.3%	36.1%

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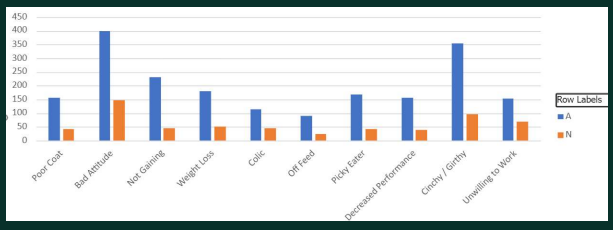
Clinical Signs and ESGD



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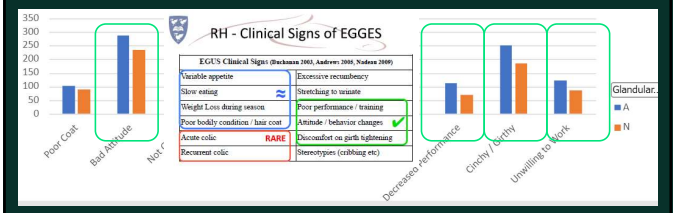
Clinical Signs and EGGD



- Hepburn. Equine Glandular Gastric Erosion Syndrome: Comparative Aspects and Treatment, ACVIM Forum, 2012

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EGUS and Colic

- **151 horses reported to have recent colic**

- **81.4% (123) had EGUS – slightly lower than total EGUS prevalence**
- **72.8% (110) had ESGD**
- **46.3% (70) had EGGD**

- **Only 10.1% of horses with ESGD had colic**
- **Only 8.9% of horses with EGGD had colic**

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Suspicion of "Ulcers"

- **If the owner suspected ulcers they were correct 85.8% of the time**
- **If the owner did not suspect ulcers they were correct 10.6% of the time**
  - Prevalence of EGUS was higher (89.4%) in horse not suspected of having ulcers

- **Owners reported 0 clinical signs, 65.5% did not suspect ulcers**
  - 34.5% of owners reporting 0 clinical signs suspect ulcers ??
- **Owners reported 1 clinical sign, 11.3% did not suspect ulcers**
- **Owners reported 2 or more clinical signs, 4% did not suspect ulcers**

- **Can owners accurately suspect ulcers?**
  - What questions/clinical signs are we asking of them?

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Diagnosis of EGUS

- **Gastroscopy** – Gold Standard
  - Greatest Value
  - Differentiate lesion location and severity
    - Dictate most appropriate treatment
    - Treatment length and which medication(s)
  - Recommend follow-up gastroscopy prior to discontinuing treatment
- Stomach block
- Response to Therapy
- Just treat for a month
  - Worse value
  - 20 - 50% of horses don't have ulcers

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Treatment Concepts – 3 Presentations

- ESGD – Squamous only
  - Moderate to high level acid suppression (Proton pump inhibitor)
- EGGD – Glandular only
  - Proton Pump inhibitor (omeprazole) + Sucralfate
  - Prostaglandin Analog (Misoprostol) +/- Sucralfate
  - All 3
  - Equally effective and equally ineffective
- ESGD + EGGD – Both
  - Proton pump inhibitor + Sucralfate
  - All 3

Glandular Adjunctive TX
- Corn or Flax seed oil
- Gastric Prokinetics
- Antibiotics
- Supplements
- Transendoscopic debulking
- Transendoscopic steroid injection

Hepburn R. EQUINE GLANDULAR ULCERATION: COMPARATIVE ASPECTS AND MANAGEMENT. ACVIM Proceedings, New Orleans, 2012

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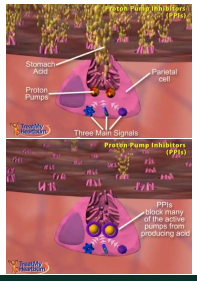
Proton Pump Inhibitors

- Weak lipophilic bases degrade easily
  - Aqueous solutions
  - pH < 7.5
- Formulation is the key to successful treatment
- Inhibits the final step in acid production
- **Suppresses acid production regardless of stimulus for up to 24 hours**
  - pH >4 for 16 hours
  - Allows mucosa to heal



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Omeprazole

- Only product currently labeled for use in horses for treatment of ulcers
  - Specially developed buffered paste to protect the omeprazole
- 96% effective in treating gastric ulcers in horses continued in training
- 4 mg/kg – 28 days
  - Ensure most ulcers heal (not all)
- Extensively studied
  - Proven safety and efficacy
- Compounded omeprazole
  - Multiple *in vivo* and *in vitro* studies show no consistent stability or clinical effect

GASTROGARD product label

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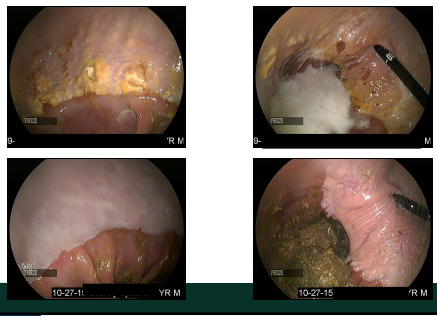
28 Day Gastrogard® Treatment



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Real-World Value

- 60 day Compounded omeprazole treatment

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Sucralfate

- Sucrose octasulfate hydroxyl aluminum salt
  - Electrostatic binding to ulcer site = mechanical barrier
  - **Stimulates PGE_2 production**
    - Increased mucus and HCO_3 production
  - **Promotes re-epithelialization**
- Increases antibiotic-mucosal contact
  - Tetracyclines strongly interact with SF in an acidic environment, leading to sustained mucosal release of antibiotic
- PBZ overdose model in foals (Geor 1989)
  - 4 gm q12h made lesions appear less active, surrounding mucosa was less hyperemic and more normal mucus coat was found
- No adult dose studies on dosing (20 mg/kg q 8-12h)
  - Human stomach SA = $0.05m^2$
  - Horse glandular portion SA = $0.15m^2$
  - Human gastritis dose = 2 gm q12h
  - Horse dose = 6 g q12h (12mg/kg/ q12hr)

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Sucralfate in EGGD

	Improvement (%)	P-value	Odds-ratio (OR)	Confidence interval (CI)
Sole G → O	4/8 (50%)			
Sole G → O + S	9/12 (75%)			
Difference between groups	25%	0.6424	1.75	0.17 – 18.79
S+G → O	26/45 (57,8%)			
S+G → O + S	36/45 (80%)			
Difference between groups	22,2%	0.0395*	2.89	1.05 – 8.50
All G → O	30/53 (56,6%)			
All G → O +S	45/57 (78,9%)			
Difference between groups	22,3%	0.0066*	3.37	1.33 – 9.12

Kranenburg, L.C., Scheepbouwer, J.H.T., van der Boom, R. A retrospective study on the effect of combined sucralfate and omeprazole therapy compared with omeprazole monotherapy for equine glandular gastric disease. ECEIM Congress 2020.

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Misoprostol

- Synthetic Prostaglandin E_1 Analogue
- Suppresses gastric acid
  - histamine-sensitive adenylate cylcase
- Cytoprotective
  - stimulation of bicarbonate and mucus secretion
  - increased mucosal blood flow
  - decreased vascular permeability
  - increased cellular proliferation and migration
- Prevent NSAID induced ulcers/bleeding in dogs
  - Same as cimetidine in horses – no effect
- Colic, inappetence - Horses
- Diarrhea, abdominal distention/bloating in man, abortion in dogs
- 5 ug/kg PO BID to TID
- No significant effect on squamous disease
- **Human safety concerns**

Murray, Equine Pharmacology, 2004

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Treatment and feeding timings

- ESGD
  - Food finished by 10 pm
  - Omeprazole at 7 am
  - Morning feed at 8 (7:30) am
  - Hay available in slow feeder or multiple hay nets throughout day
  - Evening feed 6 pm
  - Food finished by 10 pm
  - Repeat
- EGGD
  - Food finished by 10 pm
  - Omeprazole at 7 am
  - Sucralfate at 8 (7:30) am
  - Morning feed (5-15) minutes later
  - Hay available in slow feeder or multiple hay nets throughout day
  - Sucralfate at 6 pm
  - Evening feed 5-15 minutes later
  - Food finished by 10 pm
  - Repeat

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EGGD All 3 Drugs

AM
- Omeprazole after overnight fast
- Sucralfate 30 minutes later
- Feed 5-10 minutes later
- Misoprostol 10-15 minutes later

PM
- Sucralfate
- Feed 5-10 minutes later
- Misoprostol 10-15 minutes later

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Antimicrobials

- When?
  - Biopsy findings of mucosal bacterial invasion
  - Cases that worsen or become fibrinosuppurative with 1st step therapy
  - Not used alone – combine Doxy/Mino with Sucralfate administration

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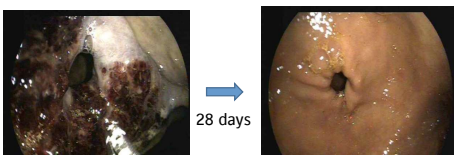
Glandular Gastric Disease

- Generally multimodal therapy
- May take several weeks to months
- May require continuous therapy to maintain



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How Quickly Do They Return????

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Adjunctive Therapy

- Housing Management
  - Increased turnout with grazing or hay available
  - Walking shown to increase gastric contractility and outflow as well as colonic motility
  - Physical and behavioral benefits

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Adjunctive Therapy

- Feeding
  - Hay fed free choice?
  - Multiple small grain meals
  - Decreased grain in ration
  - Change calorie
    - Beet pulp
  - Hay prior to feeding grain
    - saliva
    - physical barrier
    - buffering effect
  - Alfalfa Hay
    - Better buffer than grass hay
    - Ca++ , P
    - "Horse Tums"
    - 45 minutes prior to work

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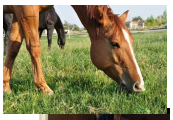
Chewing

- Grazing horses chew approx. 60,000 times a day
- 1000lb horse @1.5% BW hay; 15lbs = 25,500 chews
- 6lbs grain = 2,550 chews + 25,500 (hay) = 28,050 chews
- 12lbs grain = 5,100 chews + 25,500 (hay) = 30,600 chews



Ingredient	Chew or Jaw Sweep
2lb of oats (on ground)	1000 times
2lb of hay (on ground)	2000 times
2lb of oats (chest height)	350-500 times

Bonin et al., Comparison of mandibular motion in horses chewing hay and pellets. Equine vet J. (2007) 39 (3) 258-262

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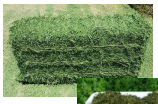
Alfalfa

- Natural buffer to acidity in the stomach (Calcium)[1]
- More effective at reducing the incidence of gastric ulcers than Bermuda grass hay[1]
- Preferably provide alfalfa at regular 5 – 6 hour intervals[2]
- **¼ - ½ flake 45 minutes prior to work**
- Hay > Chopped > Cubes > Pellets
- Saliva resulting from chewing also serves to buffer stomach acid and stomach contents for horses that have access to forage throughout the day



1)Lybbert et al., 2007, 2)Nadeau 2000

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PREVENTION

- Management/Stress Reduction
  - Removal / reduction of ulcerogenic factors
  - Turnout
  - Provide toys/distraction/pets
  - Haul horses facing backwards if feasible
  - Minimize overtraining
  - Music: Relax Trax
- Feeding changes
  - As discussed

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Relax Trax

- Specially designed to help reduce stress in horses
- Decrease cortisol level, decreased heart rates, won more money
- Quotes from users
  - "The hyper horse calmed down listened, stood quietly eyes softened" "My horses love this music" "It calms my horse and me"

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PREVENTION

- Pharmaceuticals
  - During high stress, continued ulcerogenic situations
  - Omeprazole 2 mg/kg - prevention of recurrence
  - Omeprazole 1 mg/kg - prevention
- Nutraceuticals / Supplements
  - Continuously? Research?
  - Squamous: Purina® Outlast®, Nutrena® Digestive Balance, SmartPak™ SmartGut® Ultra, Egusin®, GastriX™, ProTek GI
  - Glandular: ProTek GI, corn oil, RelyneGI (new version)??

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ULCERGARD®

- Same patented formulation as GASTROGARD
  - Cinnamon flavored/scented paste
- Same concentration as GASTROGARD but smaller dose
- 4 doses per syringe for a 1200 lb horse
- Different plunger on syringe
  - Marked in 4 dose increments
- Labeled for use in horses 6 months of age and older (different from Gastrogard)
- May be available from Veterinarian

Ulcergard Product Label

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Important Safety Information

- *Federal (USA) law restricts GASTROGARD to use by or on the order of a licensed veterinarian. GASTROGARD is indicated for the treatment and prevention of recurrence of gastric ulcers in horses and foals 4 weeks and older. In an efficacy trial, no adverse reactions were observed. Safety of in pregnant or lactating mares has not been determined. Keep this and all drugs out of the reach of children. In case of ingestion, contact a physician.*
- *ULCERGARD can be used in horses that weigh at least 600 lbs. Safety in pregnant mares has not been determined. Not for use in humans. Keep this and all medications out of the reach of children. In case of ingestion, contact a physician.*

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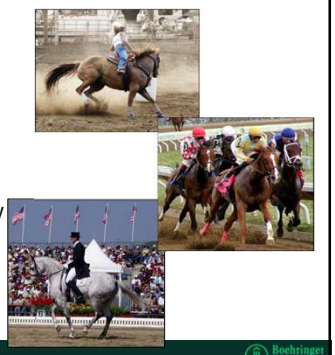
Key Points

- ESGD & EGGD are different
- EGGD are clinical signs are variable
- Appropriate Diagnosis and Treatment is imperative for successful outcomes
- Multimodal treatment is necessary for EGGD
- Consider the horse holistically when presented for performance issues



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Questions

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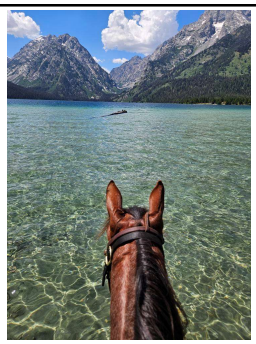

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