# Quick Review: Crohn's Disease

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**Citation**

T Fujii, B Phillips. *Quick Review: Crohn's Disease*. The Internet Journal of Gastroenterology. 2002 Volume 2 Number 1.

**Abstract**

This is a brief review of Crohn's disease, a condition first described in 1932 by Crohn BB, Ginsberg L, Oppenheimer GD. Regional ileitis: a pathological and clinical entity JAMA;99:1323

## DEFINITION

A chronic, inflammatory condition with an intermittent & unpredictable clinical pattern affecting mostly young, productive people

- Can involve the entire alimentary tract
    - Discontinuous segments
    - Most common sites
        - terminal ileum
        - proximal colon
- Extraintestinal manifestations are common
    - Eyes
    - skin
    - joints
- Variable Course: “Waxing & Waning”
- Worldwide Prevalence: 10 - 70 cases / 100,000
- Incidence: 0.5 - 6.3 cases / 100,000

Almost exclusively encountered in industrialized nations of Western Europe & the United States

- Affects all populations & ethnic groups, however, some are more-likely to be afflicted
    - Jewish 3 - 8x more-likely than non-Jewish
    - Ashkenazi Jews
        - born outside Israel: 4-fold increase (16.7 cases / 100,000)
        - compared to born in Israel (4.2 cases / 100,000)
- Aggregation in families can occur [10 - 30 %]
    - Parent-Child
    - Sibling-Sibling

However, there has never been evidence for direct mendelian transmission!

- Pattern of Onset
    - age 15 - 30
    - age 55 - 60
- Men & Women are equally-affected
- More common in urban-dwellers than rural
- Positively-associated with higher levels of education
- Cigarette smoking increases overall-risk !

## ETIOLOGY

The cause or causes of Crohn Disease remain unknown

- noncaseating granulomas within inflamed tissue suggests a possible-infectious cause
- epidemiological studies have leaned towards genetic, dietary, & environmental factors
- clinical response to immunosuppressive agents points to an immunologic cause

## THE INFECTIOUS THEORY

- histology of Crohn-segments reveals “intestinal tuberculosis”
- identification of Mycobacterium within mesenteric nodes
- however, only 23 % of patients have elevated mycobacterial antibodies (similar to healthy controls)
- Bacterial studies have demonstrated that 1/3 of patients have abnormal microflora within the small bowel
    - result of inflammation & flow stagnation

## THE LUMINAL BACTERIAL FLORA MAY PLAY A ROLE IN PERPETUATING THE INFLAMMATORY PROCESS

- Viral studies have been inconclusive

## THE IMMUNOGENETIC THEORY

- development may be genetically-determined
- thought to arise from a generalized-disorder of the intestinal immune system
    - however, a primary defect of the systemic or mucosal systems has not been identified
    - there have been many “alterations” reported - which is thought to indicate a ‘disturbed-immunoregulation”

Direct vs. Indirect Target Cell Injury is the enterocyte a target or an innocent-bystander?

## PATHOLOGY

This disease can be rapidly progressive or run an indolent, intermittent course

- Acute, Active Phase
    - aphtous mucosal ulcers
    - lymphoid aggregates
    - granulomas
    - transmural inflammation with fissures or fistulas
- Quiescent, Healing Phase
    - characterized by fibrosis with stricture formation & chronic ulcers
    - the granulomatous process may involve other tissues & organs
- Histologic Features of Regional Enteritis
    - granulomas away from ulcerations
    - granulomas within lymph nodes & other tissues
    - lymphoid aggregates within the submucosa & Subserosa
    - fissures & ulcers extending into the muscularis propria
    - transmural inflammation

## WHAT DOES CROHN DISEASE LOOK LIKE IN THE OPERATING THEATRE?

- Involved segments are rigid & thick
    - due to fibrosis & inflammatory edema which narrows the bowel lumen
- Mesenteric fat reaches over the antimesenteric border
- Mesentery is foreshortened, thick, & edematous with enlarged nodes
- Serosa may be granular & dulled by exudate
- Inflammation may extend into adjacent structures
    - leading to fistulas, abscesses, & sinus tracts
    - can distort normal anatomy
    - can lead to obstruction with matting-together of several bowel loops (both involved & uninvolved)
- Opening the involved segment
    - thickened bowel wall

    - narrow lumen
    - longitudinal ulcers
    - cobblestoning
    - aphtoid ulcers
    - dilated, proximal, uninvolved segment
- Microscopic Features of Crohn Disease
    - changes begin with the accumulation of inflammatory cells adjacent to a crypt
    - this localization leads to ulcer-formation & crypt-abscesses
    - granulomas, if present, are non-caseating
    - fistulas & sinus tracts form from confluent crypt abscesses and the associated transmural inflammation
    - transmural spread leads to serositis, which can cause adherence of adjacent structures

Thus, epithelial cell injury with necrosis is not the initial event but rather, the end-result !Differentiating Crohn disease of the colon from ulcerative colitis is the most common diagnostic dilemmain the field of “inflammatory bowel disease” so, how do we go about doing that ?Ulcerative Colitis is a contiguous, mucosal disease which begins at the rectum

- Indeterminate Colitis
    - when a clear-cut diagnosis can not be agreed upon (either Crohn disease or ulcerative colitis)
    - 10 % of all cases
    - the final diagnosis is determined by the clinical course

## THE CLINICAL FEATURES

## THE TRIAD:

- Abdominal pain, diarrhea,
- Weight loss insidious,
- Gradual onset which becomes persistent & progressive with a “waxing-waning” type course (varies from patient to patient)
- Abdominal Pain: Intermittent, Colicky Form
    - caused by distension & peristaltic contractions of the bowel as a result of either partial or complete obstruction
- Abdominal Pain: Constant Form
    - caused by parietal peritoneal inflammation
- Treating the Abdominal Pain: Multifaceted Approach
    - Dietary Measures
        - relieve or avert obstruction
    - Anti-inflammatory Agents
        - decrease inflammation & edema of the diseased segment
    - Anti-spasmodics
        - help to allay cramping
- Diarrhea: usually due to several factors
    - mucosal inflammation decreases absorption & increases secretion
    - decreased bile acid absorption leads to a decrease in fat absorption
        - ileal segment disease
        - ileal resection
        - free fatty acids in the colon decrease electrolyte & water absorption
    - the lack of an ileocecal valve (surgical resection) can lead to bacterial overgrowth within the small bowel which further interferes with nutrient digestion & absorption
- Treating the Diarrhea:
    - Dietary Measures

    - Anti-diarrheals
- Weight Loss: Common & Potentially-lethal0
    - Anorexia, Nausea, Vomiting
    - may signal an obstruction
    - the patient recognizes these “signals” and begins to eat less
    - begins a dangerous cycle !
- Consequences of Impaired Absorption & Malnutrition
    - diarrhea with dehydration & electrolyte imbalance
    - steatorrhea
    - gallstones
    - protein-losing enteropathy
    - growth retardation
    - anemia (microcytic, megaloblastic)
    - demineralization of bone ...

Malnutrition is especially-serious in children - growth retardation & delayed maturation are found in 10 - 40 % of children with Crohn disease... can be reversed with aggressive treatment ! why are renal oxalate stones common in Crohn disease ?

## CLASSIFICATION OF DISEASE

- Fibrosing/Stricturing Form
    - amenable to surgical intervention
- Fistula/Abscess Form
    - role for interventional radiology
- Aggressive-inflammatory Form
    - primarily managed by antiinflammatory therapy

## SKIN LESIONS

- Erosions
- ulcerations
- abscess
- skin tags
- hemorrhoids

## ANAL CANAL LESIONS

- Ulcers
- stenosis
- abscess
- hemorrhoids
- fissure
- fistulas (skin/vagina)
- Peri-anal Disease is common
    - 25 %, patients with ileitis
    - 40 %, patients with isolated colitis
    - 50 %, patients with ileocolitis

one-third of patients present initially with perianal disease

- Extraintestinal Manifestations: common !
    - long-list of associated conditions
    - Skin
    - eyes
    - joints
    - liver

prevalence is higher in patients with colonic disease versus small bowel disease

- Children vs. Adults: regional enteritis
    - the course of disease is similar [slowly progressive]
        - recurrent episodes of the “clinical triad”
        - only 20 % of patients remain asymptomatic for 10-20 yrs.

        - most patients usually require surgery at some point
    - growth retardation is common in children

10 % of patients die as a result from Crohn Disease

## DIFFERENTIAL DIAGNOSIS

"The signs and symptoms of Crohn disease are nonspecific"

- Infectious Diseases
- Inflammatory Conditions
- Neoplasia

Why do you operate on Crohn disease ?

"In most patients, the disease eventually advances to a stage requiring surgical intervention for alleviation of symptoms or to treat complications such as obstruction, fistula, or abscess"

- Small Bowel Obstruction: the most common complication
    - Usually Partial & Intermittent
    - Managed Conservatively, if possible...

But, as the overall disease stateprogresses (with fibrosis & stricturing), the obstruction can become complete

- Fistula Formation: a pathognomonic feature of Crohn disease
    - forms between affected bowel and any other organ/structure
    - signs & symptoms
        - Inflammatory mass
        - Fever
        - Obstructive symptoms
        - Pain

## CLASSIFICATION OF INTRA-ABDOMINAL ABSCESSES

abscesses often accompany fistulas !

- Interloop
- Intramesenteric
- Retroperitoneal
- Ileopsoas
- Enteroperitoneal
- Toxic Megacolon
    - Occurs in 6 % of patients
    - Toxic dilation can also occur in the ileum
    - Due to Severe inflammation of the submucosa
        - destroys or impairs the myenteric plexus and muscularis propria
        - this induces muscular atony and subsequent bowel distension

anticholinergics, antidiarrheals, & analgesics may precipitate toxic episodes

- Toxic Dilation: sick, sick, sick...
    - Patients are acutely ill, febrile, tachycardic, with increasing abdominal pain, diarrhea, & progressive distension
    - Diagnosis is confirmed by radiography
    - Question: how do you manage it ?
- GI Bleeding
    - massive intestinal bleeding is uncommon
        - deep ulceration into a submucosal vessel
        - colonic disease: 20-30 % of chronic rectal bleeding
- Increased risk for Small & Large Bowel Carcinoma
    - diagnosis is usually delayed
    - poor, overall prognosis

“disease specific therapy does not exist”

- Supportive Treatment
    - alleviate symptoms: pain, diarrhea
    - nutritional support: weight loss
    - suppress the inflammatory process
- Corticosteroids
    - used since the 1940's
    - exact mechanism is unclear
        - thought to cause a nonspecific immunosuppression
        - long-term therapy is dangerous and should be avoided
        - short-term courses for acute episodesPrednisone (0.5 - 0.75 mg/kg/day)
- Sulfasalazine
    - Sulfapyridne-5-ASA
    - Intestinal bacteria cleave this drug in the distal ileum
        - allows absorption of the sulfonamide portion while the 5-ASA portion stays in the intestinal lumen
        - inhibitory to the formation of prostaglandins & leukotrienes
    - Effective in achieving remission
    - Patients without symptoms do not benefit from therapy
- Antibiotics
    - broad-spectrum agents are indicated for septic episodes
    - use as “long-term suppression” is controversial
    - Metronidazole has been found to be effective in some patients
    - Unclear mechanism
    - Side Effects: GI Irritability
        - Urticaria
        - Neutropenia
        - Peripheral Neuropathy
- Immunosuppressants: Azathioprine
    - active metabolite, 6-mercaptopurine
    - a purine analog which inhibits nucleic acid production
    - interferes with the production of inflammatory cells
    - requires 3 months of treatment for an effect
    - role in long-term suppression: can maintain remission
    - side effects: bone marrow suppression/pancreatitis
- Methotrexate
    - a folic acid inhibitor with immunosuppressive & antiinflammatory effects
    - has been shown to be effective with RA, Psoriasis...
    - small trials may show a clinical benefit with ileitis
        - large trials are needed.

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### References

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