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CROHN'S DISEASE – A REVIEW OF CONTEMPORARY TREATMENT METHODS

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ABSTRACT

Background: Crohn's disease is a chronic inflammatory bowel disorder with increasing global prevalence, including in Poland. Advances in pharmacology and biologic therapies, along with nutritional and surgical strategies, have significantly changed its management, yet no curative treatment exists.

Objectives: The aim of this review was to systematize current therapeutic strategies for Crohn's disease, with emphasis on pharmacological agents, dietary interventions, and surgical approaches, and to highlight recent developments and regional perspectives.

Methods: A narrative literature review was conducted based on 51 full-text articles published in English and Polish between 2010 and 2025, retrieved from PubMed and Google Scholar. Inclusion criteria were peer-reviewed studies and reviews addressing Crohn's disease therapy. Conference abstracts, non-peer-reviewed sources, and experimental animal studies were excluded.

Results: The review identified three major groups of pharmacological agents: anti-inflammatory drugs, immunosuppressants, and biologic therapies, including recent data on JAK inhibitors and interleukin-23 antagonists. Nutritional strategies, particularly exclusive enteral nutrition, were shown to support induction of remission and reduce relapse rates. Surgical intervention remains necessary in complicated cases, though recurrence is common. Differences between international guidelines were noted, particularly regarding the role of mesalazine, enteral nutrition, and sequencing of biologic therapies.

Conclusions: Effective management of Crohn's disease requires an individualized and multidisciplinary approach. Pharmacological treatment remains the cornerstone, complemented by nutritional interventions and surgical therapy when indicated. Future progress depends on the integration of novel biologics and small

molecules, identification of predictive biomarkers, and broader access to advanced therapies.

Keywords: Crohn Disease; Drug Therapy; Biological Products; Janus Kinase Inhibitors; Surgical Procedures; Diet Therapy; Immunosuppressive Agents.

INTRODUCTION

Crohn's disease remains one of the most challenging chronic inflammatory bowel conditions, requiring regular updates of therapeutic strategies. Unlike most recent reviews focused on individual aspects of therapy, this work integrates data on pharmacological, biological, surgical, and nutritional approaches. The novelty lies in the comparative analysis of the effectiveness of different biological agents and the consideration of regional aspects of patient management. The aim of the review is to systematize current methods of Crohn's disease treatment, assess their strengths and weaknesses, and outline future directions for therapy development.

Crohn's disease is a chronic inflammatory condition involving all layers of the gastrointestinal tract wall, frequently exhibiting granulomatous features. It can affect any segment of the digestive tract—from the oral cavity to the anus—with characteristic discontinuous inflammatory lesions interspersed with areas of healthy mucosa. The exact etiology of the disease remains unclear. Initially, the inflammation is confined to the mucosal layer but may progress to deeper layers, leading to structural damage, strictures, fistula formation, and fibrosis. Systemic symptoms commonly include fatigue, low-grade fever (in approximately 30% of cases), and weight loss (reported in around 60%), which may result from malnutrition or impaired nutrient absorption. The clinical presentation varies depending on the location and severity of the inflammatory process. The most frequently affected site is the terminal ileum (in 40–50% of cases), where abdominal pain (reported by 80% of patients), diarrhea, and, less commonly, melena or a palpable mass in the right lower quadrant are predominant features. Extensive involvement of the small intestine may result in malabsorption syndrome, manifesting as anemia, steatorrhea, vitamin deficiencies, and electrolyte imbalances. Colonic involvement, observed in 20% of isolated cases and in 30–40% in combination with small bowel disease, typically presents with diarrhea, abdominal pain, and infrequently with hematochezia. The upper gastrointestinal tract may also be involved, presenting with aphthous ulcers and mucosal erosions in the oral cavity, dysphagia and odynophagia in esophageal involvement, and epigastric pain, nausea, or vomiting in the case of gastric or duodenal lesions.Perianal disease is frequently observed, especially in patients with colonic involvement. Clinical manifestations may include fissures, fistulas, abscesses, and skin tags, which may occasionally constitute the initial presentation of the disease.

The management of Crohn's disease, as well as ongoing advancements in its treatment, is of particular importance given the epidemiological data. Currently, the incidence of Crohn's disease in European Union countries is estimated at 5 per 100,000 individuals per year, while the prevalence ranges from 40 to 50 cases per 100,000 population. According to estimates, more than 15,000 individuals in Poland are affected by Crohn's disease.

The aim of this review is to provide a comprehensive summary of contemporary therapeutic strategies in Crohn's disease, with particular attention to pharmacological treatment, dietary support, and the role of surgical interventions, based on the analysis of recent literature.

METHODS

A literature review was conducted based on 51 articles retrieved from PubMed and Google Scholar. The search mainly covered the years 2010–2025 in order to include both traditional treatment methods and the most recent therapeutic strategies for Crohn's disease. Publications in both English and Polish were included in the analysis.. Articles focusing on Crohn's disease therapy, particularly pharmacological treatment, dietary interventions, and surgical management, were included. Non-peer-reviewed materials, conference abstracts, and papers unrelated to Crohn's disease were excluded.

The analyzed sources consisted mainly of clinical studies and systematic reviews. Experimental animal studies were not taken into account. The search was performed using the following key terms: "Crohn Disease", " Drug Therapy", " Biological Products". " Surgical Procedures", " Diet Therapy" and " Immunosuppressive Agents".

After screening the search results and removing irrelevant items, 51 publications were selected for analysis.

RESULTS

The literature review demonstrated that the treatment of Crohn's disease most commonly involves three main classes of pharmacological agents: anti-inflammatory drugs, immunosuppressants, and biologic therapies. Anti-inflammatory medications are primarily used during disease exacerbations, whereas immunosuppressive agents and biologics are employed for long-term disease control and maintenance of remission.

The review also emphasized the importance of appropriate dietary management, which can support pharmacological treatment, enhance patients' quality of life, and reduce the risk of disease relapse. Surgical intervention may be necessary in selected cases, particularly in the presence of complications or lack of response to medical therapy.

The analyzed studies identified the main therapeutic goals as symptom relief, induction and maintenance of remission, and prevention of relapse. Treatment efficacy depends largely on an individualized approach that considers the patient's clinical profile, the location of disease involvement, and the response to previous therapies.

The figure below summarizes the Crohn's disease treatment methods described in this article.

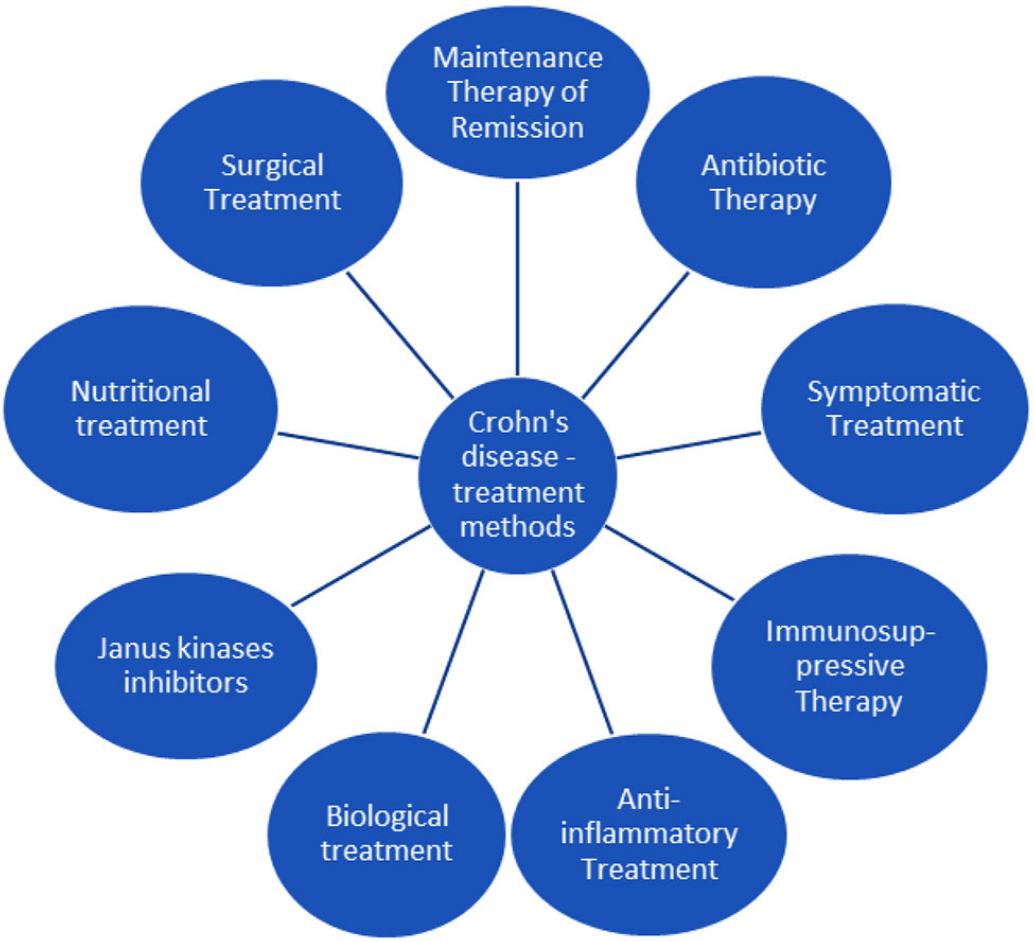

Figure 1. Diagram illustrating the treatment methods for Crohn's disease.

SYMPTOMATIC TREATMENT

An essential component of therapy for Crohn's disease is symptomatic treatment, particularly in the context of pain and diarrhea. Regarding pain management in inflammatory bowel disease (IBD), part of the therapeutic approach focuses on reducing inflammation. Nevertheless, one-third of patients continue to experience pain despite mucosal healing, and pain frequently persists even during clinical remission. Non-visceral inflammatory pain generally responds well to nonsteroidal anti-inflammatory drugs (NSAIDs), which can alleviate pain associated with arthropathies observed in IBD. However, NSAID use requires caution due to the potential risk of exacerbating IBD. A recent systematic review, which included two randomized controlled trials, did not demonstrate a statistically significant increase in disease flare-ups, and where an elevated risk was noted, it appeared highest in ileal Crohn's disease. NSAIDs may play a role in pain control for selected patients with IBD, particularly when addressing extraintestinal musculoskeletal symptoms. However, due to the risk of exacerbations, cautious use is advised. To minimize this risk, selective COX-2 inhibitors may be appropriate (1).

Another analgesic used in Crohn's disease is paracetamol, which is preferred over NSAIDs due to a lower risk of gastrointestinal irritation. Antispasmodic agents such as dicyclomine and hyoscine constitute an important drug

class, capable of relieving smooth muscle spasms in the intestines (2). These are especially valuable when pain is colicky in nature. Metamizole, an analgesic with antipyretic and mild anti-inflammatory properties, may also be considered for symptomatic treatment in cases of severe pain when other medications are ineffective or contraindicated (3).

Tramadol, an analgesic with opioid activity and additional serotonergic and noradrenergic reuptake inhibition, may be helpful in patients experiencing moderate to severe pain, especially when other options (e.g., paracetamol, antispasmodics) prove ineffective. Compared to classical opioids, tramadol may offer a more favorable safety profile in patients with IBD. Its use has been associated with lower rates of infections, bowel obstruction/ileus, and mortality compared to traditional opioids among IBD patients (4).

In the context of pain management, opioid analgesics warrant discussion. While opioids are effective for acute or cancer-related pain, evidence supporting their use in chronic pain is limited. Moreover, among patients with ulcerative colitis, opioids have not demonstrated improvements in quality of life. Instead, long-term opioid use is associated with multiple adverse effects, including constipation, nausea, vomiting, immunosuppression, sexual dysfunction, dependence, somnolence, and respiratory depression. Regular use of strong opioids in IBD has been linked to a twofold increase in premature mortality and is a prognostic factor for severe infection (1).

Despite the disadvantages of opioid use in the context of IBD, a significant proportion of IBD patients rely on opioids for pain relief. Recent studies indicate that 18%–29% of IBD patients use opioids in outpatient settings, and up to 70%–90% receive opioids during hospitalization for IBD exacerbations. It is also noteworthy that opioid utilization rates among IBD patients appear to be increasing (5).

Crohn’s disease may co-occur with psychiatric conditions such as depression and anxiety disorders. It is estimated that approximately 25% of patients with inflammatory bowel disease experience depressive symptoms. Therefore, antidepressants are proposed to play an important role in the symptomatic treatment of Crohn’s disease, not only by improving the psychological condition of patients but also by potentially influencing disease activity (6). Antidepressants—such as tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), and selective norepinephrine reuptake inhibitors (SNRIs)—modulate neurotransmitters like serotonin and norepinephrine, as well as corticotropin-releasing factor. These mechanisms affect gastrointestinal motility and modulate gut-brain signaling, ultimately resulting in a general reduction in pain (1).

Another common complaint associated with Crohn’s disease is diarrhea. Diarrhea is one of the most frequent symptoms in patients with inflammatory bowel disease (IBD), occurring in approximately 66–92% of cases (7). One of the medications used to reduce the frequency of bowel movements is loperamide (4–6 mg/day). The mechanism of action of loperamide involves delaying small intestinal transit, increasing anal sphincter pressure, and enhancing fecal continence. This prolongs the contact time of intestinal contents with the mucosa, thereby promoting greater absorption of electrolytes and water (8). Another agent used in the treatment of diarrhea in patients with Crohn’s disease is cholestyramine (4–5 g, administered 2–3 times daily). It is particularly indicated in patients who have undergone ileal resection and subsequently suffer from bile acid malabsorption. In such cases, excessive bile acids enter the colon, where they stimulate the secretion of salt and water, leading to diarrhea (9,10).

ANTI-INFLAMMATORY TREATMENT

Glucocorticosteroids (GCS) play a pivotal role in the anti-inflammatory treatment of Crohn’s disease. GCS are effective in approximately 60–80% of patients with active inflammatory bowel disease (IBD) (11). The rationale for their use in Crohn’s disease lies in their high efficacy in inducing clinical remission, rapid symptom relief, and cost-effectiveness. Although generally considered safe, glucocorticosteroids should be administered strictly in accordance with clinical indications and for a limited duration to minimize the risk of adverse effects. GCS therapy is indicated in active disease to induce remission. The choice of a specific agent depends on the severity of the flare and the anatomical location of inflammation (12). Oral prednisone at 40–60 mg/day (approximately 1 mg/kg/day) is commonly used, while in severe exacerbations, intravenous hydrocortisone (300 mg/day) or methylprednisolone (60 mg/day) may be required. For patients with inflammation limited to the ileocecal region, oral budesonide at 9 mg/day is preferred due to its low systemic bioavailability (9). While budesonide may be less effective than conventional corticosteroids in inducing remission, it is associated with a lower incidence of systemic adverse effects (13).

It is important to note that budesonide capsules are not indicated for treating lesions located in the left colon (descending colon, sigmoid colon, and rectum) (12). After achieving control of an acute flare, the glucocorticosteroid dose should be tapered over a period of 2–3 months until discontinuation (9). This approach aims to reduce the risk of steroid-related adverse effects.

Adverse effects of prolonged GCS therapy are reported in over 50% of patients treated with conventional corticosteroids and in approximately one-third of those receiving budesonide. Common side effects include

acne, moon face, striae, psychiatric disturbances, insomnia, edema, hyperglycemia, and hypertension. Musculoskeletal disorders and infections, which may result from both GCS therapy and the underlying disease, are also of concern. Osteopenia and osteoporosis are observed in 30–40% of patients with Crohn's disease, attributable to chronic inflammation, malabsorption of vitamin D and calcium, and may be exacerbated by steroid use. This problem is especially prevalent in patients with a long disease duration, low body mass index (BMI) and other nutritional deficiencies.

Bone densitometry is recommended in all Crohn's disease patients receiving GCS for more than 3 months, in those with fragility fractures, in postmenopausal women, and in men over 50 years of age. Additional limitations of GCS therapy include steroid resistance (observed in approximately 20–30% of patients) and steroid dependence, affecting 20–40% of individuals (12).

Steroid resistance is diagnosed when symptoms of active disease persist despite four weeks of prednisone at a dose of 0.75 mg/kg/day. Steroid dependence is defined as the inability to reduce the GCS dose below a specific threshold without symptom relapse. The British Society of Gastroenterology defines steroid dependence as having two or more disease flares per year requiring GCS treatment, relapse upon dose reduction below 15 mg/day, or recurrence within six months of steroid discontinuation. An alternative definition describes steroid dependence as the inability to reduce the prednisone dose (or equivalent) below 10 mg/day without relapse or the occurrence of a new flare within three months of completing a steroid course. Factors predisposing to steroid resistance include intestinal strictures, perianal disease, high Crohn's Disease Activity Index (CDAI) scores, and history of surgical resections. Steroid dependence is more frequently observed in smokers, in patients with pericolonic disease, and in those with disease onset during childhood.

In cases of confirmed steroid resistance or dependence, escalation of therapy or a change in treatment strategy should be considered. However, before proceeding, a comprehensive review of the current treatment plan is essential from both the physician's and the patient's perspective. Confirmation of active inflammation in IBD is critical and may be achieved through biomarkers such as C-reactive protein (CRP) and fecal calprotectin and/or endoscopic evaluation.

Clinical symptoms, such as diarrhea and abdominal pain, are not definitive indicators of ongoing inflammation, as they may also result from functional disorders commonly present even during remission in IBD patients. It is also necessary to assess treatment adherence and exclude coexisting infections, such as Clostridium difficile. Furthermore, identification and elimination of other contributing factors—such as NSAID use or tobacco smoking, especially in Crohn's disease—are essential.

In ambiguous cases, alternative diagnoses should be considered, including irritable bowel syndrome, lactose intolerance, small intestinal bacterial overgrowth (SIBO), or neoplastic processes. In some patients, particularly those with diarrhea and suspected steroid resistance during oral corticosteroid therapy, clinical improvement may be achieved through intravenous therapy (e.g., hydrocortisone 300–400 mg/day or methylprednisolone 60–80 mg/day). In such cases, poor bioavailability of oral steroids may be responsible for inadequate clinical response (11).

Glucocorticosteroids are not used for maintenance therapy. Their use in patients with clinically quiescent Crohn's disease does not reduce the risk of relapse over a 24-month observation period. On the contrary, long-term GCS use carries the risk of numerous adverse effects.

In the context of anti-inflammatory treatment for Crohn's disease, it is important to mention aminosalicylates. Sulfasalazine (SASP) and 5-aminosalicylic acid (5-ASA, mesalazine) are among the most long-established drugs used in the therapy of inflammatory bowel diseases (IBD). Although their efficacy in inducing and maintaining remission in ulcerative colitis (UC) has been confirmed in numerous clinical trials, the use of mesalazine in the treatment of active Crohn's disease (CD) raises serious concerns. Nevertheless, mesalazine continues to be widely used as a first-line therapy for mild and moderate forms of CD, based primarily on older scientific reports. However, most contemporary randomized studies and meta-analyses do not confirm a significant advantage of mesalazine over placebo in inducing remission, which is reflected in the recommendations of the European Crohn's and Colitis Organisation (ECCO) from 2006, which do not recommend the use of mesalazine in the active phase of the disease. Despite the lack of definitive evidence for the effectiveness of mesalazine in treating active CD, the recommendations of the British Society of Gastroenterology, the American College of Gastroenterology, and Polish guidelines allow its use at a dose of 3-4 g/day in cases of mild changes localized in the small intestine. In cases where the changes are mild or moderate and restricted to the large intestine, sulfasalazine at a dose of 3-6 g/day is recommended. Its efficacy has been demonstrated in several randomized clinical trials. It is also important to note that neither sulfasalazine nor mesalazine is effective in preventing recurrences of CD in patients who achieved remission through pharmacological treatment. However, mesalazine has documented effectiveness in reducing the frequency of recurrences following resection surgeries of the small intestine. During treatment with 5-aminosalicylates, regular monitoring of blood counts and renal parameters is necessary due to the potential nephrotoxic effects of these drugs.(11)

IMMUNOSUPPRESSIVE THERAPY

Immunosuppressive therapy in Crohn's disease (CD) is a cornerstone of treatment, especially in moderate and severe cases, where the goal is to induce and maintain remission and reduce the need for glucocorticoids. One group of drugs with immunosuppressive effects in Crohn's disease are thiopurines – azathioprine (AZA) and 6-mercaptopurine (6-MP). These represent first-line maintenance therapy. Azathioprine is a purine analog that exerts its effect by competitively inhibiting the synthesis of purine nucleotides. After oral administration, it is almost entirely converted into 6-mercaptopurine (6-MP), which then transforms into the active form – 6-thioguanine (TG). 6-MP can also be metabolized by xanthine oxidase into the inactive 6-thiouric acid or by thiopurine methyltransferase (TPMT) into 6-methylmercaptopurine (6-MMP), which also lacks biological activity. A deficiency or absence of TPMT, which occurs in approximately 0.3–11% of the population, can lead to severe adverse effects during thiopurine therapy (11,14). The most common side effects include myelosuppression (dose-dependent and usually reversible, with leukopenia being the first symptom), liver and kidney damage, and acute pancreatitis (which occurs independently of the dose in 1.3–3% of patients, typically in the 3rd–4th week of treatment, and usually resolves after discontinuation of the drug). Some patients experience intolerance symptoms such as nausea, vomiting, and abdominal pain – usually mild, although sometimes requiring a change from azathioprine (AZA) to 6-mercaptopurine (6-MP). Thiopurine therapy increases the risk of infections, including opportunistic infections, as well as certain cancers, particularly skin cancer (excluding melanoma), cervical cancer, and lymphoid malignancies. In young men (under 30 years of age) with a negative serological result for EBV, the risk of lymphoma following primary EBV infection is particularly high, thus alternative immunosuppressive agents, such as methotrexate, are recommended in this group. Due to the cancer risk, all patients should undergo dermatological care, and women should additionally participate in regular screenings for cervical cancer. Thiopurine therapy requires systematic monitoring – during the first two months, blood tests should be performed every two weeks, and then at least every three months to monitor blood counts, liver enzyme activity, and kidney function. Mild leukopenia (white blood cell count above 3500/µl) does not require dosage modification, but at lower levels, the dose should be reduced. In the case of severe leukopenia (below 2500/µl with lymphocytopenia <1000/µl), discontinuation of the drug is necessary. If liver enzyme activity exceeds three times the upper limit of normal, therapy modification should be considered, while a fivefold increase warrants discontinuation of the drug (12,14). The effectiveness and safety of thiopurine therapy can be evaluated by measuring the levels of 6-thioguanine (6TG) and 6-methylmercaptopurine (6MMP) in erythrocytes, with testing recommended after three months of treatment. Measurement of 6TG, the active metabolite, is particularly useful in cases of lack of clinical improvement or the appearance of adverse effects. A low 6TG level with no treatment effect suggests the need for a dose increase, whereas the lack of efficacy with high 6TG levels indicates that further dose increases will not be beneficial and may only intensify adverse effects (14). The recommended dose for azathioprine is 2–2.5 mg/kg body weight, while for 6-MP, it is 0.75–1.5 mg/kg body weight (9). However, therapy should begin with lower doses – 25–50 mg/day for 2 weeks, followed by a dose increase of 25 mg/day every 2–4 weeks, in combination with evaluation of tolerance and possible adverse symptoms (12). Thiopurines have a delayed onset of action, and their expected effects may only be observed after 2–3 months. Therefore, they are used primarily for maintaining clinical remission (13). They are not recommended for inducing remission (9).

Another immunosuppressive drug used in the treatment of Crohn’s disease is methotrexate (MTX). It is considered a second-line immunomodulator for patients who do not respond to or cannot tolerate 6MP/AZA therapy (13). Methotrexate has proven efficacy both in treating active Crohn's disease and in maintenance therapy. In steroid-dependent patients, it allows for gradual tapering or discontinuation of prednisone. In the active phase of the disease, to induce remission, it is administered intramuscularly at a dose of 25 mg/week for 16 weeks, and for maintenance therapy, at a dose of 15 mg/week. Methotrexate in oral formulations is ineffective (12,15). Methotrexate therapy is associated with the potential for adverse effects such as nausea, vomiting, leukopenia, and hepatic fibrosis. Less frequently, allergic pneumonitis is observed. Due to the drug's myelotoxicity and hepatotoxicity, regular monitoring of laboratory parameters is necessary, primarily blood counts, bilirubin levels, and liver enzyme activity, typically every 1–2 months. If liver enzyme activity exceeds twice the upper limit of normal, therapy should be temporarily discontinued until normalization. To reduce side effects, particularly nausea and folate deficiencies, supplementation with folic acid at a dose of 1 mg per day or 5 mg once a week is recommended, administered 1–2 days after the methotrexate dose. Methotrexate is strongly teratogenic, so its use is contraindicated in pregnant women and those planning pregnancy. Both women and men should cease therapy at least three months before attempting conception, and effective contraception is recommended during treatment and for up to six months after completion. It is worth noting that methotrexate does not increase the risk of cancer (12,14).

Another immunosuppressive drug to mention in the context of Crohn's disease is cyclosporine A. Cyclosporine A is an immunosuppressive drug that inhibits the production of interleukin-2 and other cytokines by T lymphocytes, affecting the function of both T and B lymphocytes. Its effectiveness in treating inflammatory bowel diseases (IBD) may vary due to the complexity of these diseases and the diversity of dosages used. It

also affects other inflammatory cells, such as neutrophils and mast cells, making it a versatile, although not without drawbacks, therapeutic agent – either alone or in combination with other drugs. By inducing apoptosis in T lymphocytes, it may also inhibit tumor development in the course of the disease (16). Data from uncontrolled studies suggest that parenteral cyclosporine A may be effective in treating fistulizing Crohn's disease (17). It should only be used within controlled trials in patients who are resistant to treatment and for whom surgery is not recommended (18). Cyclosporine A is generally considered less safe than other IBD therapies due to the risk of severe adverse effects, such as anaphylaxis, seizures, Pneumocystis carinii infection, and permanent kidney damage. Additionally, its use is complicated by the need for strict monitoring of drug levels due to its narrow therapeutic window. As a result, CSA is typically used as a rescue treatment in severe, refractory cases (17).

BIOLOGICAL TREATMENT

Anti-TNF agents

There are two groups of biological agents registered in treatment of Crohn’s diseases such as anti-tumor necrosis factors (infliximab, adalimumab) and new molecules vedolizumab and ustekinumab(14). Anti-TNF agents are registered in active Crohn's disease of moderate to severe severity in adult patients and of severe severity in children and adolescents, in the absence of the expected response to a complete and appropriate treatment regimen containing corticosteroids and/or immunosuppressive agents, poor tolerance of treatment or existing contraindications to treatment and active Crohn's disease with fistulas in patients who have not responded to appropriate standard treatment(19,20). Infliximab is a chimeric human-mouse IgG1 monoclonal antibody produced from a recombinant cell line. It has high affinity for the soluble and trans-membrane form of human TNF-α, but does not bind to lymphotoxin α (TNF-β). Infliximab inhibits TNF-α activity in various in vitro bioassays. In vivo, it rapidly forms stable complexes with human TNF-α, resulting in loss of biological activity by TNF-α. In Crohn's disease, treatment with infliximab is associated with a reduction in CRP levels, a reduction in the influx of inflammatory cells into affected areas of the bowel and a reduction in the presence of inflammatory markers in these areas(19). Infliximab is used in induction treatment in combination with thiopurines e.g. azathioprine, 6-mercaptopurine. In 2009 study the effectiveness of infliximab treatment was showed. 89.1% of patients were claimed to have partial or complete initial respose to treatment. In this group of individuals 46,4% presented decrease in CRP back to normal values (<3 mg/l) and 30.7% had a drop in CRP of >50%. At the en of the follow-up among the patients, 43.3% continued receiving infliximab with ongoing control of disease activity. In 20.1% of cases, infliximab was discontinued after a median duration of 6.2 months (IQR 1.4–16.6) and a median of four infusions (IQR 2–7), as the patients had achieved remission. These individuals remained in remission for a median of 47.3 months (IQR 20.8–66.4) after termiantion of infliximab treatment. Notably, 73.6% of these patients received infliximab on an episodic basis and did not require further treatment due to sustained remission (21).

Adalimumab is a recombinant human monoclonal antibody obtained by expression in Chinese hamster ovary cells. It binds specifically to human TNF and inhibits its activity by blocking its binding to TNF receptors p55 and p75 on the cell surface. Adalimumab also affects biological responses induced or regulated by TNF, including changes in the concentration of intercellular adhesion molecules responsible for leukocyte migration (ELAM-1, VCAM-1 and ICAM-1). Patients with Crohn's disease showed reduced expression of inflammatory factors in the colon (including TNFα) and rapidly decerasing level of CRP in the blood. Endoscopic examinations of the intestinal mucosa showed healing in patients taking the drug(20). In the case of adalimumab, the added benefit of combination therapy is relatively limited because adalimumab is a fully human antibody with low immunogenicity. Nonetheless, patients receiving adalimumab alongside thiopurines have shown higher drug concentrations and a reduced likelihood of developing antibodies, especially during long-term biologic treatment. Anti-TNF agents are generally considered safe, with the most frequent side effects being hypersensitivity reactions, opportunistic infections, and a slightly increased risk of certain cancers. Current research indicates that both agents are similarly effective in inducing and maintaining remission. The decision between them mainly depends on patient preference and whether thiopurines can be used in combination therapy. For patients who cannot tolerate thiopurines or experience adverse effects, adalimumab is the preferred option (14). On the basis of conducted reaserch adalimumab’ efficacy was proven comparing to placebo. Adalimumab was significantly more effective than placebo in inducing clinical remission at four weeks (24% compared to 9%). It also showed a notable benefit over placebo in achieving both a 70-point (56% vs. 34%) and a 100-point (43% vs. 24%) improvement in the Crohn’s Disease Activity Index (CDAI) score at the same time point. These findings were considered to be supported by high-certainty evidence (22). Similar results was presented in 2022 study(23).

α4-integrin inhibitors

Vedolizumab is a targeted biologic immunosuppressant that works specifically in the intestines. It is a humanized monoclonal antibody created using recombinant DNA technology in chinese hamster ovary cells.

Vedolizumab selectively binds to the α4β7 integrin found on helper T cells that are localized in the intestines. This binding prevents the T cells from attaching to the MAdCAM-1 adhesion molecule, which is primarily found on intestinal blood vessels and is crucial for retaining T lymphocytes in the gastrointestinal lining. Importantly, vedolizumab does not interfere with other integrins such as α4β1 or αEβ7. The α4β7 integrin is present on memory helper T cells that migrate to the gastrointestinal tract and contribute to the inflammation seen in Crohn's disease. By targeting this mechanism, vedolizumab helps reduce gastrointestinal inflammation Crohn's diseases. Vedolizumab blocks the interaction between integrin α4β7 and MAdCAM-1, preventing memory helper T cells, retained in the gut by the vascular endothelium, from entering the intestinal tissue. This action causes a reversible 3-fold increase in the number of these T cells in the bloodstream. Some patients treated with vedolizumab may develop antibodies against the drug, most of which are neutralizing. The presence of these antibodies is linked to faster drug clearance and reduced rates of clinical remission. Infusion-related reactions have been reported, particularly in patients who develop these antibodies.(24) In 2023 study the effectiveness and safety of vedolizumab therapy was investigated. It showed greater effectiveness of vedolizumab than placebo in achieving clinical remission during the induction phase, with 71 more patients per 1000 experiencing remission (RR 1.61, 95% CI 1.20–2.17; based on 4 studies with high-certainty evidence). It also led to a higher rate of clinical response compared to placebo, with 105 more patients per 1000 responding (RR 1.43, 95% CI 1.19–1.71; 4 studies; high-certainty evidence). Regarding safety during induction, vedolizumab may have a similar risk of serious adverse events as placebo (9 fewer per 1000; RR 0.91, 95% CI 0.62–1.33; low-certainty evidence), and is probably comparable in terms of overall adverse events (6 fewer per 1000; RR 1.01, 95% CI 0.93–1.11; moderate-certainty evidence).For the maintenance phase, vedolizumab was also more effective than placebo in sustaining clinical remission, with 141 more patients per 1000 maintaining remission (RR 1.52, 95% CI 1.24–1.87; 3 studies; high-certainty evidence). In terms of safety during maintenance, it may be similar to placebo for serious adverse events (3 fewer per 1000; RR 0.98, 95% CI 0.68–1.39; low-certainty evidence), and probably shows no difference in overall adverse events (no difference per 1000; RR 1.00, 95% CI 0.94–1.07; moderate-certainty evidence) (25).

Another example of anti-α4-integrin drug is natalizumab. Its mechanism of action is similar to vedolizumab. In the metaanalysis comparing these two drugs to each other and placebo no significant difference between vedolizumab and natalizumab was observed. It was proven that both of these drugs have comparative effect in inducing clinical remission and imroving quality of life in anti-TNF-naive and anti-TNF-exposed patients and similar adverse effects rate (26).

IL-12, IL-23 inhibitors

Ustekinumab is a fully human IgG1κ monoclonal antibody that binds with high specificity to the p40 protein subunit common to the cytokines IL-12 and IL-23, inhibits their activity by preventing the binding of these cytokines to their IL-12Rβ1 protein receptor located on the surface of immune cells. Ustekinumab, being unable to bind to IL-12 or IL-23, which are attached to IL-12Rβ1 receptors on the cell surface, does not affect complement activity or participate in the phenomenon of antibody-dependent receptor cell cytotoxicity. IL-12 and IL-23 are heterodimeric cytokines secreted by activated antigen-presenting cells such as macrophages and dendritic cells. They participate in the body's immune response; IL-12 stimulates natural killer (NK) cells and CD4+ T cell differentiation towards a Th1 phenotype, while IL-23 induces the Th17 pathway.(27) A single induction dose is given intravenously. Maintenance treatment consists of doses of the drug administered subcutaneously every 8 or 12 weeks, depending on the risk assessment of severity and previous treatment. Ustekinumab has a very good safety profile. The risk of severe infections appears to be lower than with anti-TNF drugs, and no increased risk of carcinogenesis has been found(14) A retrospective cohort study performer in pediatric patients showed its effectiveness and safety. Thirteen patients who had previously not responded to anti-TNFα therapy were included in the study—eight (61.5%) with Crohn's disease and five (38.5%) with ulcerative colitis . The median patient age was 13 years (IQR: 11.5–14), and ustekinumab was started at a median of 3 years (IQR: 2.3–7) after diagnosis. Clinical remission was achieved in 10 patients (76.9%). There were no significant differences in baseline characteristics between those who did and did not reach clinical remission. Biochemical remission was observed in six patients (46.2%). Among patients in remission, there were significant improvements in BMI, reductions in CRP, and decreased reliance on corticosteroids. Follow-up endoscopy in seven patients showed remission in six. Reported adverse events included two infections and one case of headache. A group of medications similar to Il-12/IL-23 inhibitors are selective IL-23 inhibitors. These drugs like risankizumab, guselkumab, and mirikizumab target the IL-23p19 subunit to suppress IL-23 activity and reduce inflammation in Crohn's diseases and they do not interfere with IL-12 . This review evaluates their efficacy, safety, and overall therapeutic potential in Crohn's disease treatment. These agents have shown significant success in inducing clinical remission and achieving endoscopic healing in patients with moderate to severe Crohn's disease, including those unresponsive to anti-TNF therapies. Risankizumab, in particular, yielded strong outcomes in key clinical trials such as ADVANCE, MOTIVATE(28), and FORTIFY, with remission rates reaching up to 45% and consistent normalization of inflammatory markers. Both guselkumab and mirikizumab also demonstrated notable effectiveness in both induction and maintenance phases, with encouraging long-term results. IL-23 inhibitors generally exhibited a favorable safety profile, with low incidences of serious side

effects, including infections and cancer. Overall, these selective IL-23 blockers offer a promising and targeted treatment option for moderate to severe Crohn's disease, with high rates of clinical and endoscopic remission and a reassuring safety record (29).

JANUS KINASES INHIBITORS

Upadacitinib is a selective and reversible inhibitor of janus kinases (JAKs). JAKs are intracellular enzymes that transmit signals for cytokines and growth factors involved in a broad spectrum of cellular processes, including inflammatory responses, haematopoiesis and immune surveillance. The JAK family consists of four enzymes, JAK1, JAK2, JAK3 and TYK2, which, acting in pairs, phosphorylate and activate signal transducers and activators of transcription (STAT proteins). JAK1 plays an important role in signal transduction for pro-inflammatory cytokines, JAK2 in erythrocyte maturation and JAK3 in immune surveillance and lymphocyte function. In human cell assays, upadacitinib preferentially inhibits signal transduction by JAK1 or JAK1/3 with functional selectivity towards cytokine receptors that signal via JAK2 pairs. Pro-inflammatory cytokines that transmit signals through the JAK1 pathway are involved in the pathology of inflammatory bowel diseases. Inhibition of JAK1 by upadacitinib modulates signal transduction by JAK-dependent cytokines that cause inflammation and the subjective and physical symptoms of inflammatory bowel disease.(30) The study GETAID was conducted on population of patients who had been treated at least one biological drug before starting upadacitinib and 53.8% had undergone at least one previous intestinal resection. After 12-weeks period SFCR (steroid free clinical remission) was assesed. SFCR was achieved in 107 out of 197 patients (54.3%). Clinical response was observed in 129/197 (65.5%), while clinical remission was observed in 111/197 (56.3%) of patients. The scores of abdominal pain and stool decreased respectively from 2 (1–2) to 0 (0–1) and from 4 (2–7) to 1 (0–4). 38 patients had endoscopic and/or radiological evaluation at week 12 (ileocolonoscopy $n = 11$; MRI $n = 15$; and IUS $n = 13$), with a response observed in 18 patients (47.4%). Endoscopic response was observed in 4 out of 11 patients, while radiological response was observed in 11 out of 28 patients. Ten study showed dercrease in levels of CRP from 10.0 (4.0–25.0) mg/L at baseline to 4.0 (1.0–12.7) and calprotectin 700 (438–1600) µg/g to 207 (57–700) µg/g. The improvement of biomarkers level was confirmed in 90/173 (52.0%).(31) Moreover the reaserch work in 2025 presented outcomes after 12 weeks treatment which are similar to the results of previous study and after 6 months. Of the 179 patients with 6-month follow-up, 119 (66.5%) demonstrated clinical response. At baseline, corticosteroids were used in 77 out of 311 patients (24.8%), and 22 out of 54 (40.7%) continued steroid use at 12 weeks. Among those who achieved clinical remission, 132 out of 146 (90.4%) were corticosteroid-free at 12 weeks, and 94 out of 100 (94%) remained steroid-free at 6 months. Of the patients who had both baseline and 6-month follow-up endoscopies, endoscopic remission was observed in 44 out of 103 (42.7%) overall, including 42 out of 97 (43.3%) who were on the 30-mg dose.(32).

The table below summarizes the biological treatments used in the management of Crohn's disease. It presents the mechanism of action of individual classes of biologic drugs, efficacy and safety profile.

Table 1. Comparison of Biologic Therapies in Crohn's Disease

Drug Class	Mechanism of Action	Efficacy	Safety Profile
Anti-TNF agents	Bind to TNF-α (tumor necrosis factor alpha), neutralizing its pro-inflammatory activity. Infliximab is chimeric (mouse-human), Adalimumab is fully human.	Infliximab: 89.1% initial response; 46.4% normalized CRP; 43.3% maintained remission long-term. Adalimumab: 24% remission at 4 weeks (vs. 9% placebo); CDAI improvement of 70 points (56% vs. 34%). Similar efficacy in maintenance.	Generally safe; risks include infusion reactions (especially with infliximab), infections, and slightly increased malignancy risk.

α4-Integrin inhibitors	Bind selectively to α4β7 integrin (Vedolizumab), preventing T-cell adhesion to MAdCAM-1 and migration to the gut. Natalizumab blocks α4-integrin more broadly.	Vedolizumab: RR 1.61 for induction remission; 71 more per 1000 patients in remission vs placebo; 141 more per 1000 in maintenance remission. Similar efficacy to Natalizumab.	Excellent gut-selective safety; rare infusion reactions and anti-drug antibodies. No increased malignancy or systemic infections.
IL-12/ IL-23 inhibitors	Binds to the p40 subunit shared by IL-12 and IL-23 cytokines, blocking activation of Th1 and Th17 pathways.	Pediatric study: 76.9% achieved clinical remission; 46.2% biochemical remission; significant CRP and steroid reduction; endoscopic remission in 6 of 7 follow-ups.	Very good safety profile; lower infection risk than anti-TNF; no increased cancer risk observed.
Selective IL-23 inhibitors	Target IL-23p19 subunit, selectively inhibiting IL-23-driven inflammation without affecting IL-12.	Risankizumab: up to 45% remission in ADVANCE/ MOTIVATE/FORTIFY trials; normalization of inflammatory markers. Guselkumab, Mirikizumab also showed strong remission and mucosal healing outcomes.	Favorable profile; low incidence of infections and malignancies. Promising for long-term therapy.
JAK inhibitors	Selective and reversible JAK1 inhibitor, blocking intracellular signaling of pro-inflammatory cytokines via JAK-STAT pathway.	GETAID study: 54.3% steroid-free remission at 12 weeks; 56.3% clinical remission; CRP decreased from 10.0 to 4.0 mg/L; calprotectin from 700 to 207 µg/g. 6-month follow-up: 66.5% clinical response, 94% steroid-free. Endoscopic remission in 42.7%.	Generally well tolerated; ongoing evaluation of long-term safety. Slightly increased infection risk possible.

NUTRITIONAL TREATMENT

Enteral nutrition

For patients with Crohn's disease, both enteral nutrition (EN) and parenteral nutrition (PN) are recommended by the European Crohn's and Colitis Organisation (ECCO) and the European Society of Clinical Nutrition and Metabolism (ESPEN) guidelines, particularly for those who are malnourished and undergoing major gastrointestinal surgery, or as a supplementary therapy alongside an oral diet. Enteral nutrition (EN) is a liquid-based diet that eliminates solid foods and provides complete caloric needs. It is especially recommended during disease flare-ups, typically over a 6–8 week period to help induce remission. EN can be taken orally—as a beverage, powder, pudding-like snack—or administered through a feeding tube, all with comparable effectiveness. Currently, EN is available in three main types based on protein and fat composition: elemental, semi-elemental, and polymeric. Elemental formulas are made up of easily absorbed nutrients such as amino acids, simple sugars, and medium-chain triglycerides. Semi-elemental formulas include peptides of varying lengths, simple carbohydrates like glucose or starch, and medium-chain triglycerides. Polymeric formulas contain intact proteins, complex carbohydrates, and long-chain triglycerides (33). The subtype of EN is an exclusive enteral nutrition (EEN). EEN is advised as the first-line treatment for children and adolescents with active Crohn's disease, offering a safe and highly effective approach to induce remission, promote mucosal healing, and improve nutritional status, bone metabolism, growth, and overall quality of life(34). EEN consists of providing a nutritionally complete liquid formula exclusively—replacing all regular food and drinks—for a set period, typically 6 to 8 weeks. Oral intake is preferred, though alternative methods such as tube feeding or stoma may be used when oral feeding is not feasible or insufficient to meet nutritional needs. The method of

administration, whether continuous or in bolus form, does not influence treatment effectiveness. Polymeric formulas, which are generally better tolerated and more palatable, are recommended. Specialized or modified formulas are reserved for particular cases, such as cow's milk protein allergy or specific digestive or absorption issues.(35) EEN is the primary treatment for mild to moderate Crohn's disease in children and adolescents, as it leads to disease remission in 80–85% of cases and helps reduce of steroids, which can negatively affect growth(36). However, besides the promising results of EEN over steroids in children, the outcomes in adults are not so convincing and steroids maintain agents with better remission rate(37). EEN may affect gut microbiota because it reduces bacterial diversity, quantity of *F. prausnitzii* spp. (which produce anti-inflammatory protein) and decreases fecal butyrate production. Another limitations of EEN include its unpleasant taste and the challenge patients face in adhering to a liquid-only diet for an extended period. These issues often reduce patient compliance with the treatment.

Parenteral nutrition

Parenteral nutrition (PN), including its complete form—total parenteral nutrition—delivers nutrients directly into the bloodstream via a central venous catheter. According to European Chron's an Colitis Organisation (ECCO) PN can be used to improve nutritional status before surgery in Crohn's disease patients, either as a supplement to EN or as an alternative when EN is not feasible or is contraindicated(38). PN is typically recommended for malnourished patients undergoing an acute inflammatory flare to allow for bowel rest. It is also indicated when postoperative complications impair gastrointestinal function and oral or enteral feeding is not possible for at least seven days. Other clinical situations where PN is appropriate include bowel obstruction or partial blockage, high-output fistulas, bowel ischemia, severe bleeding, anastomotic leaks, or active disease leading to significant gut dysfunction.(39)

Low FODMAP diet

The low FODMAP (fermentable, oligosaccharides, disaccharides, monosaccharides, and polyols) diet involves eliminating certain short-chain carbohydrates that are poorly absorbed and highly fermented by gut bacteria, often triggering symptoms like diarrhea, bloating, abdominal pain, and distention. Individuals following this diet should avoid honey and specific fruits such as apples, watermelon, and dates (high in fructose), as well as onions, garlic (rich in fructans), and legumes like beans and lentils (sources of galactans). Sucrose, however, is permitted. While this dietary approach has been shown to relieve gastrointestinal symptoms, it does not appear to improve calprotectin levels or reduce intestinal inflammation. It is generally recommended for patients with silent IBD who experience IBS-like symptoms, which affect up to 57% of those with Crohn's disease. A notable drawback is the decreased intake of prebiotics such as inulin, fructo-oligosaccharides, and fructose, which can lead to a reduction in beneficial Bifidobacteria and contribute to dysbiosis.(39)

The specific carbohydrate diet

The Specific Carbohydrate Diet (SCD) permits the intake of monosaccharides while excluding disaccharides and most polysaccharides. Allowed foods include meats, eggs, oils, fruits, nuts, low-lactose dairy products like dry-curd cottage cheese and 24-hour homemade fermented yogurt, and vegetables high in amylose. Prohibited items on the SCD include sucrose, maltose, isomaltose, lactose, potatoes, corn, okra, soy, fluid milk, fresh cheeses high in lactose, as well as food additives and preservatives. Gottshall recommended following the SCD for at least one year after symptom resolution, which can make long-term adherence challenging due to work or social constraints. Research indicates that the SCD can alleviate symptoms, enhance quality of life, and in some cases, maintain remission without medication. In pediatric patients, it has also been shown to support mucosal healing and normalize inflammatory markers such as CRP, fecal calprotectin, and serum albumin.(39)

SURGICAL TREATMENT OF PATIENTS WITH CROHN'S DISEASE

Indications for surgical treatment in Crohn's disease can be divided into urgent, emergency, and selective indications. In cases of urgent indications, surgery is required immediately to avoid serious complications. An indication for urgent surgery is the lack of significant improvement within 7–10 days of intensive conservative treatment for a severe flare of extensive Crohn's disease. The most common reason for surgical treatment is selective indications, which include:

1. External and internal fistulas
2. Septic complications in the abdominal cavity
3. Extensive inflammatory changes in the anal region
4. Presence or suspicion of malignancy
5. Chronic disability associated with persistent symptoms despite appropriate conservative treatment
6. Delayed physical development and growth retardation in children. (40)

Emergency indications include:

1. Complete obstruction due to small bowel stricture,
2. Massive bleeding,
3. Perforation with diffuse peritonitis.

Bowel obstruction is one of the most common complications of Crohn's disease and can result from chronic inflammation, scarring, or narrowing of the intestinal lumen. Surgery becomes necessary when there is a risk of perforation, in cases of multiple or long strictures that cannot be treated endoscopically, and when pharmacological or endoscopic treatments do not provide sufficient improvement in clinical symptoms. Additionally, surgical intervention is required when there is suspicion of malignancy. The decision for surgical treatment includes resection of the affected segment of the intestine with primary anastomosis. A key principle in the surgical treatment of Crohn's disease is to remove only the section of the intestine affected by the complication, in order to avoid the development of short bowel syndrome (41). Currently, if technically feasible, instead of resection, surgical dilation of small bowel strictures can be performed. Strictureplasty is used in the case of short, fibrous strictures or when other treatment options are contraindicated or too risky. During strictureplasty, the surgeon reshapes or dilates the narrowed segment of the intestine to restore its normal flow of food contents while preserving as much healthy bowel as possible. The aim of this procedure is to improve bowel patency and alleviate symptoms of obstruction, such as abdominal pain, bloating, nausea, and constipation, which may occur due to the presence of strictures (42). The best surgical approach for Crohn's disease of the small intestine is conservative resection. Nowadays, if technically feasible, surgical dilation of small bowel strictures, or strictureplasty, is increasingly performed instead of resection. In the case of large bowel diseases, the type of surgery depends on the location and extent of the pathological changes. When the right or left colon is affected, a hemicolectomy is performed. If the changes are more extensive, colectomy with ileorectal anastomosis is usually necessary, or even proctocolectomy with the creation of a permanent ileostomy. Changes in the anal region pose a significant surgical challenge. Perianal and ischiorectal abscesses should be incised and drained. Low fistulas can heal after being cut and left to granulate. On the other hand, extensive ulcers in the anal region do not heal solely through local surgical interventions. In some patients, the only effective treatment may be the removal of the diseased focus located higher, although in some cases this may require the creation of a permanent ileostomy or colostomy (9).

MAINTENANCE THERAPY OF REMISSION

Currently used therapeutic strategies for maintaining remission in Crohn's disease include the use of 5-aminosalicylates, thiopurines (such as azathioprine and 6-mercaptopurine), methotrexate, and infliximab. To maintain remission in moderate and severe forms of Crohn's disease, the use of 6-mercaptopurine or azathioprine is recommended. Azathioprine and 6-mercaptopurine are also effective in chronic active disease and corticosteroid-dependent Crohn's disease. One of the most significant advancements in recent years in the treatment of Crohn's disease is the introduction of biological therapy. The use of infliximab – an antibody directed against tumor necrosis factor-alpha (TNF-α) – has already shown high efficacy in inducing remission (43–45). Infliximab may be a treatment option for patients who have achieved remission with this medication. Alternative therapies include a combination of infliximab with azathioprine, and methotrexate in remission induced by methotrexate. Corticosteroids are not recommended for long-term maintenance therapy. Maintenance treatment usually lasts for many years and is often continued indefinitely as long as the disease remains in remission and the patient tolerates the therapy well. This is due to the fact that the risk of relapse after discontinuing treatment is very high -reaching up to 70–90% within 1–2 years (46,47). Discontinuation of treatment may be considered when the patient has maintained stable remission for at least two years, has no clinical symptoms, endoscopic examinations show no inflammatory changes, and inflammatory markers are within normal ranges. Additionally, it is important that there have been no previous relapses following the end of therapy. Even under such circumstances, the decision to stop treatment should be made with great caution, in consultation with a gastroenterologist, and with close monitoring of the patient’s condition.

ANTIBIOTIC THERAPY

Antibiotics are used in the treatment of perianal fistulas and in cases of septic complications. The duration of fistula treatment should range from 4 to 8 weeks. The most commonly used medications are metronidazole, ciprofloxacin, and levofloxacin. Metronidazole is effective against anaerobic bacteria and certain parasites, while ciprofloxacin has high efficacy against E. coli and bacteria from the Enterobacteriaceae family (9,48,49). Prolonged use of metronidazole is associated with the risk of peripheral neuropathy (50). Ciprofloxacin combined with metronidazole may be more effective than monotherapy(51).

The table below summarizes the known treatment methods for Crohn's disease. It includes the description of action of each method, its advantages and limitations.

Table 2. Comparison of Treatment Methods for Crohn's Disease

Method of treatment	Description	Advantages	Limitations
Symptomatic treatment	Treatment to relieve symptoms	Rapid symptom relief	Does not target disease mechanism, may mask clinical activity
Anti-inflammatory therapy	Medications that reduce inflammation	Well tolerated	Limited efficacy in more severe case
Immunosuppressive therapy	Drugs that suppress the immune response	Effective in long-term control	Immune deficiency, toxic effects on other organs
Biologic therapy	Moderate to severe disease, refractory cases	High efficacy in inducing and maintaining remission	Risk of immunogenicity and infusion/ allergic reactio
Janus kinase (JAK) inhibitors	Blocking intracellular inflammatory signaling pathways	Targeted anti-inflammatory mechanism of action, reduction in corticosteroid use	Risk of infections, requires further research in the context of long-term use.
Nutritional therapy	Includes elemental diets, exclusive enteral nutrition or parenteral nutrit	Potential to induce remission without medication	Requires specialized dietary supervision
Surgical treatment	Resection of affected bowel segments, drainage of abscesses, management of strictures or fistulas	Immediate relief; resolution of local disease	Not curative, risk of recurrence, surgical complications
Maintenance therapy	Long-term treatment to prevent relapse	Prolongs symptom-free periods	Requires ongoing monitoring
Antibiotic therapy	Treatment of infectious complications	Helpful in the treatment of fistulas, abscesses, and as supportive therapy	Does not eliminate the cause, risk of adverse effects

DISCUSSION

The findings of the literature review indicate that the management of Crohn's disease requires a comprehensive and personalized approach, encompassing pharmacotherapy, nutritional interventions, and surgical treatment. Due to the absence of a curative therapy, the primary goals of treatment are induction and maintenance of remission, symptom alleviation, and prevention of complications and relapses.

Symptomatic treatment continues to play a significant role in the daily care of patients. Analgesics and

antidiarrheal agents may improve quality of life, although they do not affect the underlying pathophysiology of the disease. Nonetheless, these agents should be used cautiously, as they may mask symptoms of complications or lead to adverse effects (1,4,7). Anti-inflammatory therapy demonstrates limited efficacy in Crohn's disease, in contrast to ulcerative colitis. Nevertheless, in selected cases—particularly in mild disease—it may offer some clinical benefit (13,14).

Immunosuppressive agents (e.g., azathioprine, mercaptopurine, methotrexate) constitute the cornerstone of long-term therapy, particularly in maintaining remission and reducing dependency on corticosteroids. These medications exhibit a delayed onset of action, and their effectiveness is often limited by adverse effects and the need for regular toxicity monitoring (12,15,17,18).

Biological therapy has revolutionized the treatment paradigm for Crohn's disease. Anti-TNF agents and interleukin inhibitors enable effective control of inflammation, even in patients who are refractory to conventional therapies (21-23,25-29). However, the risk of adverse events (e.g., infections) necessitates careful patient selection and ongoing clinical monitoring (22,26).

Janus kinase (JAK) inhibitors represent a novel class of immunomodulatory agents that have shown promising results in clinical trials, though further studies are needed to evaluate their long-term safety and efficacy (30-32).

Nutritional therapy, often underestimated, plays a critical role in the management of Crohn's disease. Elemental diets and approaches such as exclusive enteral nutrition (EEN) can be effective in inducing remission without the systemic side effects commonly associated with pharmacological agents (33–37). Nutritional strategies may be particularly relevant in pediatric populations (34, 35) and in perioperative settings (38).

Surgical intervention remains indispensable in the presence of complications such as fistulas, strictures, abscesses, or perforations (41,42). Although not curative, surgery may provide substantial symptomatic relief and improve patient functioning. It is important to note, however, that surgery does not eliminate the risk of recurrence and may result in short bowel syndrome in cases requiring extensive resection (2,40).

Maintenance therapy is a key component of long-term disease management. Depending on the therapeutic response, either immunosuppressants or biologics are employed, with the primary goal of preventing relapses and preserving quality of life (43-47).

Antibiotic therapy plays a role in the management of Crohn's-related complications such as abscesses or perianal fistulas. While not utilized to reduce systemic inflammation, antibiotics can serve as an adjunct to other therapeutic modalities (48-51).

In summary, effective management of Crohn's disease necessitates an individualized treatment strategy that considers disease activity, anatomical location, presence of complications, and patient-specific factors and preferences. Advances in pharmacotherapy continue to improve disease control; however, further research into pathogenic mechanisms and curative therapies remains essential.

However, international guidelines do not always fully agree on therapeutic strategies. For example, the role of mesalazine in Crohn's disease is still debated, and the use of exclusive enteral nutrition is emphasized in pediatric practice but rarely adopted in adults. Differences also exist between ECCO, AGA, and national guidelines regarding the timing and sequencing of biologic therapies.

This review has certain limitations. The literature search was limited to articles published in English between 2010 and 2025, and only PubMed and Google Scholar databases were used. No meta-analysis was performed, and conclusions are therefore based on a narrative synthesis of the available studies.

Future research should focus on long-term outcomes of novel therapies, predictors of treatment response, and strategies to improve access to innovative drugs while ensuring cost-effectiveness.

CONCLUSIONS

Current therapeutic strategies for Crohn's disease primarily focus on symptom control, as the precise etiology of the disease remains unknown. The goals of therapy are to induce and maintain remission, reduce inflammation, and prevent relapses and complications. Therapeutic approaches should be individualized based on the location and extent of inflammatory lesions, severity of symptoms, and response to prior treatment.

Management of Crohn's disease requires not only pharmacotherapy but also comprehensive lifestyle support, particularly regarding appropriate nutritional interventions. In complicated cases, such as the presence of fistulas, abscesses, or intestinal strictures, surgical intervention may be necessary. However, surgical procedures do not constitute a definitive cure, as the disease may recur in other segments of the gastrointestinal tract.

The efficacy of treatment is significantly enhanced by the collaboration of a multidisciplinary team, including gastroenterologists, dietitians, surgeons, and psychologists. Such an approach contributes to a reduction in hospitalizations and improvement in patients' daily functioning. At the same time, ensuring equitable access to advanced therapies, especially biological agents, remains a significant challenge.

Although Crohn's disease continues to represent a substantial therapeutic challenge, advances in the development of novel biological therapies and the implementation of a multidisciplinary care model have markedly improved prognosis and quality of life for affected patients. In conclusion, effective management of Crohn's disease relies on a balanced combination of pharmacotherapy, nutritional intervention, and surgery, with individualized treatment tailored to the clinical characteristics and specific needs of the patient.

DISCLOSURE

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