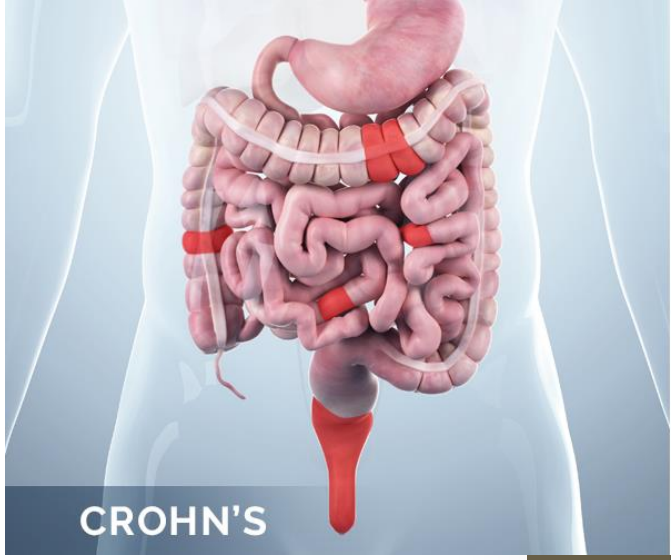

Crohn's Disease

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DEFINITION

Crohn's disease (CD) is an idiopathic inflammatory disorder of unknown etiology with genetic, immunologic, and environmental influences

ACG Clinical Guideline: Management of Crohn's disease in Adults doi: 10.1038/ajg.2018.27;

INTRODUCTION

- The prevalence of CD appears to be higher in urban areas than in rural areas, and also higher in higher socio-economic classes
- **CD can affect any part of the gastrointestinal (GI) tract from the mouth to the anus.**
- In the 75% of patients with small intestinal disease, the terminal ileum is involved in 90%.
- CD is a transmural process
- The peak age of incidence of CD is in the third decade of life, with a decreasing incidence rate with age
- Although more females than males have CD, the incidence rates among young children have been higher in males than in females during the past decade, and over time we may see an equalization of the sex distribution

PATHOLOGY AND PATHOGENESIS

- Although the etiology is complex, the most widely accepted hypothesis purports CD as an immune-mediated condition in genetically susceptible individuals, where disease onset is triggered by environmental factors that perturb the mucosal barrier, alter the healthy balance of the gut microbiota, and abnormally stimulate gut immune responses
- Active CD is characterized by focal inflammation and formation of fistula tracts, which resolve by fibrosis and stricturing of the bowel
- The bowel wall thickens and becomes narrowed and fibrotic, leading to chronic, recurrent bowel obstructions

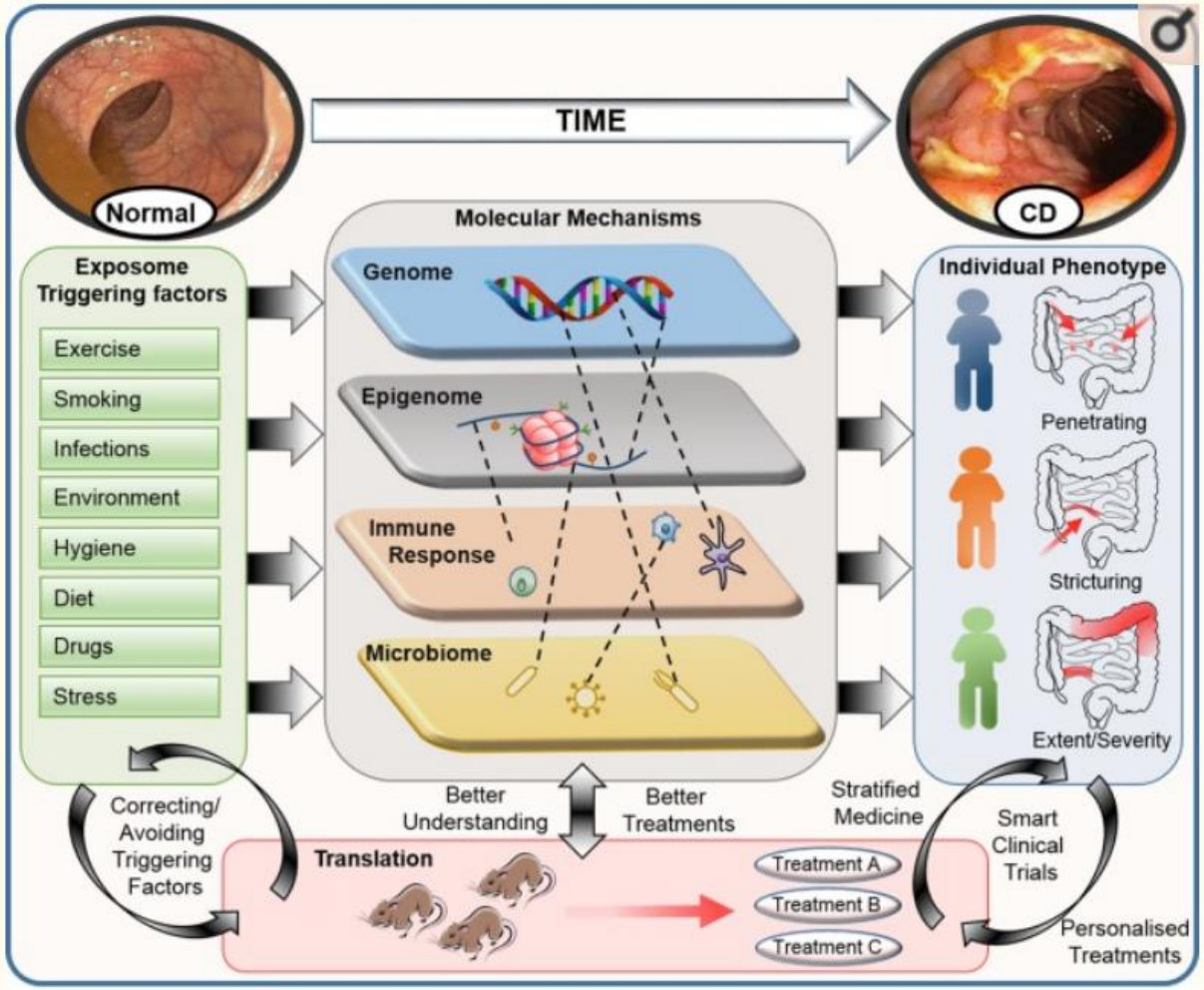
ACG Clinical Guideline: Management of Crohn's disease in Adults doi: 10.1038/ajg.2018.27; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4447044/

GENETICS

- The successful genome-wide association studies (GWASs) have provided a rational framework for new mechanistic insights and directions for research in CD
- These most strongly and consistently implicate themes involving defective intracellular bacteria killing and innate immunity (*CARD15/NOD2*, *IRGM*, *IL23R*, *LRRK2*, and *ATG16L1*) and de-regulated adaptive immune responses, namely the interleukin-23 (IL-23) and T helper 17 (Th17) cell pathway (*IL23R*, *IL12B* (encoding IL-12p40), *STAT3*, *JAK2*, and *TYK2*)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4447044/

PATHOGENESIS



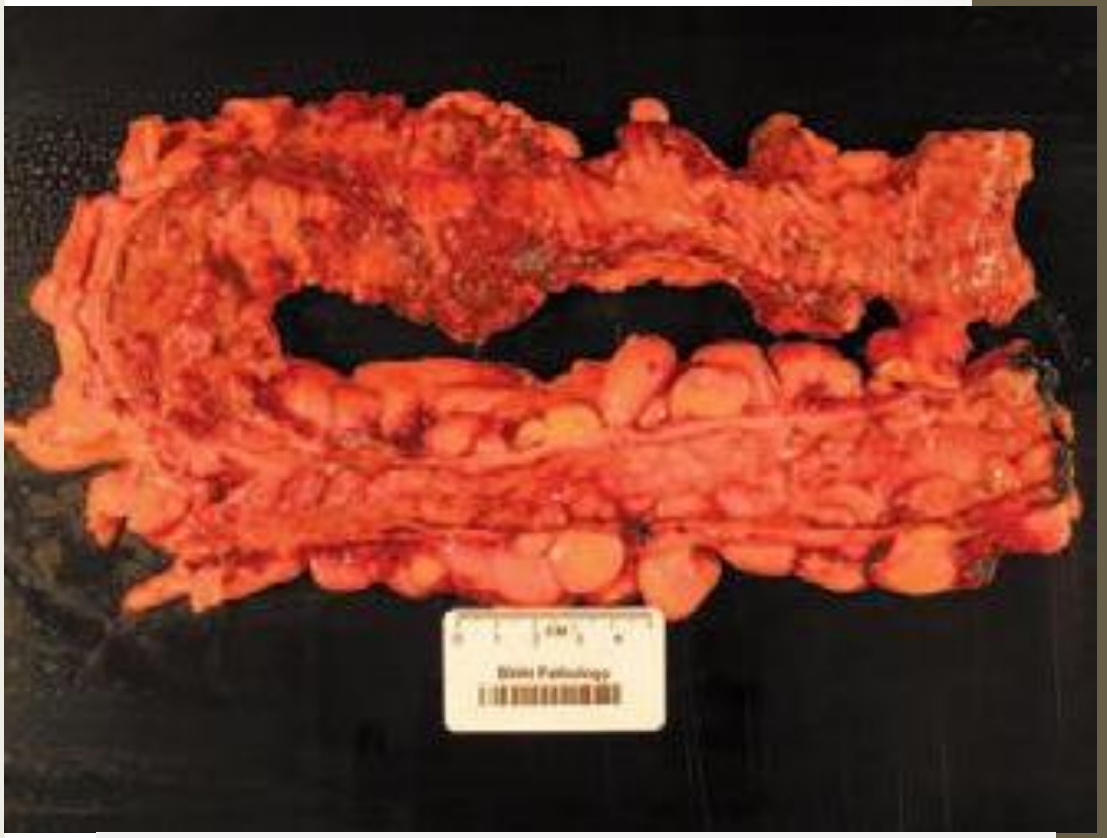
Crohn's disease (CD): multi-layer interactions in pathogenesis and clinical translation

Individual patients with CD have a unique pathogenic signature comprised of different contributions from each of these factors (stratification of patients on the basis of these signatures may lead to more focused, personalized, and successful therapies)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4447044/

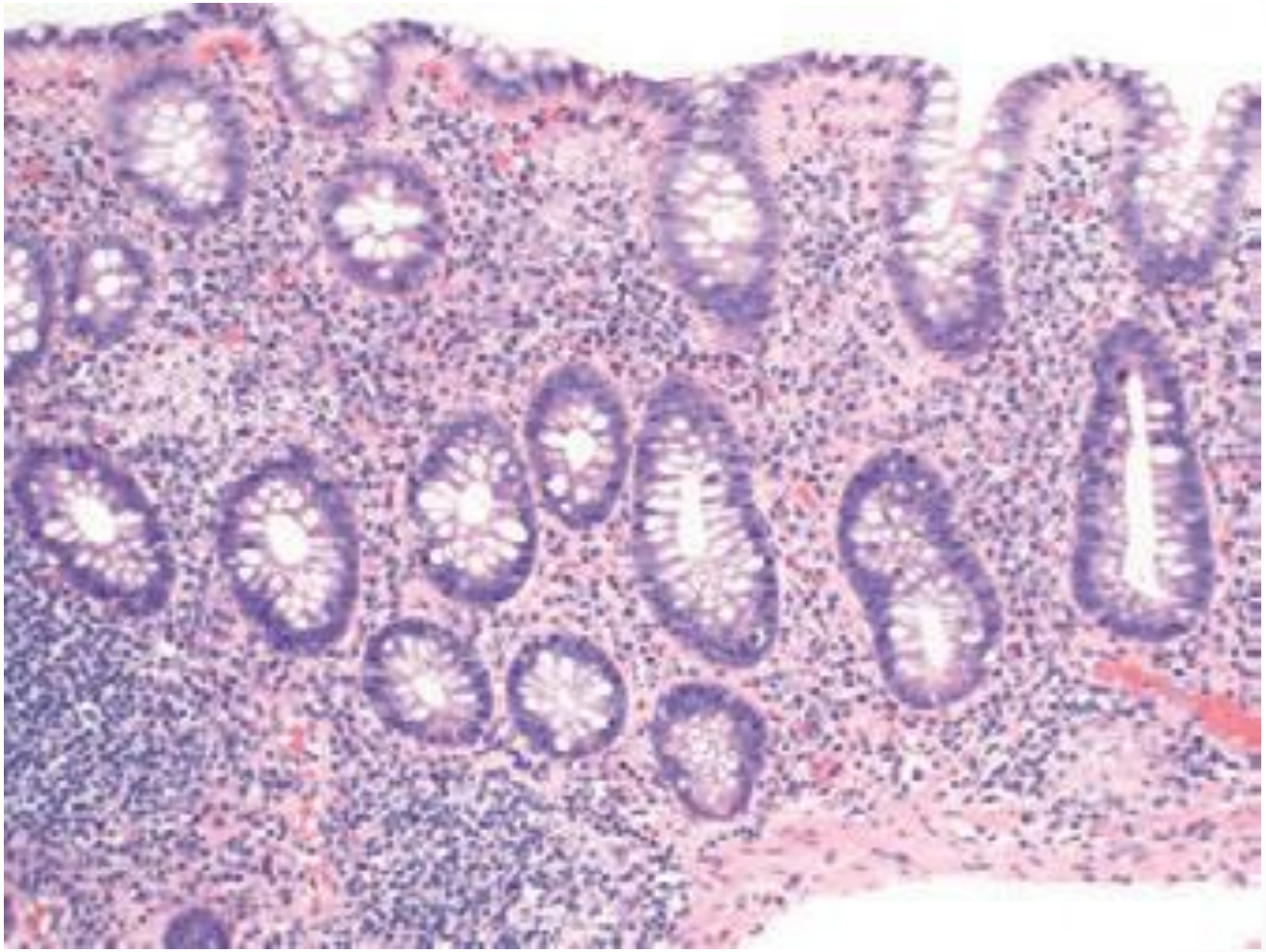
CD: MACROSCOPIC FEATURES

- CD is segmental with skip areas in the midst of diseased intestine
- Endoscopically, aphthous or small superficial ulcerations characterize mild disease; in more active disease, stellate ulcerations fuse longitudinally and transversely to demarcate islands of mucosa that frequently are histologically normal
- This "cobblestone" appearance is characteristic of CD, both edoscopically and by barium radiography
- Active CD is characterized by focal inflammation and formation of fistula tracts, which resolve by fibrosis and stricturing of the bowel
- The bowel wall thickens and becomes narrowed and fibrotic, leading to chronic, recurrent bowel obstructions



CD of the colon showing thickening of the wall, with stenosis, linear serpiginous ulcers and cobblestoning of the mucosa.

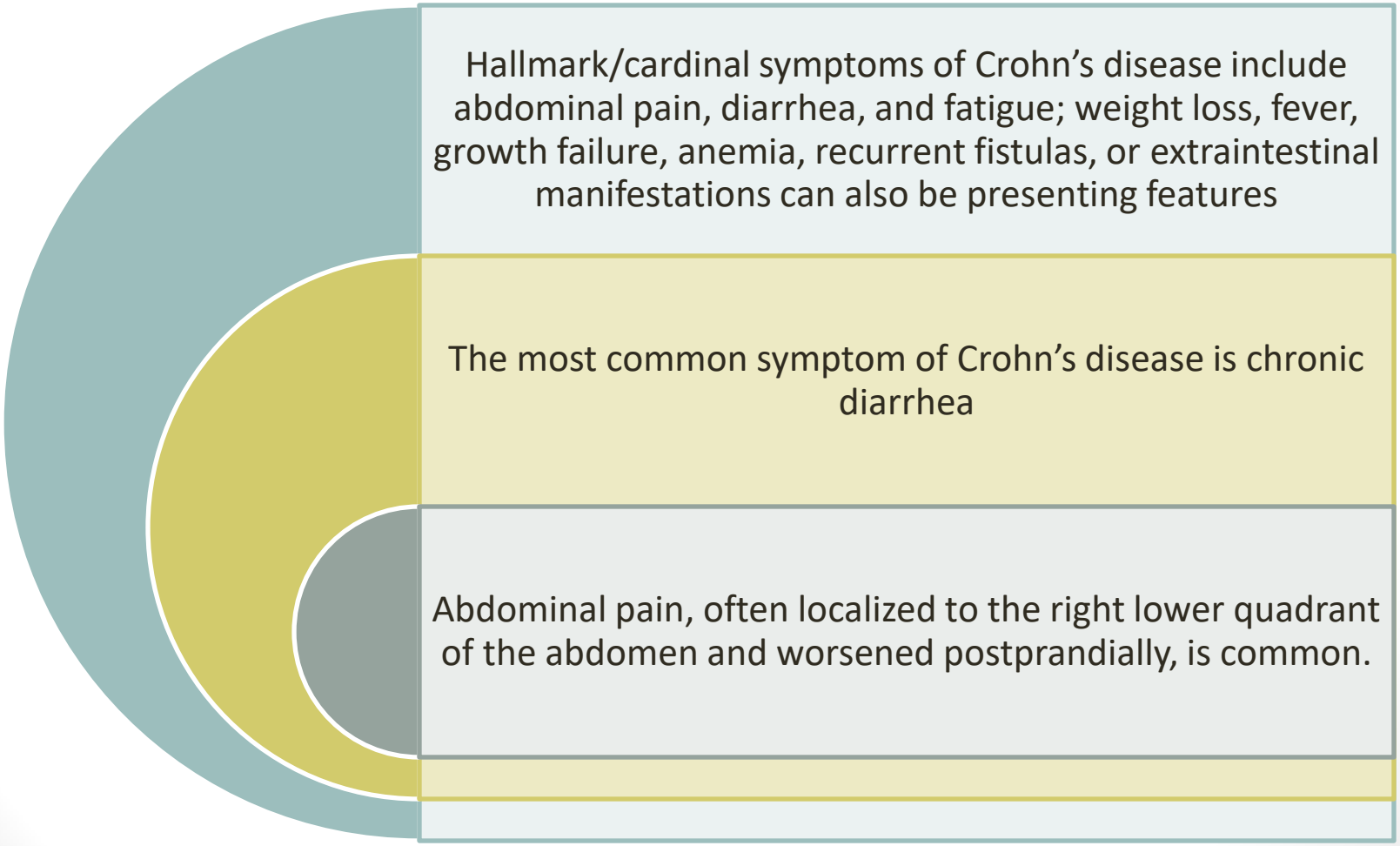
CD: MICROSCOPIC FEATURES



Medium-power view of Crohn’s colitis showing mixed acute and chronic inflammation, crypt atrophy, and multiple small epithelioid granulomas in the mucosa

Harrison's Principles of Internal Medicine, 20e

CLINICAL FEATURES



ACG Clinical Guideline: Management of Crohn's disease in Adults doi: 10.1038/ajg.2018.27;

CLINICAL FEATURES

The site of disease also influences the clinical manifestations!

- ***Ileocolitis*** - a chronic history of recurrent episodes of right lower quadrant pain and diarrhea. Sometimes the initial presentation mimics acute appendicitis with pronounced right lower quadrant pain, a palpable mass, fever, and leukocytosis
- Pain is usually colicky; it precedes and is relieved by defecation
- A low-grade fever is usually noted
- High-spiking fever suggests intraabdominal abscess formation
- Weight loss is common—typically 10–20% of body weight—and develops as a consequence of diarrhea, anorexia, and fear of eating
- Over several years, persistent inflammation gradually progresses to fibrostenotic narrowing and stricture; diarrhea will decrease and be replaced by chronic bowel obstruction

CLINICAL FEATURES

The site of disease also influences the clinical manifestations!

- ***Jejunoileitis -*** extensive inflammatory disease is associated with a loss of digestive and absorptive surface, resulting in malabsorption and steatorrhea
- Intestinal malabsorption can cause anemia, hypoalbuminemia, hypocalcemia, hypomagnesemia, coagulopathy, and hyperoxaluria with nephrolithiasis in patients with an intact colon
- Diarrhea is characteristic of active disease; its causes include (1) bacterial overgrowth in obstructive stasis or fistulization, (2) bile acid malabsorption due to a diseased or resected terminal ileum, and (3) intestinal inflammation with decreased water absorption and increased secretion of electrolytes

CLINICAL FEATURES

The site of disease also influences the clinical manifestations!

- ***Colitis and perianal disease -*** present with lowgrade fevers, malaise, diarrhea, crampy abdominal pain, and sometimes hematochezia
- Gross bleeding is not as common as in Ulceritive Colitis and appears in about one-half of patients with exclusively colonic disease
- Pain is caused by passage of fecal material through narrowed and inflamed segments of the large bowel
- Colonic disease may fistulize into the stomach or duodenum, causing feculent vomiting, or to the proximal or mid-small bowel, causing malabsorption by “short circuiting” and bacterial overgrowth
- Perianal disease affects about one-third of patients with Crohn’s colitis and is manifested by incontinence, large hemorrhoidal tags, anal strictures, anorectal fistulae, and perirectal abscesses

CLINICAL FEATURES

The site of disease also influences the clinical manifestations!

- ***Gastroduodenal disease -*** symptoms and signs of upper GI tract disease include nausea, vomiting, and epigastric pain
- Patients usually have an *Helicobacter pylori*–negative gastritis
- The second portion of the duodenum is more commonly involved than the bulb
- Fistulas involving the stomach or duodenum arise from the small or large bowel and do not necessarily signify the presence of upper GI tract involvement.
- Patients with advanced gastroduodenal CD may develop a chronic gastric outlet obstruction

CLINICAL FEATURES

Extraintestinal manifestations

- **arthropathy** (both axial and peripheral);
- **dermatological** (including pyoderma gangrenosum and erythema nodosum (Figure 1));
- **ocular** (including uveitis (Figure 2), scleritis, and episcleritis);
- **hepatobiliary disease** (i.e., primary sclerosing cholangitis).

Other extraintestinal complications

- thromboembolic (both venous and arterial);
- metabolic bone diseases;
- osteonecrosis;
- cholelithiasis;
- nephrolithiasis.

A number of other immune-mediated diseases are associated with Crohn's disease, including asthma, chronic bronchitis, pericarditis, psoriasis, celiac disease, rheumatoid arthritis, and multiple sclerosisions

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CLINICAL FEATURES : Extraintestinal manifestations

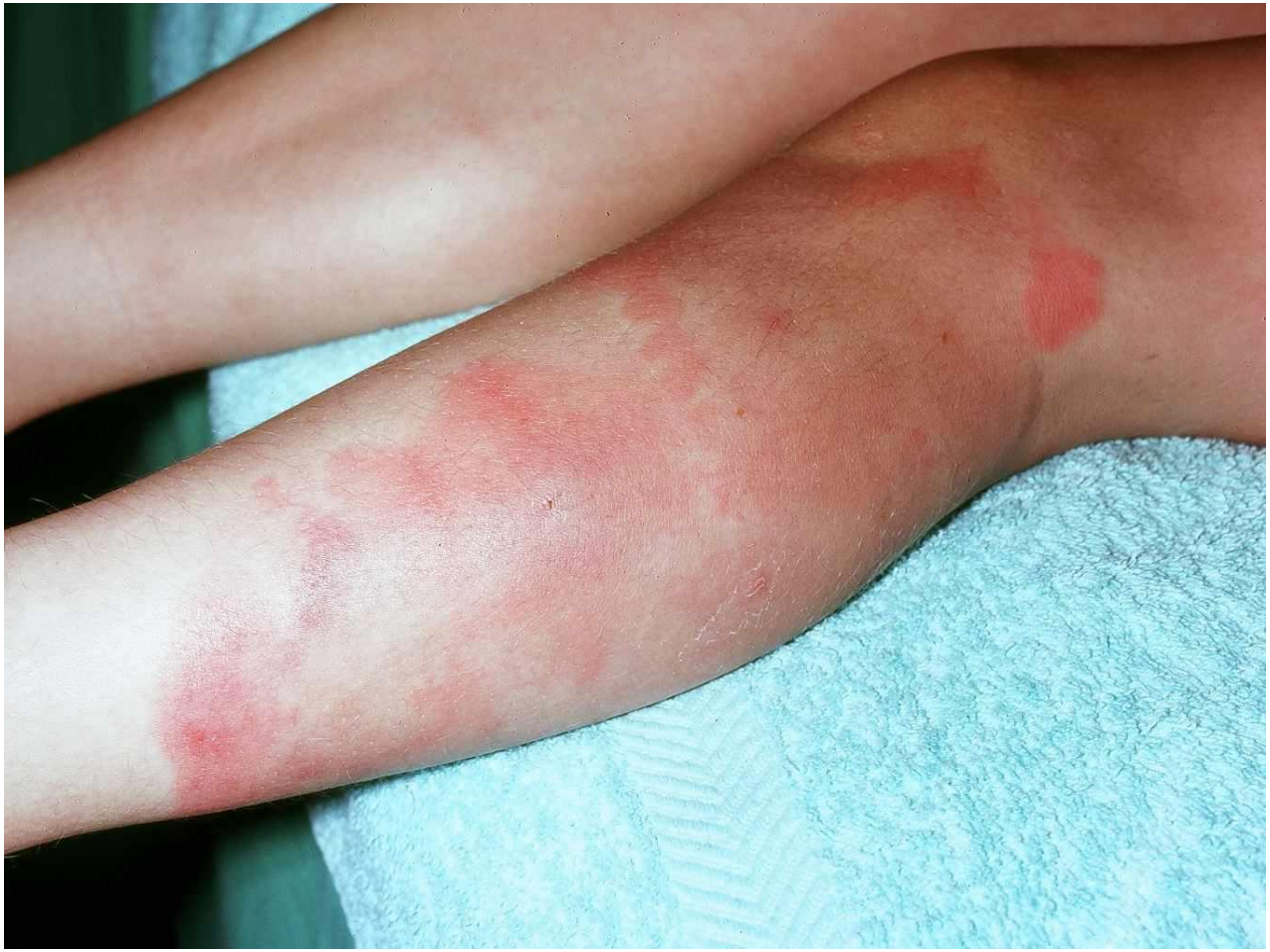

Figure 1. Erythema nodosum on legs.

https://www.verywellhealth.com/erythema-nodosum-1943012

CLINICAL FEATURES: Extraintestinal manifestations

Figure 2. Uveitis: a form of eye inflammation. It affects the middle layer of tissue in the eye wall (uvea)

https://www.stepwards.com/?page_id=2371

CLINICAL FEATURES: Extraintestinal manifestations

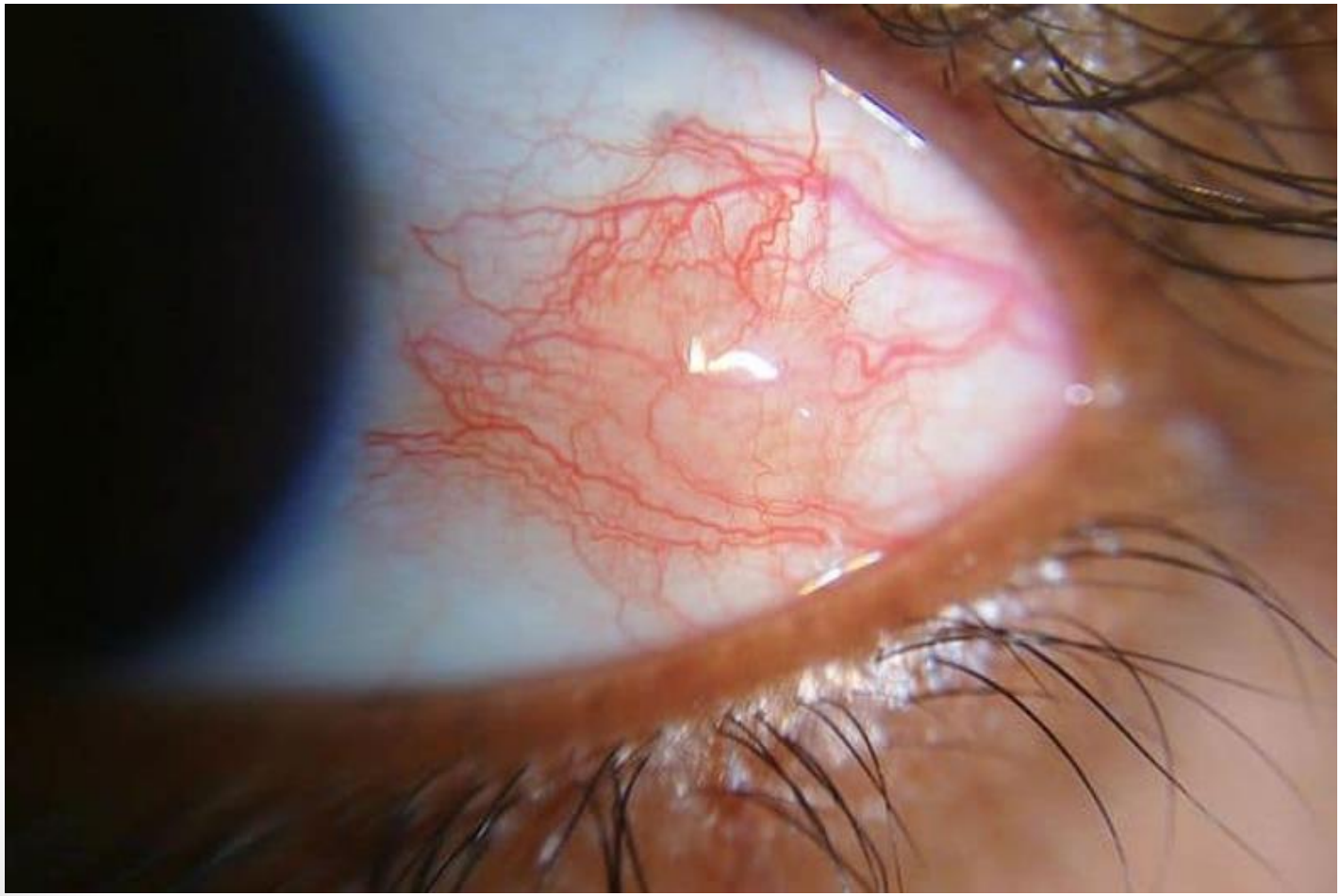

Figure 3. Episcleritis and scleritis are characterized by red, inflamed-looking whites of the eye, mild pain, and watery eyes

https://www.stepwards.com/?page_id=2371

DIAGNOSIS

Routine laboratory investigation

- Initial laboratory investigation should include evaluation for inflammation, anemia, dehydration, and malnutrition.

Stool examination

- **Routine fecal examinations and cultures** should be carried out to eliminate bacterial, viral, or parasitic causes of diarrhea.
- **Testing for *Clostridium difficile*** (should be considered even in the absence of antecedent antibiotics) — should be carried out within 2 hours of passage of stools.
- **A check for occult blood or fecal leukocytes**
- **Lactoferrin, α1-antitrypsin**. The main reason for listing this test is to rule out intestinal inflammation, rather than using it as a positive diagnostic test. It may not be available in developing countries, but it can be undertaken relatively inexpensively and easily with rapid-turnaround slide-based enzyme-linked immunoassay (ELISA) tests.
- **Calprotectin** — a simple, reliable, and readily available test for measuring IBD activity — may be better for UC than CD; the rapid fecal calprotectin tests could be very helpful in developing countries.

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DIAGNOSIS

Routine laboratory investigation

Blood examination

- Complete blood count (CBC)
- Erythrocyte sedimentation rate, C-reactive protein levels correlate imperfectly with inflammation and disease activity
- Electrolytes and albumin, ferritin, calcium, magnesium, vitamin B12.
- Serum ferritin may be elevated in active IBD, and may be in the normal range even in the face of severe iron deficiency
- Liver enzyme and function testing — international normalized ratio (INR), bilirubin, albumin.
- Human immunodeficiency virus (HIV) — additional opportunistic infection work-up, hepatitis B virus (HBV), hepatitis C virus (HCV), varicella zoster virus (VZV), immunoglobulin G (IgG)
- Perinuclear antineutrophil cytoplasmic antibody (p-ANCA) and anti-*Saccharomyces cerevisiae* antibodies (ASCA) for cases of unclassified IBD.
- — Positive p-ANCA and negative ASCA tests suggest UC.
- — Negative p-ANCA and positive ASCA tests suggest CD.
- Celiac antibody testing should be pursued unless presentations include obviously nonceliac features such as fistulas, perineal disease, and blood in the stool

World Gastroenterology Organization, 2015 ;

DIAGNOSIS

Endoscopy

Colonoscopy with intubation of the terminal ileum and biopsy is recommended as part of the initial evaluation of patients with suspected IBD.

Mucosal changes suggestive of CD include mucosal nodularity, edema, ulcerations, friability, and stenosis

- Upper endoscopy should only be performed in patients with upper gastrointestinal signs and symptoms.
- Video capsule endoscopy (VCE) is a useful adjunct in the diagnosis of patients with small bowel Crohn's disease in patients in whom there is a high index

Endoscopic scoring systems: the Crohn's Disease Endoscopic Index of Severity (CDEIS) and the Simple Endoscopic Score for Crohn's disease (SES-CD) of suspicion of disease.

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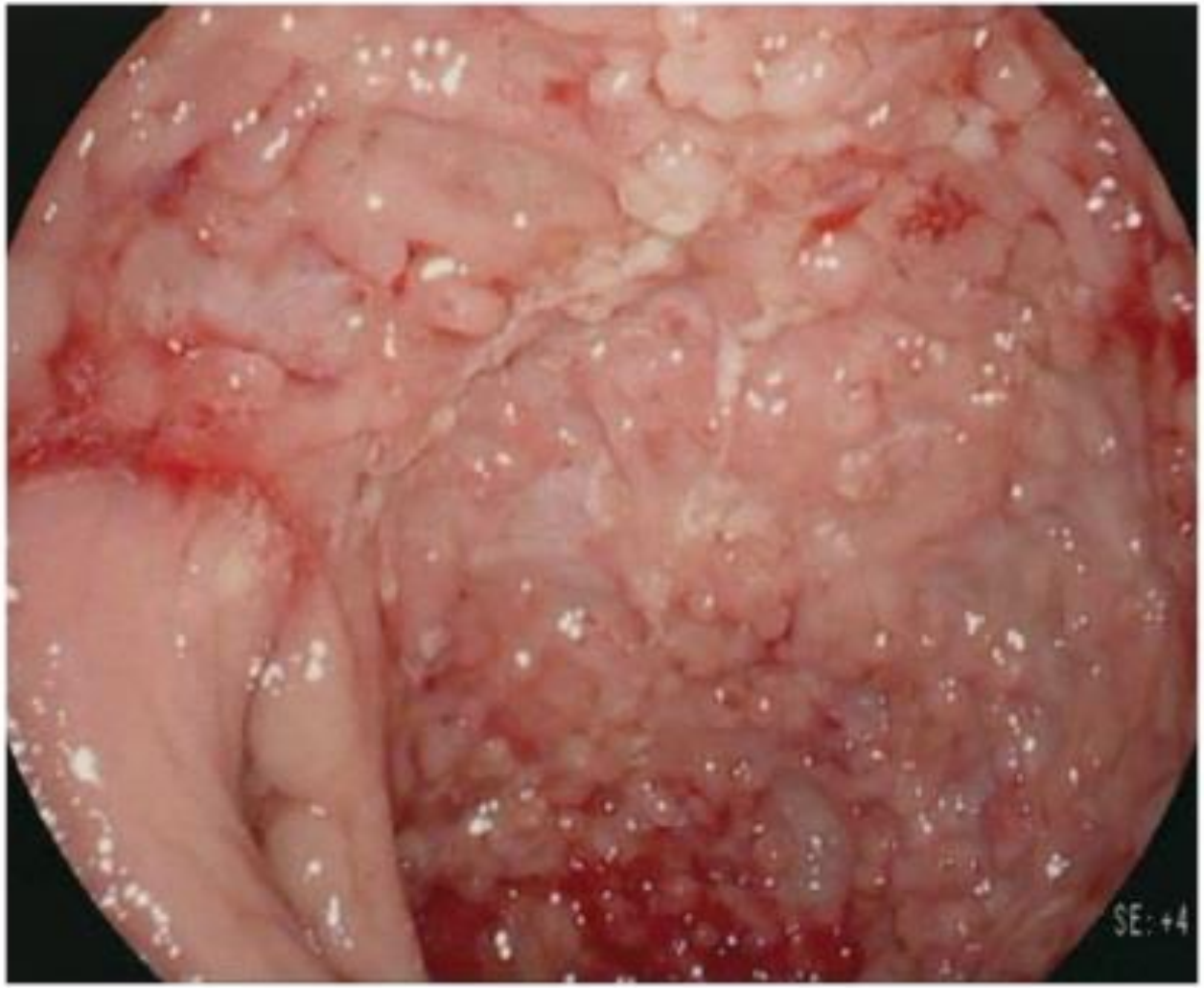
DIAGNOSIS



High-definition white-light endoscopy of severe Crohn's disease with multiple longitudinal ulcers and spontaneous bleeding of the inflamed mucosa.

https://www.hindawi.com/journals/grp/2012/301541/fig1/

DIAGNOSIS

Imaging studies

Computed tomography enterography (CTE) is sensitive for the detection of small bowel disease in patients with Crohn's disease and is comparable to magnetic resonance enterography (MRE).

Because of the absence of any radiation exposure, MRE should be used preferentially in young patients (<35 y.o.) and in patients in whom it is likely that serial exams will need to be performed

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Classification of Disease Severity in Crohn's Disease

There is no "gold standard" for determining disease activity.

Disease activity depends on heterogeneous clinical measures, impact on quality of life, complications of disease, and complications of therapy.

These assessments are important in that they allow the clinician to make decisions about disease management.

Status	CDAI Score	Description from ACG Guidelines
Remission	< 150	Asymptomatic or without any symptomatic inflammatory sequelae
Mild to moderate	150 to 220	Ambulatory and able to tolerate oral alimentation without manifestations of dehydration, systemic toxicity, abdominal tenderness, painful mass, intestinal obstruction, or > 10% weight loss
Moderate to severe	220 to 450	Failed to respond to treatment for mild to moderate disease, or those with more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting, or significant anemia
Severe	> 450	Persistent symptoms despite the introduction of conventional corticosteroids or biologic drugs as outpatients, or individuals presenting with high fevers, persistent vomiting, evidence of intestinal obstruction, significant peritoneal signs such as involuntary guarding or rebound tenderness, cachexia, or evidence of an abscess

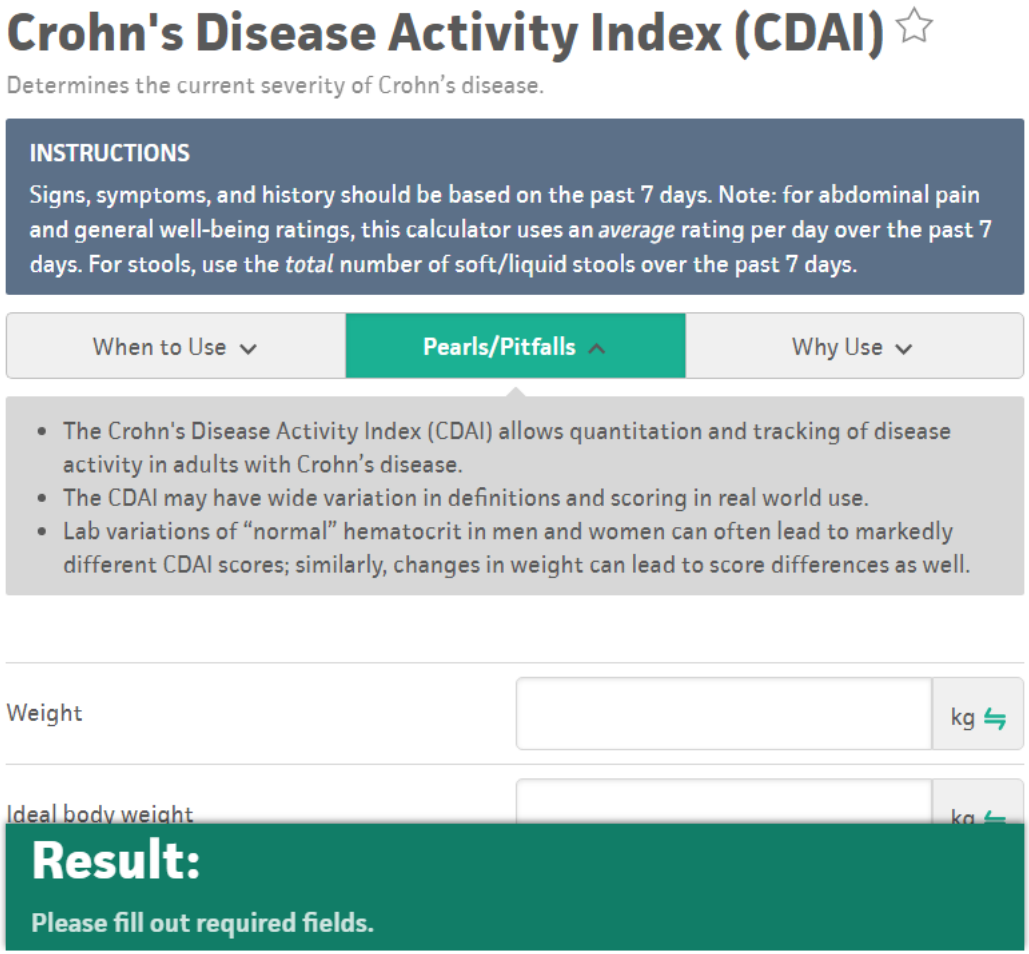
CRP is usually increased

ACG = American College of Gastroenterology; CDAI = Crohn's Disease Activity Index.

Source: American College of Gastroenterology.[23]

https://www.ncbi.nlm.nih.gov/books/NBK424370/table/T5/

The Crohn's Disease Activity Index (CDAI)



The Crohn's Disease Activity Index (CDAI) allows quantitation and tracking of disease activity in adults with Crohn's disease.

The CDAI may have wide variation in definitions and scoring in real world use.

Lab variations of "normal" hematocrit in men and women can often lead to markedly different CDAI scores; similarly, changes in weight can lead to score differences as well.

CDAI of 150-450 is used as a marker of active Crohn's disease. The higher the score, the more severe the disease activity.

https://www.mdcalc.com/crohns-disease-activity-index-cdai#pearls-pitfalls

DIAGNOSIS

Monitoring disease activity

- Fecal calprotectin and fecal lactoferrin measurements may have an adjunctive role in monitoring disease activity.
- Serum CRP is relatively nonspecific for the inflammation of Crohn's disease, but in select patients serial measurements may have a role in monitoring disease activity and response to therapy.
- Periodic cross-sectional imaging (CTE, MRE) may be considered in monitoring response to therapy in certain patients with small bowel Crohn's disease.
- Mucosal healing as determined by endoscopy is a goal of therapy.
  - a. Endoscopic scores have been developed that are reliable in measuring degree of mucosal healing and may be used to monitor response to therapy.
  - b. Evaluation of the ileum for post-operative endoscopic recurrence by colonoscopy within a year after ileocolonic resection may help guide further therapy.

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DIFFERENTIATING BETWEEN UC AND CD

	Typical UC features	Typical CD features
Clinical	• Frequent small-volume diarrhea with urgency • Predominantly bloody diarrhea	• Diarrhea accompanied by abdominal pain and malnutrition • Abdominal mass • Perianal lesions
Endoscopic and radiological	• Diffuse superficial colonic inflammation • Involvement of rectum, but this can be patchy • Shallow erosions and ulcers • Spontaneous bleeding	• Discontinuous transmural asymmetric lesions • Mainly involving ileum and right-sided colon • Cobblestone appearance • Longitudinal ulcer • Deep fissures
Histopathological	• Diffuse inflammation in mucosa or submucosa	• Granulomatous inflammation

World Gastroenterology Organization, 2015 ;

Management of CD

- *The goal of treatment is to:*
- Improve and maintain patients' general well-being (optimizing the quality of life, as seen from the patient's perspective)
- Treat acute disease:
- — Eliminate symptoms and minimize side effects and long-term adverse effects
- — Reduce intestinal inflammation and if possible heal the mucosa
- Maintain corticosteroid-free remissions (decreasing the frequency and severity of recurrences and reliance on corticosteroids)
- Prevent complications, hospitalization, and surgery
- Maintain good nutritional status

World Gastroenterology Organization, 2015 ;

Management of CD

Diet and lifestyle considerations

- The impact of diet on inflammatory activity in UC/CD is poorly understood, but dietary changes may help reduce symptoms:
- During increased disease activity, it is appropriate to decrease the amount of fiber. Dairy products can be maintained unless not tolerated.
- Smoking cessation benefits patients with CD in relation to their disease course
- Reduction of stress and better stress management may improve symptoms or the patients' approach to their disease

World Gastroenterology Organization, 2015 ;

MEDICAL THERAPY

- Medical treatment of CD is usually divided into **induction** and **maintenance therapy**
- These phases of treatment involve achieving control of inflammation relatively quickly (over 3 months or less) and then sustaining that control for prolonged periods of time (beyond 3 months)
- Treatment is generally chosen according to the patient's risk profile and disease severity, with a goal of controlling inflammation and, consequently, symptoms arising from active inflammation
- Medical therapy used to treat CD includes the categories of 5-aminosalicylates (5-ASA), antibiotics, corticosteroids, immunomodulators, and biologics (the anti-TNF agents infliximab, adalimumab, certolizumab pegol; agents targeting leukocyte trafficking, including vedolizumab, natalizumab; and the anti-p40 (anti-IL-12/23) antibody, ustekinumab).

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MEDICAL THERAPY

5-aminosalicylates

- Sulfasalazine (in the doses of 3–6 g daily) is an effective therapy for treatment of symptoms of patients with mild to moderately active colonic CD and/or ileocolonic CD, but not in those with isolated small bowel disease

Corticosteroids

- Corticosteroids (such as prednisone and methylprednisolone) are used primarily for the treatment of flares of CD.
- Oral formulations may be used for mild to moderate disease, whereas systemic corticosteroids are used for moderate to severe disease. They have historically been used as a "bridge" to permit symptom control until immunomodulators and/or biologic agents become effective and enable mucosal healing.
- Systemic corticosteroids are ineffective for maintenance therapy in patients with CD.
  - The appropriate prednisone equivalent doses used to treat patients with active CD are at doses ranging from 40 to 60 mg/day
  - Higher doses, such as 1 mg/kg body weight per day of prednisolone, have also been studied. These doses are typically maintained for 1–2 weeks and tapered at 5 mg weekly until 20 mg and then 2.5–5.0 mg weekly.
  - Corticosteroid tapers should generally not exceed 3 months.

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MEDICAL THERAPY

Antimicrobial therapy

- Although widely used in the past, the primary role of antibiotics for the treatment of luminal CD is not established.
- Metronidazole is not more effective than placebo at inducing remission in patients with CD.
- Broad-spectrum antibiotics are used for the treatment of pyogenic complications (e.g., intra-abdominal and mesenteric abscesses) in patients with CD.
- Metronidazole may be helpful to prevent postoperative recurrence in CD.

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MEDICAL THERAPY

Immunomodulators

- In patients with moderate-to-severe CD who remain symptomatic despite current or prior corticosteroid therapy, the thiopurine analogs (6-mercaptopurine and azathioprine) may be used
- Methotrexate, when given subcutaneously (SC) or intramuscularly (IM), is also effective as a steroid-sparing agent
- Thiopurine agents and methotrexate are not effective agents for short-term induction in active, symptomatic disease because of their relatively slow onset of action, between 8 and 12 weeks.
- The use of methotrexate in combination with steroids is effective for treatment of moderately active steroid-dependent/resistant CD
- Azathioprine (at maximal doses of 1.5–2.5 mg/kg/day), 6-mercaptopurine (at maximal doses of 0.75– 1.5 mg/kg day), or methotrexate (15–25 mg SC/IM once weekly) may be used in treatment of active CD
- Azathioprine and 6-mercaptourine are effective therapies and should be considered for treatment of patients with Crohn's disease for maintenance of remission

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Medical Therapy

Anti-TNF agents

- The anti-TNF antibodies (infliximab, adalimumab, and certolizumab pegol) are effective for treatment of patients with CD who respond inadequately to treatment with corticosteroids, thiopurines, and methotrexate
  - Before initiation of anti-TNF therapy, assessment for latent and active tuberculosis and other latent opportunistic infections such as histoplasmosis and blastomycosis when potentially present should be initiated
  - Assessment for the presence of viral hepatitis should be performed in all CD patients before the initiation of anti-TNF therapy.

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MEDICAL THERAPY

- ***NOVEL AGENTS***
- Some of the other agents under different stages of development for the treatment of patients with CD include other anti-integrins such as etrolizumab (which is a dual action anti-integrin that inhibits both α 4β 7 and α Eβ 7) or ozanimod (a potent sphingosine1-phosphate receptor modulator that inhibits the egress of lymphocytes from lymph nodes)
- Several other agents in early phases of development include the anti-IL-23 agents, risankizumab and brazikumab, and the selective Janus kinase-1 inhibitors, filgotinib and upadacitinib (formerly ABT-494)

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MEDICAL THERAPY

Agents targeting leukocyte trafficking

- Inhibitors of leukocyte trafficking (Natalizumab, an anti-α 4 integrin antibody etc) recently have expanded the therapeutic options for patients with CD

Agents targeting IL-12/23 (anti-p40 antibody)

- Ustekinumab should be given for moderate-to-severe Crohn's disease patients who have failed previous treatment with corticosteroids, thiopurines, methotrexate, or anti-TNF inhibitors, or who have had no prior exposure to anti-TNF inhibitors

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MEDICAL THERAPY

MAINTENANCE THERAPY OF LUMINAL CROHN'S DISEASE

- Once remission is induced with corticosteroids, a thiopurine or methotrexate should be considered
- Corticosteroids are not indicated for long-term treatment of CD because of lack of efficacy for maintenance of remission and adverse effects
- There are several studies that have demonstrated that azathioprine 2.5 mg/kg/day and 6 mercaptopurine 1.5 mg/kg/day are effective for the maintenance of remission in CD
  - Oral 5-aminosalicylic acid has not been demonstrated to be effective for maintenance of medically induced remission in patients with Crohn's disease, and is not recommended for long-term treatment
- Anti-TNF therapy, specifically infliximab (5 or 10 mg/kg every 8 weeks), adalimumab, and certolizumab pegol, should be used to maintain remission of anti-TNF-induced remission

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Case Report 1.4.

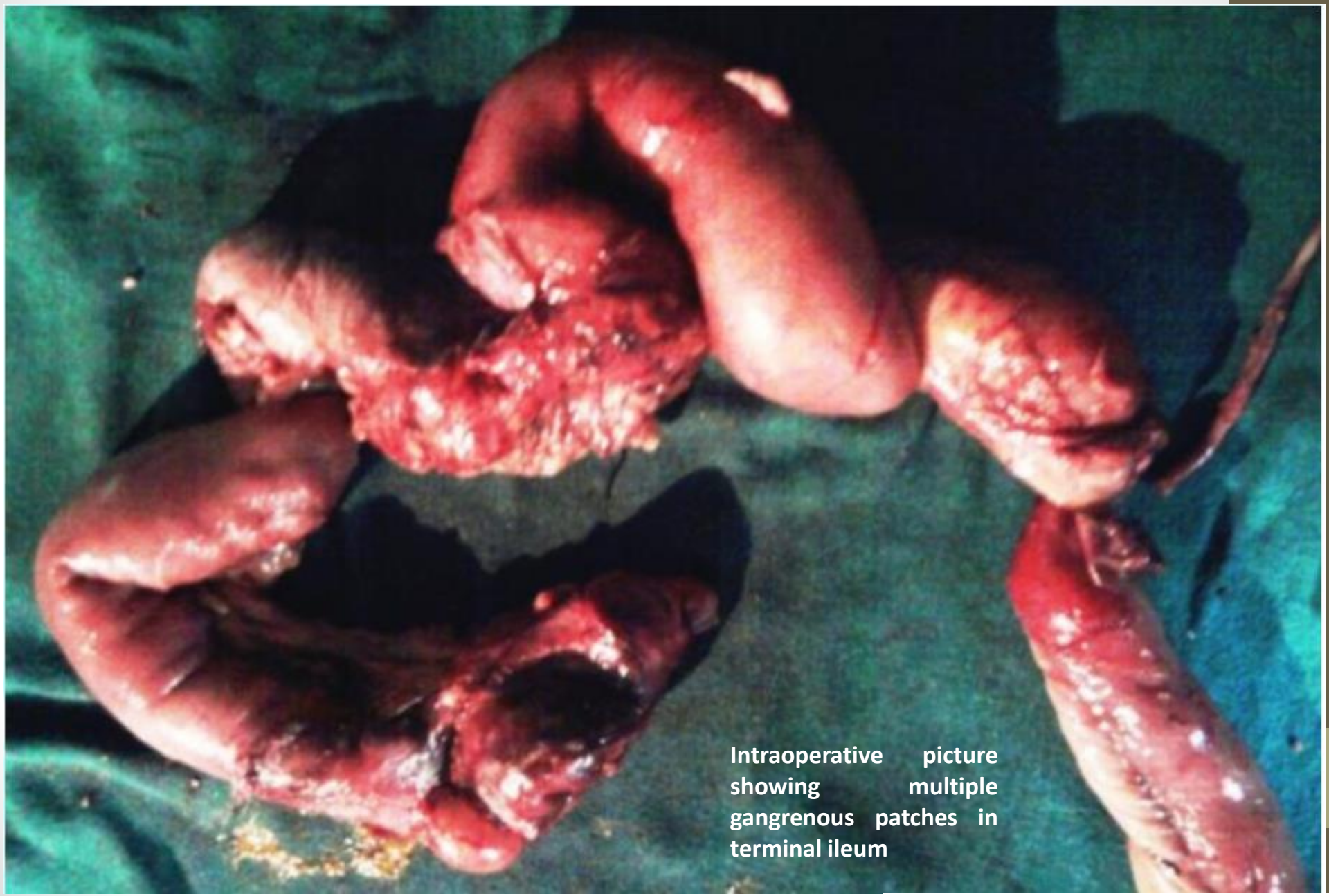
- A 65-year male chronic smoker was admitted to the medicine ward in hospital as a case of acute exacerbation of chronic obstructive pulmonary disease with history of diarrhea and abdominal pain for the last 14 days.
- However patient developed features of acute intestinal obstruction in the form of severe abdominal pain, gross abdominal distention, absolute constipation while on medical treatment for 4-5 days.
- In view of patients acute abdominal condition exploratory laparotomy was performed.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3336915/

Case Report 2.4.

- Intraoperatively the entire small bowel was grossly dilated with dense interloop adhesions in the terminal ileum with multiple gangrenous patches.
- About 500-600 ml pus present in between the adhered loops of bowel was suggestive of an old terminal ileal perforation

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3336915/



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3336915/

Case Report 4.4.

- The gangrenous bowel was resected out and an ileostomy with a distal mucus fistula was made.
- Histopathological examination showed narrowed areas of ileum with thickening and congestion of all the layers along with focal non caseating granulomas in the serosal layer.
- Chronic inflammatory infiltrates were present in all the layers with acute inflammatory cells in the serosal layer. Thus, a diagnosis of Crohn's disease leading to chronic intestinal obstruction with superadded bacterial infection of serosal layer was made.
- Postoperatively, the patient was put on broad spectrum antibiotics and chest care was taken.
- The patient was doing well for a period of more than one month after surgery but unfortunately he had collapse of right lung with pleural effusion and died of respiratory cause.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3336915/

Case Report 1.12.

- The patient was a 27 years old female with a chief complaint of diarrhea for 3 months, and fever and night sweating for more than 2 months

- Three months ago, the patient began having yellow watery diarrhea at a frequency of 3-4 times a day, and mushy stool that occasionally contained mucus, accompanied with periumbilical and the right abdominal dull pain

- The symptoms failed to respond to medical treatment

Int J Clin Exp Med 2016;9(10):20362-20366 www.ijcem.com /ISSN:1940-5901/IJCEM0025649

Case Report 2.12.

- During about two months, she developed low-grade fever (37.4-38.0°C), usually in the afternoon, night sweating, fatigue, anorexia and weight loss
- Colonoscopy showed no significant abnormality in the colon mucosa
- Chest X-ray was not remarkable
- Purified protein derivative tuberculin (PPD) test was strongly positive, and a diagnosis of intestinal tuberculosis was made
- On April 11, 2012, the patient began receiving anti-TB treatment with isoniazid, rifampicin and ethambutol in another hospital
- Two weeks later, ethambutol was withdrawn

Case Report 3.12.

- However, the symptoms were not significantly relieved
- She had a persistent fever (the highest temperature 39.5°C) and productive cough
- She was sent to our clinic for further diagnosis and treatment, where laboratory tests showed that the autoantibody spectrum, anti-O and rheumatoid factor were within the normal range
- TB antibody test in another hospital a month ago was weakly positive
- The abdominal contrast-enhanced CT showed no abnormal signs, and the diagnosis of TB infection was questioned
- Oral anti-TB treatment with isoniazid and rifampicin was continued, but high fever remained unrelieved, accompanied with multiple oral ulcers
- Gastroscopy and lung CT scan in another hospital were not remarkable, and the diagnosis of Behcet's disease (type of vasculitis) was suspected
- No other special drug was administered

Case Report 4.12.

- A diagnosis of Behcet's disease was made in the outpatient department of rheumatology of our hospital, and oral prednisone (15 mg daily) was prescribed
- However, the patient still had intermittent fever (39.0°C), and she visited our hospital again for further treatment
- Since the onset of the disease, she had lost about 10 kg body weight
- She had been previously healthy and prone to develop mouth ulcers that were difficult to heal
- Admission examination: T 36.4°C, P 102 bpm, R 18/min, BP 107/73 mmHg; conscious; mild anemia appearance; obvious body weight loss; superficial lymph nodes impalpable; heart and lungs not remarkable; abdomen soft, right side abdomen tender without rebound pain; liver and spleen not palpable below costal margin; no percussion pain over liver and kidney areas; no edema in the lower extremities
- Laboratory examinations: **hemoglobin 109 g/L**, **platelet count 577** × 109/L, urine leukocytes 1+, **stool occult blood positive**; stool culture: not abnormal; blood biochemistry: globulin 37.00 g/L, total cholesterol 5.76 mmol/L; **coagulation: activated partial thromboplastin time 50.70 sec, fibrinogen 7.30 g/L, ultra-sensitive C-reactive protein 84.4 mg/L, ESR 86-95 mm/h**

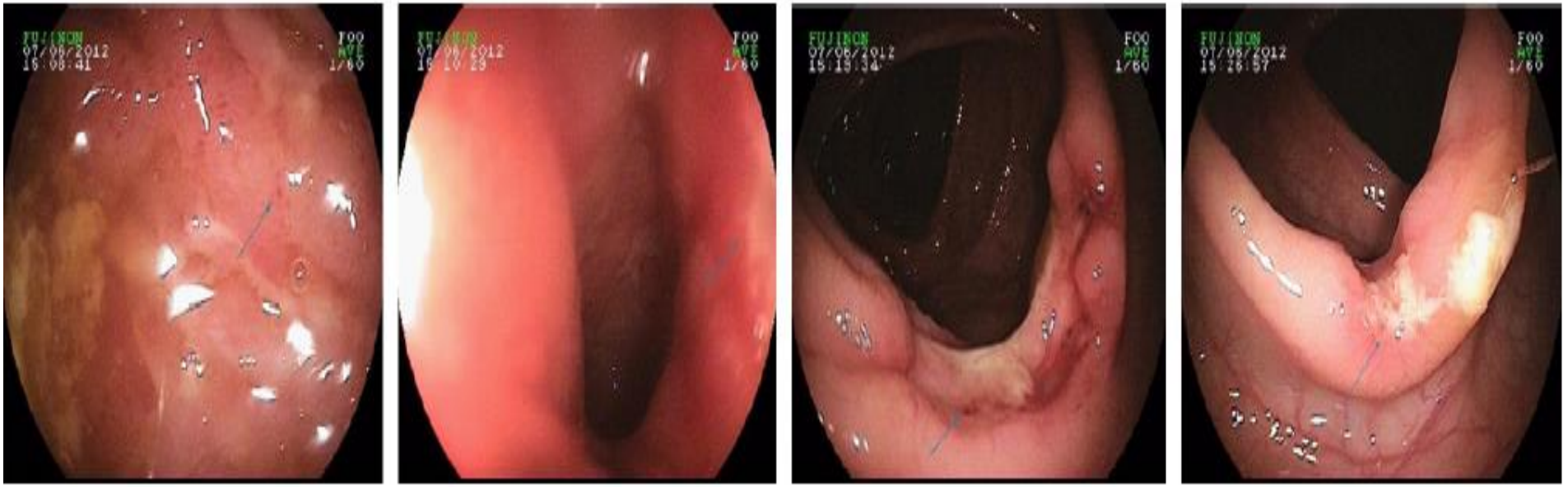
Case Report 5.12.

- TB antibody negative; PPD strongly positive; immune function monitoring: serum complement C31.87 g/L; rheumatology detection: ANA, ENA, ANCA normal
- Protein electrophoresis: γ globulins within normal range, immunoglobulin normal; infection related detection: to luidine Red agglutination test: HIV, cytomegalovirus, EB virus, TORCH four, Weil-Felix reaction, Widal reactions are normal
- Procalcitonin 0.06 ng/ml, ferritin 183.3 ng/ml
- Eye examination: normal
- **Examinations in other hospitals:** thyroid function, tumor markers, protein electrophoresis γ globulin, coagulation, Legionella antibodies, Mycoplasma pneumoniae antibodies, ANA, ANCA, parasite eggs (roundworm, hookworm, whipworm, pinworm) not remarkable; chlamydia antibody (+)
- Liver function: globulin, abdominal ultrasonography: cholestasis, sediment ocean stones, uterine adnexa normal; thyroid ultrasound: no exception, colonoscopy, lungs, pelvic, intestinal CT normal; cerebrospinal fluid normal; bone marrow puncture: normal

Case Report 6.12.

- **Capsule endoscopy after admission showed multiple ulcers of the jejunum and ileum!**
- Enteroscopy showed congestion, edema and easy bleeding of the terminal ileum, and multiple shallow ulcers measuring 0.3 * 0.4-0.8 * 1.0 cm, from which biopsy specimens were obtained
- Multiple irregular ulcers of different sizes and shapes were seen from the anus 20 cm to the ileocecal valve; nodular change was seen in part of the ulcer edges; the lesions were in a jumping distribution; and the mucosa between the ulcers was normal

Case Report 7.12.



Enteroscopy showed congestive necrosis in the small intestine and multiple deep ulcers in the colon.

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Case Report 8.12.

- Shallow ulcers were seen in the local anal canal mucosa
- Positron emission tomography-computed tomography (PET-CT) showed the following:

1) multiple small patches were seen in the colon and small intestine, where the punctate metabolism was increased; no obvious thickening and swelling were seen in the intestinal wall, based on which inflammatory infection or tuberculosis was suspected;

2) no significant high metabolic tumor lesion was seen in other organs of the

Case Report 9.12.

- Pathology study suspected the diagnosis of severe chronic inflammation in the terminal ileum, ascending colon and sigmoid colon mucosa; acute active (moderate) reactive lymphoid follicular hyperplasia and inflammatory necrosis
- Further examinations were suggested to exclude Behcet's disease, Crohn's disease and intestinal tuberculosis
- Immunohistochemistry excluded lymphoma and parasitic infection
- Ultrasonic colonoscopy showed that the colonic mucosa was clear, **intestinal wall with slightly thickened, submucosa showed High echo, muscularis propria was involved, the ultrasound presentation is consistent with the diagnosis of Crohn's disease, and did not supported lymphoma**

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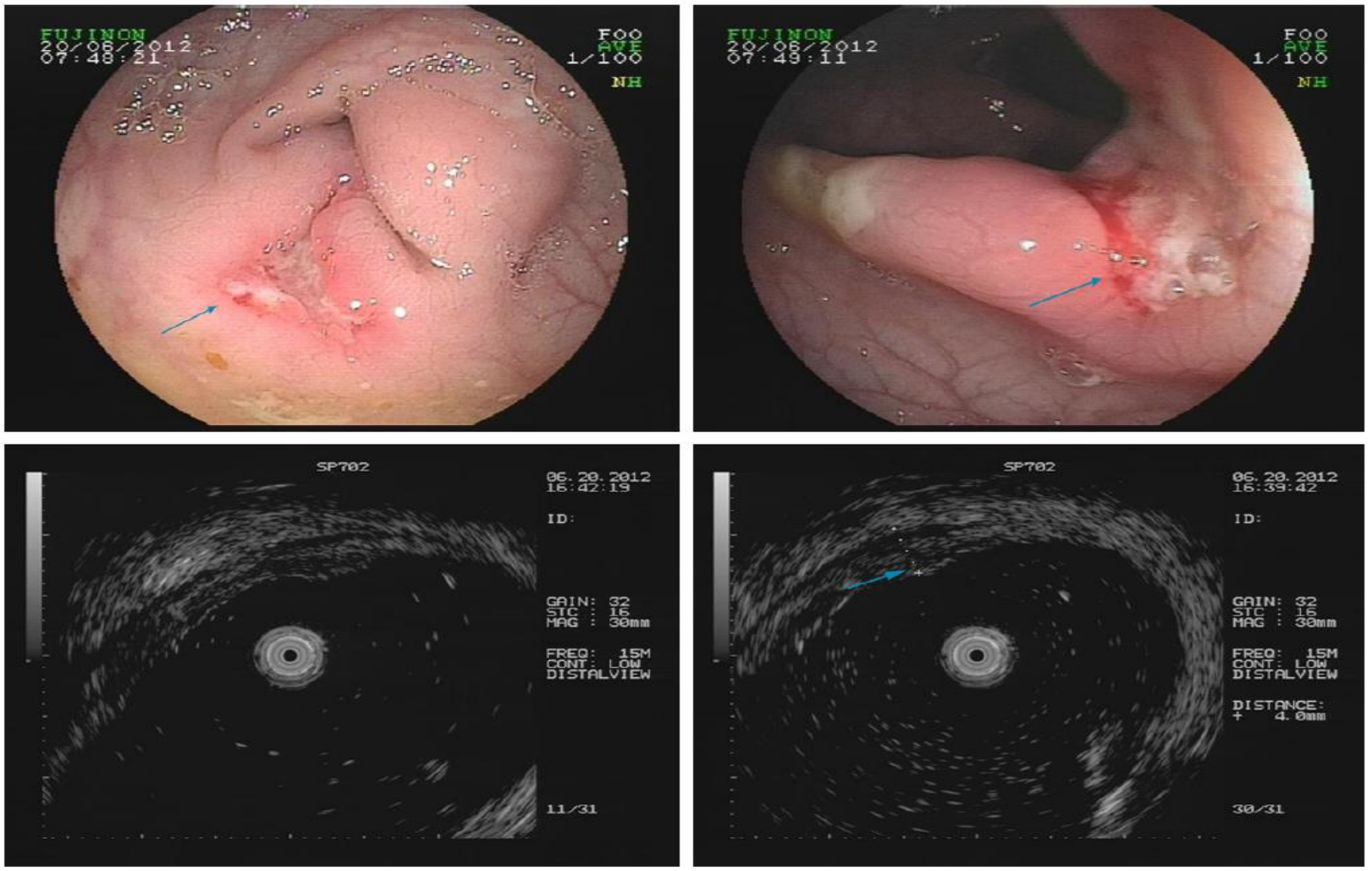
Case Report 10.12.



Ultrasound colonoscopy showed the Ultrasonic echo is higher than other diseases in the submucosa.

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Case Report 11.12.

- Treatment with methylprednisolone (60 mg * 5 d) and quinolone antibiotics were initiated on June 20, 2012, followed by oral prednisone (50 mg) for a month
- After the hormone therapy, temperature of the patient returned to normal, diarrhea disappeared, and appetite was improved, with occasional abdominal discomfort
- Ultra-sensitive C-reactive protein re-examination showed 36-26 mg/L and ESR 64 mm/h
- Gradually hormone was replaced by immunosuppressive agents after one month.

DISTINGUISHING BETWEEN TUBERCULOSIS AND CROHN'S DISEASE

Features	TB	CD
Clinical	• History of TB or current TB • Positive TB contact • Less frequent fistulas, abdominal abscesses, or perianal involvement • Abnormal CXR (not universal) • Rarely involves the rectum	• Fistulas • Bowel wall abscess • Anal perirectal disorders • Bloody stools • Bowel perforation • Recurrence after intestinal resection
Endoscopic	• Superficial, irregular transverse ulcers without predominant segmental distribution • Pseudopolyps • Cecum > ileum • ICV involved (gaping)	• May appear similar to changes in TB • TB features less common in intestinal TB (favoring CD): — Longitudinal ulceration — Cobblestoning — Aphthous ulceration — Ileum > cecum — ICV may be stenosed or ulcerated

World Gastroenterology Organization, 2015 ;

Case Report 12.12.

Discussion

- Intestinal tuberculosis and Crohn's disease are among important intestinal inflammatory diseases, the incidence of which is on the rise in recent years
- The diagnosis of Crohn's disease mainly depends on the following evidence: 1) discontinuous or segmental lesions; 2) cobblestoning and longitudinal ulcers; 3) inflammatory lesions of the entire intestinal wall; 4) non-caseous granuloma; 5) the presence of fistula; and 6) anal lesions (excluding intestinal tuberculosis, amoebic dysentery, Yersinia infection, chronic intestinal infection, eliminate intestinal lymphoma, diverticulitis, ischemic colitis and Behcet's disease). 1, 2, 3 are suspected, plus 4, 5, 6 any one can be diagnosed. 4 plus 1, 2, 3 any two can be diagnosed
- The diagnosis of tuberculosis mainly depends on the presence of the caseous necrotizing granulomatous bowel wall or mesenteric lymph nodes, histological biopsy, positive culture
- Intestinal tuberculosis: support: PPD strong positive, fever, suppressed menstruation and tuberculosis symptoms. nonsupport: anti-TB therapy is invalid, intestinal change is not typical
- In the short term, it is necessary to review colonoscopy, endoscopic ultrasound is an important means to identify the Crohn's disease
- When the treatment is invalid of the patient, the diagnosis and the relevant checks need to reconsider.