Crohn’s Disease

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What is Crohn’s Disease? (1)

- Chronic inflammation of gastrointestinal (GI) tract due to:
  - Imbalance between inflammatory mediators
  - Genetics and environmental factors

- Symptoms:
  - Rectal bleeding
  - Abdominal Pain
  - Diarrhea, nausea and vomiting

Image from: http://emedicine.medscape.com/article/172940-overview
Prevalence/Epidemiology of Disease (1)

- Epidemiology
  - Adults = 201/100,000 adults
  - Children = 43/100,000

- Increased rates in:
  - Upper socioeconomic classes
  - Influenced by increased access to health care
  - European Jewish population

Mechanism of Disease (2)

- Chronic inflammation from T-cell activation leads to tissue injury in GI tract
  - Activation of type 1 T-helper (Th1) cells from defective regulation

- Activity of ulceration of superficial mucosa
  - Encourages invasion of deep mucosal layers by inflammatory cells

Image from: http://emedicine.medscape.com/article/172940-overview#a3
Risk Factors (3-5)

- Family history
- Environment
- Measles virus
- Breastfeeding
Exacerbating Factors (6-9)

- Intercurrent infections
  - Upper respiratory tract and enteric infections
- Smoking
- Stress
  - Controversial but anecdotal evidence
- Oral contraceptives
  - Preliminary evidence
Medications
What is Prednisone? (10-13)

- Glucocorticoid receptor agonist
- Prevent digestive inflammation

Image from: http://www.millersurgery.co.uk/conditions/crohns-disease-and-colitis/
Mechanism of Action (14,15)

Inflammatory cytokines (ex. TNFα, NDKB) → Prednisone → Transcription of proinflammatory genes
Effectiveness of Prednisone - Wild et al. (16)

Decreased L:M ratios by 50% = improved intestinal permeability

Decreased TNFα levels in non-relapsed individuals

Side effects: Immunosuppressant Effect (17)

- Typically:
  - Pro-inflammatory cytokines
  - Vasodilation
  - Leukocyte migration to infection site

- Prednisone side effects:
  - High blood pressure
  - Increased susceptibility to infection
What is Infliximab/Remicade? (18)

- Monoclonal antibody that works against TNF-α
- Apoptosis of T-lymphocytes and monocytes
- Down regulation of other pro inflammatory cytokines

Decreases inflammation AND induces apoptosis

Image from: https://openi.nlm.nih.gov/imgs/512/173/4282853/PMC4282853_gnl-09-18f1.png
Mechanism of Action

Image from: http://www.peterbullartstudio.co.uk/webcontent/wp-content/gallery/technical/technical30.jpg
Effectiveness of Infliximab (19)

Side Effects (20, 21)

- Most serious: higher risk of infection associated with mycobacteria
- Tuberculosis
- Lymphoma
- Acute and delayed hypersensitivity reactions

Current Research
Bacteriome and Mycobiome Research (22, 23)

- Dysbiosis associated with several diseases, particularly inflammatory bowel diseases [IBD]

- Liguori et al. (2015) analyzed bacterial and fungal composition of mucosa-associated microbiota of Crohn’s Disease patients (CD) and healthy subjects (HS)

- Hoarau et al. (2016) identified fungal and bacterial species associated with CD dysbiosis
Liguori et al., 2015
Hoarau et al., 2016

- *Candida tropicalis* abundance is significantly increased in CD patients
- Abundance of *Serratia marcescens* (*S. marcescens*) and *Escherichia coli* (*E. coli*) is elevated in CD patients
- Interactions between *C. tropicalis* and potential bacterial pathogens play an important role in CD
Conclusion
References


References


