

Comprehensive Insight into Crohn's Disease: Diagnosis, Clinical Presentation, Complications and Treatment”: Review

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Abstract:

Immune-related in nature, Crohn's disease (CD) is classified as an inflammatory bowel disease (IBD). Genetic, environmental, and microbiological variables combine to produce its etiology. Beyond its potential to impact any area of the gastrointestinal system, the pathophysiology includes elevated levels of interleukin (IL)-12, IL-17, and Th1 profile, as well as the impairment of tolerance responses and a jump in pro-inflammatory interleukins. Intestinal neoplasia, enteric fistulae, and fibrotic strictures are among the long-term consequences of unchecked inflammation. As a result, it is crucial to reduce inflammatory early and effectively. In addition to blood in the stool or rectum, signs and symptoms include exhaustion, anorexia, loss of weight, persistent diarrhea, and stomach discomfort. This situation may also be linked to extra-intestinal manifestations such erythema nodosum, anterior uveitis, osteoporosis, and arthritis, as well as disorders involving musculoskeletal, cutaneous, ophthalmic, hepatic, and hematological changes. Currently, the diagnostic inquiry might include clinical history, tests like ileocolonoscopy, capsule endoscopy, and fecal calprotectin, as well as therapies to bring about and sustain remission. In this regard, biological substances, anti-inflammatory medications like corticosteroid and immunomodulators (for quick symptom relief during anti-tumor necrosis factor α therapy commencement), surgery, and non-pharmacological treatments all play a part in its treatment. Antibody production and infusion responses, infections, malignancies linked to immune-modulating medications and biologics, and damage to the liver and bone marrow are examples of adverse therapeutic reactions. In addition to providing more recent data for therapeutic therapy of CD, this review aims to provide a brief overview of its pathogenesis, surveillance, and related illnesses.

Keywords; IBD, Crohn diseases, gastrointestinal diseases, autoimmune diseases

1. Introduction

Similar to ulcerative colitis, Crohn's disease is a kind of inflammatory bowel disease (IBD), however it frequently manifests more quietly. According to Dolinger *et al.*, (2024), Crohn's disease is an inflamed gastrointestinal disorder that is mediated by the immune system and affects the full thickness of the colon wall. Any region of the gastrointestinal system might be affected. According to statistics from Minnesota, within 90 days of evaluation, 19% of individuals have stricturing or fistulizing illness. Within 20 years after assessment, intestinal problems such as fistulae, phlegmons, strictures, and abscesses affect around half of the population. According to population-based research conducted in Minnesota and Northern Europe, only 6–14% of individuals have disease migration, with ileal, ileocolonic, or colonic commitment appearing every third of the time (Claytor *et al.*, 2023). In contrast to colonic commitment, pathology in the ileal, ileocolonic, or gastrointestinal tract's upper part indicates a higher risk of stricturing and fistulizing (Click *et al.*, 2022). The eyes, skin, liver, and joints are frequently affected by extra intestinal symptoms of Crohn's disease (Faggiani *et al.*, 2024).

The precise cause of inflammatory bowel disease (IBD) remains uncertain. Nonetheless, there is strong indication that the illness could be caused by an immunological reaction that is not suitable for external antigens such as medications, poisons, infections, or gut microorganisms in a host that is genetically vulnerable. More than 71 Crohn's disorder susceptibility loci along with greater than 200 IBD-associated alleles have been found via extensive genomic investigations (Akanyibah *et al.*, 2024).

Some phenotypes of Crohn's illness are linked to genetic variations. For instance, people with Crohn's disease who present with ileal inclusion and more severe symptoms at younger ages have been shown to have NOD2/CARD15 alterations. Surgery is frequently necessary for these patients. In the future, it is anticipated that genotyping will offer prognostic data on the severity of diseases. Genetic screening is still mostly used as a research technique today (Kayali *et al.*, 2025).

2. Epidemiology

Globally, the prevalence of Crohn's disease (CD) ranges from 0.1 to 16 cases per 100,000, with higher rates observed in Europe. The pattern of IBD prevalence has shifted over the last 20 years, increasing in regions with previously low frequency, such as Asia and the Middle East, while simultaneously continuing to climb in the West (Abood *et al.*, 2024).

According to recent worldwide research, IBD prevalent is rising but recurrence is constant in Western nations, whereas newly Westernized nations in regions like Asia and Latin America are seeing increased incidence patterns (Forbes *et al.*, 2024). The beginning of CD is most common between the ages of 15 and 30 and 40 and 60, according to its bimodal pattern. According to Forbes *et al.*, (2024), Crohn's disease is more common in cities than in rural regions.

Ethnicity is one factor influencing the gender-specific proportions of Crohn's disease (CD) and ulcerative colitis (UC). In Asia, more men than women suffer with Crohn's disease, despite the fact that women are almost twice as likely as men to have it in Europe and the USA. There is no sex-related variation in UC development (Blumenstein & Sonnenberg, 2023). An intriguing link between age and sex in IBD epidemiological was found in a newly released study that included 16 areas from Europe, North America, Australia, and New Zealand. The study found that women had a decreased incidence of CD in infancy up to the age of 10–14. But after that, there was a significant rise in the incidence of CD in the 25–29 and across-35 age categories (Shah *et al.*, 2018).

A number of the main risk factors for the occurrence of IBD is family history, which raises the disease's prevalence rate by 10 to 15 times in first-degree family members who are not afflicted and by around 3 times in close relatives (Mohammed & Amin, 2022). Epidemiological evidence indicates that smoking is the primary cause of several illnesses, such as cancer, respiratory and cardiovascular conditions, diabetes mellitus, and inflammatory bowel disease (Wang *et al.*, 2022).

3. Clinical presentation

In the initial phases of the sickness, inflammation causes vague symptoms including fever and malaise. Intestinal damage is the cause of both diarrhea and stomach discomfort. Ileocecal inflammation may cause discomfort in the right bottom quadrant. Vitamin shortages and malabsorption might result from terminal ileal injury. Based on which part of the gut is most affected, anemia can result from either feces blood loss or vitamin B12 deficiency. Because fistulae occur when inflammation is extracted, the surrounding tissues may malfunction (Caruso *et al.*, 2024).

Diarrhea, stomach discomfort, and generalized symptoms such as weariness and weight loss are frequent presenting signs of CD, which is most common in those aged 20 to 30. Although less often, rectal bleeding can happen if the distal colon is affected. Frequently misconstrued as irritable

bowel syndrome, symptoms might change over time. Longer intervals are linked to increased intestinal blockage and surgery; the median median diagnosed delay is 9 to 18 months from the start of symptoms (Sigall Boneh *et al.*, 2024).

Arthropathy, cutaneous (pyoderma gangrenosum, erythema nodosum), and ophthalmic symptoms are examples of extra-intestinal indications (Rogler *et al.*, 2021). A minimum of a single joint indication is present in 24% of cases with IBD, followed by ocular manifestations (27%), and extraintestinal skin manifestations (35%), according to Kilic *et al.*, (2024). The commonly used Montreal classification methodology categorizes CD phenotype according to the following factors: illness place (ileal, colonic, ileocolonic, isolated upper), disease behavior (non-stricturing/nonpenetrating, stricturing, penetrated, perianal), and age at assessment (<16, 17–40, >40 years old) (Atreya *et al.*, 2022). CD may progress to strictures and penetration illness consequences such fistulas and abscesses development as a result of recurrent cycles of bowel inflammation (Zhou *et al.*, 2023).

Extra-intestinal symptoms are known to occur in a gender-specific manner (Algaba *et al.*, 2021). The relationship between primary sclerosing cholangitis (PSC) and gender is the most well-known. Male sex is obviously a risk factor in this case (van Munster *et al.*, 2024). Similarly, joint, skin, and eye involvement appear to be more likely in women, while ankylosing spondylitis and the exceedingly uncommon amyloidosis possess a greater common in males (Omar *et al.*, 2024).

4. Complications

Examining the variations in osteoporosis risk by gender is very fascinating. For instance, in an immense retrospective German research, the percentage of males with osteopenia or osteoporosis (53.9%) was much greater compared to the percentage of premenopausal women with IBD (29.6%), despite the fact that women with Crohn's disease had an elevated long-term risk of osteoporosis. The threat in this research is comparable to that of postmenopausal women with IBD (47%) (Lourenço *et al.*, 2024).

According to multiple researches, male gender therefore seems to be a separate risk factor for the occurrence of bone density decrease (Severs *et al.*, 2018). This problem needs further attention, screening, and prevention because it is undoubtedly underappreciated in routine medical procedures. But according to certain research, women and stoma consumers are also more likely to develop osteoporosis, which should be taken into account in routine clinical treatment (Hu *et al.*, 2024).

Regardless of their gender, people with IBD are more likely to develop colorectal cancer (CRC) than the general population (Fanizza *et al.*, 2024). But there are additionally blatantly gender-specific distinctions. Compared to women with Crohn's disease, males with IBD are more likely to acquire colorectal cancer (CRC) (Jess *et al.*, 2012). According to 171,000 human years of follow-up, men are almost 60% more likely than women to be at risk (RR 1.6, 95% CI: 1.2 to 2.2). Forty years following the first diagnosis of IBD, the cumulative incidence of colorectal cancer (CRC) was 3.5% for women and 8.3% for males (Blumenstein and Sonnenberg, 2023). Male individuals who have IBD are not the only ones at increased risk for colorectal cancer (CRC); this is true for everyone else as well and is primarily caused by a range of medical conditions. According to Lu *et al.*, (2022), patients who are men are more prone to tobacco use and consume larger amounts of alcohol, cooked meat, and fatty meats.

5. Pathogenesis

Crohn's disease is complex; the disorder is caused by a combination of environmental, nutritional, immunological, transmissible, and genetic variables (Basiji *et al.*, 2025). The pathophysiology of CD involves connections between the immune processes of innate and adaptive immunity. The inflammation and anti-inflammatory mechanisms are dysregulated, and cytokines are released in overabundance (Alula and Theiss, 2023). Innate and acquired processes comprising intestinal macrophages, neutrophils, and helper T-cells (Th) contribute to the overactive immune response by increasing inflammatory chemicals such as tumor necrosis factor- α (TNF- α). Important mediators in the inflammatory chain of Crohn's disease include Th1 and Th17. Cytokines such as interleukins (ILs) 2, 12, and 18 and interferon- γ were discovered to be abundant in colonic Crohn's disease lesions (Kong *et al.*, 2023).

According to histology, the GI tract's mucosa is made up of three different cell types: immune system cells, paneth cells, and goblet cells (Wang and Shen, 2024). These cells are essential for preserving the intestines' foundational strength and protection, and they actively participate in homeostasis. As consequence, any damage to the intestines may interfere with physiological processes, which could lead to negative reactions in the body related to consumption and digestion (Yang and Shen, 2021). Furthermore, changes in the microbiota can cause inflammation of the mucus membrane in response to intestinal destruction of tissue, which attracts

monocytes and natural killer (NK) cells to fight against the infection or injury (Jing *et al.*, 2024).

Crohn's disease is polygenic, as evidenced by the more than 100 genetic variations that have been linked to the condition to date. The likelihood to acquire Crohn's disease may be significantly influenced by immunoreactivity to gut flora, according to involved genes. Through antibody response disruption or intestinal lining deterioration, connections among genes and the surroundings may contribute to the etiology of Crohn's disease by increasing the sensitized immune system's stimulation by intestinal bacteria (Buffet-Bataillon *et al.*, 2025).

One well-established environmental associated with the onset of Crohn's disease and several other unfavorable health consequences is smoking. According to To *et al.*, (2016), tobacco has been linked to an increased risk of Crohn's disease, illness flare-ups, and surgical need. In addition, in a retrospectively cohort analysis of participants with Crohn disease in Spain, smokers (n = 1535), contrasted with nonsmokers (n = 1689), showed a greater demand for steroids, immunosuppressive medicines, and anti-tumor necrosis factor (TNF) biologic therapy (Mínguez and Nos, 2024). Hence, it is recommended that all individuals with Crohn's disease quit cigarettes.

6. Diagnosis

Anemia, a lack of iron, a lack of vitamin D, and high markers of inflammation such as C-reactive protein, erythrocyte sedimentation rate, and fecal calprotectin are common in those with Crohn's. With roughly sensitivity of 0.87 and specificity of 0.67, fecal calprotectin is a great deal of sensitive screening tests for IBD; nevertheless, in individuals with discrete small bowel illness, the findings may be negative (Bohra *et al.*, 2023).

Biopsy ought to be performed endoscopically on individuals who exhibit signs of inflammatory processes, gastrointestinal complaints, or systemic symptoms. Inconsistent regions of inflammation with ulceration, erythema, mucosal edema, and/or luminal constriction are the hallmarks of Crohn's disease (Figure 6-1). Transmural inflammatory with architectural deformation, lymphoid infiltrates, and/or granulomas are characteristics of tissue histology, which is still the mainstay of diagnosing (Figure 6-2). Crosssectional ultrasound using magnetic resonance enterography is frequently useful in individuals without bleeding from the rectal in order to pinpoint the endoscopic approach by identifying areas of intestinal tract inflammatory (Mosli *et al.*, 2015).

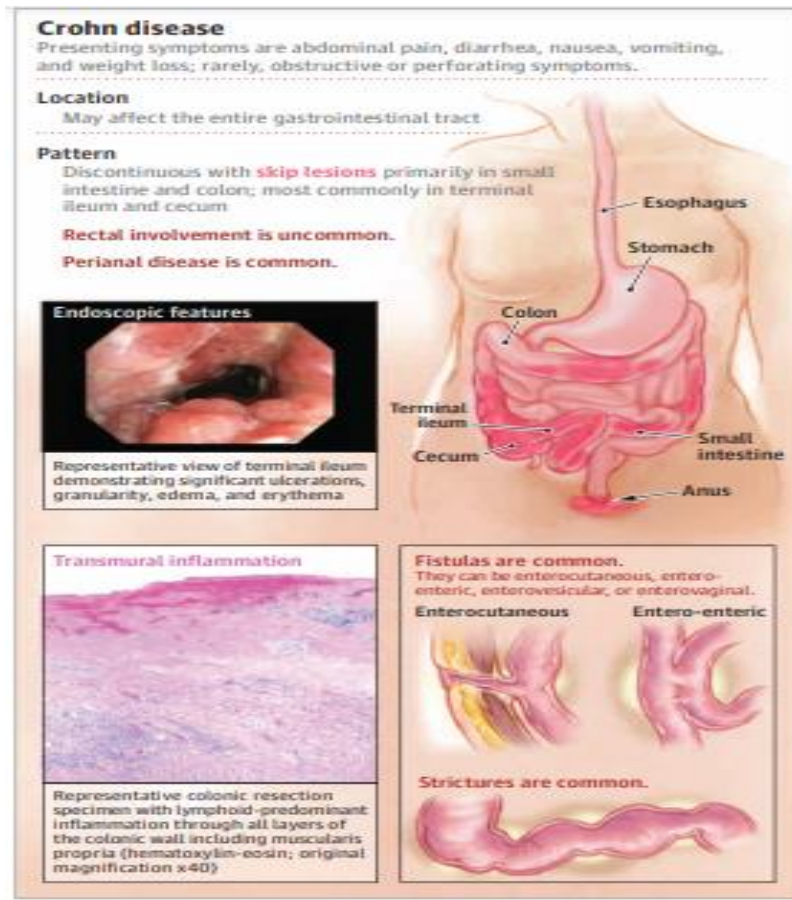


Figure 6-1: Characteristics of Crohn's illness (Cushing & Higgins, 2021)

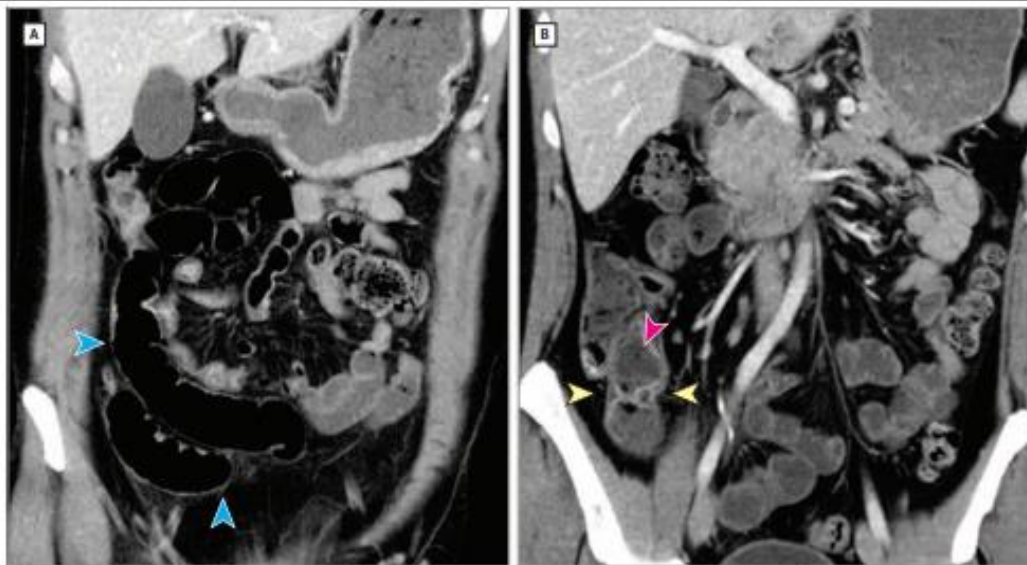


Figure 6-2: Scanning of the Abdomen and Pelvis Using Helical Computed Tomography (Coronal computed tomography views show slightly increased

enhancement in the mucosa of the terminal ileum near the ileocecal valve with areas of slight wall thickening and mural stratification with predominantly intramural fat (yellow arrowheads), as well as feculent luminal contents (pink arrowhead). More proximal loops of ileum are slightly dilated (blue arrowheads) (Cushing & Higgins, 2021).

Luminal constriction and stratified mural enrichment are examples of radiologic results. Additionally, abscesses in the abdomen and fistulae, which are consequences of Crohn's disease, can be detected by cross-sectional imaging. A capsule-based endoscopy to detect ulcerative lesions and a balloon enteroscopy to take biopsies may be necessary for certain individuals with a gastrointestinal illness who are not accessible with a regular colonoscope (Minordi *et al.*, 2024).

The manifestations of Crohn's disease might be confused with those of other gastrointestinal disorders that are inflammatory or cancerous. Since a result, the medical record should be carefully considered since it may frequently assist in determining alternative causes (Cushing & Higgins, 2021).

The first evaluation should include risk classification for complex Crohn's illness. Future difficulties are more likely to occur in patients with prior-onset Crohn's disease, small bowel place, perianal participation, prior intestinal blockage, fistula, or an abscess, prior intestines resections, early corticosteroid usage, and current smoking. According to Amadu and Soldera (2024), these individuals in particular need early, efficient treatment and careful observation to keep inflammation under control and avoid further problems from the condition.

7. Treatment

A. Medical Management

The choice of clinical therapy is depend on the patient's risk profile and severity of disease.

1. Mild-to-moderate disease could be treated by oral mesalamine, immunomodulators such as thiopurines (6-mercaptopurine, azathioprine), methotrexate, and steroids.

• **Mesalamines** (5-ASAs) and **sulfasalazine** (5-ASA with a sulfapyridine moiety) have an impact that reduces inflammation. Compared to ulcerative colitis, the use of 5-ASAs in Crohn's disease is less recognized. These drugs are ineffective when used for small bowel illness; however they may be tested for mild cases of Crohn's disease in the colon (Siddiqui *et al.*, 2025).

• **Corticosteroids;** they are primarily employed to maintain Crohn's disease until immunomodulator or biologic treatment takes operation, especially in moderate-to-severe cases, and to promote remission of flare-ups (Plotkin *et al.*, 2024).

• **Immunomodulators;** are steroid-sparing medications useful for mild Crohn's disease maintain treatment? These drugs are not utilized for active Crohn's illness induced remission because of their comparatively sluggish start of effect, which lasts 8 to 12 weeks. Steroids and immunomodulators, however, may be used together at first. Azathioprine 1.5–2.5 mg/kg/day, 6-mercaptopurine 0.75–1.5 mg/kg/day, and methotrexate (MTX) 15–25 mg every week are the dosages suggested for Crohn's disease (Martin and Sadowski, 2024).

2. Moderate-to-severe disease (including fistulizing disease) is preferred treating with binding immunomodulators and biologics or biologics alone.

• **Corticosteroids;** they are employed sparingly to prevent adverse reactions and are mostly utilized to produce remission in moderate-to-severe Crohn's illness (Plotkin *et al.*, 2024).

• **Immunomodulators;** act as supplements that lessen the immunogenicity of biologics. Interestingly, immunomodulator and anti-TNF combo treatment works better than either drug alone (Duan *et al.*, 2024).

• **Anti-TNF agents** (infliximab, adalimumab, and certolizumab pegol); stop the TNF inflammation cascade's aftereffects. These medications work well for Crohn's disease that is immunomodulator-refractory or steroid-resistant. Within two weeks of starting, medical benefit is observed, indicating a comparatively quick effect commencement. Fistulizing illness can be effectively treated with anti-TNF medications, which also lower the chance of endoscopic recurrent following surgery (Chanchlani *et al.*, 2024).

• **Leukocyte trafficking agents** suppress a memory T cell subset's integrin $\alpha4\beta7$ adhesion protein specifically to stop the T cells from attaching to gut mucous cells. This method of action has anti-inflammatory properties that are particular to the stomach. The medication in this class used to treat Crohn's disease is vedolizumab. With or without immunomodulators, this medication was discovered to be more successful than a placebo at causing and sustaining treatment in Crohn's disease (Feagan, 2024).

• **IL-12/23 agents** (ustekinumab, risankizumab); are efficacious in patients who failed prior corticosteroid, immunomodulator, or anti-TNF treatment. Ustekinumab is a nonselective IL-12/23 inhibitor, while risankizumab is a

selective IL-23 inhibitor. The side effect profile of these agents is relatively favorable according to safety surveillance data in psoriasis patients (Roshanov and Khanna, 2025).

- **JAK inhibitors;** focus on Janus kinases, which are involved in aberrant immune system reactions. The first oral selective JAK inhibitor treatment for Crohn's disease to receive FDA approval is upadacitinib. Individuals who have had unsuccessful biological and traditional therapies for Crohn's disease can benefit from this medicine (Farkas *et al.*, 2024).

B. Surgical Management

Surgery is necessary when problems from Crohn's disease occur, such as dysplasia, malignancy, recurring abscess, perforated intestine, and intestinal blockage from fibrostenotic strictures, fistulization in spite of effective medicinal therapy, or clinically resistant illness. Fibrostenotic disease, the most prevalent surgical warning, can be managed by stricturoplasty and surgical excision. For endoscopic dilatation, short segmental strictures can be taken into consideration (Ullrich and Frischer, 2024).

Simple fistulas—defined by superficial or low transsphincteric fistulas without accompanying proctitis—may be treated with fistulotomy. The implantation of chronic seton may be necessary for complex fistulas. Injection of mesenchymal stem cells into the fistula tract to decrease inflammation is being researched and shows promise (Pal *et al.*, 2024).

When doing an ileocelectomy on those with Crohn's disease who have multiple danger signs for an anastomotic leakage, a diversion ileostomy is typically taken into consideration instead of a main anastomosis. Among these hazards include weight reduction, steroid usage, and smoking (Doğru *et al.*, 2024).

C. Treatment Monitoring

In 2023, the American Gastroenterological Association (AGA) suggested that the existence of clinical signs and biomarker levels could be used to track the effectiveness of Crohn's disease therapy (Chavannes *et al.*, 2024). Individuals in remission can receive biomarkers every 6 to 12 months, whereas those who need therapy escalation may need to take them more regularly.

Serum CRP and fecal calprotectin are proposed indicators. For the purpose of ruling out active inflammation and avoiding routine endoscopic examination of disease activity, goals ought to be below 150 µg/g for calprotectin as well as fewer than 5 mg/L for CRP.

Additionally, the AGA suggested the following:

- Biomarkers are substances every two to four months to evaluate therapy response throughout active illness.
 - Endoscopic or radiologic confirmation of illness loss within three years of symptomatic reduction
- Six to twelve months after symptoms have subsided; a follow-up endoscopy should be carried out to record the healing of the mucosal surfaces.

For individuals who have not experienced any symptoms 12 months following surgical healing, a fecal calprotectin level of below fifty $\mu\text{g/g}$ is adequate to rule out illness recurrence. For these individuals, routine endoscopic evaluation is not necessary. Asymptomatic patients with little danger of postoperative resurgence or those with a greater risk but already taking preventative medicine may be treated with a similar biomarker and target. Endoscopic examination is recommended for high-risk individuals who are not taking preventative medicine in order to monitor disease activity (Li *et al.*, 2024).

D. Dietary Management

Diet is still a therapeutic adjunct. Given that people with Crohn's illness are susceptible to starvation and micronutrient problems, dietitian advice and nutritional supplements are strongly advised throughout therapy. For instance, vitamin B12 deficiency is more likely to occur in people who have past experiences of terminal ileum dysfunction or resection (Gibson *et al.*, 2024).

Some dietary interventions, including basic and semielemental eating habits, successfully decrease mucosal inflammation, according to data mostly from the juvenile community. Yet, due to low adherence, these diets have mostly failed in adults. Additionally, benefits are short-lived since inflammation returns once a nonrestrictive diet is resumed (Faggiani *et al.*, 2025).

8. Conclusions

In addition to discussing the clinical care of these individuals, this article gives a summary of the immunologic features of CD. Detection can be aided by identifying symptoms of digestion such exhaustion, anorexia, diarrhea, and stomach discomfort. Extraintestinal signs and related conditions such arthropathy, erythema nodosum, episcleritis, and anterior uveitis may also accompany these signs and symptoms. The assessment process also heavily relies on imaging studies and laboratory testing, including Fecal Calprotectin, with endoscopic operations being the first-line method. In this detection scenario, ileocolonoscopy and capsule endoscopy are both crucial tools. The

foundation of disease management is comprised of non-pharmacological and pharmacological medications, with surgical therapy being considered in certain cases. These treatments include biological agents and anti-inflammatory medications such as corticosteroids and immunomodulators. Lastly, medications that done toward the immune system are being studied additionally , and further investigation is required to detection the best course of action for peoples with CD, taking into account their unique phenotypes.

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نظرة شاملة على مرض كرون: التشخيص، العرض السريري، المضاعفات، والعلاج: مراجعة
مستخلص البحث:

يُصنف داء كرون (CD) باعتباره مرضًا التهابيًا معويًا، وهو مرض مناعي بطبيعته. تجتمع العوامل الوراثية والبيئية والميكروبيولوجية لتحديد مسبباته. وإلى جانب تأثيره المحتمل على أي منطقة من الجهاز الهضمي، تشمل الفيزيولوجيا المرضية ارتفاع مستويات الإنترلوكين-12 (IL-12)، والإنترلوكين-17، وTh1، بالإضافة إلى ضعف استجابات التحمل وزيادة كبيرة في الإنترلوكينات المؤيدة للالتهابات. ومن بين العواقب طويلة المدى للالتهاب غير المسيطر عليه، تكوّن الأورام المعوية، والناسور المعوي، والتضيقات الليفية. لذا، من الضروري الحد من الالتهاب مبكرًا وبفعالية. وبالإضافة إلى وجود دم في البراز أو المستقيم، تشمل العلامات والأعراض الإرهاق، وفقدان الشهية، وفقدان الوزن، والإسهال المستمر، واضطراب المعدة. قد ترتبط هذه الحالة أيضًا بمظاهر خارج الأمعاء مثل الحمى العقدية، والتهاب العنقية الأمامي، وهشاشة العظام، والتهاب المفاصل، بالإضافة إلى اضطرابات تشمل تغيرات عضلية هيكلية، وجلدية، وعينية، وكبدية، ودموية. في الوقت الحالي، قد يشمل الاستقصاء التشخيصي التاريخ السريري، وفحوصات مثل تنظير القولون اللفائفي، والتنظير الداخلي بالكبسولة، وكالبروتكتين البرازي، بالإضافة إلى علاجات لتحقيق الهدأة والحفاظ عليها. في هذا الصدد، تلعب المواد البيولوجية، والأدوية المضادة للالتهابات مثل الكورتيكوستيرويدات ومعدلات المناعة (لتخفيف الأعراض بسرعة أثناء بدء العلاج بعامل نخر الورم ألفا)، والجراحة، والعلاجات غير الدوائية، دورًا في علاجها. ومن أمثلة التفاعلات العلاجية الضارة: إنتاج الأجسام المضادة واستجابات التسريب، والالتهابات، والأورام الخبيثة المرتبطة بالأدوية المعدلة للمناعة والبيولوجية، وتلف الكبد ونخاع العظم. بالإضافة إلى توفير بيانات أحدث للعلاج العلاجي لمرض كرون، تهدف هذه المراجعة إلى تقديم لمحة عامة موجزة عن مسببات المرض ومراقبته والأمراض المرتبطة به.

الكلمات المفتاحية: مرض التهاب الأمعاء، مرض كرون، أمراض الجهاز الهضمي، أمراض المناعة الذاتية.