Supportive module 2 "Basics of diagnosis, treatment and prevention of major gastroenterological diseases"

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Supportive module 2: Basics of diagnosis, treatment and prevention of major gastroenterological diseases

Chronic Disease of The Colon: Irritable Bowel Syndrome and Ulcerative Colitis

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Plan of the Lecture

The Same for Irritable Bowel Syndrome and Ulcerative Colitis



- Definition
- Epidemiology
- Mechanisms
- Classification
- Clinical presentation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic guidelines

Definition Irritable Bowel Syndrome

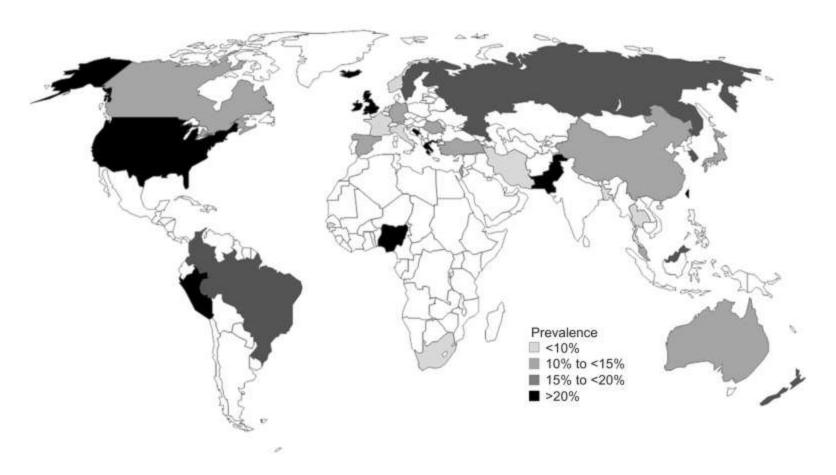
Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder that affects the large intestine (colon) and commonly causes changes in the pattern of bowel movements with cramping, abdominal pain, bloating, gas, diarrhea and constipation but without any evidence of underlying damage and is diagnosed using clinical criteria.

Epidemiology

- Irritable Bowel Syndrome (IBS) affects around 11% of the population globally
- Up to 30% of people who experience the symptoms of IBS will consult physicians
- There is a female predominance in the prevalence of IBS
- There is 25% less IBS diagnosed in those over 50 years and there is no association with socioeconomic status
- Patients diagnosed with IBS are highly likely to have other functional disease and have more surgery than the general population
- There is no evidence that IBS is associated with an increased mortality risk.

Epidemiology

Irritable Bowel Syndrome

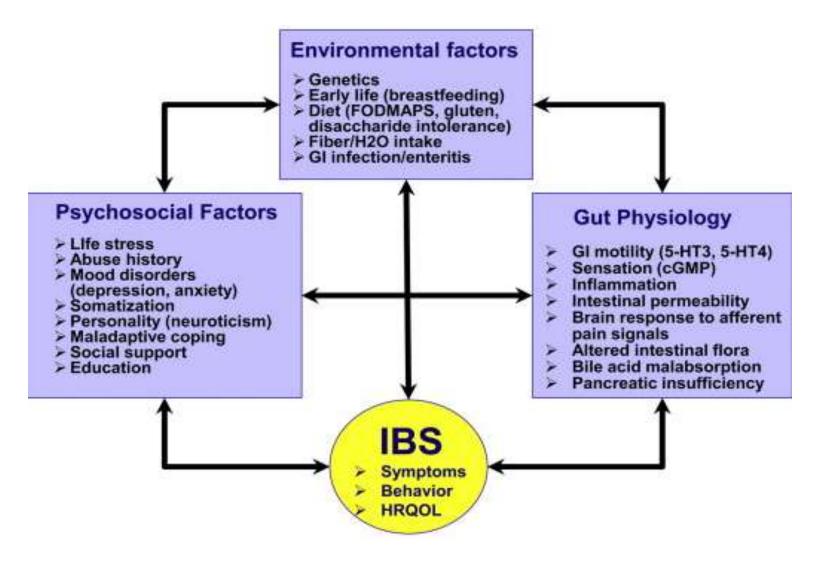


Worldwide prevalence of irritable bowel syndrome, as reported by country.

Risk Factors & Etiology

- While the causes are still unknown, it is believed that the entire gut brain axis is affected
- The risk of developing IBS increases six-fold after acute gastrointestinal (GI) infection
- Psychological factors may play a role in the persistence and perceived severity of symptoms
- Antibiotic appears to increase the risk of developing IBS
- Women report more IBS symptoms than men
- IBS occurs in all age groups with no difference seen in the frequency of subtypes by age
- IBS was associated with lower socioeconomic status
- The relative risk of IBS is twice as high in individuals with a biological relative with IBS.

Risk Factors & Etiology

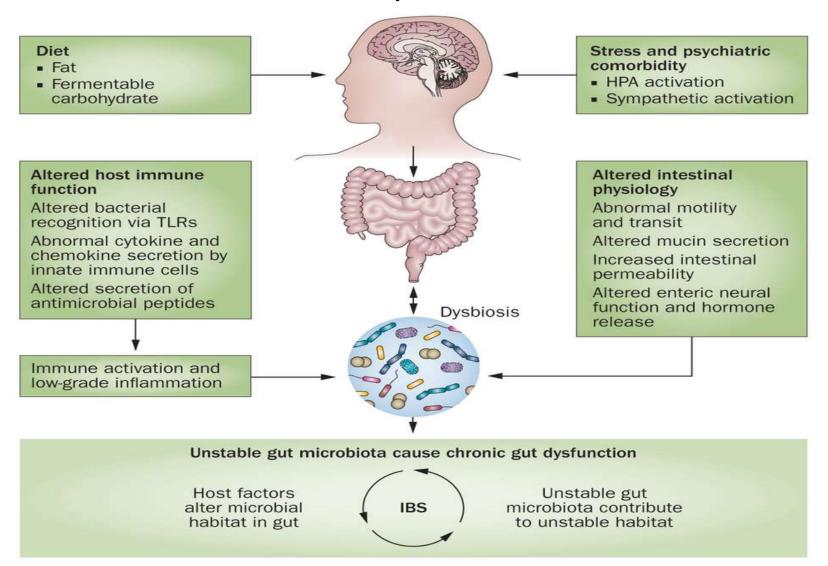


Mechanism

- Motor abnormalities of the GI are detectable in some patients include increased frequency and irregularity of luminal contractions, prolonged transit time in constipation-predominant IBS, and an exaggerated motor response to cholecystokinin and meal ingestion in diarrhea-predominant IBS
- Visceral hypersensitivity (increased sensation in response to stimuli)
 is a frequent finding in IBS and results from stimulation of various
 receptors in the gut wall that transmit signals via afferent neural
 pathways to the dorsal horn of the spinal cord and ultimately to the
 brain
- These abnormalities are secondary to psychological disturbances rather than being of primary relevance

Mechanism

Irritable Bowel Syndrome: Gut Flora



International Classification of Diseases

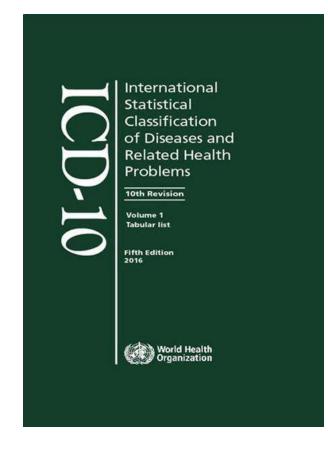
XI Diseases of the digestive

K58 Irritable bowel syndrome

K58.0Irritable bowel syndrome with

diarrhoea

K58.9Irritable bowel syndrome without diarrhoea



Irritable Bowel Syndrome: Clinical Types

- IBS with constipation (constipation-predominant): stomach pain and discomfort, bloating, abnormally delayed or infrequent bowel movement, or lumpy/hard stool
- IBS with diarrhea (diarrhea-predominant): stomach pain and discomfort, abnormally frequent bowel movements, an urgent need to move bowels, or loose/watery stool
- IBS with alternating constipation and diarrhea
- Pain-predominant.

Irritable Bowel Syndrome: Clinical Types

IBS-Constipation	IBS-Diarrhea
≥ 25% Hard or lumpy < 25% Loose or watery	≥ 25% Loose or watery < 25% hard or lumpy
	type & lency
frequ	ency
IBS-Mixed Pattern	IBS-Unspecified
≥ 25% Hard or lumpy	< 25% Hard or lumpy

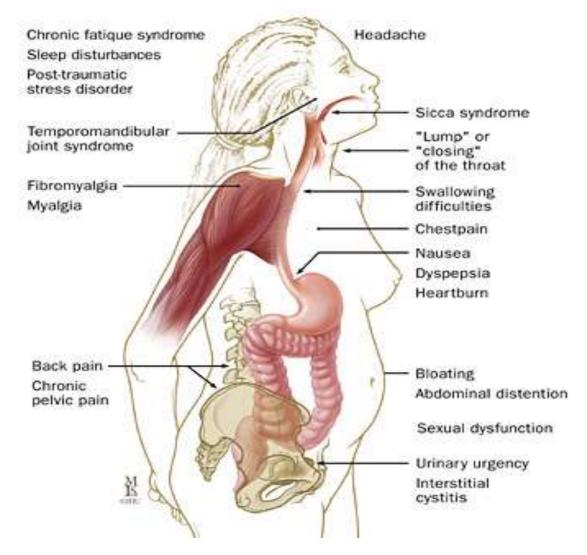
Irritable Bowel Syndrome: Rome IV (2016) (sub-typing by predominant stool pattern)

- IBS with constipation (IBS-C): hard or lumpy stools for ≥25% of bowel movements and loose (mushy) or watery stools for ≤25% of bowel movements
- 2. IBS with diarrhoea (IBS-D): loose (mushy) or watery stools for ≥25% of bowel movements and hard or lumpy stool for ≤25% of bowel movements
- Mixed IBS (IBS-M): hard or lumpy stools for ≤25% of bowel movements and loose (mushy) or watery stools for ≤25% of bowel movements
- 4. Unspecified IBS: insufficient abnormality of stool consistency to meet criteria for IBS-C, IBS-D, or IBS-M.

Signs and Symptoms

- The primary symptoms are abdominal pain or discomfort in association with frequent diarrhea or constipation and a change in bowel habits
- Symptoms usually are experienced as acute attacks that subside within one day, but recurrent attacks are likely
- There may also be urgency for bowel movements, a feeling of incomplete evacuation (tenesmus), bloating, or abdominal distension
- In some cases, the symptoms are relieved by bowel movements
- People with IBS, more commonly than others, have gastroesophageal reflux, genitourinary disturbances, chronic fatigue, fibromyalgia, headache, backache, and psychiatric symptoms such as anxiety
- About a third of people who have IBS also report sexual dysfunction typically in the form of a reduction in libido.

Signs and Symptoms



History

- In assessing the patient with IBS, it is important not only to consider the primary presenting symptoms, but also to identify precipitating factors and other associated gastrointestinal and extra gastrointestinal symptoms
- It is vital also to seek out and directly question for the presence of alarm symptoms and to consider, in the relevant context, other explanations for the patient's symptoms (e.g., bile acid diarrhea, carbohydrate intolerance, microscopic colitis)
- The history is critical and involves both the identification of those features regarded as typical of IBS and also the recognition of "red flags," or other features that suggest alternative diagnoses.

Physical Exam

- A physical examination reassures the patient and helps detect possible organic causes
- A general examination is carried out for signs of systemic disease
- Abdominal examination:
 - Inspection
 - Palpation
 - Auscultation
- Examination of the perianal region:
 - Digital rectal examination.

Complications Irritable Bowel Syndrome

- Diarrhea and constipation can aggravate hemorrhoids
- With diarrhea or constipation, or both, social engagements are often disrupted or broken (this, in turn, may lead to social isolation, depression and further withdrawal)
- Sexual intimacy may be impacted, sexual activity can become unappealing and even painful.

Diagnosis

- A diagnosis is usually suspected on the basis of the patient's history and physical examination, without additional tests
- Confirmation of the diagnosis requires the confident exclusion of organic disease in a manner dictated by an individual patient's presenting features and characteristics
- In many instances (e.g., in young patients with no alarm features), a
 secure diagnosis can be made on clinical grounds alone
- In clinical practice, whether in the setting of primary or specialist care, clinicians usually base a diagnosis of IBS on their evaluation of the whole patient (often over time) and consider a multiplicity of features that support the diagnosis (apart from pain and discomfort associated with defecation, or change in stool frequency or form).

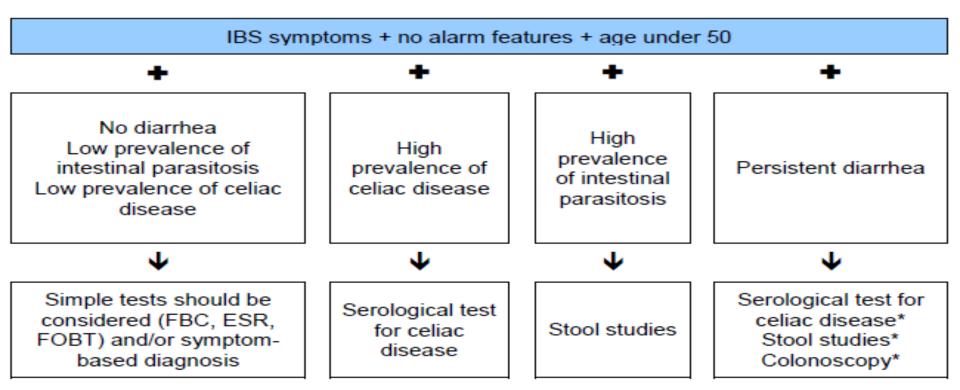
Diagnosis

Irritable Bowel Syndrome: Rome III (2006) diagnostic criteria

- Recurrent abdominal pain or discomfort three days per month in the last three month associated with two or more of:
 - Improvement with defecation
 - Onset associated with a change in frequency of stool
 - Onset associated with a change in form of stool

Diagnosis

Irritable Bowel Syndrome: Diagnostics Algorithm



Notes: ESR, erythrocyte sedimentation rate; FBC, full blood count; FOBT, fecal occult blood test.

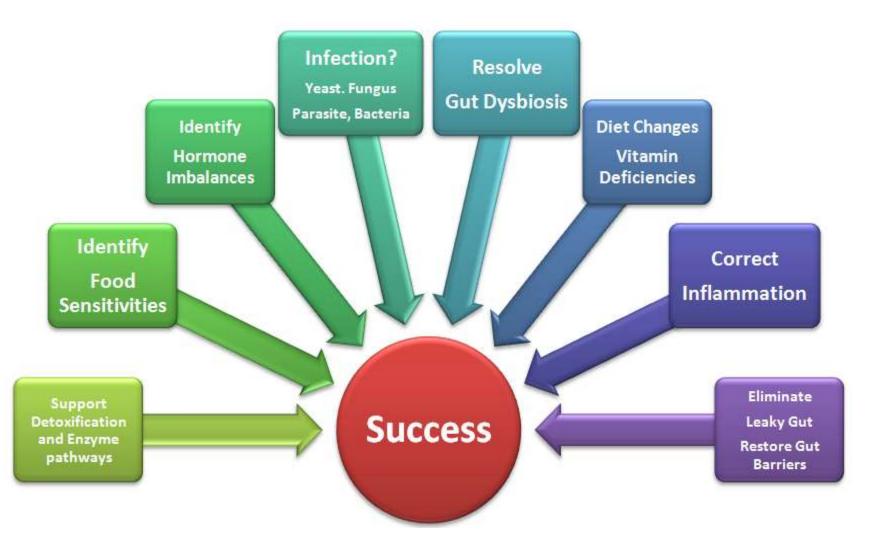
Esophagogastroduodenoscopy and small intestinal biopsy for enteropathy, giardiasis, and changes associated with small-intestinal bacterial overgrowth (SIBO) may be recommended in high-resource areas in selected cases

^{*} Where relevant—i.e., when there is a high prevalence of celiac disease, parasitosis, inflammatory bowel disease, or lymphocytic colitis.

Management

- Management consists primarily of providing psychological support and recommending dietary measures
- Dietary measures may include fiber supplementation; polycarbophil compounds; judicious water intake; caffeine avoidance; legume avoidance; lactose, fructose limitation or avoidance; probiotics
- Pharmacologic treatment is adjunctive and should be directed at symptoms; pharmacologic agents include anticholinergics, antidiarrheals, tricyclic antidepressants, prokinetics, bulk-forming laxatives, serotonin receptor antagonists, chloride channel activators, antispasmodics, rifaximin
- Patient education remains the cornerstone of successful treatment of irritable bowel syndrome (many patients successfully manage their symptoms with attention to dietary triggers).

Management



Prognosis

- IBS tends to last a life time and the symptoms often come and go
- The symptoms usually persist throughout life and may get aggravated with certain stressful life situations
- Many patients may have long symptom-free years interspersed between periods of severe symptoms
- IBS does not shorten lifespan or lead to major life threatening complications in most patients
- Nearly one half of all patients who suffered from abdominal pain in childhood have been seen to suffer from IBS after three decades
- Female gender, younger age and weight loss during the episode of acute gastroenteritis are seen to be the strongest links to development of post infectious IBS.

Prophylaxis

- It is not possible to prevent IBS
- Proper self-care may help ease symptoms and may extend the time between episodes
- Self-care includes quitting smoking, avoiding caffeine and foods that make symptoms worse, and getting regular exercise.

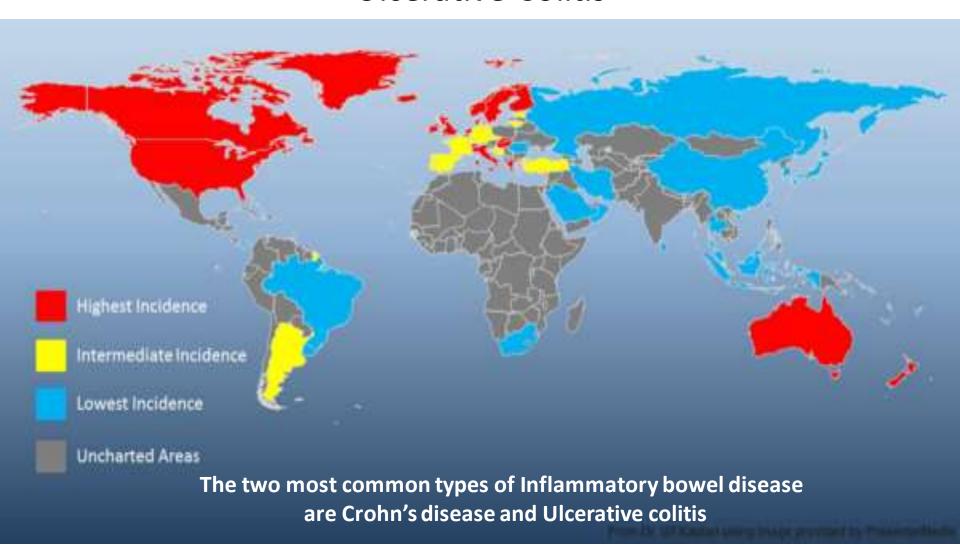
Definition

- Ulcerative colitis (UC) is a chronic idiopathic autoimmune disease characterized by diffuse mucosal inflammation of the colon, that may involve the sigmoid colon (i.e., proctosigmoiditis), the descending colon (i.e., left-sided colitis), the ascending colon (i.e., right-sided colitis), the rectum (i.e., proctitis), or the entire colon (i.e., pancolitis)
- The hallmark clinical symptom is bloody diarrhea often with prominent symptoms of rectal urgency and tenesmus
- The clinical course is marked by exacerbations and remissions, which may occur spontaneously or in response to treatment changes or intercurrent illnesses
- Complications may include megacolon, inflammation of the eye, joints, or liver, and colon cancer.

Epidemiology

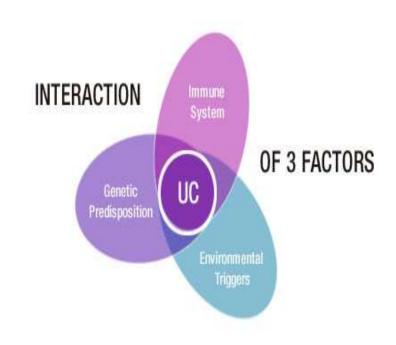
- Each year it newly occurs in 1 to 20 people per 100,000 and 5 to 500 per 100,000 individuals are affected
- The disease is more common in North America and Europe
- Often it begins between 15 and 30 years of age or among those over
 60
- Males and females appear to be affected equally
- It has also become more common since the 1950s
- Together, UC and Crohn's disease affect approximately 500,000 to 2 million people in the United States
- With appropriate treatment the risk of death appears the same as that of the general population.

Epidemiology



Risk Factors & Etiology

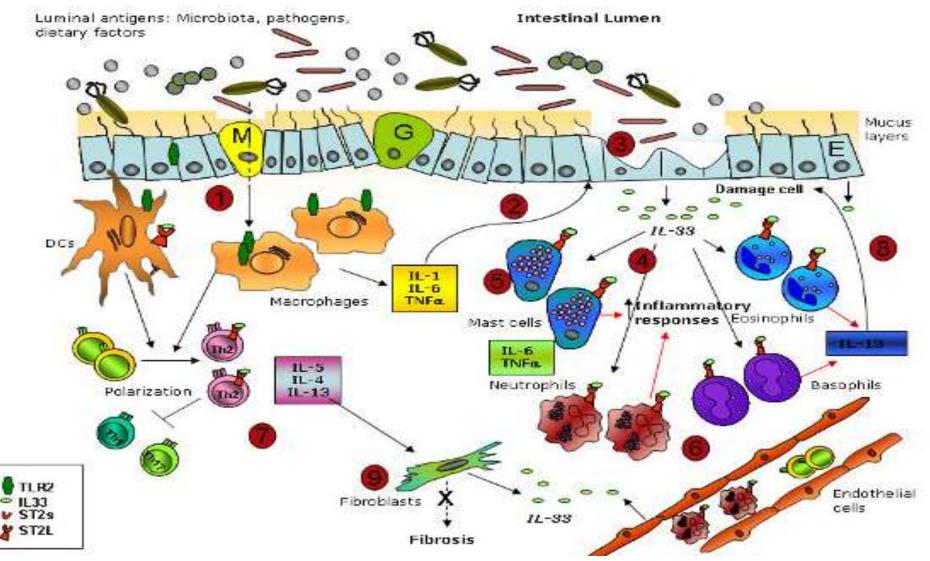
- The exact etiology is unknown, but certain factors have been found to be associated with the disease, and some hypotheses have been presented
- Predisposing factors potentially contributing to UC include genetic factors, immune system reactions, environmental factors, nonsteroidal anti-inflammatory drug (NSAID) use, low levels of antioxidants, psychological stress factors, a smoking history, and consumption of milk products.



Mechanism

- A variety of immunologic changes have been documented
- Subsets of cytotoxic to the colonic epithelium T cells accumulate in the lamina propria of the diseased colonic segment
- This change is accompanied by an increase in the population of B cells and plasma cells, with increased production of immunoglobulin G (IgG) and immunoglobulin E (IgE) as anticolonic and anticytoskeletal antibodies
- Microscopic changes include inflammation of the lamina propria, crypts of Lieberkühn and abscesses
- The ulcerated areas are soon covered by granulation tissue that leads to the formation of polypoidal mucosal excrescences, which are known as inflammatory polyps or pseudopolyps
- An increased amount of destroying epithelial barrier colonic sulfatereducing bacteria has been observed in some patients.

Mechanism



International Classification of Diseases

XI Diseases of the digestive

K51 Ulcerative colitis

K51.0 Ulcerative (chronic) pancolitis

backwash ileitis

K51.2 Ulcerative (chronic) proctitis

K51.3 Ulcerative (chronic) rectosigmoiditis

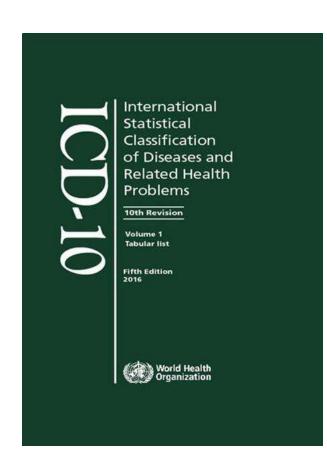
K51.4 Inflammatory polyps

K51.5 Left sided colitis

left hemicolitis

K51.8 Other ulcerative colitis

K51.9 Ulcerative colitis, unspecified



Ulcerative Colitis: Montreal classification (Localization)

- E1 (ulcerative proctitis): involvement limited to the rectum (proximal extent of inflammation is distal to the rectosigmoid junction)
- E2 (left-sided UC, also called distal UC): involvement limited to a portion of the colorectum distal to the splenic flexure
- E3 (extensive UC, also called pancolitis): involvement extends proximal to the splenic flexure.

Classification

Ulcerative Colitis: Montreal classification (Severity)

- S0: clinical remission (asymptomatic)
- S1 (mild UC): passage of ≤4 stools per day (with or without blood), absence of any systemic illness, and normal levels of inflammatory markers
- S2 (moderate UC): passage of >4 stools per day but with minimal signs of systemic toxicity
- S3 (severe UC): passage of ≥6 bloody stools daily, pulse rate of at least 90 bpm, temperature of at least 37.5°C (99.5°F), hemoglobin level of <105g/L (10.5 g/dL), and ESR of at least 30 mm/hour
- Fulminant disease correlates with >10 bowel movements daily, continuous bleeding, toxicity, abdominal tenderness and distension, blood transfusion requirement, and colonic dilation (expansion).

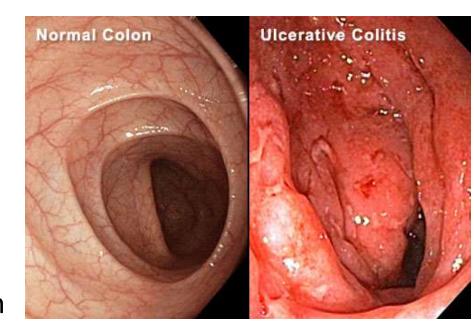
Signs and Symptoms

Ulcerative Colitis: Most Common Symptoms

UC symptoms will vary from person to person, range from mild to severe and may change over time

The most common symptoms are:

- Diarrhoea
- Cramping pains in the abdomen
- Tiredness and fatigue
- Feeling generally unwell or feverish
- Loss of appetite and weight loss
- Anemia.



Signs and Symptoms

Ulcerative Colitis: Extraintestinal Manifestations

- Osteoporosis
- Oral ulcerations
- Arthritis
- Primary sclerosing cholangitis
- Uveitis
- Pyoderma gangrenosum
- Deep venous thrombosis
- Pulmonary embolism.



History

- Patients predominantly complain of rectal bleeding, with frequent stools and mucous discharge from the rectum
- Some patients also describe tenesmus
- Onset is typically insidious
- In severe cases, purulent rectal discharge causes lower abdominal pain and severe dehydration, especially in the elderly population
- UC manifests as an intense inflammatory reaction in the large intestine
- Rarely, patients have persistence of small intestinal inflammation following proctocolectomy and pull-through
- In some cases, UC has a fulminant course marked by severe diarrhea and cramps, fever, leukocytosis, and abdominal distention
- UC is associated with various extracolonic manifestations.

Physical Exam

- Findings from abdominal examination are usually unremarkable
- Physical findings are typically normal in patients with mild disease, except for mild tenderness in the lower left abdominal quadrant
- Patients with severe disease can have signs of volume depletion and toxicity, including the following:
 - Fever
 - Tachycardia
 - Significant abdominal tenderness
 - Weight loss.

Complications

- Intestinal Complications
 - Strictures (usually benign, but can lead to obstruction)
 - Fistulae, abscesses, perforation and toxic megacolon
 - Infectious Colitis
 - Malignancy
- Extraintestinal
 - Arthritides
 - Ophthalmologic
 - Dermatologic
 - Urinary
 - Other (aphthous ulcers, pericholangitis, primary sclerosing cholangitis, cholelithiasis, anemia, hypercoagulable state, etc.).

Ulcerative Colitis: Clinical Data

- The clinical history can be used to differentiate the various etiologies of chronic diarrhea in patients who have not previously been diagnosed with UC
- For the patient with established UC, the presence of constitutional symptoms and extraintestinal manifestations, particularly arthritis and skin lesions, may provide clues to the severity of the disease
- Physical examination should target the gastrointestinal, dermatologic, and ocular systems
- The presence of finger clubbing increases the likelihood of UC in patients with bowel symptoms (positive likelihood ratio [LR] = 3.8), but its absence does not reduce the likelihood (negative LR = 0.8).

Ulcerative Colitis: Initial Diagnostic Workup

- A complete blood count and erythrocyte sedimentation rate
- Electrolyte studies and renal function tests
- Liver function tests
- X-ray
- Urinalysis
- Stool culture
- C-reactive protein
- Sigmoidoscopy.



Ulcerative Colitis: Endoscopic

- Full colonoscopy to the cecum and entry into the terminal ileum is attempted only if the diagnosis of UC is unclear
- Endoscopic findings in ulcerative colitis include loss of the vascular appearance of the colon, erythema and friability of the mucosa; superficial ulceration, pseudopolyps
- Ulcerative colitis is usually continuous from the rectum, with the rectum almost universally being involved
- There is rarely perianal disease, but cases have been reported
- The degree of involvement endoscopically ranges from proctitis or inflammation of the rectum, to left sided colitis, to pancolitis, which is inflammation involving the ascending colon.

Ulcerative Colitis: Histologic

- Biopsies of the mucosa are taken to definitively diagnose UC and differentiate it from Crohn's disease, which is managed differently clinically
- Microbiological samples are typically taken at the time of endoscopy
- The pathology in UC typically involves distortion of crypt architecture, inflammation of crypts (cryptitis), frank crypt abscesses, and hemorrhage or inflammatory cells in the lamina propria
- In cases where the clinical picture is unclear, the histomorphologic analysis often plays a pivotal role in determining the diagnosis and thus the management
- By contrast, a biopsy analysis may be indeterminate, and thus the clinical progression of the disease must inform its treatment.

- The clinical history can be used to differentiate the various etiologies of chronic diarrhea in patients who have not previously been diagnosed with UC
- For the patient with established UC, the presence of constitutional symptoms and extraintestinal manifestations, particularly arthritis and skin lesions, may provide clues to the severity of the disease
- Physical examination should target the gastrointestinal, dermatologic, and ocular systems
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Ulcerative Colitis: Severity Index

SIGN OR SYMPTOM	MILD	MODERATE	SEVERE
Albumin (g per dL)	Normal	3.0 to 3.5	< 3.0
Body temperature	Normal	37.2 to 37.8°C	> 37.8°C
Bowel movements	< 4 per day	4 to 6 per day	> 6 per day
ESR (mm per hour)	< 20	20 to 30	> 30
Hematocrit (%)	Normal	30 to 40	< 30
Pulse (beats per minute)	< 90	90 to 100	> 100
Weight loss (%)	None	1 to 10	> 10

Ulcerative Colitis: Differentiation

CLINICAL CHARACTERISTICS	
Perianal lesions common; frank bleeding less common than in ulcerative colitis	
udden onset; pathogens present in stool; ain may be a predominant feature	
Meets Rome II criteria for irritable bowel yndrome	
offects older age groups; vascular disease often present; sudden onset, often painful	
lecent antibiotic use; Clostridium lifficile toxin detectable in stool	

- Current medical approaches focus on treating active disease to address symptoms, to improve quality of life, and thereafter to maintain remission
- The long-term benefits of achieving mucosal healing remain unclear
- The treatment chosen for active disease is likely to depend on clinical severity, extent of disease and the person's preference, and may include the use of mesa-lamine (aminosalicylates), corticosteroids or biological drugs
- These drugs can be oral or topical (into the rectum), and corticosteroids may be administered intravenously in people with acute severe disease
- Surgery may be considered as emergency treatment for severe ulcerative colitis that does not respond to drug treatment
- People may also choose to have elective surgery for unresponsive or frequently relapsing disease that is affecting their quality of life.

Ulcerative Colitis: Medications

- First-line medical therapies contain mesa-lamine (5-aminosalicylic acid), which acts topically from the colonic lumen to suppress the production of numerous proinflammatory mediators
- Corticosteroids are often use in conjunction with mesa-lamine drugs to bring about remission of ulcerative colitis
- Cyclosporine is a powerful drug that was designed to prevent rejection after organ transplantation, but it can be effective treatment to induce remission in people with refractory UC, although it cannot be used long-term (to maintain remission) due to potentially toxic side effects
- Biologic treatments (infliximab, adalimumab, golimumab, and vedolizumab) are sometimes used to treat refractory ulcerative colitis alone or in combination with other treatments
- Iron deficiency anemia should be treated with iron supplements.

http://www.aafp.org/afp/2007/1101/p1323.html

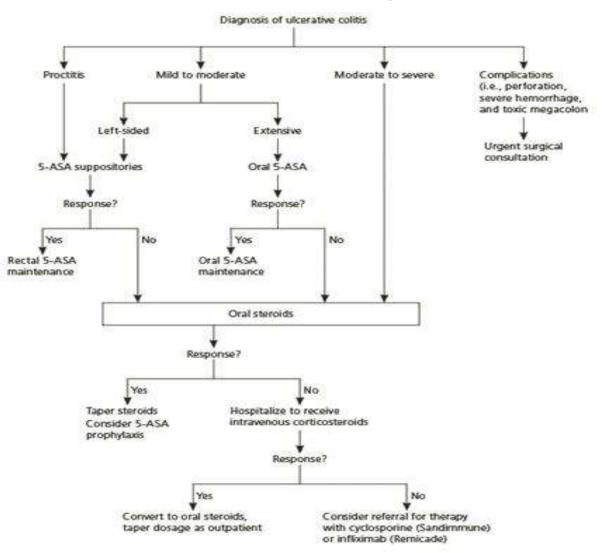
Ulcerative Colitis: Bacterial Recolonization

- Probiotics (such as Escherichia coli Nissle, or Lactobacillus acidophilus) have demonstrated the potential to be helpful in the treatment of UC
- Fecal bacteriotherapy involves the infusion of human probiotics through fecal enemas
 - UC typically requires a more prolonged bacteriotherapy treatment than *Clostridium difficile* infection to be successful, possibly due to the time needed to heal the ulcerated epithelium
 - The response of UC is potentially very favorable with 68% of sufferers experiencing complete remission
 - There have been several reported cases of patients who have remained in remission for up to 13 years.

Ulcerative Colitis: Helminthic Therapy

- Inflammatory bowel disease including UC is less common in the developing world, and some have suggested that this may be because intestinal parasites are more common
- Helminthic therapy using the whipworm Trichuris suis has been shown in a randomized control trial from Iowa to show benefit in patients with UC
- The therapy tests the hygiene hypothesis which argues that the absence of helminths in the colons of patients in the western world may lead to inflammation.

Ulcerative Colitis: Algorithm



Ulcerative Colitis: Surgery

- The gastrointestinal aspects of UC can generally be cured by surgical removal of the large intestine, though extraintestinal symptoms may persist
- This procedure is necessary in the event of: exsanguinating hemorrhage, frank perforation, or documented or strongly suspected carcinoma
- Surgery is also indicated for patients with severe colitis or toxic megacolon
- Patients with symptoms that are disabling and do not respond to drugs may wish to consider whether surgery would improve the quality of life.

Ulcerative Colitis: Dietary Modification

- Removing meat and alcohol from the diet has a significant impact in the reduction of the relapses for UC patients
- Pilot studies have introduced greater plant fibers in a diet, which has had an impact in increasing butyrate levels in the colon countering the hydrogen sulfide levels from meat and alcohol
- Lactose intolerance is noted in many patients and if it is restricted, calcium may need to be supplemented to avoid bone loss
- Patients with abdominal cramping or diarrhea should avoid fresh fruit, caffeine, carbonated drinks, high fructose corn syrup and sorbitol-containing foods
- The carbohydrate diet has been promoted as helping with the symptoms of various auto-immune and gastrointestinal problems, including UC.

Prognosis

- The risk of proximal extension of proctitis over 10 years is 41% to 54%
- The risk of proximal extension of left-sided colitis may be higher
- Disease extent may regress over time, with regression rates estimated from a crude rate of 1.6% to an actual rate of 71% after 10 years
- Benign stricture rarely causes intestinal obstruction
- The risk of colonic malignancy is higher in cases of pancolitis and in cases in which onset of the disease occurs before the age of 15 years
- The most common cause of death is toxic megacolon.

Prophylaxis

- UC cannot be prevented, but there are steps that can be taken to reduce or eliminate symptoms
- Dietary changes, including avoiding certain foods (e.g., dairy products, cabbage, broccoli, beans, spicy foods) and increasing dietary fiber, may help in some cases
- Other foods that may increase UC symptoms include raw fruits, popcorn, alcohol, coffee, chocolate, and soda
- Patients should eat small, frequent meals
- If the condition is active, bland, soft foods may cause less discomfort
- Depressed patients should seek counseling or contact a health care provider
- Exercise, even mild exercise such as walking, biofeedback techniques, yoga, meditation, and hypnosis can help reduce stress.

Abbreviations

IBS - Irritable Bowel Syndrome

GI – gastrointestinal

UC - Ulcerative colitis

Diagnostic and treatment guidelines

Pharmacological Management of IBS

<u>Irritable Bowel Syndrome: a Global Perspective</u>

2014 American College of Gastroenterology Monograph on the Management of

<u>Irritable Bowel Syndrome and Chronic Idiopathic Constipation</u>

<u>Irritable bowel syndrome in adults: diagnosis and management</u>

ACG Releases Recommendations on the Management of Irritable Bowel Syndrome

<u>Ulcerative Colitis in Adults</u>

Guidelines for the management of inflammatory bowel disease in adults

<u>Ulcerative Colitis Treatment & Management</u>

<u>Ulcerative Colitis: Diagnosis and Treatment</u>

<u>Ulcerative colitis: management</u>