

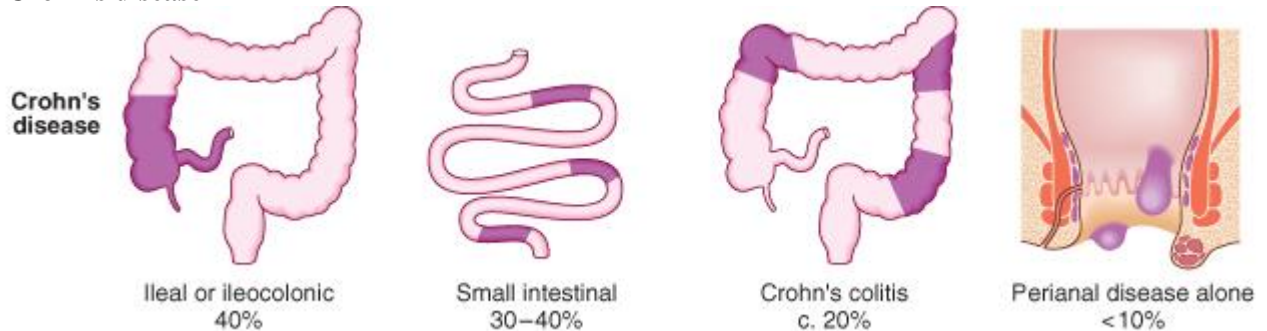
## Lecture 6[2hrs]

### Physical signs

#### \*Ulcerative colitis

- \*With extensive disease, patients have abdominal tenderness.
- \*Patients with toxic colitis have severe pain, bleeding, fever, and tachycardia.
- \*Those with megacolon [ hepatic tympanic on percussion].
- \* Patients with proctitis have a tender anal canal and blood on rectal examination.

#### 2- Crohn's disease



Crohn's disease is characterized by patchy, transmural inflammation the entire wall of the bowel is edematous and thickened. There are deep ulcers that appear as linear fissures thus the mucosa between them is described as cobblestone. The bowel wall thickens and becomes narrowed and Fibrotic, leading to chronic recurrent bowel obstructions, which may affect any part of the gastrointestinal tract. It may be defined by location (terminal ileal, colonic, ileocolic, upper gastrointestinal), or by a pattern of disease (inflammatory, fistulating, or stricture formation). The rectum is often spared.

#### Histological

The earliest lesions of the CD are aphthoid ulcerations, non-caseating granulomas. Chronic inflammation through all layers of the bowel wall from mucosa to serosa that is accompanied by fissures that penetrate deeply into the bowel wall and sometimes form fistulous tracts or local abscesses. Granulomas can be seen in lymph nodes, mesentery, peritoneum, liver, and pancreas

#### Clinical Features of Crohn's disease include

- \*Watery Diarrhea and does not contain blood or mucus. Due to bile acid malabsorption.
- \*Abdominal pain [due to sub-acute intestinal obstruction, inflammation, biliary or renal stone],
- \*Weight loss due to Malabsorption or patient avoids food since eating provokes pain.
- \*Fever, malaise, anorexia, and vomiting [from jejunal obstruction].
- \*Aphthous ulcer, refractory DU. \*Bloody diarrhea, the passage of mucus if there is colonic involvement.

#### Physical examination

- \*Evidence of wt. loss, Anemia, glossitis and angular stomatitis due to malabsorption
- \*Abdominal tenderness most marked over the inflamed area.
- \*Abdominal mass due to matted loops of thickened bowel or intra-abdominal abscess.
- \*Perianal skin tags, fissures, or fistulae.

#### Investigations of IBD

##### Blood tests

- Elevated sedimentation rate[ESR] and C-reactive protein.
- Hypoalbuminemia as a consequence of protein-losing Enteropathy.
- Anemia results from iron, folic acid, or Vit. B12 Malabsorption.
- Leukocytosis.
- ASCA [anti-Saccharomyces cerevisiae antibodies]. pANCA[perinuclear antineutrophil cytoplasmic antibodies].

ASCA 40-60% positive in CD and 5% in UC

pANCA 60-65% in UC and 20-25 in CD

##### Bacteriology

\*Stool cultures to exclude superimposed enteric infection in a patient who presents with an exacerbation of IBD\*Stool for Calprotectin.

\*Blood culture for the patient with colitis or Crohn's disease

### **Endoscopy**

#### **Endoscopic appearance in UC include**

\*In UC the disease is continuous and more severe in the distal colon and rectum.

\*The mucosa is erythematous, loss of vascular patterns and contact bleeding and in more severe disease a fine granular surface, petechial hemorrhages, spontaneous bleeding, discrete ulcers, and purulent exudates, inflammatory polyps (pseudo polyps).

\*The mucosa may appear normal in remission but in patients with many years of disease it appears atrophic and featureless and the entire colon becomes narrowed

#### **Endoscopic appearance in Crohn's colitis include**

The appearance may be identical to UC but skip lesions, strictures and deeper ulcers are characteristic

### **Barium studies.**

Is a less sensitive investigation than colonoscopy for the investigation of colitis.

\*In long-standing UC the colon is shortened and loss of haustra to become tubular and pseudo polyps are seen.

\*Contrast study of the small bowel is normal in UC

\*Contrast study of small bowel in CD [Affected areas are narrowed and ulcerated, multiple strictures are common.]

### **Plain abdominal radiographs**

Show colonic dilatation, mucosal edema [thumb-printing], or evidence of perforation.

In small bowel Crohn's disease, there may be evidence of intestinal obstruction or displacement of the bowel loop by a mass.

### **Radionuclide scans**

Radio-labeled white cell scans show areas of active inflammation.

### **MRI**

Is very accurate in delineating pelvic or perineal involvement by Crohn's disease.

### **Complications of IBD**

#### **1-Intestinal**

\***Toxic Megacolon.** defined as acute colonic dilatation with a transverse colon diameter of >6 cm (on imaging examination). Develop as a result of the extension of the inflammatory process to the muscularis propria and serosa causing atony leading to the accumulation of gas and fluid within the lumen and subsequent colonic dilatation, perforation, and peritonitis. This complication occurs in both UC and CD most commonly during the first attack of colitis. Predisposing factors for the development of toxic megacolon include the administration of NSAID, narcotics, anticholinergics.

Toxic megacolon may complicate any severe inflammatory condition of the bowel like bacterial colitis, pseudomembranous colitis

\***Perforation** of the small intestine or colon may occur.

\***Fistula and perianal disease.** Fistulous connections between loops of affected bowel or between bowel and bladder or vagina are a specific complication of Crohn's disease and do not occur in UC.

1-Enterointestinal fistulae. Causes diarrhea and Malabsorption due to blind loop syndrome.

2-Enterovesical fistulae. Causes recurrent urinary tract infections and pneumaturia.

3-Enterovaginal fistula. Causes a feculent vaginal discharge.

4-Perianal or ischiorectal [abscess, fissures, and fistulae].

#### **\*Cancer**

Both chronic UC and CD predispose to adenocarcinoma of the colon .the risk of cancer is directly related to the extent of colonic involvement and duration of disease. Patients with extensive colitis >8 years are at increased risk of colon cancer. Small bowel adenocarcinoma is a rare complication of Crohn's disease. Patients with long-standing extensive colitis are therefore entered into a surveillance colonoscopy program beginning 8-10 y after diagnosis.

And patient with left side colitis after 10-15 years. Surveillance is to perform colonoscopy with

Multiple random biopsies .patients who have no evidence of dysplasia or only low-grade dysplasia are screened every year to every 2 years. While those with high-grade dysplasia should be considered for proctocolectomy because of the high risk of colon cancer development.

About 50% to 60% of patients with IBD have extra-intestinal manifestations(EIMs).

### **2-Extra Intestinal manifestations [EIMs] that Parallel disease activity include**

\*Conjunctivitis, Iritis, Episcleritis

\*Mouth ulcers

\*Portal pyemia, Liver abscess

\*Mesenteric or portal vein thrombosis

\*Venous thrombosis

\*Arthralgia of large joints. It is asymmetric, polyarticular, migratory and most often affects large joints of the upper and lower extremities

\*Erythema nodosum [EN].These are hot, red, and tender nodules found on the anterior surface of the lower legs, ankles, calves, thighs, and arms. Measuring 1 to 5 cm in diameter.

\*Pyoderma gangrenosum [PG].Lesions are commonly found on the dorsal surface of the feet and legs but may occur on the arms, chest, and face. PG usually begins as a pustule and then spreads concentrically to involve healthy skin. Lesions then ulcerate with violaceous edges surrounded by a margin of erythema.

### **3-The Extra intestinal [EIMs] that run a course independent of disease activity include**

\*Autoimmune hepatitis.

\*Sclerosing cholangitis, Cholangiocarcinoma.

\*Gallstones.

\*Sacroilitis/Ankylosing spondylitis.

\*Metabolic bone disease.

\*Amyloidosis.

\*Oxalate calculi.

Calcium oxalate stones develop secondary to hyperoxaluria, which results from increased absorption of dietary oxalate. Normally dietary calcium combines with luminal oxalate to form insoluble calcium oxalate which is eliminated in the stool. In patients with the ileal disease, non absorbed fatty acids bind calcium and leave oxalate unbound. The unbound oxalate is then delivered to the colon where it is readily absorbed especially in the presence of colonic inflammation.

### **Differential diagnosis of IBD**

**\*Conditions that can mimic UC or CD.**

#### **Infective**

\*Bacterial. Salmonella, shigella, campylobacter, enteropathic.Ecoli, gonococcal proctitis, pseudomembranous colitis.

\*Viral. Herpes simplex and Chlamydia proctitis \*Protozoa. Amoebiasis

#### **Non-infective**

\*Vascular. Ischemic colitis, Radiation proctitis

\*Idiopathic.Collagenous colitis, Behcet's disease

\*Drugs. NSAID\*Colonic carcinoma\*Diverticulitis

#### **\*Differential diagnosis of small bowel Crohn's disease**

\* right iliac fosse mass.Caecal carcinoma and Appendix abscess

\*Infection. [TB, yersinia, actinomycosis]

\*Mesenteric adenitis\*Pelvic inflammatory disease \*Lymphoma

### **Management**

The aims of therapy are to

\*Treat attacks[ induction therapy]\*Prevent relapses [maintenance therapy]

\*Detect carcinoma at an early stage.\*Select patients for surgery.

### **Drugs used in the treatment of IBD include**

**1-Corticosteroids.** Glucocorticoids are used to induce remission in mild-to-severe UC and CD.

\*Prednisolone [30-40 mg/day orally] for 2w and then reduced slowly over 8 W.

Severe active colitis can be treated by IV methyl-Prednisolone [60mg daily] by infusion, once improvement occurs the patient is converted to oral steroid.

\*Steroid foam or liquid retention enemas for procto-sigmoiditis Patient with very active procto-sigmoiditis those who are unable to retain enemas need oral steroids

\*Systemic and local steroid can be used for extensive disease

Side effects of glucocorticoids include

Acne, hypertension, hirsutism, cataracts, striae, hyperglycemia, hyperlipidemia, insomnia, episodes, adrenal suppression, and weight gain, hyperactivity, acute psychotic

**2-5-Amino-Salicylic-Acid** [5-ASA] and Sulfasalazine [sulfapyridine bound to 5-ASA] which acts by modulating intestinal inflammatory activity. A high concentration of 5-ASA is delivered to the colon using the preparations mesalazine or olsalazine. Dose 2 - 4.8 g/d. Doses of 1.5-4 g/d maintain remission in 50 to 75% of patients with UC and CD.

liquid or foam retention enemas are used for treating active proctitis. [500mg twice a day] or oral with local for more extensive disease. aminosalicylates are considered first-line agent

side effects of sulfasalazine (attributed to the sulfa moiety) include nausea dyspepsia, headache, interference with folic acid absorption, and occasionally hemolytic anemia, agranulocytosis, hepatitis, or pneumonitis. Patients taking sulfasalazine should be given folate 1 mg

### **3-immunomodulators drugs**

#### Azathioprine

For Patient who relapse frequently after courses of steroids or who require maintenance steroid therapy

**Azathioprine**[1.5-2mg/kg daily] is a prodrug that is converted to 6-MP Both are used to maintain remission in UC and CD these are purine analogs that interfere with nucleic acid metabolism and cell growth and exert cytotoxic effects on lymphoid cells. This immunosuppressant drug exerts its maximal effect only after 6-12 W and steroid therapy should continue until this time. Side effects are bone marrow suppression, nausea, vomiting, or acute pancreatitis.

**Methotrexate** for CD. a folic acid antagonist and has antimetabolite and anti-inflammatory actions dose 15-25 Mg Weekly SC or IV

\***Cyclosporine** Cyclosporine is a potent inhibitor of cell-mediated immunity for induction of remission in a patient with steroid-refractory UC **dose 4 mg kg IV.**

### **4-Biological therapy**

#### Anti-TNF agents include

infliximab, adalimumab, certolizumab[ monoclonal antibody against TNF] for a severe CD with refractory perianal and Entero- cutaneous fistulas or UC

\***Infliximab** [5 mg/kg)0,2,6 and then every 8 W] -

Side effects include sepsis, reactivation of tuberculosis, fungal infection, and T-cell lymphoma. Infusion reactions, characterized by chest pain, shortness of breath, rash, and hypotension, are more common

#### Anti-adhesion molecules

##### Natalizumab

monoclonal antibodies against lymphocyte adhesion molecules indicate for CD unresponsive to biological therapy

#### **agents targeting IL-12/23**

#### **Induction therapy for UC Based on Disease Severity**

##### **\*Mild Disease**

##### **5-Aminosalicylates**

Topical (distal colitis)

Oral (distal/extensive colitis)

Combination

##### **\*Moderate Disease**

##### **5-Aminosalicylates**

Topical (distal colitis)

Oral (distal/extensive colitis)

Combination

## **Glucocorticoids**

Topical (distal colitis), Oral (distal/extensive colitis) or Combination

Azathioprine or 6-mercaptopurine

Infliximab or adalimumab

### **\*Severe Disease**

IV glucocorticoids

Cyclosporine

Infliximab, adalimumab, or vedolizumab

## **Maintenance therapy for UC**

\*5-Aminosalicylates

Topical (distal colitis)

Oral (distal/extensive colitis)

Combination

\*Azathioprine or 6-mercaptopurine

\*Infliximab or adalimumab

## **Drugs used treatment of Small Bowel Crohn's Disease include**

\*Corticosteroids [Prednisolone 30-40 mg/day] reducing over 6-8 weeks

\*Azathioprine [1.5-2 mg/kg] for a patient who relapses after stopping steroids or who are steroid dependent.

\*Budesonide [this is a potent synthetic corticosteroid which reduces mucosal inflammation 9mg equivalent to 30 mg of Prednisolone. following absorption the drug undergoes first-pass metabolism in the liver, adrenocortical suppression is minimized and steroid side effects are reduced.

## **Metabolic bone disease**

The patient should encourage exercising, adequate calcium intake and bisphosphonate should be given if osteoporosis is documented.

## **Nutritional therapy**

The best advice for the majority of the patient is to eat a well-balanced diet with protein, mineral, and Vit, supplements. Patients with small bowel stricture should avoid nuts, raw fruit, and vegetable which may precipitate intestinal obstruction. Patient with proctitis and constipation needs dietary fibers.

## **Management of complications**

### **\*Fulminant colitis**

This is a life-threatening complication that needs intensive medical and surgical management

The patient should be monitored for clinical signs of peritonitis, fever, tachycardia, stool frequency, and volumes and abdominal x-ray are taken daily for evidence of toxic dilatation or perforation.

Steps in the management of fulminant UC are

\*IV fluids\*Blood Transfusion if Hb<10 gr.

\*IV methylprednisolone [60mg daily] or hydrocortisone.\*Antibiotic for infection

\*Nutritional support \*SC heparin for prophylaxis of thromboembolism

\*Avoidance of opiates and antidiarrheal agents

\*Urgent colectomy If improvement has not occurred within 5-7 days or the patient deteriorates.

### **Perianal disease**

\*Ciprofloxacin (500 mg bid).

\*Metronidazole dose is 15 to 20 mg/kg per day in three divided doses; it is usually continued for several months

\*Abscess requires drainage.

\*Infliximab may induce remission in resistant cases

## **Dysplasia and colorectal cancer**

Patients with long-standing UC or colonic CD are at increased risk of colorectal cancer. The most important risk factors colonic cancer in IBD are severity, extension, duration

Patients with long-standing UC or colonic CD are at increased risk of colorectal cancer

Pancolitis more than 8 years is associated with the highest risk.

**Indication for Surgery at UC include.**

\*Colonic dysplasia or carcinoma, \*Colonic perforation, \*Growth retardation, \*refractory disease  
\*Toxic megacolon, \*Uncontrollable colonic hemorrhage, \*Intolerable or unacceptable side effects of medical therapy, \*Systemic complications that are recurrent or unmanageable like Arthritis, Pyoderma gangrenosum, Surgery involves removal of the colon and the rectum with ileostomy or ileal anal pouch.

**The indications for surgery in Crohn's Disease**

Are similar to those for UC and fistulae, abscesses, perianal disease, and small or large bowel obstruction. Because CD is chronic and recurrent with no clear surgical cure, as little intestine as possible should be resected.

**Prognosis**

-90% of UC patients have intermittent disease activity. -10% have continuous symptoms

-1/3 of those with pancolitis undergo colectomy within 5 y of diagnosis.

-80% of CD undergoes surgery at some stage

-70% of these require more than one operation during their lifetime.

**Microscopic Colitis**

Characterized by watery diarrhea[secretory] with normal-looking mucosa. Mucosal biopsies revealed chronic inflammation in the absence of crypt architectural distortion. it is more common in females and associated with rheumatoid arthritis, DM, and Coeliac disease.

Types of microscopic colitis include

1-Lymphocytic colitis. Characterized by an increased number of intraepithelial lymphocytes.

2-Collagenous colitis. Characterized by a subepithelial collagen band >10 micrometers thick.

**Treatment**

\*Antidiarrheal drugs, bismuth, aminosalicylates, and topical steroid enema