## **Crohn's Disease**



## Introduction

- Crohn's Disease is an idiopathic, chronic, transmural inflammatory process of the bowel that can affect any part of the gastro intestinal tract from the mouth to the anus.
- Most cases involve the small bowel, particularly the terminal ileum.

## Prevalence

- Higher number of cases of Crohn's disease found in western industrialized nations.
- Males and females are equally affected.
- Smokers are three times more likely to develop Crohn's disease.
- Crohn's disease tends to present initially in the teens and twenties.

## Aetiology

- Incompletely understood
- Complex interplay of genetic and environmental factors.
- Although CD shares some features with Chronic infection, no causative organism has ever been demonstrated.
- Smoking increases the risk
- Relationship between the gut mucosa and the normal gut bacteria becomes deranged, resulting in uncontrolled intestinal inflammation.

#### Microbes

- A.V. Singh et al. have suggested that *Mycobacterium avium subspecies paratuberculosis* (MAP) were identified in 100% of subjects with CD ;75% of attendants of MAP infected animals were positive.
- Psychrotrophic bacteria such as Yersinia spp and Listeria spp contribute to Crohn's disease.



Mycobacterium avi

sis colonies from stool tient

## Pathogenesis

- An **increased permeability** of the mucous membrane.
- This may lead to increased passage of luminal antigens, which then induce a cell-mediated inflammatory response.
- This results in the release of proinflammatory cytokines, such as interleukin-2 and tumour necrosis factor,
- which coordinate local and systemic inflammatory responses.
- potentially genetically determined increase in gut permeability, combined with an abnormal immune-mediated response to colonisation of the gut with subspecies of the normal enteric microflora, may initiate the disease.

#### Pathophysiology of CD



## Pathology

- The terminal ileum is most commonly involved (60 per cent), either in isolation or in combination with colonic disease.
- Colitis alone occurs in up to a third of cases and the remainder are patients with more proximal small bowel involvement.
- The stomach and duodenum are affected in around 5 per cent
- Perianal lesions are common, affecting up to 50– 75 per cent

#### **Distribution of gastrointestinal Crohn's disease :Data from American Gastroenterological Association**





## Pathology (Macroscopically)

- A fibrotic thickening of the intestinal wall with a narrow lumen and fat wrapping (encroachment of mesenteric fat around the bowel,
- There is usually dilated bowel proximal to the stricture and deep mucosal ulcerations with linear or snake-like patterns in the strictured area itself.
- Oedema in the mucosa between the ulcers gives rise to a cobblestone appearance.

- The transmural inflammation (which is a key feature of CD) may lead to segments of bowel becoming adherent to each other and to surrounding structures, inflammatory masses with mesenteric abscesses and fistulae into adjacent organs.
- The serosa is usually opaque, with thickening of the mesentery and enlarged mesenteric lymph nodes.

CD is characteristically discontinuous, with inflamed areas separated from normal intestine, so-called 'skip' lesions. Crohn's disease of the ileocaecal region showing typical thickening of the wall of the terminal ileum with narrowing of the lumen



# Colonic Crohn's disease. Note the normal mucosa on either side of the inflammatory stricture



## Microscopically

- There are focal areas of chronic inflammation involving all layers of the intestinal wall with lymphoid aggregates.
- Non-caseating giant cell granulomas are found
- Multifocal arterial occlusions are found in the muscularis propria, which is thickened.
- There is deep, fissuring ulceration within affected areas.
- Characteristically, and unlike in UC, there may be completely normal areas immediately next to areas of severe inflammation.

### Section of Colectomy Showing Transmural Inflammation





## **Classification of CD**

On the behavior of disease as it progresses:

• **Stricturing** disease causes narrowing of the bowel which may lead to bowel obstruction or changes in the caliber of the feces.



#### Stricturing

## **Classification of CD**

- **Penetrating** disease creates abnormal passage ways between the bowel and other structures such as the skin.
- Inflammatory disease causes inflammation without causing strictures or fistulae.



#### Inflammatory



#### Penetrating

## **CLINICAL FEATURES**



## **Clinical features(Acute)**

- Acute ileal inflammation and symptoms and signs resembling those of acute appendicitis,
- Perforation of the small intestine, resulting in a local or diffuse peritonitis.
- Fulminant colitis but this is considerably less common than in UC

## **Clinical features(chronic)**

- Commonly presents with features of chronicity.
- Manifests as mild diarrhoea extending over many months, occurring in bouts accompanied by intestinal colic.
- pain, particularly in the right iliac fossa, and a tender mass may be palpable.
- Intermittent fevers, secondary anaemia and weight loss are common.
- After months of repeated attacks with acute inflammation, the affected area of intestine begins to narrow with fibrosis, causing obstructive symptoms.
- Children developing the illness before puberty may have retarded growth and sexual development.
- With progression of the disease, adhesions and **transmural fissuring**, intra-abdominal abscesses and fistula tracts may develop.

## **Clinical features(chronic)**

 Fistulation may occur into adjacent loops of bowel (enteroenteric

fistulae), and, most notably the (healthy) sigmoid loop may become adherent to the affected terminal ileum, resulting

in ileosigmoid fistulation and profuse diarrhoea.

Fistulation may also occur into the bladder (ileovesical) or the female genital tract and, less commonly, the duodenum. Fistulation into the abdominal wall (enterocutaneous fistulation) may also develop spontaneously, but more commonly occurs as a

complication of abdominal surgery.

## **Clinical features(chronic)**

- colitis and proctitis
- Perianal abscesses and fistulae, rectovaginal fistula
- In severe cases, the perineum may become densely fibrotic, rigid and covered with multiple discharging openings (watering-can perineum).

#### Complications



#### Intestinal Complications of Crohn's Disease Sore or Ulcer

- The cells in lining of the intestines are shed and replaced on a regular basis in a healthy body.
- When the lining of the intestine is irritated, cells may be shed more frequently, causing ulcers.
- The sores and ulcers are most common in ileum, colon or rectum.
- Ulcers can be serious if they go through the intestines and damage an artery.
- This can lead to life-threatening bleeding.

#### Fistula

- Sores and ulcers can become deep and form tunnel through the tissues of nearby organs:
- > The rectum
- Other parts of the intestine
- ➤ The bladder
- The vagina
- > The skin.
- These tunnels are called "fistulas," and can become infected.
- Fistulas require special treatment, such as medication or even surgery.



#### Abscess

- An abscess is a collection of pus that has formed as a result of fistula due to an infection.
- An abscess must be drained in order to heal or surgery may be recommended to remove the infected portion of bowel.

#### **Bowel Obstruction**

- The most common complication of Crohn's disease is blockage of the intestine, known as a bowel obstruction occurs in up to 30 % of people.
- A bowel obstruction occurs because the disease tends to thicken the intestinal wall with swelling and scar tissue, narrowing or even blocking the passage.

#### Cancer

- Crohn's disease may increase risk of developing cancer.
- If the inflammation is mainly in small intestine, risk of cancer of the small intestine is increased.
- The risk of cancer gets higher as great as 32 times the normal rate if the whole colon is involved.

#### Perforation

- A perforation is a hole in the bowel.
- The size, location, and seriousness of the hole can vary.
- Small perforations often seal themselves off.
- More serious bowel perforations may require a surgery and removal of the damaged area.

#### **Toxic Megacolon**

- More serious complications of Crohn's disease is called "toxic megacolon," which occurs when the large intestine stops working and expands suddenly.
- This can cause it to bleed excessively, or even rupture which can be very dangerous.

#### **Systemic Complications of Crohn's Disease**

#### Osteoporosis

- Osteoporosis is a threat to people with Crohn's disease because of:
- Low calcium and vitamin D intake
- Poor absorption of nutrients in the body
- The use of corticosteroids
- In a cohort study of 6207 patients with chronic inflammatory bowel disease, osteoporotic fractures were found in 25% of patients and vertebral fractures in 7%; in addition, the age at fracture occurrence was 10–15 years younger than in healthy controls. A 40% increase in the fracture risk has been reported in patients with Crohn's disease.
- Similarly, Klaus et al. reported that 22% of 293 patients with Crohn's disease had one or more vertebral fractures and that 35% of patients with vertebral fractures were younger than 30 years of age.

#### **Systemic Complications of Crohn's Disease**

**Joint Problems** 

- Up to 25 percent of people with Crohn's disease will have joint complications.
- This may include intermittent joint tenderness or arthritis include ankylosing spondylitis.



Anky

## **Skin Problems**

- Erythema nodosum presents as red nodules on the shins is due to inflammation of the underlying subcutaneous tissue and is characterized by septal panniculitis.
- Skin complications occur in about 15 percent of people with Crohn's disease.



Erythema nodosum on the back and leg of a person with Crohn's Disease

#### **Systemic Complications of Crohn's Disease**

- Pyoderma gangrenosum is a painful ulcerating nodule.
- Clubbing, a deformity of the ends of the fingers, also be a result of Crohn's disease.





Pyoderma gangrenosum on the leg of a person with Crohn's Disease

Clubbing

#### **Systemic Complications of Crohn's Disease**

#### **Eye Problems**

- Eye complications occur in about 5 percent of people with Crohn's disease. These include:
- Iritis (inflammation of the colored part of the eyes)
- Uveitis (inflammation of the middle layer of the eye)
- Episcleritis (inflammation of the white part of the eyes)





## Extraintestinal manifestations of Crohn's disease

#### **Related to disease activity**

- Erythema nodosum
- Pyoderma gangrenosum
- Arthropathy
- Eye complications (iritis/uveitis)
- Aphthous ulceration
- Amyloidosis

#### Unrelated to disease activity

- Gallstones
- Renal calculi
- Primary sclerosing cholangitis
- Chronic active hepatitis
- Sacroiliitis
#### Diagnosis



- Crohn's disease does not diagnose with complete certainty.
- A colonoscopy is 70% effective in diagnosing the disease via direct visualization of the colon and the terminal ileum.
- Capsule endoscopy help in endoscopic diagnosis.
- 30% of Crohn's disease involves only the ileum, cannulation of the terminal ileum is required in making the diagnosis.

## Investigations

#### Laboratory

- Anaemia
- fall in serum albumin, magnesium, zinc and selenium.
- Acute phase protein measurements (C-reactive protein and orosomucoid) may correlate with disease activity.

## Endoscopy(Colonoscopy)

- Patchy inflammation.
- Inflamed mucosa that are irregular and ulcerated, with a mucopurulent exudate.
- The earliest appearances are aphthous ulcers surrounded by a rim of erythematous mucosa.
- These become larger and deeper with increasing severity of disease.
- There may be stricturing,

## Endoscopy image of colon showing serpiginous ulcer in Crohn's disease



# Upper gastrointestinal endoscopy,

- Deep longitudinal ulcers
- cobblestone mucosa in the duodenum, stomach
- Enteroscopy may reveal jejunal ulcerationand stricturing.

#### **CT** scan showing Crohn's disease in the fundus of the stomach



#### Endoscopic image of Crohn's colitis showing deep ulceration



#### **Radiologic Tests**

- A barium X-ray where barium sulfate suspension is ingested and fluoroscopic images of the bowel are taken to check inflammation and narrowing of the small bowel.
- Identifying anatomical abnormalities when strictures of the colon are too small for a colonoscope to pass through, or in the detection of colonic fistulae.





## Aphthoid ulcers (target sign)

 <u>Pathology</u>: mucosal ulcers with surrounding translucent mound of edema.



## Fissure ulcers (Rose thorn appearanc • <u>Pathology:</u> transmural ulcers



## Nodular pattern

#### • <u>Pathology:</u> Submucosal edema of the villi.



Ulcero-nodular pattern (Cobble stone appearance)

 <u>Pathology</u>: transverse & longitudinal fissure ulcers with intervening edematous mucosa.



# Straightening of the mesenteric border & sacculation of the ante-mesenteric border



## **Stricture** (String sign of Kantor)

 Pathology: edema &/or fibrosis with ulcerated mucosa (resembling frayed string).





## U/S

Intestinal manifestations	<ul> <li>Mural thickening.</li> <li>Mural hypervascularity</li> <li>Loss of layering (partial or total).</li> <li>Reduced or absent peristalsis of the involved segment.</li> <li>Non compressibility of the involved segment.</li> </ul>
Extra-intestinal manifestations	<ul> <li>Mesenteric creeping fat.</li> <li>Mesenteric lymphadenopathy.</li> </ul>
Complications	<ul> <li>Obstruction.</li> <li>Phlegmon / abscess.</li> <li>Perforation.</li> </ul>

## Mural thickening



## Mural hyper-vascularity



## Loss of layering

## •<u>Pathology</u>: transmural edema, inflammation or fibrosis.

The bowel wall is formed of 5 alternating hyper & hypoechoic layers AKA the gut signature).



## **Mesenteric creeping fat**

Uniform hyper-echoic mesenteric fat.
(usually at the cephalic margin of terminal ileum).



### **Mesenteric lymphadenopathy**

Multiple oval hypoechoic masses in the mesentery.



## Obstruction

#### Dilated hyperperistaltic fluid filled segments.



### Abscess



## Fluid collection with thickened wall containing air or echogenic debris



## Fistula

#### bright echoes with distal acoustic shadows outside the boundaries of bowel loops.



## Phlegmon

Heterogenous hypoechoic mass with irregular borders.
No identifiable wall or fluid.





## CT

CT is less sensitive than in detection of early mucosal changes (i.e ulceration).
 CT is more sensitive than in detection of extraluminal changes (mural or extraintestinal).

## CT

## 1ry intestinal manifestations

- Mural thickening.
- Mural hyper-enhancement.
- Mural stratification.
- Stricture.

## Extra-intestinal manifestations

- Mesenteric fibrofatty proliferation (creeping fat)
- Mesenteric stranding (hazy fat).
- Mesenteric lymphadenopathy.
- Mesenteric hypervascularity (Comb sign).

#### **Complications**

- Obstruction.
- Phlegmon / Abscess.
- Perforation.
- Fistula.

Circumferential mural thickening In acute non cicatrizing phase: In chronic cicatrizing phase: Mural thickening, with loss of mural stratification and increased luminal narrowing.



- Normally the bowel wall measures less than 2 mm if well distended).
- The mean diameter in Crohn's disease is 10 mm.
- If > 10 mm suspect pseudomembranous enterocolitis.

## Mural hyper-enhancement.

- Segmental hyper-attenuation of distended small bowel loops relative to nearby normalappearing loops
- Mural hyper-enhancement indicates *active disease*.



## Stricture

 Sometimes associated with proximal dilatation due to partial obstruction.



# Mesenteric fibro-fatty proliferation (Creeping fat):

- Adjacent to the actively inflamed segment.
- Of high density than the normal fat.
- Produce mass effect with displacement of the adjacent bowel loops (DD with T.B).



## Mesenteric hypervascularity (Comb sign)

Pathology: engorged vasa recta.



## Phlegmon

• ill-defined inflamed mass of mixed attenuation

### Abscess

- Well defined mass of fluid attenuation,
- Thick enhancing wall
- Containing air or contrast material.



## Obstruction

• Proximal dilatation of small bowel loop > 2.5 cm.

## **Perforation**

• Pneumoperitoneum.
## **Fistula**

 The track of the fistula is better demonstrated on barium studies while the sequelae of these tracks are better demonstrated on CT (e.g air in the urinary bladder in entero-vesical fistula).

#### **Crohn's Disease & Ulcerative Colitis**

- Ulcerative colitis mimics the symptoms of Crohn's disease, as both are inflammatory bowel diseases that can affect the colon.
- Sometimes its not possible to tell the difference, in those case the disease is classified as indeterminate colitis.

#### Treatment

- Remission may be prolonged in Crohn's disease.
- Symptoms controlled with medication, lifestyle changes and surgery.
- Adequately controlled Crohn's disease may not significantly restrict daily living.
- Treatment for Crohn's disease is only when symptoms are active and involve first treating the acute problem, then maintaining remission.



### Medication

- Antibiotics use to reduce inflammation.
- Prolonged use of corticosteroids has significant side.
- Alternatives include aminosalicylates alone, though only a minority are able to maintain the treatment, and many require immunosuppressive drugs.



# Medicine Used in Treatment of Crohn's Disease

- 5-aminosalicylic acid (5-ASA)
- Prednisone and methylprednisolone
- Immunomodulators such as azathioprine, mercaptopurine, methotrexate, infliximab, adalimumab.
- Hydrocortisone should be used in severe attacks of Crohn's disease.



#### Lifestyle Changes

 Dietary adjustments, proper hydration and smoking cessation reduce symptoms.

 Consume balanced diet with proper portion control & eat small meals frequently instead of big meals.

• Do regular exercise and take enough sleep.

Identifying foods that trigger symptoms.

## Surgery

- Crohn's cannot be cured by surgery.
- Surgery required in case of obstructions, fistulas and/or abscesses, or if the disease does not respond to drugs.
- After the first surgery, Crohn's usually shows up at the site of the resection though it can appear in other locations.
- After a resection, scar tissue builds up which can cause strictures.
- A stricture is when the intestines become too small to allow excrement to pass through easily which can lead to a blockage.
- For patients with an obstruction due to a stricture, two options for treatment are strictureplasty and resection of that portion of bowel.

#### **Diet for Crohn's Disease**

- Drink lots of fluid to keep body hydrated and prevent constipation.
- Take multivitamin-mineral supplement to replace lost nutrients .
- Eat a high fiber diet when CD is under control.
- During a flare up, limit high fiber foods and follow a low fiber diet.
- Avoid lactose-containing foods if one has lactose intolerance or use lactase enzymes and lactase pretreated foods.
- Try small frequent meals.
- Eating a high protein diet with lean meats, fish and eggs, may help relieve symptoms of Crohn's.

#### **Diet for Crohn's Disease**

- Take pre-digested nutritional drinks to give bowel a rest and replenish lost nutrients.
- Limit caffeine, alcohol and sorbitol .
- Limit gas-producing foods such as broccoli, cabbage, cauliflower, brussels sprouts, dried peas ,lentils, onions, and carbonated drinks.
- Reduce fat intake if part of the intestines has been surgically removed.
- If the ileum has been resected, a Vitamin B<sub>12</sub> injection may be required.
- Studies found that fish oil and flax seed oil may be helpful in managing .
- The role of prebiotics such as psyllium & probiotics helpful in the healing process.



# THANK YOU ③