Infiltrative Intestinal Disease in Horses: A Review
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Overview
Infiltrative intestinal disease

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


Clinical signs of IBD
• CHRONIC WEIGHT LOSS
• Diarrhoea
• Recurrent colic
• Appetite–
• Depression/lethargy
• Oedema
• Pyrexia
• Skin lesions

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

IBD: The boundaries are not well defined
Granulomatous enteritis
Lymphocytic plasmacytic enterocolitis
Inflammatory Bowel Disease (IBD)
Systemic manifestation of eosinophilic enterocolitis??
Eosinophilic enterocolitis??
Reaktion pattern rather than specific diagnosis??
Clinical signs

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Diagnosis of IBD

Approach to chronic weight loss:

- History
- Nutrition
- Other factors
- Clinical exam
- Clinical pathology
- Peritoneal fluid analysis
- Other diagnostics

Clinical pathology

- Hypoproteinemia
- Neutrophilia
- Anaemia
- Hyperfibrinogenemia

Clinical examination

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

Clinical pathology in IBD

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<tr>
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Ancillary diagnostic tests

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<th>Rectal biopsy diagnostic</th>
<th>Malabsorption indicated by OGTT</th>
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<td>Granulomatous Enteritis</td>
<td>59%</td>
<td>90%</td>
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<td>82%</td>
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<tr>
<td>MEED</td>
<td>50%</td>
<td>38%</td>
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Ancillary diagnostic tests

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

OGTT


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…?)


The IBD Complex

Granulomatous enteritis

Lymphocytic plasmacytic enterocolitis

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Idiopathic focal eosinophilic enteritis (IFEE)
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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
- Aetiology and pathogenesis unknown
- Surgical resection an option

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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.

Gross Pathology: MEED

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

Eosinophilic infiltration

Overview
IBD
Lawsonia
Lymphosarcoma

Enlargement of ileal Peyer’s patches

Overview
IBD
Lawsonia
Lymphosarcoma

The IBD Complex

Granulomatous enteritis
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Idiopathic focal eosinophilic enteritis (IFEE)

Photographs courtesy of D. Knottenbelt
Proliferative enteropathy

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

**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)

**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)

**Epidemiology**

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

**Clinical findings**

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

**References**

Abdominal ultrasonography

- Thickened small intestinal walls
- Non-specific finding!
- Normal wall thickness 0.16± 0.05cm

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)

Overview

- IBD
- Lawsonia
- Lymphosarcoma

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 its use?
- Erythromycin not ideal
  - prokinetic!
  - side effects!
- Metronidazole
  - 10-15 mg/kg q 8-12h PO

Reference: Professor Derek Knottenbelt

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

Outcome

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

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

Reference:

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.