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## Infiltrative Intestinal Disease in Horses: A Review

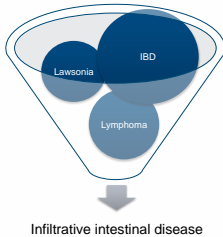
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 School of Veterinary Medicine  
 College of Medical, Veterinary and Life Sciences  
 University of Glasgow  
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Overview IBD Lawsonia Lymphosarcoma

### Overview




Infiltrative intestinal disease

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### What is IBD?

- A group of infiltrative bowel diseases that produce similar clinical signs to one another (primarily chronic weight loss) (T Mair 2002)
- Aetiology mostly unknown
- Histopathology normally required to differentiate




T Mair (2002) Chronic weight loss. In: Manual of Equine Gastroenterology, WB Saunders Ltd

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### Clinical signs of IBD

- CHRONIC WEIGHT LOSS
- Diarrhoea
- Recurrent colic
- Appetite- ↑ ↔ ↓
- Depression/lethargy
- Oedema
- Pyrexia
- Skin lesions



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### The IBD Complex

Granulomatous enteritis	Lymphocytic plasmacytic enterocolitis
Inflammatory Bowel Disease (IBD)	
Multisystemic eosinophilic epitheliotropic disease (MEED)	Idiopathic focal eosinophilic enteritis (IFEE)

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### IBD- The boundaries are not well defined

Granulomatous enteritis	Lymphocytic plasmacytic enterocolitis
Inflammatory Bowel Disease (IBD)	
Systemic manifestation of eosinophilic enterocolitis??	Reaction pattern rather than specific diagnosis?

Eosinophilic enterocolitis??

Lymphoma?

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### Clinical signs

	Weight loss	Diarrhoea	Colic	Dermatitis
Granulomatous Enteritis	98%	30%	11%	11%
Lymphocytic-plasmacytic enteritis	95%	35%	20%	0%
MEED	100%	63%	4%	63%
Eosinophilic enterocolitis	7%	0%	100%	0%

Schumacher, J., Edwards, J.F., Cohen, N.D., 2000. Chronic idiopathic inflammatory bowel diseases of the horse. J. Vet. Intern. Med. 14, 258-265.

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### Diagnosis of IBD

Approach to chronic weight loss:

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### Clinical pathology

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### Clinical pathology in IBD

	Low serum protein	Low serum albumin	Anaemia	High GGT
Granulomatous Enteritis	64%	91%	87%	0%
Lymphocytic-plasmacytic enteritis	35%	55%	10%	0%
MEED	58%	79%	10%	73%
Eosinophilic enterocolitis	14%	14%	0%	0%

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### Clinical examination

- Peripheral/ dependent oedema
- Rectal
  - enlarged mesenteric lymph nodes
  - thickened bowel wall

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### Ancillary diagnostic tests

	Rectal biopsy diagnostic	Malabsorption indicated by OGTT
Granulomatous Enteritis	50%	90%
Lymphocytic-plasmacytic enteritis		82%
MEED	50%	38%
Eosinophilic enterocolitis		Not determined

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### Ancillary diagnostic tests

- Abdominocentesis
  - Usually normal
  - Occasionally eosinophilia/ neoplastic cells
  - Elevated myeloperoxidase (Gruelke et al 2008)
- Rectal biopsy-
  - 50% cases pathological change (Lindberg et al 1996)
- Oral glucose absorption test (OGTT)

Gruelke, S., Franck, T., Gangl, M., Péters, F., Saliccia, A., Deby-Dupont, G., Serteyn, D., 2008. Myeloperoxidase assay in plasma and peritoneal fluid of horses with gastrointestinal disease. Can. J. Vet. Res. 72, 37.  
Lindberg, R., Nygren, A., Persson, S.G.B., 1996. Rectal biopsy diagnosis in horses with clinical signs of intestinal disorders: a retrospective study of 116 cases. Equine Vet. J. 28, 275-284.

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### OGTT

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### Exploratory laparotomy

- Allows full thickness small intestinal wall biopsies
- At least 3 biopsies, including mesenteric lymph node if possible
- Laparoscopic intestinal biopsy (Schambourg and Marcoux 2006)

• *Are these horses good candidates for surgery (hypoalbuminaemia, catabolic state....?)*

Schambourg, M.M., Marcoux, M., 2006. Laparoscopic Intestinal Exploration and Full-Thickness Intestinal Biopsy in Standing Horses: A Pilot Study. Vet. Surg. 35, 689-696.

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### Specific diagnosis in IBD

Type of cellular infiltrate and degree of inflammation

↓

Specific diagnosis

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### The IBD Complex

Granulomatous enteritis Lymphocytes, macrophages & plasma cells	Lymphocytic plasmacytic enterocolitis Lymphocytes and plasma cells
Multisystemic eosinophilic enteropathy Eosinophils and lymphocytes	Idiopathic focal eosinophilic enteritis Eosinophils and lymphocytes

Inflammatory Bowel Disease (IBD)

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Inflammatory Bowel Disease (IBD)

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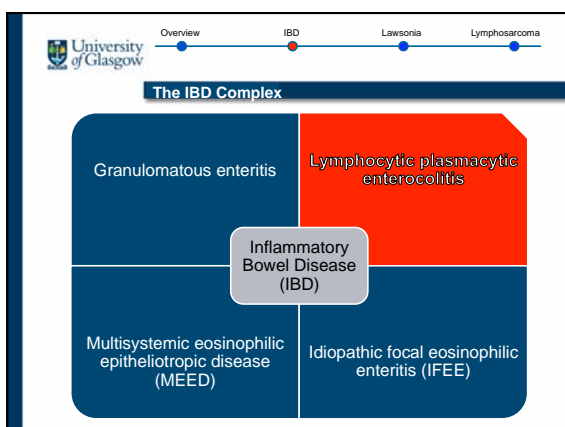
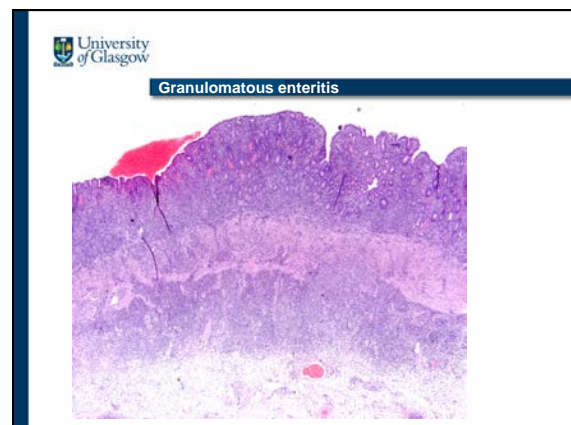
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### Granulomatous enteritis

- First reported in 1974
- Histologically similar to Crohn's disease in humans
- Majority (75%) < 4 years old (Schumacher et al 2000)
- Macrophage aggregation and villous atrophy
- Aetiopathogenesis unknown
- Surgical resection an option

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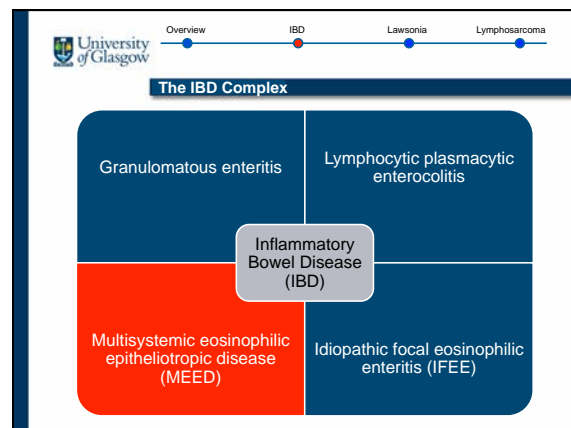
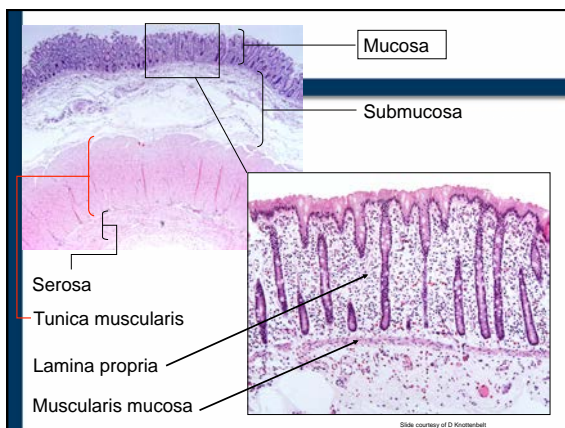
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### Lymphocytic plasmacytic enterocolitis

- Common in small animals
- Infiltration of lamina propria with lymphocytes and plasma cells- no granulomatous change
- RARE in equines
- Association with lymphosarcoma in other species- not reported in equines.



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**Multisystemic eosinophilic epitheliotropic disease (MEED)**

- Unlike other forms of IBD- affects multiple organ systems (GI, skin, liver, pancreas)
- Intestinal changes: Eosinophilic enterocolitis
- Dermatological changes: Exfoliative dermatitis
- Unknown aetiology
- By definition for a diagnosis of MEED to be made- multiple organs need to be involved.

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**Multisystemic eosinophilic epitheliotropic disease**




Photograph courtesy of Dr. Verrynken

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**Multisystemic eosinophilic epitheliotropic disease**



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**Multisystemic eosinophilic epitheliotropic disease**



Photograph courtesy of Dr. Verrynken

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**Multisystemic eosinophilic epitheliotropic disease**



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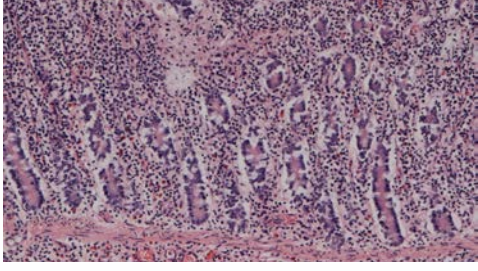
**Gross Pathology- MEED**

- Thickening of small and large intestinal walls
- Involvement of ileocaecal valve
- Ulceration of colonic mucosa
- Mesenteric lymphadenopathy

Reference: Bosseler, L., Verrynken, K., Bauwens, C., de Vries, C., Deprez, P., Ducatelle, R., Vandenaabeele, S., 2013. Equine multisystemic eosinophilic epitheliotropic disease: A case report and review of literature. N. Z. Vet. J. 61, 177–182.

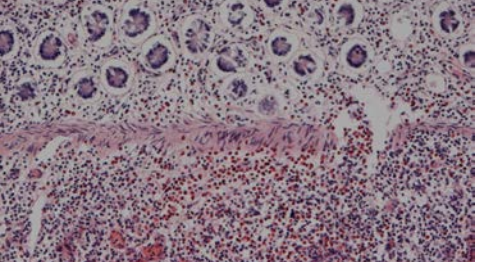
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**Eosinophilic infiltration**



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**Enlargement of ileal Peyer's patches**



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**The IBD Complex**

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**Idiopathic focal eosinophilic enteritis (IFEE)**

- Rare
- Aetiology unknown
- Similar histologically to eosinophilic enterocolitis but differing clinical presentation
- Present with acute colic
- Distended small intestine with segmental or focal circumferential infiltration with eosinophils

Archer, D.C., Barrie Edwards, G., Kelly, D.F., French, N.P., Proudman, C.J., 2006. Obstruction of equine small intestine associated with focal idiopathic eosinophilic enteritis: An emerging disease? Vet. J. 171, 504–512.

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**Idiopathic focal eosinophilic enteritis (IFEE)**



Photographs courtesy of D. Kusterbaal

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**Idiopathic focal eosinophilic enteritis (IFEE)**



Photographs courtesy of D. Kusterbaal

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### Proliferative enteropathy

- *Lawsonia intracellularis*
- Obligate intracellular anaerobic Gram negative organism
- Inhabits the enterocyte cytoplasm
- An emerging disease of increasing prevalence

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### Aetiopathogenesis

- *Lawsonia intracellularis*
- Also causes disease in pigs
- Has been identified in dog, cat and rodent faeces
- ??Infection due to ingestion of faeces from another infected species??
- Infection with equine strain of *L. intracellularis* results in more severe disease. (Vannucci et al 2012)





Vannucci, F.A., Pusterla, N., Mapes, S.M., Kelley, M., Gebhart, C.J., 2012. Evidence of host adaptation in *Lawsonia intracellularis* infections. *J. Equine Vet. Sci.* 32, 4.

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### Pathology

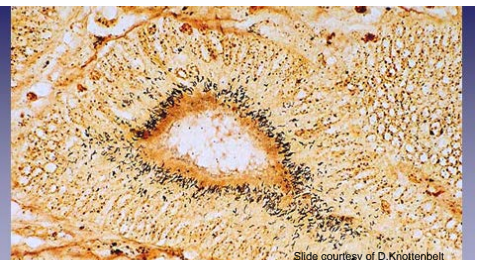
- Gross thickening of ileal mucosa ± muscularis
- Intracellular bacteria within apical cytoplasm of crypt epithelial cells
- Warthin-Starry silver stain
- Immunohistochemistry gold standard for diagnosis (Pusterla and Gebhart 2013)



Pusterla, N., Gebhart, C.J., 2013. Equine proliferative enteropathy - a review of recent developments: Equine proliferative enteropathy - a review of recent developments. *Equine Vet. J.* 45, 403-409.

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### Histopathology




Slide courtesy of D.Kröttenbelt

Warthin- Starry silver stain- large number of black organisms.

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### Epidemiology

- Typically affects foals/weanlings (4-7months old)
- Now reported in adult horses (Shimizu et al 2010)
- Worldwide distribution




Shimizu, C., Shibahara, T., Takai, S., Kasuya, K., Chikuba, T., Murakoshi, N., Kobayashi, H., Kubo, M., 2010. *Lawsonia intracellularis* and Virulent *Rhodococcus equi* Infection in a Thoroughbred Colt. *J. Comp. Pathol.* 143, 303-308.

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### Clinical findings

- Often non specific
- Weight loss
- Oedema
- Colic
- Anorexia
- Hypoalbuminaemia ± leukocytosis/ neutropaenia






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### Abdominal ultrasonography

- Thickened small intestinal walls
- Non-specific finding!
- Normal wall thickness  $0.16 \pm 0.05\text{cm}$



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### Diagnosis

- Combination of both molecular and serological techniques recommended (Pusterla and Gebhart 2013)
- Maximises high specificity but variable sensitivity of PCR and ELISA
- Comparative study has shown good agreement between serological methods (Gebhart et al 2012)

Gebhart, C.J et al 2012. Comparative study of serology assays for equine proliferative enteropathy., in: American Association of Equine Practitioners. Anaheim, California, pp. 502–503.  
Pusterla, N., Gebhart, C.J., 2013. Equine proliferative enteropathy - a review of recent developments. Equine proliferative enteropathy - a review of recent developments. Equine Vet. J. 45, 403–409.

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### Treatment

- Lipophilic or amphoteric antibiotics essential
  - Intracellular nature of organism
- Rifampin + erythromycin estolate
  - Prolonged
  - Similar regimen for treatment of R equi infections
- Note: Rifampin can be used on its own BUT:
  - Resistance develops rapidly
  - Treatment for human TB – should we be restricting it's use?
- Erythromycin not ideal
  - prokinetic!
  - side effects!
    - Diarrhoea / hyperthermia / clostridial enteritis
- Metronidazole
  - 10-15 mg/kg q 8-12h PO

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### Treatment –other options

- Azithromycin (± Rifampin)**
  - Azithromycin**
    - 10 mg/kg PO q 24h for 5 days
    - Then 10 mg/kg q 48h
  - High / persistent intracellular concentrations
- Oxytetracycline 6.6mg/kg IV q12hrs for 7 days then doxycycline 10mg/kg PO q 12hrs for 2 weeks

Reference: Professor Derek Knottenbelt

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### Outcome

- Survival of 53/57 horses in one study
- Survivor yearlings sold for average of 68% less than half siblings

Frazer, M.L., 2008. *Lawsonia intracellularis* Infection in Horses: 2005-2007. J. Vet. Intern. Med. 22, 1243–1248.

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### Prevention

- Test herdmates of affected animals
- Vaccination.....?
- No licensed equine vaccine
- BUT the rectal administration of the porcine vaccine has been described in horses and resulted in protection..... Very small numbers

Pusterla, N., Vannucci, F.A., Mapes, S.M., Nogradi, N., Collier, J.R., Hill, J.A., DiFrancesco, M., White, A.M., Akana, N.K., Simonek, G., 2012. Efficacy of an avirulent live vaccine against *Lawsonia intracellularis* in the prevention of proliferative enteropathy in experimentally infected weanling foals. Am. J. Vet. Res. 73, 741–746.

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### Alimentary lymphosarcoma

- Finally....
- Alimentary lymphosarcoma is an important cause of infiltrative intestinal disease but will be covered in detail in Professor Knottenbelt's lecture on intestinal neoplasia
- Lymphocytic-plasmacytic enteritis may be an early stage of this condition