Pathology

Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC) — Causes and Treatment

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Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the gastrointestinal tracts and is comprised of two major disorders: ulcerative colitis (UC) and Crohn's disease (CD). Both diseases have characteristic and overlapping findings, which will be discussed in detail throughout this article.

Introduction

Although the two inflammatory bowel diseases almost have the same general symptoms, they are two separate disorders because each affects different areas of the gastrointestinal tract.

Crohn’s disease commonly affects the terminal ileum and the start of the colon, but it can also attack any point in the GI tract, i.e. from the mouth to anus. Ulcerative colitis specifically affects the colon. It is important to know the characteristic signs and symptoms of the two diseases for proper treatment.
Definitions of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

Crohn’s disease
Is characterized by **transmural inflammation** (entire wall thickness) **with skip lesions**, affecting any point along the GI tract. The particular affected area can vary among every affected individual.

The inflammation can occur as patches in the intestine leaving un-inflammatory section **(skip lesions)**, while in ulcerative colitis this is not observed.

Is associated with the development of **fistulas** which are channels or open connections between two areas such as one twist of colon to another or colon to skin, bladder, or vagina.

**Ulcerative colitis**

Is characterized by frequent episodes of inflammation that affect the innermost layer of the rectum and colon (mucosal layer) causing ulcers and soreness in the GI tract (no fistula formation). The combination of inflammation and ulceration can cause abdominal
discomfort and frequent emptying of the colon.

Both are long-lasting and persistent when not carefully managed in their early stages. Long-term remission can be observed with treatment for these inflammatory diseases.

**Risk Factors of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)**

The exact pathophysiology of inflammatory bowel disease (IBD) is unclear, but a number of risk factors are associated with their development.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td><strong>Age and gender</strong></td>
<td>• Most cases of IBD start at age between 15 and 40 years. • In Crohn’s disease, there is a slight female predominance which suggests hormonal factors in the disease progression.</td>
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<td><strong>Racial and ethnicity</strong></td>
<td>• The racial and ethnic differences are significantly dependent on environmental &amp; lifestyle factors in addition to the underlying genetic differences. • IBD occurs more in the developed, urban, and northern areas rather than undeveloped, rural and southern climates. • It occurs more commonly in Jewish patients. • It more common in Caucasians.</td>
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<td><strong>Genetic susceptibility</strong></td>
<td>• IBD usually runs in the family, 25% of patients with IBD have a first degree relative (parent-children, siblings, and parent-siblings) with the disorder. • Genetics have major threat of having Crohn’s disease rather than ulcerative colitis with more risks when both parents are affected.</td>
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<td><strong>Smoking</strong></td>
<td>• <strong>Ulcerative colitis:</strong> Current studies suggest that smoking is not a risk factor for development of UC and, in fact, may even be protective of or reduce disease symptoms. • <strong>Crohn’s disease:</strong> Smoking increases risk of Crohn’s disease two fold. It also increases the risk of recurrence of CD.</td>
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<tr>
<td><strong>Diet</strong></td>
<td>• Suggested that certain food antigens may precipitate development of IBD and Suggested that Western diet (e.g. processed, fried, and sugary foods) is associated with increased risk of Crohn’s disease, and also ulcerative colitis.</td>
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<tr>
<td><strong>Obesity</strong></td>
<td>• Excessive obesity may contribute in development of IBD due to intra-abdominal accumulation of fat, leading to mucosal inflammation and disease development.</td>
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<td><strong>Infections</strong></td>
<td>• The GI tract naturally contains beneficial bacteria that are harmless and help in digestion. • Imbalance and/or alterations in the gut commensal microorganisms may contribute to the development of IBD. • It has been suggested that multiple pathogens (e.g., <em>Shigella</em>, <em>Salmonella</em>, <em>Campylobacter</em>, <em>Clostridium difficile</em> spp.) can trigger an inflammatory response which can’t be controlled by the mucosal immune system.</td>
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<td><strong>Antibiotics</strong></td>
<td>• Antibiotics may alter the gut flora and increase the risk of IBD.</td>
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<tr>
<td><strong>Oral contraceptives &amp; Hormone replacement therapy</strong></td>
<td>• Hormone therapy can have thrombotic effects on the microvasculature which predisposes for IBD. Women using OCP or HRT have an increased risk of developing IBD.</td>
</tr>
<tr>
<td><strong>Appendectomy</strong></td>
<td>• Several studies have shown that an appendectomy may protect patients from the occurrence of UC. The mechanism is yet unknown.</td>
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</tbody>
</table>
Psychosocial factors

• Psychosocial factors (e.g. stress) may have a role in exacerbations of symptoms in patients with IBD, possibly though stimulating the enteric nervous system and the release of proinflammatory cytokines.

Classification of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

Crohn’s disease classification

The classification of Crohn’s disease is based on the inflammation (clinical behaviour), anatomical distribution (location) and operative history (age). There are generally two types which hold different values for the mentioned features:

- Vienna class
- Montreal class

Vienna class

This was used to classify patients as: A1 is the age below 40 years and A2 is the age above 40 years, location were L1, L2, L3 and L4 representing ileal, colonic, ileocolonic and upper respectively. In addition, the behaviours were of 3 kinds B1, B2 and B3 indicating

Montreal class

An updated classification. It was modified to: in which the age group was identify clearly designating A1 for below 16 years age group as children are now becoming the victims of this disease, A2 for 17-40 years of age and A3 for the age above 40. The identified locations remained the same by slight clarifying L4 as isolated upper disease. And lastly, a P type behaviour was added defined as

Ulcerative colitis classification

This specific type of IBD is classified by considering the area of colon affected, along with its severity.

- Class I/S1 - Mild UC
- Class II/S2 - Moderate UC
- Class III/S3 - Severe UC

Class I/S1 - Mild UC

Passing up to four stools per day together with blood and normal inflammatory markers (ESR) with absence of any systemic illness. The affected area is restricted to rectum (ulcerative proctitis).

Class II/S2 - Moderate UC

Passing four or more stools per day and has negligible signs of systemic noxiousness.

Class III/S3 - Severe UC

Passing six or more blood containing stools regularly, a pulse rate of >90 bpm, temperature of >37.5°C, and blood haemoglobin <10.5 g/100 ml. Elevated ESR >30 mm/h. Youngster below 16 years having prolonged ulcerative colitis are inclined to have
severe symptoms. ESR is a terminology used for erythrocyte sedimentation rate.

Clinical Features of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

IBDs, when symptomatic, have nearly the same presentation. The affected area is the main key way of distinguishing Crohn’s disease from the ulcerative colitis. The signs and symptoms of inflammatory bowel diseases usually range from mild to severe conditions. Symptoms may develop suddenly.

Signs and symptoms include:

- Abdominal pain due to inflammation and ulceration
- Bloody stool
- Ongoing diarrhea that causes intensified intestine cramping
  - **Diarrhea** that sustain sleeplessness
- Low grade fever lasting more than a day
- Mouth sores
- Fatigue and stress
- Nausea and vomiting
- Severe abdominal/pelvic pain
- Abnormal eating habits and difficulty in absorption and digestion

Characteristic Crohn’s disease symptoms:

- Perianal disease with fistula formation
- Delayed growth
- Skin and joint inflammation
- Liver inflammation

Particular ulcerative colitis symptoms

- Rectal pain
- Rectal bleeding with mucous and pus
- Perseverance to defecate
- Incapability to have a bowel movement despite urgency

Diagnosis of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

When crohn’s disease or ulcerative colitis are suspected, diagnosis is confirmed with biopsy and radiological exams. There is no specific test for the IBDs, besides biopsy, one has to go through multiple options for the investigations.

Blood tests

**Hemoglobin**

Patients are usually anemic and the efficiency of red blood cells is inadequate for transmission of oxygen to the tissues. Also, the early signs of infections can be interpreted.
Stool tests

Identifying fecal occult will help in investigating the root cause behind these deadly diseases.

Other Diagnostic Tests

Colonoscopy

![Endoscopic image of ulcerative colitis showing loss of vascular pattern of the sigmoid colon, granularity and some friability of the mucosa.](image)

This specific procedure is performed with the help of an endoscope. A few tissue samples can be taken out during the procedure for histological analysis. Groups of inflammatory cells known as granulomas are associated with Crohn’s.

Flexible sigmoidoscopy

The sigmoid is the last segment of the colon and is examined with an endoscope known as a slender.

X-ray

Perforated colon can be diagnosed by the standing abdominal X-ray and is a severe complication.

Computerized tomography (CT)

It is a focused X-ray to show the more detailed X-ray analysis. This scan can be performed for abdomen and pelvis inflammation. This is equally helpful in ulcerative colitis as well as Crohn’s disease.

Magnetic resonance imaging (MRI)

Magnetic field together with radio waves is created in this procedure for detail analysis of tissues and organs. MRI is predominantly valuable for assessing a fistula near the anal area and it is termed as pelvic MRI; CT does this, too.
Investigations of Crohn’s disease

Capsule endoscopy

In this particular procedure in which to swig a capsule consisting of a small camera to take pictures that are transmitted to a computer belt. After the procedure, the camera expels out of the body with the stool.

Investigations for ulcerative colitis

CT enterography combined with magnetic resonance (MR) enterography

Unlike conventional imaging procedures, ulcerative colitis is diagnosed with more precision by using combination of CT and MR enterography revealing soreness in the bowel. MR enterography is a substitute source. Soreness is the patch making pattern caused by the ulcerative colitis.

Chromoendoscopy

Ulcerative colitis with colorectal cancer can be examined by chromoendoscopy in which technician uses a spray dye to spot abnormal tissue variations.

Differential Diagnosis of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

The following comparison may help in distinguishing between both diseases:

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Ulcerative Colitis</th>
<th>Crohn’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross blood in stool</td>
<td>Yes</td>
<td>Occasionally</td>
</tr>
<tr>
<td>Mucus</td>
<td>Yes</td>
<td>Occasionally</td>
</tr>
<tr>
<td>Systemic symptoms</td>
<td>Occasionally</td>
<td>Frequently</td>
</tr>
<tr>
<td>Pain</td>
<td>Occasionally</td>
<td>Frequently</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>Rarely</td>
<td>Yes</td>
</tr>
<tr>
<td>Significant perineal disease</td>
<td>No</td>
<td>Frequently</td>
</tr>
<tr>
<td>Fistulas</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Small intestinal obstruction</td>
<td>No</td>
<td>Frequently</td>
</tr>
<tr>
<td>Colonic obstruction</td>
<td>Rarely</td>
<td>Frequently</td>
</tr>
<tr>
<td>Response to antibiotics</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Recurrence after surgery</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>ANCA-positive</td>
<td>Frequently</td>
<td>Rarely</td>
</tr>
<tr>
<td>ASCA-positive</td>
<td>Rarely</td>
<td>Frequently</td>
</tr>
</tbody>
</table>

Endoscopic

| Rectal sparing                | Rarely             | Frequently      |
| Continuous disease            | Yes                | Occasionally    |
| “Cobblestoning”               | No                 | Yes             |
| Granuloma on biopsy           | No                 | Occasionally    |

Radiographic

| Small bowel significantly abnormal | No | Yes |
| Abnormal terminal ileum          | No | Yes |
| Segmental colitis                | No | Yes |
Treatment of Crohn’s Disease (Ileitis) and Ulcerative Colitis (UC)

Treatment of IBD can be divided into:

- **Pharmacological treatment**
- **Surgical treatment**

**Anti-inflammatory medications**

**5-aminosalicylates**

5-ASA agents, such as **sulfasalazine** are effective in Inducing and maintaining remission in UC, with limited role in Inducing and maintaining remission in CD. The most useful for treatment of active Crohn’s disease involving the colon.

**Corticosteroids**

Corticosteroids are effective in treatment of moderately severe UC or CD. Corticosteroids don’t play any role in maintaining remission of either UC or CD. They can be given orally as prednisone (40–60 mg/d) or parenterally as hydrocortisone (300 mg/d) or methylprednisolone (40–60 mg/d). Because of systemic side effects of standard corticosteroids, another medication called **budesonide** (9 mg/day) which is used for 2–3 months has the same potent effect of prednisone but with less side effects.

**Immunosuppressors**

**Azathioprine & 6- Mercaptopurine**

They are purine analogs that are used mainly in the treatment of corticosteroids-dependent IBD and used as glucocorticoid-sparing agents in UC & CD.

**Methotrexate**

It’s effective in inducing and maintaining remission in active CD, and allows to reduce the dosage of glucocorticoids.

**Biological therapies**

The first approved biological therapy in treatment of Crohn’s disease refractory to previous regimens or moderate to severe active ulcerative colitis.

**Antibiotics**

Antibiotics can lessen the quantity of drainage and occasionally dissolve fistulas in patients with Crohn’s disease. Regularly recommended antibiotics include Metronidazole and ciprofloxacin depending on the severity.

**Anti-diarrheals**

A fiberous supplement including psyllium powder or methylcellulose help relieve
moderate diarrhea by adding fiber bulk to the stool. Loperamide is effective for severe diarrhea.

Supplements

Iron and vitamin supplements on daily basis. They will overcome iron deficiency and vitamin B-12 fulfill body needs and encourages regular growth and development. Calcium supplements can reduce the risk of osteoporosis that occur in crohn’s disease.

Surgery

Surgery is indicated for patients with persistent disease despite conservative treatment.

Strictureplasty is carried out in case of Crohn’s disease in which the impaired section is separated from the small intestine. In case of ulcerative colitis, proctocolectomy is done to remove the complete colon as well as rectum. And creating a hole in abdomen (ileal stoma) will help to pass the stool.

Review Questions

The correct answers can be found below the references.

1. Which area of the body is affected in ulcerative colitis?
   A. Ileum
   B. Colon
   C. Anus
   D. Vagina

2. Which part of the GI tract is removed during surgery in Crohn’s disease?
   A. Rectum
   B. Colon (large intestine)
   C. Ileum (small intestine)
   D. Mouth

3. What are the main causes of Crohn’s disease?
   A. Genetics
   B. Environment
   C. Immunity
   D. All of the above

References


**Correct answers:** 1B, 2C, 3D

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