

Inflammatory Bowel Disease

Objectives:

NOT FOUND.

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Resources: 435 team + 436 Slides

- <u>Editing file</u>
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Inflammatory Bowel Disease

IBD : 8:58 minutes **Definition**:

IBD is comprised of two major disorders: <u>ulcerative colitis (UC)</u> and <u>crohn's disease(CD)</u>. These disorders have both distinct and overlapping pathologic and clinical characteristics. So it's clinically useful to distinguish between these two conditions because of differences in their management.

Epidemiology:

-More common in the west, but the incidence is increasing in the developing countries including saudi arabia.

- IBD can present at any age:

- The peak: 15-30 years.
- A second peak is 50 years old in our community we just see the peak of (15-30) cus people who are at age of 50 did not live in the environment that promotes the disease .



Etiology:

Both diseases has no clear cause, but there are multiple factors which hypothesized to Play Role:

1- Environmental factors:					
Smoking	Appendectomy	Persistent infection(triggered by organisms and the body exaggerates in response and unregulated inflammation happens)	Defective mucosal integrity	Dysbiosis	Dysregulated immune response
-increases the chance for crohn's disease. -has a protective role in Ulcerative colitis.	have a protective role in Ulcerative colitis.	-mycobacteria -helicobacter sp. -measles,mumps -listeria. -toxigenic -E.coli.	-altered mucus. -increased permeability. -cellular starvation. -impaired restitution.	(<u>change in</u> <u>microbiota</u> <u>of the gut):</u> ↓protective bacteria ↑aggressive commensals	-loss of tolerance -aggressive cellular activation. -defective apoptosis.
2- Diet:	Western diet and Frozen food increase the chance of developing IBD, especially in children less 10 years-old.				



Ulcerative Colitis

Definition: UC is a chronic inflammatory disease characterized by recurrent episodes of inflammation limited to the mucosal layer of the rectum and colon. **Starts at the rectum then extends proximally.**

General characteristics	 Involves the rectum in all cases and can involve the colon either partially or entirely: A. Ulcerative proctitis: rectum alone. B. Ulcerative proctosigmoiditis: rectum and sigmoid colon. C. Left-sided colitis: disease that extends beyond the rectum and as far proximally as the splenic flexure. D.Extensive colitis: beyond the splenic flexure. E.Pancolitis: whole colon. Ulcerative proctitis and Ulcerative proctosigmoiditis" most common" "A+ B" = 40-50% of patients Extending beyond the sigmoid "C+ D" = 30-40% of patients Pancolitis "E" = 20% of patients Ulcerations are not deep . from a clinical point of view we just divide them into (A+B+C) , for example if someone gets extensive colitis , he will be treated as if he got pancolitis . The course is unpredictable and characterized by periodic exacerbation and periods of complete remission. Blood in the stool could be: A. Proctitis: fresh blood or blood-stained mucus that is either mixed with the stool or streaked on the surface. The stool could be normal or hard. B. If the disease extends beyond the rectum, blood is usually mixed with stool or grossly bloody diarrhea may be noted. 	
Clinical features	 Diarrhea (bloody diarrhea). Also called large bowel diarrhea , (they will present with <u>frequency</u> and <u>small amounts</u>) because ulcerations is usually in the rectum , so the rectum cant hold the stool that's why they have <u>urgency</u>). Since it's almost always associated with bloody diarrhea its is more accompanied with anemia. Rectal bleeding (Hematochezia) Crampy abdominal pain. Start when the patient develop "left sided colitis". Tenesmus recurrent need to evacuate the bowel. Passage of mucus. Extraintestinal symptoms: skin lesions, jaundice, arthritis. In moderate to severe disease: anorexia, nausea, vomiting, fever, weight loss. When its only limited to the rectum or sigmoid, the patient won't have severe symptoms 	
Diagnosis	 NO SINGLE MODALITY IS ENOUGH FOR DIAGNOSIS! Combination of clinical picture, laboratory, endoscopy, pathology are required for the diagnosis of UC. Colonoscopy and mucosal biopsy are the gold standard investigation for the diagnosis of UC : 1- stool culture for C. difficile, ova and parasites - to rule out infectious diarrhea. 2- fecal leukocytes. 	



	 3- Colonoscopy: Vascular markings are lost. colon mucosa will disappear Petechiae, exudates, touch friability and frank hemorrhage "rectal bleeding" may be present. Colonic involvement is <u>continuous</u> in ulcerative colitis, in contrast to the patchy nature of Crohn's disease. Superficial ulcerations 	
Pathology	 Inflammation is not transmural, it is limited to the mucosa. Chronic inflammation PMNs accumulate in the crypts of the colon (crypt abscesses) Chronic changes including branching of crypts, atrophy of glands, and loss of mucin in goblet cells. They have pseudo-polyps (thats is the mucosa trying to re-generate) 	
Complications	 Hemorrhage. Perforation. Colon cancer: The risk correlates with extent and duration of colitis. However, in distal proctitis there is no increased risk for colorectal cancer. Toxic megacolon: is the leading cause of death in UC and affects <5% of patients. It is associated with a risk of colonic perforation. (It is a transverse colon with a diameter of more than 5-6 cm with loss of haustration) Iron deficiency anemia Electrolyte disturbances and dehydration secondary to diarrhea Sclerosing cholangitis (SC) Cholangiocarcinoma—Half of all bile duct cancers are associated with UC. Growth retardation. Psychosocial issues (e.g., depression) often due to chronicity and the disabling nature of the disease. 	
Goals of therapy In both CD and UC:	 Induce and maintain remission. Ameliorate symptoms. Improve pts quality of life. Adequate nutrition. Prevent complication of both the disease and medications. 	
Management	 1- Medical: Rule out infections before start treatment (always First thing to do even if it's not the first visit) <u>How? Stool culture.</u> E.g. Salmonella gastroenteritis Even if the patient is a known case of UC , because you don't want to start with steroids and suppress their immune response while they have infection . 	 2- Surgical: often curative (unlike Crohn's disease) and involves total colectomy because there is great chance they will get the cancer in another area Indications for surgery include:
	a. 5-ASA Aminosalicylates : (oral, rectal) work very well with UC but <u>no rule in Crohn's</u> Sulfasalazine (topical application as a suppository) is the mainstay of treatment. Preferred over topical steroids because they are effective as maintenance therapy. Remission rates as high as 93% have been reported.	a. Severe attacks that fail to respond to medical therapy.b. Complications of a severe attack (e.g., perforation, acute dilatation).c. Chronic continuous disease with an impaired quality of life.



• It is effective in <u>induction and maintaining remissions.</u>	d. Dysplasia or carcinoma
5-ASA (mesalamine) is the active component.	
• 5-ASA enemas can be used for proctitis and distal	
colitis.	
give two forms (oral and rectal) if its beyond the rectum	
like rectosigmoiditis, more effective. id 5ASA didnt	
work you give steroids for induction and	
immunomodulators for maintenance.	
b. Systemic corticosteroids are used for acute exacerbations.	
Good for induction of remission ONLY.	
never for maintenance, because of the side effects.	
Systemic: Prednisolone	
• Local acting: enema.	
c. Immunomodulators agents in patients with refractory disease	
may prevent relapses but are not effective for acute attacks.	
(Azithyoprine - Methotrexate) just for maintanance.	
d. Anti TNF therapy (infliximab): if not responding.	
induction and maintaining remissions.	
Contraindicated in the presence of infections.	

Crohn's disease (CD)

Definition:

Is a disorder of uncertain etiology that is characterized by chronic transmural inflammation of the gastrointestinal tract. It's also called (regional enteritis).

Location:

- CD may involve the entire gastrointestinal tract from mouth to the perianal area.
 - 80% Small bowel.
 - 50 % ileocolitis. Most common base of crohn's
 - 20 % colon.
 - \circ 30% perianal disease.
 - UGI < 5 % Upper GI (mouth, stomach, esophagus)





Clinical manifestation:	 Fever, Fatigue and malaise. Early manifestation Abdominal pain (usually RLQ pain), nausea and vomiting. early manifestation Non-bloody diarrhea. late manifestation Malabsorption and weight loss. Weight loss is a late manifestation. The pain is often associated with diarrhea, which is usually watery and does not contain blood or mucus. Extraintestinal manifestation :,Arthritis, Eye involvement: (uveitis - iritis - episcleritis), Skin disorders. Others: Primary sclerosing cholangitis more with UC, Venous and arterial 	
	 thromboembolism ,Renal stones ,Bone loss and osteoporosis ,Vitamin B12 deficiency, aphthous oral ulcers, painless pyoderma gangrenosum and painful erythema nodosum (more details will be mentioned below). Crohn's colitis presents in an identical manner to ulcerative colitis, but <u>rectal sparing</u> and the <u>presence of perianal disease</u> are features which favour a diagnosis of <u>Crohn's disease</u> 	
KEY POINTS IN CD :	 Phlegmon/abscess: walled off inflammatory mass without bacterial infection Crohn's patients are more prone to have fistulas and abscesses than UC patients Fistula: are tracts or communications that connect two epithelial-lined organs a. With other loop of the intestine (enteroenteric). b. With bladder (enterovesical). c. Vagina (enterovgainal). d. With skin (enterocutaneous) Perianal disease: Anorectal diseases (in 30%) Include fissures, abscesses, perianal fistulas (almost exclusively to Crohn's) e. Severe oral involvement: aphthous ulcers. Rarely f. Esophageal involvement: odynophagia and dysphagia. g. Gastroduodenal CD: upper abdominal pain and symptoms of gastric outlet obstruction. h. Gallstones. Usually the inflammation affects the ileum, and the reabsorption of bile salts happens there, normally bile salts bind to cholesterol and make it water soluble, so Without enough bile salts, cholesterol can form stones. i. Increased risk of renal stones (calcium oxalate calculi), inflammation of the small bowel result in accumulation of oxalate in the blood. 	
	The diagnosis of CD is usually established with endoscopic findings or imaging studies in a patient with a compatible clinical history. 1. Compatible clinical history. 2. Endoscopic findings: (the most accurate test) : A. Colonoscopy: B. Wireless capsule endoscopy. (helpful in pediatrics, and useful for identification of small bowel inflammation)	



Diagnosis	Endoscopic features include focal ulcerations adjacent to areas of normal appearing mucosa along with polypoid mucosal changes that give a cobblestone. -You would also see non-caseating granulomas. $\underbrace{\begin{aligned} \hline \hline$		
	3. Imaging studies in a patient:		
	 a. small bowel follow through (SBFT) not done anymore b. computed tomography: CTS or CT enterography c. Magnetic resonance imaging (MRI) or MR enterography best imaging modality for CD. 		
	4. Serologic markers: (used when the diagnosis still unclear) :		
	 Inflammatory marker: ESR, CRP Antineutrophil cytoplasmic antibodies (ANCA) : positive in UC Anti-Saccharomyces cerevisiae antibodies (ASCA) : positive in CD Stool markers: fecal calprotectin. done very often, it detects any inflammation in the small bowel (it won't tell us if its crohn's or gastroenteritis) but at the very least it would tell us there is an inflammation ongoing, meaning it has good sensitivity and not specific. Inflammation would give a positive fecal calprotectin It CAN differentiate between IBS and (IBD or any inflammation) 		
	- Induce and maintain remission.		
Goals of therapy	 Ameliorate symptoms Improve patient quality of life Adequate nutrition Prevent complication of both the disease and medications 		
	1- Medical: Rule out infections (again. First thing to do) How? Stool culture.		
	 a. corticosteroids (systemic = prednisone <u>or</u> long acting = budesonide): for acute exacerbations and if no response to metronidazole. Good for induction of remission ONLY not maintenance b. Immunomodulators (azathioprine,Methotrexate): in conjunction with steroids if the patient does not respond to above agents.Good for induction of remission AND maintenance c. Anti TNF therapy (infliximab) 		



Management:	 d. Bile acid sequestrants (cholestyramine or colestipol): for patients with terminal ileal disease who cannot absorb bile acids e. Antidiarrheal agents generally not a good choice (may cause ileus) 5-ASA has NO role in treating Crohn's disease 	
	2- Surgical: eventually required in most patients we don't want the patient to have short bowel syndrome	
	 Indications for surgery include: small bowel Obstruction, severe perianal disease unresponsive to medical therapy, difficult fistulas (especially between bowel and bladder, vagina), major bleeding, severe disability and perforation or abscess) Conservative surgery, just resect that one affected part, unlike ulcerative colitis you resect the whole bowel. Ileostomy is very helpful, it evacuates the stool if the condition is so severe . because the biggest problem which causes more pain and inflammation is that when the feces gets trapped inside the ulcers. 	
	3- Nutritional supplementation and support: Parenteral nutrition is sometimes necessary.	





Extraintestinal manifestations (BOTH CD AND UC)

Fig. 22.55 Systemic complications of inflammatory bowel disease. (See also Chs 19 and 20.)

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CD and ulcerative colitis share a number of extraintestinal manifestations :

- Eye lesions:
 - Epi-scleritis
 - Anterior **uveitis**: independent course.
 - o iritis.
- Skin lesions:
 - Erythema nodosum: especially in Crohn's disease; parallels bowel disease activity.
 - Pyoderma gangrenosum: especially in UC; parallels bowel disease activity in 50% of cases.
- Arthritis: most common extraintestinal manifestation of IBD.
- Venous and arterial thromboembolism
- Bone loss and Osteoporosis.
- Renal stones
- Gallstones in Crohn's disease (ileal involvement).
- Primary Sclerosing cholangitis in UC.
- Vitamin B12 deficiency





<u>Sum Up :</u>

	Ulcerative colitis	Crohn's disease
Age group	Any	Any
Gender	M = F	Slight female preponderance
Incidence	Stable	Increasing
Ethnic group	Any	Any; more common in Ashkenazi Jews
Genetic factors	HLA-DR*103; colonic epithelial barrier function (HNF4a, LAMB1, CDH1)	Defective innate immunity and autophagy (NOD2 ATG16L1, IRGM)
Risk factors	More common in non-/ex-smokers Appendicectomy protects	More common in smokers
Anatomical distribution	Colon only; begins at anorectal margin with variable proximal extension	Any part of gastrointestinal tract; perianal disease common; patchy distribution, skip lesions
Extra-intestinal manifestations	Common	Common
Presentation	Bloody diarrhoea	Variable; pain, diarrhoea, weight loss all common
Histology	Inflammation limited to mucosa; crypt distortion, cryptitis, crypt abscesses, loss of goblet cells	Submucosal or transmural inflammation common; deep fissuring ulcers, fistulae; patchy changes; granulomas
Management	5-ASA; corticosteroids; azathioprine; biological therapy (anti-TNF); colectorny is curative	Corticosteroids; azathioprine; methotrexate; biological therapy (anti-TNF); nutritional therapy; surgery for complications is not curative; 5-ASA not effective

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Feature	CD	UC			
	Characteristics of CD and UC				
Location	SB or colon	colon			
Anatomic distribution	Skip lesions	Continuous			
Rectal involvement	Rectal spare	Involved in >90%			
Gross bleeding	Only 25%	Universal			
Peri-anal disease	1/3	Rare			
Fistulization	Yes	No			
Granulomas	30%	No			
Endoscopic features of CD and UC					

Mucosal involvement	Discontinuous	Continuous	
Aphthous ulcers	Common	Rare	
Surrounding mucosa	Relatively normal	Abnormal	
Longitudinal ulcer	Common	Rare	
Cobble stoning	In severe cases	No	
Mucosal friability	Uncommon	Common	
Vascular pattern	Normal	distorted	
Pathologic features of CD and UC			
Transmural inflammation	Yes	Uncommon	
Granulomas	30%	No	
Fissures	Common	Rare	
Fibrosis	Common	No	
Submucosal inflammation	Common	Uncommon	

SUMMARY

	Ulcerative colitis	Crohn's disease	
Age of onset	* The peak :15 - 30 years * A second peak 50		
Etiology	* Genetic factors: NOD2/CARD15 *		
Involvement	 * limited to the mucosal layer of the colon * Start rectum then extend proximally * can be presented as: proctitis proctosigmoiditis / Left-sided colitis Extensive colitis / Pancolitis 	 * transmural inflammation may involve the entire gastrointestinal tract. * the most common presentation is ileocolitis 	
Clinical features	 * diarrhea * rectal bleeding * tenesmus * passage of mucus * crampy abdominal abdominal pain * blood – stained mucus Streaked onto the surface of stool → in case of proctitis * blood is usually mixed with stool or grossly bloody diarrhea → disease extends beyond the rectum * anorexia, nausea, vomiting, fever, weight Loss → in case of excessive and pancolitis * <u>complications :</u> (Hemorrhage -Perforation Toxic megacolon - cancer) 	 * Fatigue * Diarrhea and Weight loss " late symptoms because crohn's typically affect small area " * Abdominal pain * Fever * Phlegmon/abscess (with no pus) * fistulas (due to transmural involvement) * Perianal disease * aphthous ulcers * Esophageal involvement →odynophagia and dysphagia. * Gastroduodenal CD → upper abdominal pain and gastric obstruction symptoms * gallstones * <u>Extraintestinal mnifistatiom:</u> (Arthritis - Eye involvement - Skin disorders " eg: erythema nodosum" - Primary sclerosing cholangitis - thromboembolism - Renal stones - osteoporosis ,Vitamin B12 deficiency). 	
Investigation : CD need different modalities and it difficult to be diagnosed	* Colonoscopy	 * Colonoscopy * Wireless capsule endoscopy (before use it we have to insure that there is no stricture in small bowe) * SBFT (we used to use it in the past) * CT * MRI * Serologic markers 	
Findings	 * The vascular markings are lost * superficial ulceration * continuous involvement * pathology : - crypt abscesses - signs of chronic inflammation 	 * skip lesions * cobblestone * Serologic markers: - ERS , CRP - antibodies : (pANKA) , (ASCA) - stool markers : fecal calprotectin (to investigate if there is inflammation or not so 	

		can help in differentiation between IBD and IBS)
Management : To induce and maintain remission, improve quality of life and prevent complications	 * Role out infection * 5 ASA therapy → indicates and maintain remission * corticosteroid * Immunomodulators → maintain remission - Azathioprine - Methotrexate * biological therapy: - Anti TNF therapy → indicates and maintain remission 	 * Role out infection * corticosteroid * Immunomodulators → maintain remission - Azathioprine - Methotrexate * biological therapy: - Anti TNF therapy → indicates and maintain remission
Surgery indications " last option, but do not wait until the patient is very sick and can not survive during surgery"	 * Severe attacks that fail to respond to medical therapy * Complications * impaired quality of life * Dysplasia or carcinoma 	 *Obstruction, *severe perianal disease unresponsive to medical therapy *major bleeding * severe disability

QUESTIONS

_1/ A 35-year-old white man presents with diarrhea, weight loss, and RLQ pain. On examination, a tender mass is noted in the RLQ; the stool is guaiac-positive. Colonoscopy shows segmental areas of inflammation. Barium small bowel series shows nodular thickening of the terminal ileum.

- a. Ulcerative colitis
- b. Crohn disease
- c. Ischemic colitis
- d. Diverticulosis

2/ A 75-year-old African American woman, previously healthy, presents with low-grade fever, diarrhea, and rectal bleeding. Colonoscopy shows continuous erythema from rectum to mid-transverse colon. The cecum is normal.

- a. Ulcerative colitis
- b. Crohn disease
- c. Ischemic colitis
- d. Diverticulosis

3/19-year-old woman presents with a 3-month history of crampy abdominal pain not related to eating. She also has bloody diarrhea, is fatigued, and has lost 5 pounds. She has both constipation and diarrhea. She has tender red sores on the anterior aspects of her lower extremities and decreased range of motion at the lumbar spine. She has anemia with a hemoglobin of 1 0.8 g/dl.

Which of the following is the most likely diagnosis?

- a. Inflammatory bowel disease
- b. Infectious colitis
- c. Irritable bowel disease
- d. Anal fissure

4/ A 32-year-old woman has a history of chronic diarrhea and gallstones and now has rectovaginal fistula. Which of the following is the most likely diagnosis?

- A. Crohn disease
- B. Ulcerative colitis
- C. Systemic lupus erythematosus
- D. Laxative abuse

5/ A 24-year-old male presents to your office having with worsening RLQ cramping abdominal pain for the past 2 months. He reports having diarrhea on and off for the past 1 to 2 years. He previously had colonoscopy with a terminal ileum biopsy showing ulceration, acute inflammation, and noncaseating granulomas. Two months ago he was placed on mesalamine. He has lost 20 lb since then despite attempting to increase his dietary intake. He denies any other medical problems and takes no other medications. His physical examination reveals mild tenderness in the RLQ with normal bowel sounds. There are no anal fissures or fistulae. His stool is negative for occult blood. Vital signs are as follows: Temperature = 98.7°F, RR = 15, BP = 122/78 mm Hg, pulse = 65. BMI 21. Laboratory test results show normal liver/renal function. CBC shows Hgb 9.9 g/dL, MCV 82 fL, WBC 10.1 × 103/mm3. X-ray abdomen reveals nonspecific gas pattern without free air or distended bowel loops. CT enterography reveals thickened mucosa in distal ileum with adjacent mesenteric stranding; there is no fistula, abscess, or free air present. What would be the single most effective intervention recommended to this patient?

- A. Loperamide
- B. Azathioprine
- C. Infliximab
- D. Surgical resection

answers :1/B 2/A 3/A 4/A 5/C