VETERINARY MEDICINE

INFLAMMATORY BOWEL DISEASE IN HORSES

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Large Animal Internal Medicine Resident

Summary

Introduction

Classification

Diagnosis

Treatment

Prognosis

Clinical case

INTRODUCTION

Malabsorption syndromes in the horse

EQUINE VETERINARY EDUCATION
Equine vet. Educ. (2006) **18** (6) 299-308

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TABLE 1: Important causes of malabsorption syndrome in the adult horse

Extensive small intestinal resection
Chronic inflammatory bowel diseases
Granulomatous enteritis
Idiopathic eosinophilic enterocolitis
Multisystemic eosinophilic epitheliotrophic disease
Lymphocytic/plasmacytic enterocolitis
Alimentary lymphoma (lymphosarcoma)
Amyloidosis (Hayden *et al.* 1988)
Enteric infections
Mycobacterial infection
Rhodococcus equi (rare in adult horse)
Enteric fungal infections
Idiopathic villous atrophy
Congestive heart failure
Intestinal ischaemia
Parasitism - cyathostominosis
Intestinal fibrosis

Inflammatory bowel disease

Definition:

A group of gastrointestinal tract disorders recognized as an infiltration of the mucosa and submucosa with different types of inflammatory cells.

Pathogenesis:

A group of gastrointestinal tract disorders recognized as an infiltration of the mucosa and submucosa with different types of inflammatory cells.

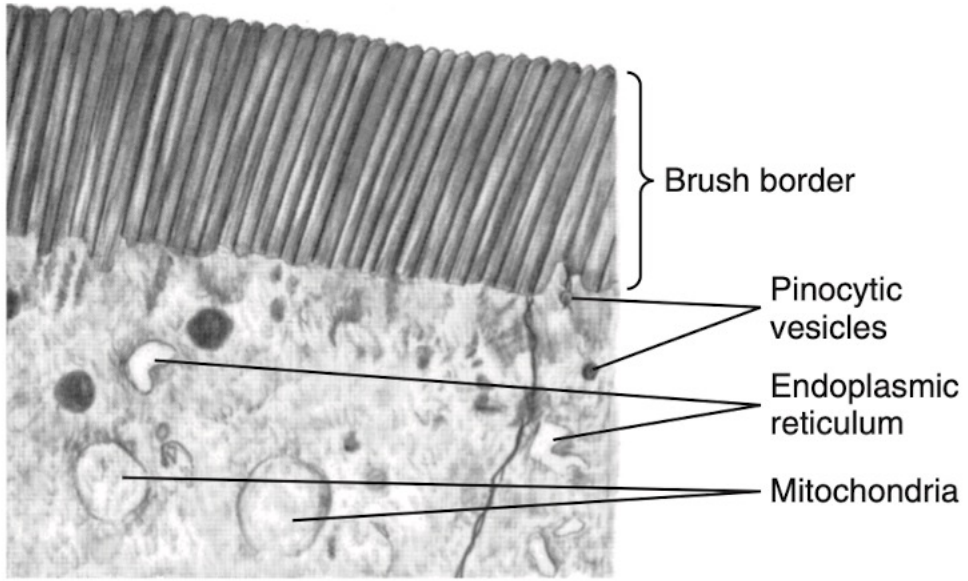
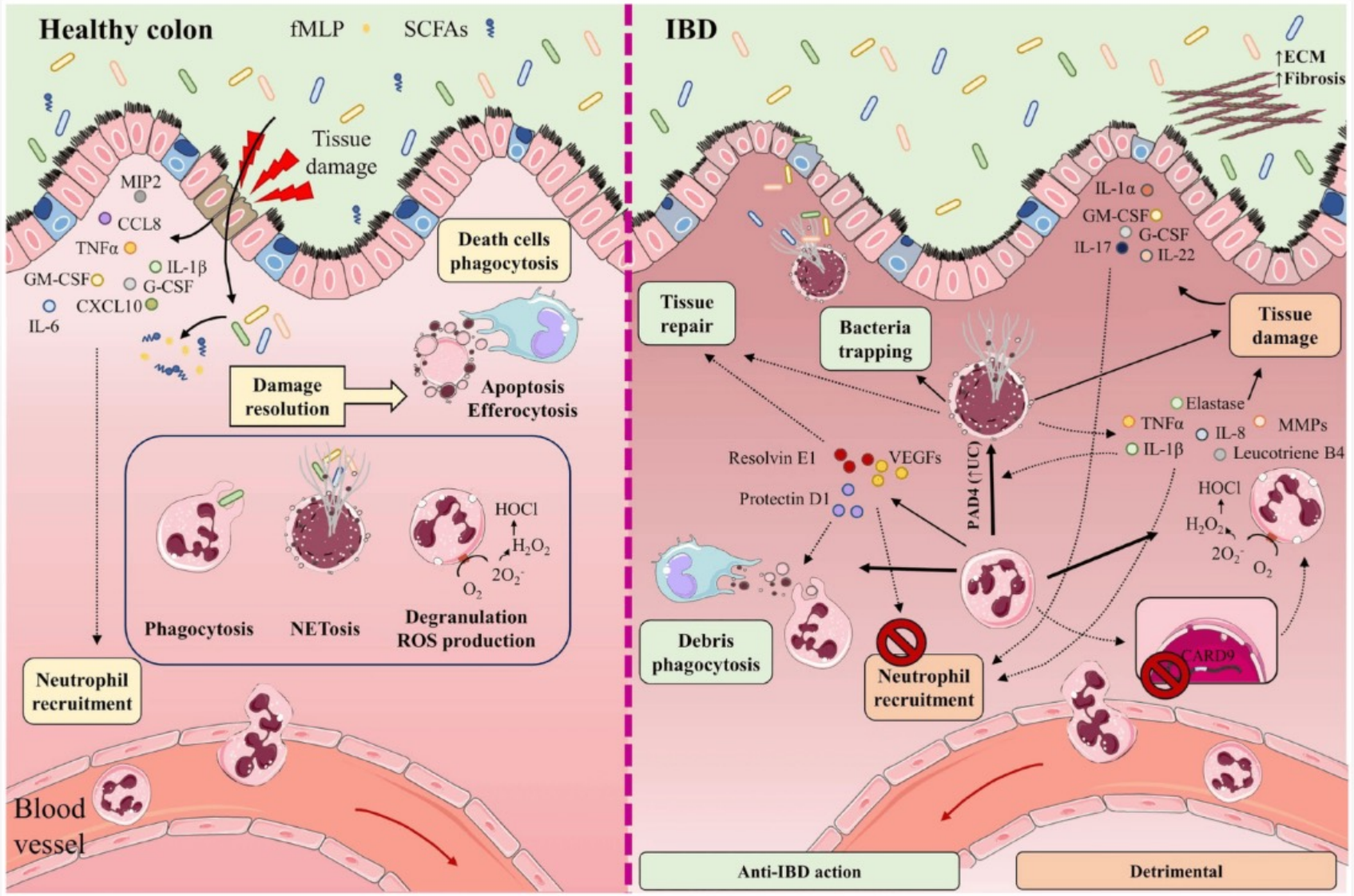


Figure 66-7. Brush border of a gastrointestinal epithelial cell, also showing absorbed pinocytic vesicles, mitochondria, and endoplasmic reticulum lying immediately beneath the brush border. *(Courtesy Dr. William Lockwood.)*

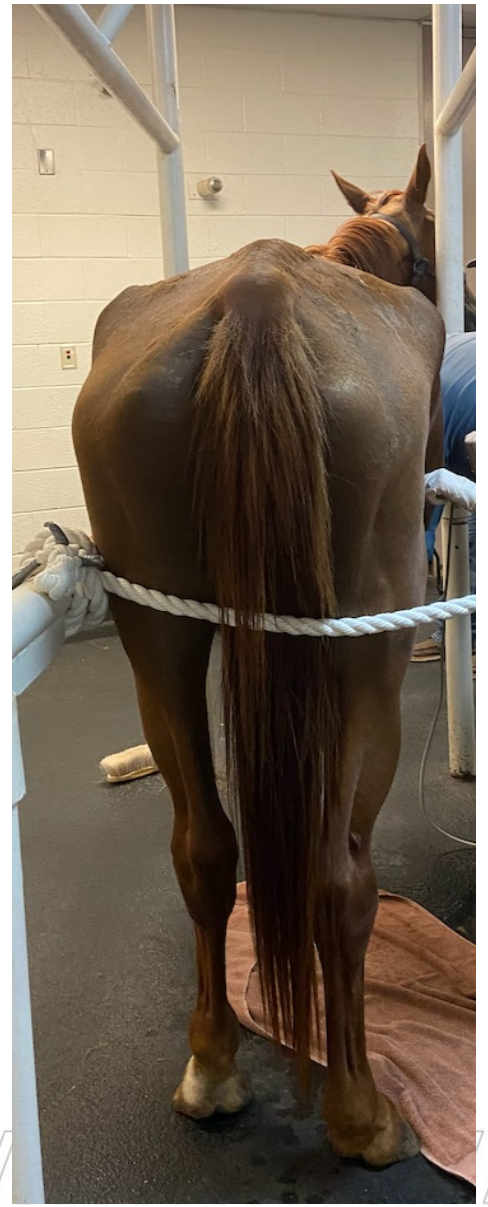
Guyton and Hall (2020)

Saez A. et al. (2023)



Clinical signs

- Weight loss
- Recurrent colic episodes
- Lethargy
- Diarrhea



CLASSIFICATION

Classification:

- Granulomatous enteritis (GE)
- Lymphocytic-plasmacytic enteritis (LPE)
- Eosinophilic enterocolitis (EE)
  - Multisystemic eosinophilic epitheliotropic disease (MEED)
  - Diffuse eosinophilic enterocolitis (DEE)
  - Idiopathic focal eosinophilic enteritis (IFEE) or colitis (IFEC)

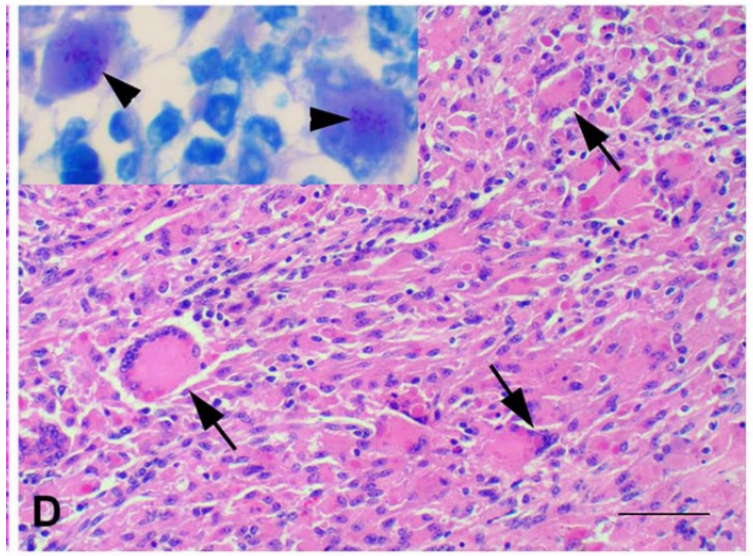
EQUINE VETERINARY EDUCATION
Equine vet. Educ. (2022) **34** (9) 493-500
doi: 10.1111/eve.13537

Review Article

Inflammatory bowel diseases in horses: What do we know?

V. Vitale

Granulomatous enteritis



Saied AA, Bryan LK, Bolin DC. (2019)

- Characterized by infiltration of macrophages, lymphocytes, epithelioid and giant cells that form granulomas or diffuse granulomatous infiltrates.
- Lesions are found in the mucosa, submucosa, and are occasionally delineated by fibroblasts.
- Marked villous atrophy, crypt hyperplasia, lymphangiectasis, edema, mucosal erosion and/or ulceration.
- The portion most severely affected is usually the ileum.
- Affected horses can be of any age, sex or breed. However, young Standardbreds have been over-represented.

Lymphoplasmacytic enterocolitis

- Characterized by infiltration of lymphocytes and plasma cell at the level of the lamina propria of the gastrointestinal tract.
- Thickened villi and villous blunting or atrophy.
- Affected horses can be of any age, sec or breed.
- Speculated that LPE may precede the development of intestinal lymphoma.

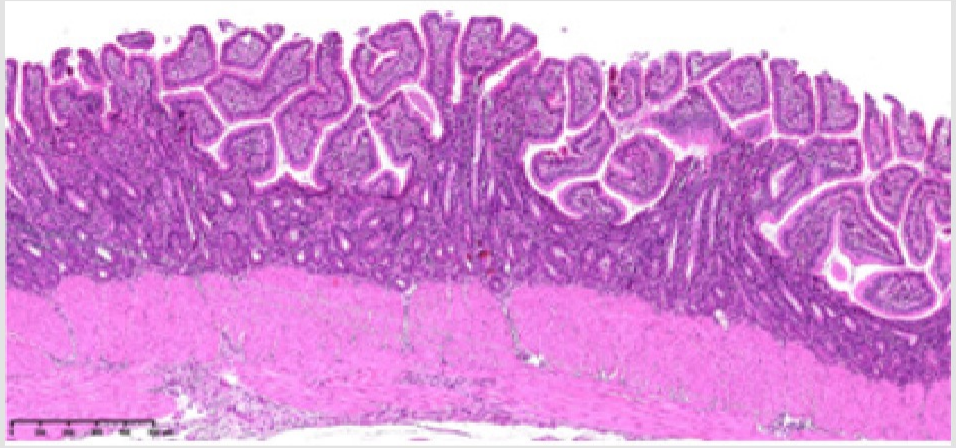


Figure 1: Representative histopathological images of the predominant lymphocytic-plasmacytic inflammatory infiltrate of the jejunum mucosa, crypt glands hyperplasia and marked villous atrophy.

Pinto P. (2021)

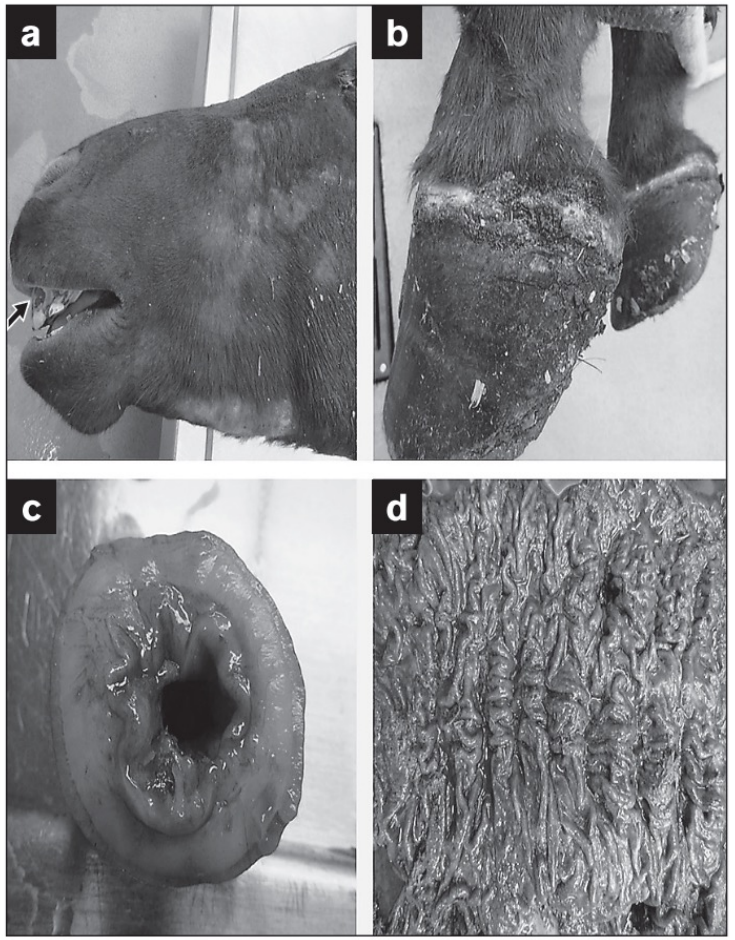
Eosinophilic enterocolitis

- Characterized by infiltration of eosinophils at the level of the intestinal mucosa.
- Gross lesions can be seen distributed intermittently or segmentally in any part of the GI tract.

- **Multisystemic eosinophilic epitheliotropic disease (MEED)**
- **Diffuse eosinophilic enterocolitis (DEE)**
- **Idiopathic focal eosinophilic enteritis or colitis (IFEE/IFEC)**

Multisystemic eosinophilic epitheliotropic disease (MEED)

- Uncommon form
- Abnormal infiltration of eosinophils and the formation of eosinophilic granulomas in the mucosa, submucosa, or parenchyma of various organs.
- Clinical findings can be variable.



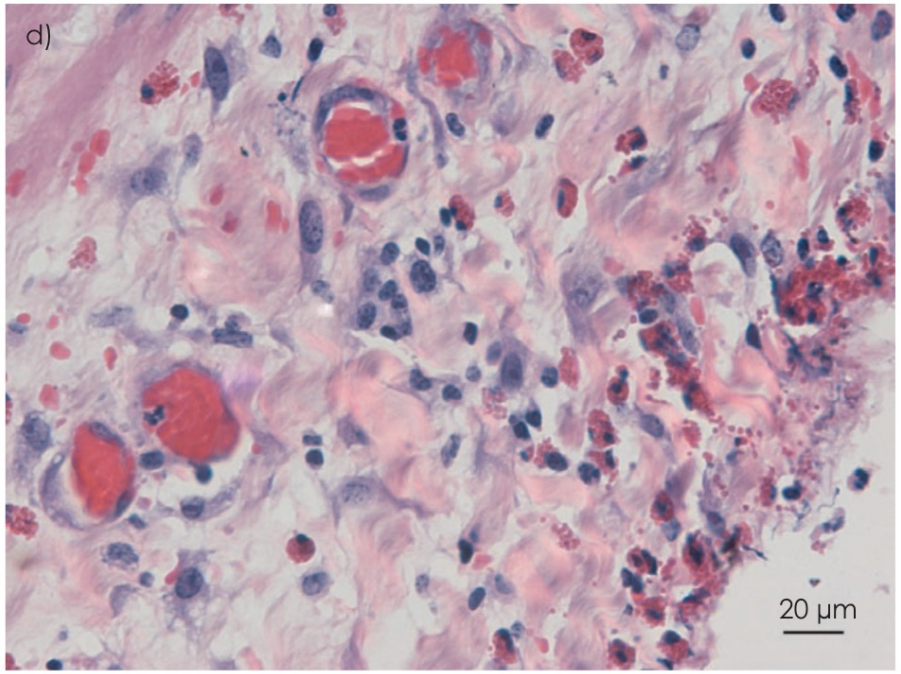
Inflammatory bowel disease characterized by multisystemic eosinophilic epitheliotropic disease (MEED) in a horse in Saskatchewan, Canada

Claudia Cruz Villagrán, Debora Vogt, Ashish Gupta, Enrique Aburto Fernández

Diffuse eosinophilic enterocolitis (DEE)

- Emerging cause of abdominal pain (colic).
- No clear cause has been identified.
- Diffuse infiltration on the GI tract mucosa, specially small intestine.

Bont M. et at. (2016)



H&E photomicrograph of serosal layer with hyperaemia and diffuse eosinophilic infiltrate.

Idiopathic focal eosinophilic enteritis or colitis (IFEE/IFEC)

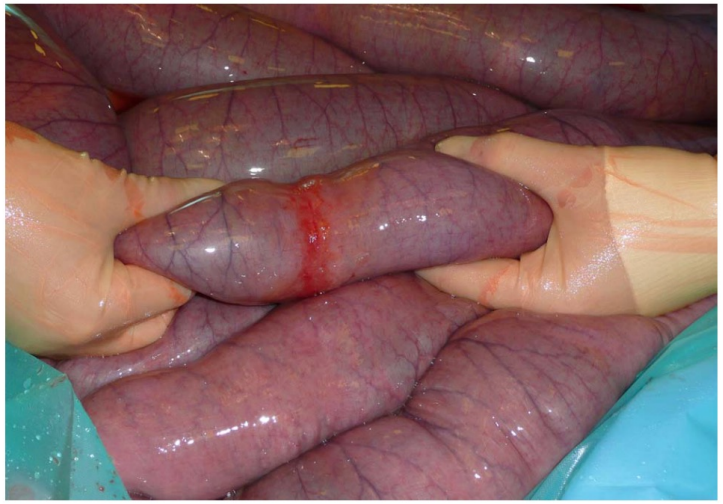


Figure 1. The typical visual appearance of an idiopathic focal eosinophilic enteritis IFEE lesion at laparotomy. The lesion is grossly hyperaemic and spans all or part of the circumference of the small intestine (small bowel). Palpably the tissues are markedly thickened at the site of the lesion and most commonly there is obstruction of ingesta proximal to the lesion(s) resulting in a simple obstruction of the bowel.

doi:10.1371/journal.pone.0112072.g001

- Emerging cause of abdominal pain (colic).
- No clear cause has been identified.
- Circumferential mural bands, this may cause constriction of the intestinal lumen.

DIAGNOSIS

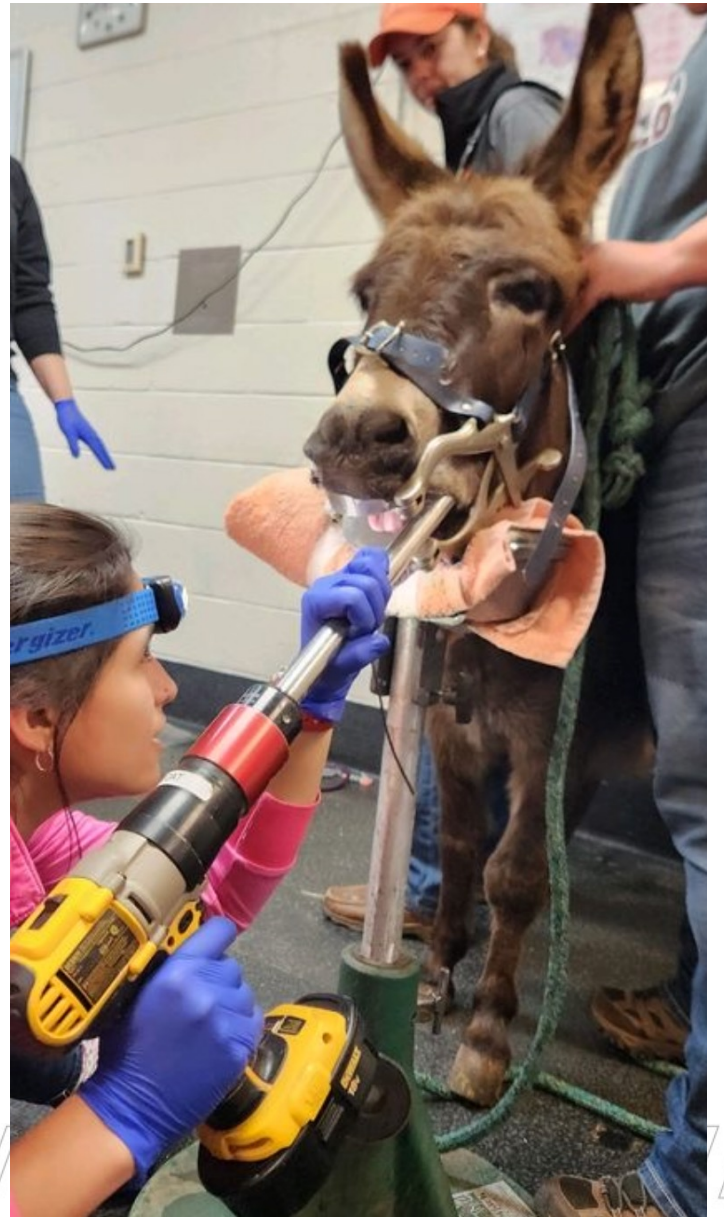
Diagnosis

History:

- Mild or recurrent colic
- Diarrhea

Physical exam:

- Evaluation of teeth
- Fecal/parasite load
- Body condition score
- Ventral or limb edema
- Skin and coat examination



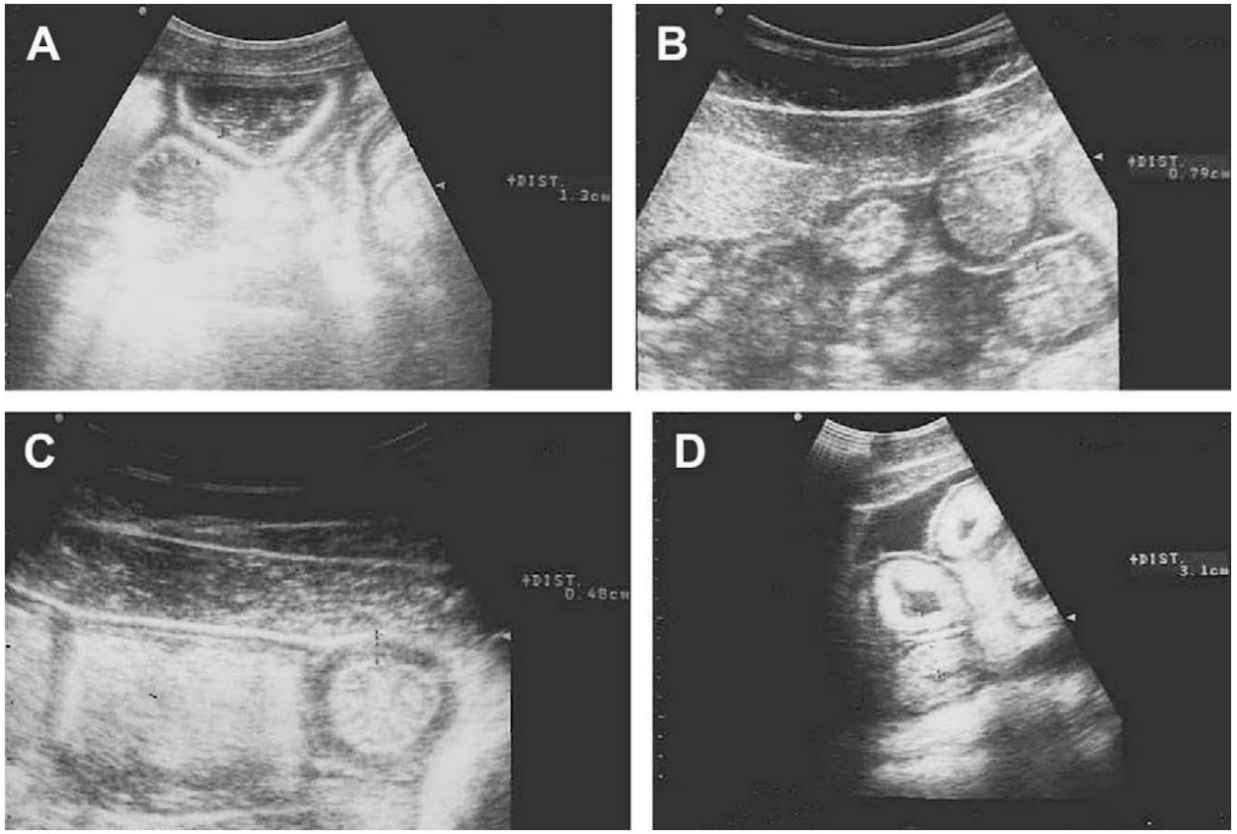
Transabdominal ultrasound:

- Thickened bowel
- Abdominal masses vs lymphadenopathy

Abdominocentesis:

- Normal transudate
- +/- Eosinophils

Kalck K. (2009)



Absorption test

- Glucose absorption test (GAT)
- D-xylose

Kalck K. (2009)

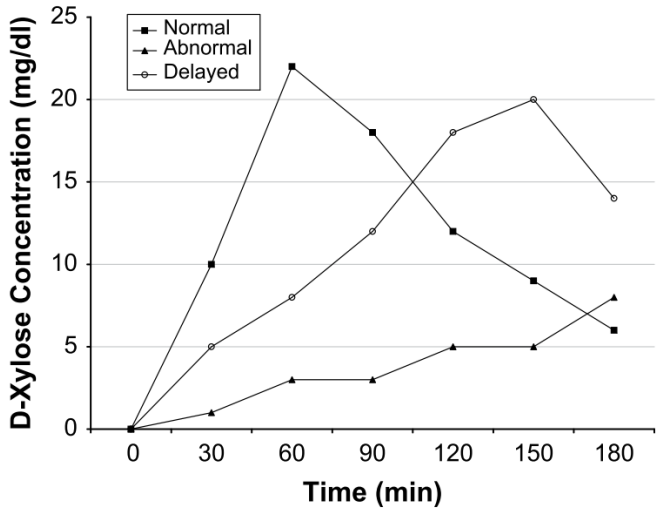


Fig. 3. D-xylose curves. Examples of possible curves from D-xylose absorption tests. The squares represent a curve of a normal horse, with peak D-xylose concentration greater than 20 mg/dL by 60 minutes. The triangles represent a flat line resulting from a horse with complete malabsorption. The open circles represent a delayed response that may occur with partial absorption in the small intestine.

Biopsy - histopathology:

- Exploratory laparotomy
- Exploratory laparoscopy
- Duodenal biopsy
- Rectal biopsy

Article

Retrospective Evaluation of the Most Frequently Observed Histological Changes in Duodenal and Rectal Mucosal Biopsies in Horses with Recurrent Colic

Natalia Siwińska [1], Agnieszka Żak-Bochenek [2,*], Marzena Paszkowska [3], Maciej Karczewski [4], Dorota Długopolska [5] and Wolfram Haider [6]

Table 1. Table showing the type of cellular infiltration in the lamina propria of the duodenum, along with its degree, number of horses, and % distribution in the studied horse population.

Infiltration Degree	Cell Type					
	Lymphocytes	Plasma Cells	Neutrophils	Eosinophils	Macrophages	Mott Cells
mild	9 (15%)	11 (18.3%)	28 (46.6%)	33 (55%)	-	-
moderate	40 (66.6%)	40 (66.6%)	5 (8.3%)	1 (1.6%)	2 (3.3%)	3 (5%)
marked	9 (15%)	8 (13.3%)	2 (3.3%)	4 (6.6%)	-	-
SUM	58 (96.6%)	59 (98.2%)	35 (58.2%)	38 (62.3%)	2 (3.3%)	3 (5%)

Note: A significant number of horses showed infiltration composed of more than one type of cell, so, although the infiltration concerned all horses from the study population, the sum is not equal to 100%.

TABLE 1: Flow chart for the diagnostic investigation of suspected IBD

	Horses presented with: Weight loss despite good appetite Chronic diarrhoea Recurrent colic		
First step	Check the diet. Exclude: Dental problems Intestinal parasites (Kalck, 2009; Metcalfe et al., 2013; Schumacher et al., 2000).	Complete physical examination (including rectal examination): Skin lesions¤ Ventral/limb oedemas¤ (Kalck, 2009; Metcalfe et al., 2013; Schumacher et al., 2000).	Blood work: Exclude infection, hepatic and renal diseases. Anaemia¤, especially in GE due to chronic disease and malabsorption of elements involved in erythropoiesis (Lindberg et al., 1985; Schumacher et al., 2000). Frequently hypoproteinaemia and hypoalbuminaemia¤ (Boshuizen et al., 2018; Kaikkonen et al., 2014; Metcalfe et al., 2013; Oliver-Espinosa, 2018) Elevated hepatic enzymes¤ in MEED, if there's liver involvement (Bosseler et al., 2013; Kalck, 2009; Lindberg et al., 1985; Schumacher et al., 2000).
Second step	Transabdominal ultrasonography: Sometimes increased thickness of small intestine¤ (Boshuizen et al., 2018; Kalck, 2009). Occasionally lymphoadenopathy¤ (Kalck, 2009).	Abdominocentesis: Usually normal transudate in IBD (Kalck, 2009; Oliver-Espinosa, 2018). It may be altered in case of peritonitis, intra-abdominal neoplasia or abscess (Edwards et al., 2000; Oliver-Espinosa, 2018).	
Third step	Absorption tests: Decreased in case of diffuse infiltrative disease of small intestine¤ (Boshuizen et al., 2018; Kaikkonen et al., 2014; Kalck, 2009; Metcalfe et al., 2013).	Histopathology of noninvasive biopsy samples (duodenal or rectal): Infiltration with inflammatory cells¤ (Lindberg et al., 1996; Metcalfe et al., 2013; Boshuizen et al., 2018). Not useful in segmental diseases (Kalck, 2009). Limitation: lack of standardisation for the interpretation (Oliver-Espinosa, 2018).	
Fourth step	Laparoscopy/Laparotomy: For collection of full-thickness intestinal samples (Kalck, 2009) May also help to exclude/confirm presence of intra-abdominal masses (Kalck, 2009; Lindberg et al., 1996; Oliver-Espinosa, 2018).		

GE, Granulomatous enteritis; MEED, Multisystemic eosinophilic epitheliotropic disease; ¤ = red flags of possible IBD

Vitale V. (2022) Inflammatory bowel disease in horses: What do we know?

Table 1. *Differential diagnoses for the main clinical symptoms of equine IBD*

Chronic/recurrent colic	Hypoproteinaemia/weight loss	Chronic diarrhoea
Alimentary lymphoma	Alimentary lymphoma	Alimentary lymphoma
Crib-biter/windsucker[1,2]	Amyloidosis	Disruption of intestinal flora
Congestive heart failure*	Congestive heart failure	Enteric bacterial infection
Dental abnormalities[1]	Dental abnormalities	*Brachyspira* spp.[8, 9]
Displacement of the colon	Enteric bacterial infection	*Salmonellosis*
Enteric bacterial infection	*Lawsonia intracellularis*	Enteric parasitic infection
Lawsonia intracellularis	*Mycobacterium avium* spp.	*Cyathostominosis*
Enteric parasitic infection	*Rhodococcus equi*	*Giardia* spp.[10]
Cyathostominosis	Enteric fungal infection	*Strongylus vulgaris*
Strongylus vulgaris	*Aspergillus fumigatus*	Hyperlipidaemia
Enterolithiasis	*Histoplasma capsulatum*	Impaction
Gas colic, intermittent	Enteric parasitic infection	Intestinal muscular hypertrophy[6]
Gastrointestinal ulceration	*Cyathostominosis*	Liver disease
Impaction	*Parascaris equorum*	NSAID toxicity/right dorsal colitis
Intestinal adhesions	External bleedings or burns	Peritonitis
Intestinal diverticulum	Gastrointestinal ulceration	Sand ingestion/accumulation
Intestinal fibrosis[3]	Grass sickness[5]	
Intestinal muscular hypertrophy[4]	Immunodeficiency	
Intussusception	Intestinal muscular hypertrophy[4, 6]	
Liver disease	Kidney disease	
Miscellaneous neoplasia	Liver disease	
Neural dysfunction/ grass sickness	Lymphatic obstruction	
NSAID toxicity/right dorsal colitis	Malnutrition	
Obstruction, intra- or extraluminal	Miscellaneous neoplasia	
Peritonitis	NSAID toxicity/right dorsal colitis	
Sand ingestion/accumulation	Pancreatic insufficiency	
Urogenital disease	Pleuritis/peritonitis	
	Pulmonary disease[7]	

Modified after: Archer (2009), Kalck (2009), Lecoq & Lavoie (2009), Mair *et al.* (2006), *Mair & Hillyer (1997), Love *et al.* (1992) and Roberts (1983)

Olofsson (2016). Immunopathological Aspects of Equine Inflammatory Bowel Disease.

TREATMENT

Treatment

- Dietary adjustments
- Endoparasites control
- Corticosteroids

Box 4
Sample dosing schedule for horse with inflammatory bowel disease

This schedule is intended only to serve as a starting point, because all horses respond differently, and the dosing schedule should be adjusted to meet each individual horse's needs.

Medication: dexamethasone 2 mg/mL

0.05 mg/kg IM daily for 3 weeks

0.03 mg/kg IM daily for 3 weeks

Re-evaluate horse clinically

0.03 mg/kg PO daily for 3 weeks

0.03 mg/kg PO every other day for 6 weeks

Abbreviations: IM, intramuscularly; PO, orally.

TABLE 2: Alternative medical treatment proposed for IBD cases

Treatment	Hypothesised/documented effect	Reference
Metronidazole	Antimicrobial and anti-inflammatory	Kalck, 2009
Hydroxyurea	Antineoplastic drug used in humans suffering from hypereosinophilia syndrome; suggested for the treatment of MEED in horses	Bosseler et al., 2013
Sulfasalazine	Colon-specific prodrug used for the treatment of Crohn's disease in humans; reported to be successful in one horse with chronic diarrhoea without a definitive diagnosis	Valle et al., 2013
Cyclosporine, Azathioprine, Chlorambucil, Mycophenolate	Immune suppressive drugs used in dogs with IBD; not studied in horses	Craven and Washabau, 2019
Probiotics	Applied for a variety of GIT disorders in humans and small animals; inconsistent results in horses	Jergens and Simpson, 2012; Schoster et al., 2014; Grześkowiak et al., 2015; Schoster et al., 2016; Schoster, 2018; Kim et al., 2019
Polyunsaturated fatty acids (PUFA) supplementations	Used in humans and dogs with IBD to decrease the production of arachidonic acid-derived pro-inflammatory eicosanoids in favour of anti-inflammatory eicosanoids; not studied in horses	Calder, 2013; Kalenyak et al., 2019
Faecal microbioma transplant (FMT)	Approved for the use only in humans with *Clostridium difficile* infection; recently gained interest in small animals, ruminants and horses	Cammarota et al., 2014; DePeters and George, 2014; Julliand and Grimm, 2016; Costa and Weese, 2018; Mullen et al., 2018; Pereira et al., 2018; Murcia, 2019

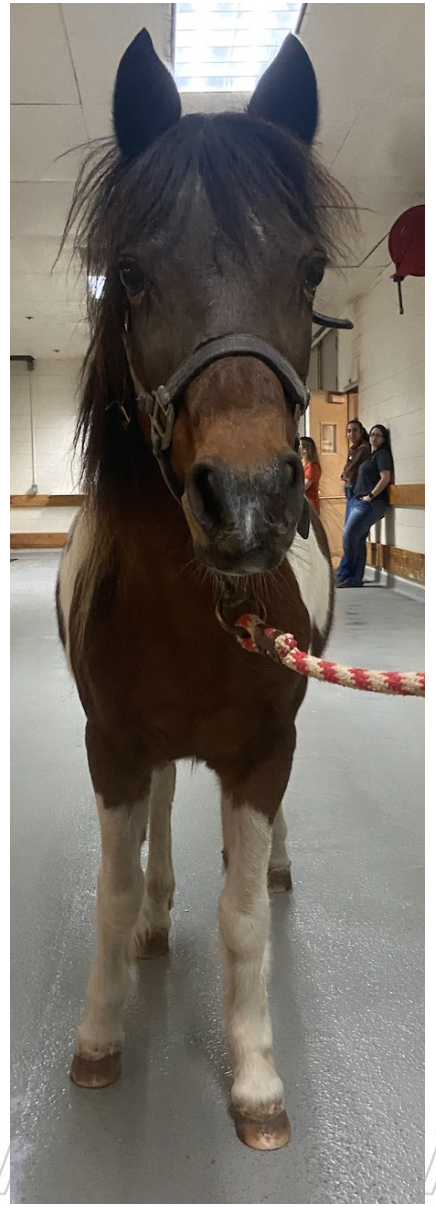
GIT, Gastrointestinal tract; IBD, Inflammatory bowel disease; MEED, Multisystemic eosinophilic epitheliotropic disease

PROGNOSIS

Prognosis

- The overall prognosis for the disease is reported to be guarded to poor.
- If the disease is focal, surgical resection of the affected bowel can be curative.
- Patients may require lifelong , low-dose treatment with corticosteroids.

CLINICAL CASE



Signalment

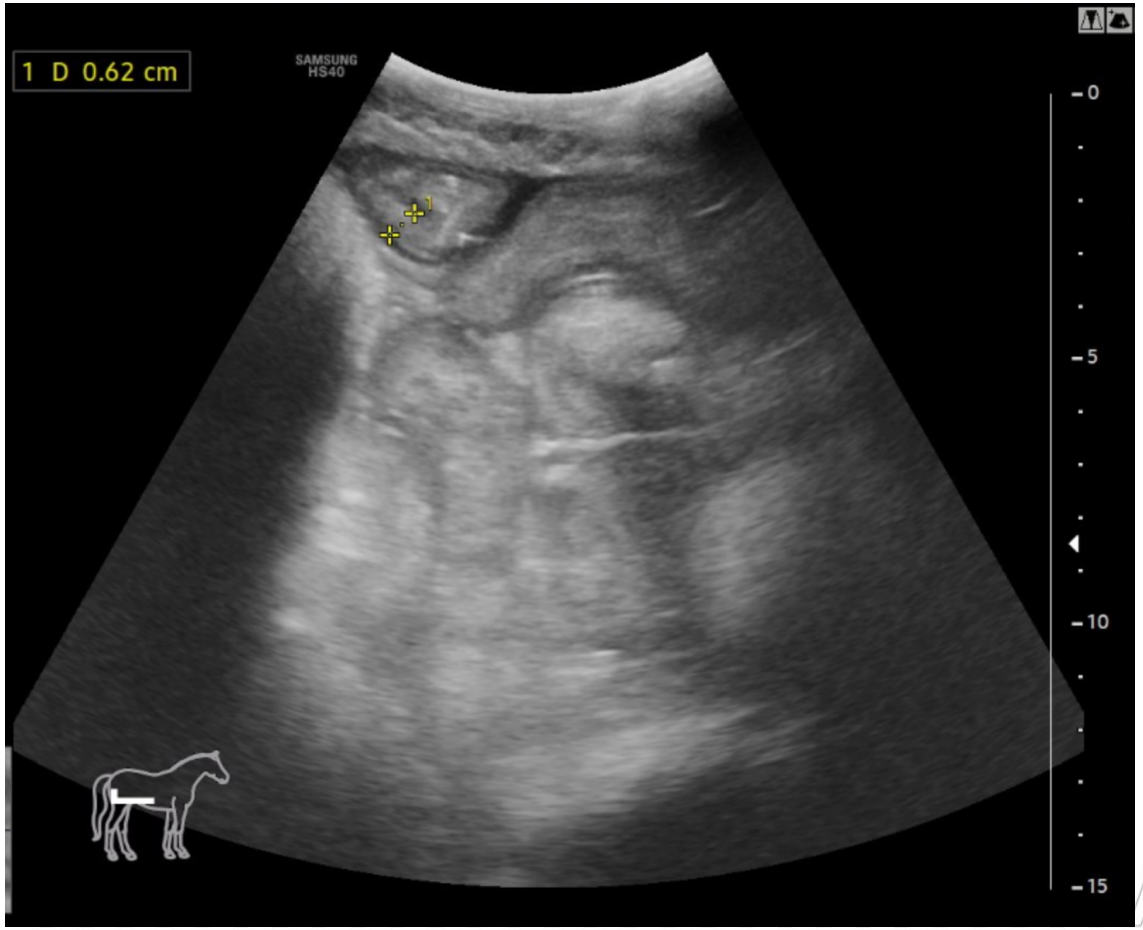
- 15 years old Shetland Pony
- Colic signs started ~ 15 hours before presentation. During that afternoon, Pony was evaluated by her rdvm and she was given Flunixin meglumine (1.1 mg/kg)
- However, signs of colic came back during the night.
- During the morning, she was given another dose of Flunixin meglumine.
- The patient was brought to the clinic that morning.

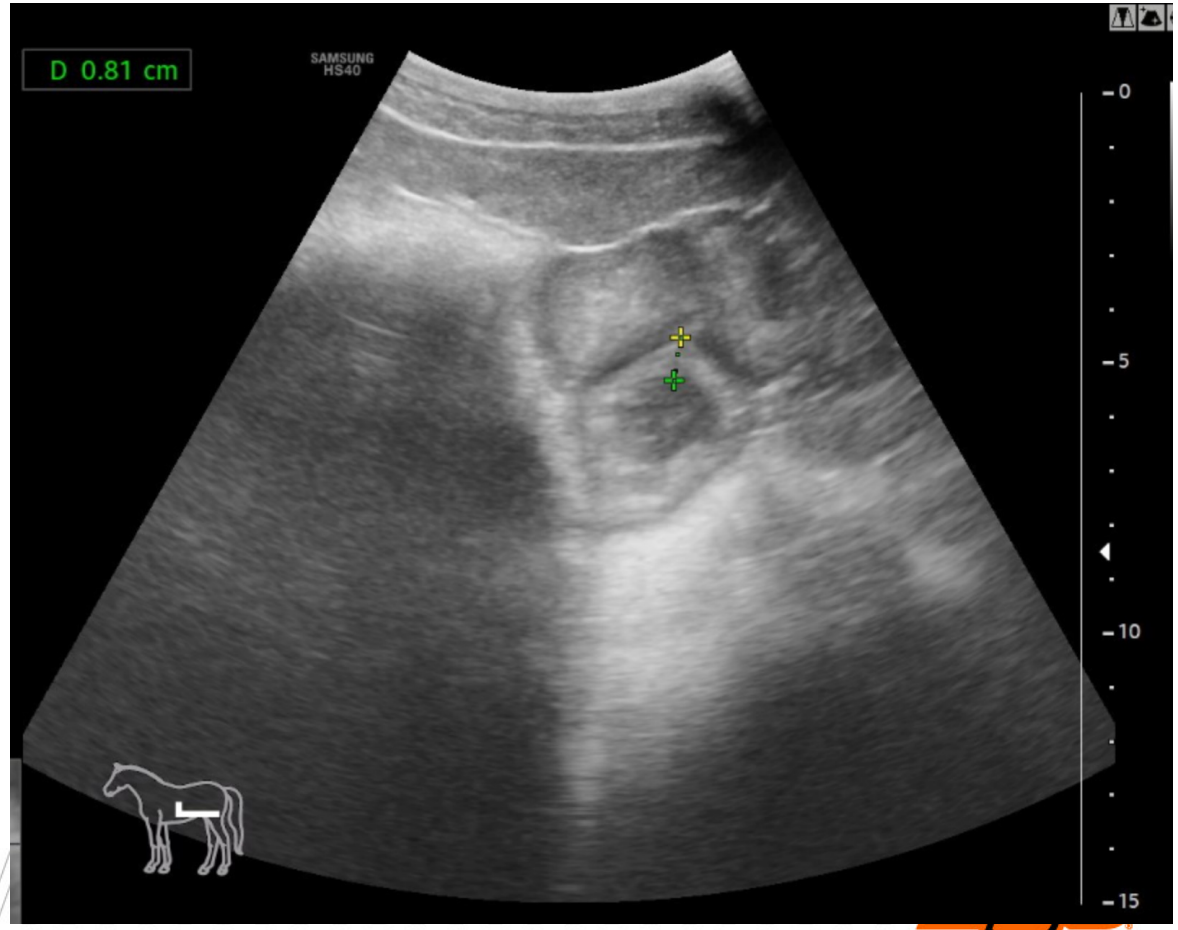
Bloodwork

Test	Results	Unit	Lowest Value	Highest Value
WBC	10.0	10^3/µL	5.1	12.5
RBC	9.1	10^6/µL	6.5	11.6
HGB	15.0	g/dL	11.0	17.0
HCT	45	%	32	47
MCV	49	fL	34	58
MCH	16.5	pg	12.0	19.7
MCHC	34	g/dL	31	38
Platelet Count	191	10^3/µL	100	400
Platelet Estimate	Adequate			
Neutrophils	67	%	30	65
Bands	0	%	0	1
Lymphocytes	24	%	25	70
Monocytes	1	%	1	7
Eosinophils	8	%	0	11
Basophils	0	%	0	3
Absolute Neutrophils	6700	/µL	2700	7000
Absolute Lymphocytes	2400	/µL	1500	5500
Absolute Monocytes	100	/µL	0	800
Absolute Eosinophils	800	/µL	0	925
Absolute Basophils	0	/µL	0	170

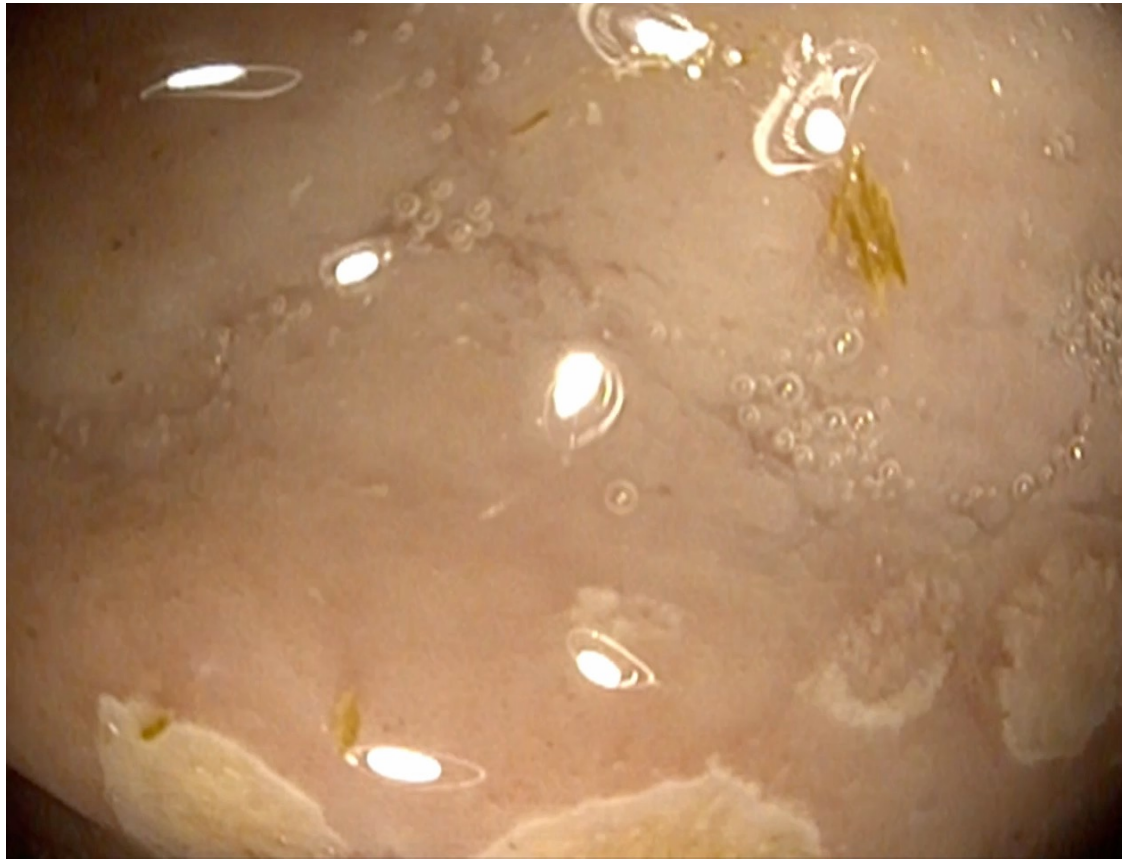
Test	Results	Unit	Lowest Value	Highest Value
TOTAL PROTEIN	6.7	g/dL	5.6	8.0
ALBUMIN	3.0	g/dL	2.2	3.9
GLOBULIN	3.7	g/dL	2.2	5.6
A/G RATIO	0.8		0.5	2.4
AST (SGOT)	246	IU/L	148	420
Alk Phosphatase	419	IU/L	50	325
GGT	12	IU/L	2	36
Total Bilirubin	1.7	mg/dL	0.4	3.4
BUN	24	mg/dL	8	26
Creatinine	1.0	mg/dL	1.0	2.0
BUN/CREAT RATIO	24		5	21
PHOSPHORUS	4.0	mg/dL	2.0	5.1
Glucose	108	mg/dL	68	120
CALCIUM	12.3	mg/dL	10.8	13.5
SODIUM	136	mEq/L	132	146
POTASSIUM	3.6	mEq/L	2.4	4.7
NA/K RATIO	38		24	58
CHLORIDE	104	mEq/L	95	110
CHOLESTEROL	109	mg/dL	70	160
TRIGLYCERIDE	229	mg/dL	14	65
CPK	718	IU/L	45	360
LDH	611	IU/L	81	390

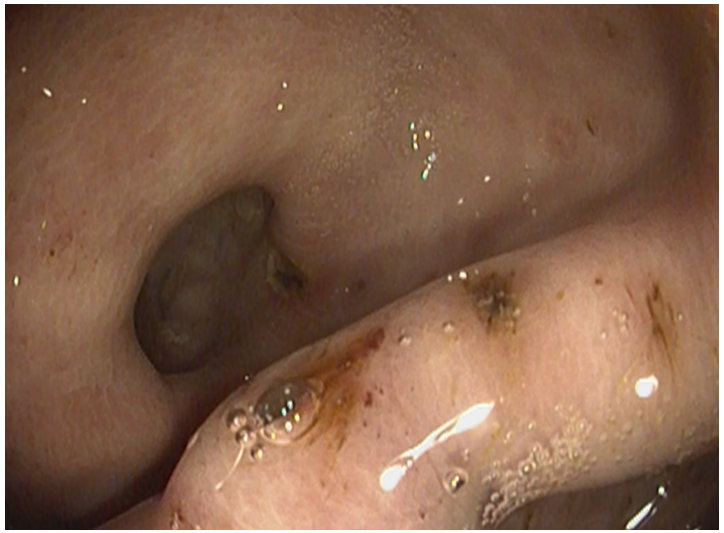
Abdominal ultrasound

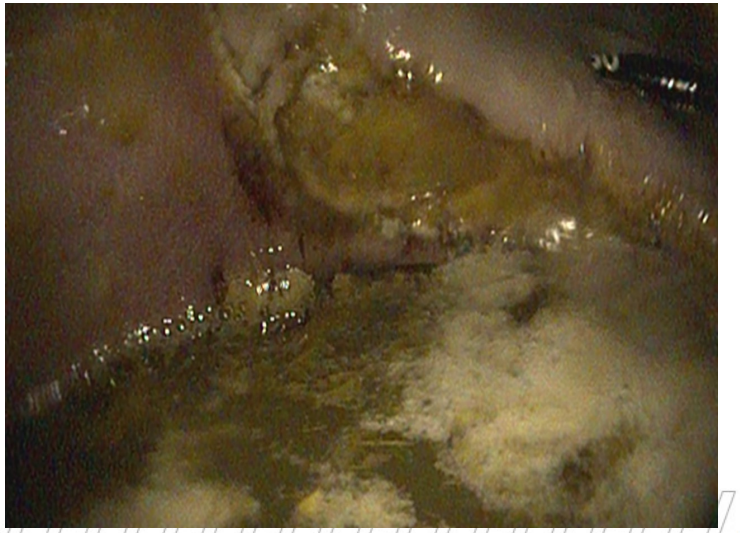




Gastroscopy







Histopathology

Diagnosis

(11.17.2023)

Duodenum: Moderate, chronic, diffuse eosinophilic duodenitis with regional ulceration and marked neutrophilic infiltrate.

Comments

(11.17.2023)

Two small tissue pieces are examined, both of which have mild to moderate crush artifact. In one section, the lamina propria is diffusely infiltrated by increased numbers of eosinophils, suggesting a possible hypersensitivity. In the other section, the mucosa is ulcerated and replaced by numerous viable and degenerate neutrophils; this region presumably reflects the endoscopically described plaques. There is no evidence of a neoplasm or infectious agent in the examined sections. Unfortunately a cause remains unclear. This is the final report. Please call with any questions.

Treatment

- Initial treatment – Prednisolone
  - 1.5 mg/kg for 5 days orally once a day
  - 0.75 mg/kg orally once a day until recheck (~ 3 weeks)

- After recheck – Prednisolone
  - 0.75 mg/kg orally once a day for 7 days
  - 0.5 mg/kg orally once a day for 7 days
  - 0.25 mg/kg orally once a day for 7 days
  - 0.25 mg/kg orally every other day for 7 days

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Large animal Internal Medicine

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