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Crohn's Disease

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Dedication

This study is wholeheartedly dedicated to our beloved parents, who have been our source of inspiration and gave us strength when we thought of giving up, who continually provide their moral, spiritual, emotional, and financial support. To our brothers. sisters, relatives, mentor, friends, classmates and department who shared their words of advice and encouragement to finish this study.

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(In the name of Allah, most Kindness and most Merciful)

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My special thanks to my family, which support and motivate me in all time of my life especially during period of study, and give me possibility of a university education.

Abstract

Crohn’s disease is an inflammatory bowel disease that causes chronic inflammation of the gastrointestinal tract. If you have been diagnosed with Crohn’s disease or are looking for more information about the condition, we are here to help , Although the goal of manage- ment is to control the inflammation and induce a clinical remission with pharmacologic therapy, most patients will eventually require surgery for their disease. Unfortunately, surgery is not curative and patients still require ongoing therapy even after surgery for disease recurrence. Importantly, given the risks of complications from both Crohn disease and the medications used to treat the disease process, primary care physicians play an important role in optimizing the preventative care management to reduce the risk of complications

Heading terms: crohns disease, crohn’s disease, crohn disease, inflammatory bowel disease, and inflammatory bowel diseases. Presenting symptoms are often variable and may include diarrhea, abdominal pain, weight loss, nausea, vomiting, and in certain cases fevers or chills.

Keyword: crohn’s disease, epidemiology, risk factors, diagnosis

Table of Contents

Introduction

Crohn's disease is an entity which comprises a heterogeneous spectrum of intestinal and extraintestinal manifestations, each one requiring individual approaches for diagnosis and management. Medical management has evolved greatly during the last decade: innovations have included the introduction of new therapeutical agents for prophylaxis and for management of complications. Yet, the introduction of new biologic agents, such as anti-TNF antibody,[1] or immunomodulators, such as azathioprine/6 mercaptopurine,[2] has not significantly changed the longterm prognosis and natural history of patients with Crohn's disease,[3] Patients with Crohn's disease still tend to require surgery as time progresses, and the timing of surgery is critical. This review article will focus on the indications for surgical treatment, on the preoperative evaluation of Crohn's patients, on surgical options specific to different gastrointestinal locations affected by the disease, and on new minimally invasive approaches to this disease. Crohn's disease is a chronic infl ammatory disease of the gastrointestinal tract with symptoms evolving in a relapsing and remitting manner. It is also a progressive disease that leads to bowel damage and disability. All segments of the gastrointestinal tract can be aff ected, the most common being the terminal ileum and colon. Infl ammation is typically segmental, asymmetrical, and transmural. Most patients present with an inflammatory phenotype at diagnosis, but over time complications (strictures, fistulas, or abscesses) will develop in half of patients, often resulting in surgery,[4] Current therapeutic strategies aim for deep and prolonged remission, with the goal of preventing complications and halting the progressive course of disease. Crohn's disease (CD) follows a relapsing and remitting course that typically results in progressive bowel damage,[5]Although CD presents in several clinical patterns such as inflammatory, penetrating, and stricturing with or without perianal involvement, the disease behavior, in general, evolves as a result of cumulative bowel damage (CBD),[6]Advanced body-imaging techniques such as magnetic resonance enterography (MRE) and computed tomography enterography (CTE) allow detailed assessment of structural changes incurred as a result of the ongoing disease process (e.g., mucosal enhancement, bowel wall thickness),[7]Crohn's disease (CD) and ulcerative colitis form the two main entities of inflammatory bowel diseases (IBD), which are marked by chronic idiopathic inflammation of the gastrointestinal (GI) tract. Specifically, CD is characterised by transmural inflammation, causing thickening and narrowing of the GI wall and eventually leading to the disabling development of deep ulcerations, fistulae, strictures and abscesses,[8]Furthermore, chronic deep transmural inflammation causes irreversible structural damage and, as in patients with ulcerative colitis, increases the probability of the onset of colitis-associated neoplasia,[9]Within recent years, fostered by several

breakthroughs in available medical therapies, therapeutic goals in the treatment of CD have evolved dramatically. Inflammatory bowel disease (IBD) is a set of chronic, relapsing/remitting gastrointestinal diseases with long-term effects on patients' quality of life and well-being. The two major types of IBD are ulcerative colitis (UC) and Crohn's disease. Commonly used systemic therapies, including corticosteroids (CS), immunosuppressants (IS), and anti-tumor necrosis factor alpha agents (anti-TNFs), are not effective for many patients and increase the risk for opportunistic infections, non-Hodgkin lymphoma, and other undesired side effects,[10]

Epidemiology

The prevalence of CD has an incidence of 3 to 20 cases per 100,000,[11] Crohn disease is more common in the industrialized world, particularly in North America and Western Europe, though the incidence is rising in Asia and South America,[12-13] There may be a slightly higher predominance of CD in women and it is more common in individuals of Ashkenazi Jewish origin than in non-Jews. The exact pathogenesis of CD is unknown, although there are a number of genetic and environmental factors that have been shown to increase the risk of the disease and lead to the aberrant gut immune response characteristic of the disease,[12] In epidemiologic studies, the rates of disease incidence and prevalence have their interpretations. Generally, the high incidence rate is in association with the presence of predisposing factors while the prevalence of a disease is correlated with geographical variations,[14-15]

Risk factor

Risk factors for the development of CD appear to be related to changes in the gut microbiome or disruptions to the intestinal mucosa and genetics.

Environmental Risk Factors

Crohn disease appears to be triggered by alterations in the gut microbiome or disruption in the intestinal mucosa,[16] Patients with IBD oftenhave a dysbiosis that results in a reduction in the diversity of the gut microbiome,[17] Although the literature surrounding the specifics is evolving, the exact mechanism by which alterations in the gut microbiome predispose to CD is still not fully understood. Gastrointestinal infections, nonsteroidal anti-inflammatory drugs, and antibiotics have all been implicated in the development of IBD,[12,16,18,19] However, none of these associations has been substantiated with large epidemiological studies. In one study, patients with enteric infections from salmonella or campylobacter had an increased risk of developing IBD within the first year of their illness,[18] Also, sustained use of nonsteroidal antiinflammatory drugs, especially in women, may increase the risk of IBD,[20] Antibiotic exposure early in life has also been associated with an increased risk of developing CD,[21] In women, both hormone replacement therapy and oral contraceptives may increase the risk of IBD,[19,22,23] The best-studied environmental risk factor, cigarette smoking, doubles the risk of developing CD,[24] This risk is increased in both current and former smokers,[25] Studies have also suggested that appendectomy may increase the risk of CD but this may be due to inaccurate classification of appendicitis which in truth was actually CD,[26] The role of diet in the development of CD also remains unclear. Some studies have suggested that diets high in sugar, omega-6 fatty acids, polyunsaturated fatty acids, total fat, oil, and meat increase the risk of CD whereas a diet high in fiber and fruit decreased the risk of CD,[27-28] However, further studies are still needed to clarify the role of diet and the risk of developing CD.

Genetic Risk Factors

Although family history does portend an increased risk, only 10% to 25% of patients with IBD have a first-degree relative with the disease,[12] In twin studies, concordance rates for CD in monozygotic twins range from 20% to 50% compared with 10% in dizygotic twins,[29,30] Crohn disease is more common in patients of Ashkenazi Jewish origin than in non-Jews and is less frequently seen in African Americans or Hispanics,[12] Although genetic risk factors are still being elucidated, there are more than 200 genes that have been associated with the development of IBD. The first gene discovered was the NOD2 locus on chromosome 16,[31,32] Homozygotic changes at NOD2 have a 20 to 40 times higher risk of developing CD, while being heterozygous increases the risk by 2 to 4 times,[31,32] A number of other genetic foci involving multiple different pathways (eg, autophagy, adaptive immunity, and epithelial function) have also been associated with CD.[33,34]

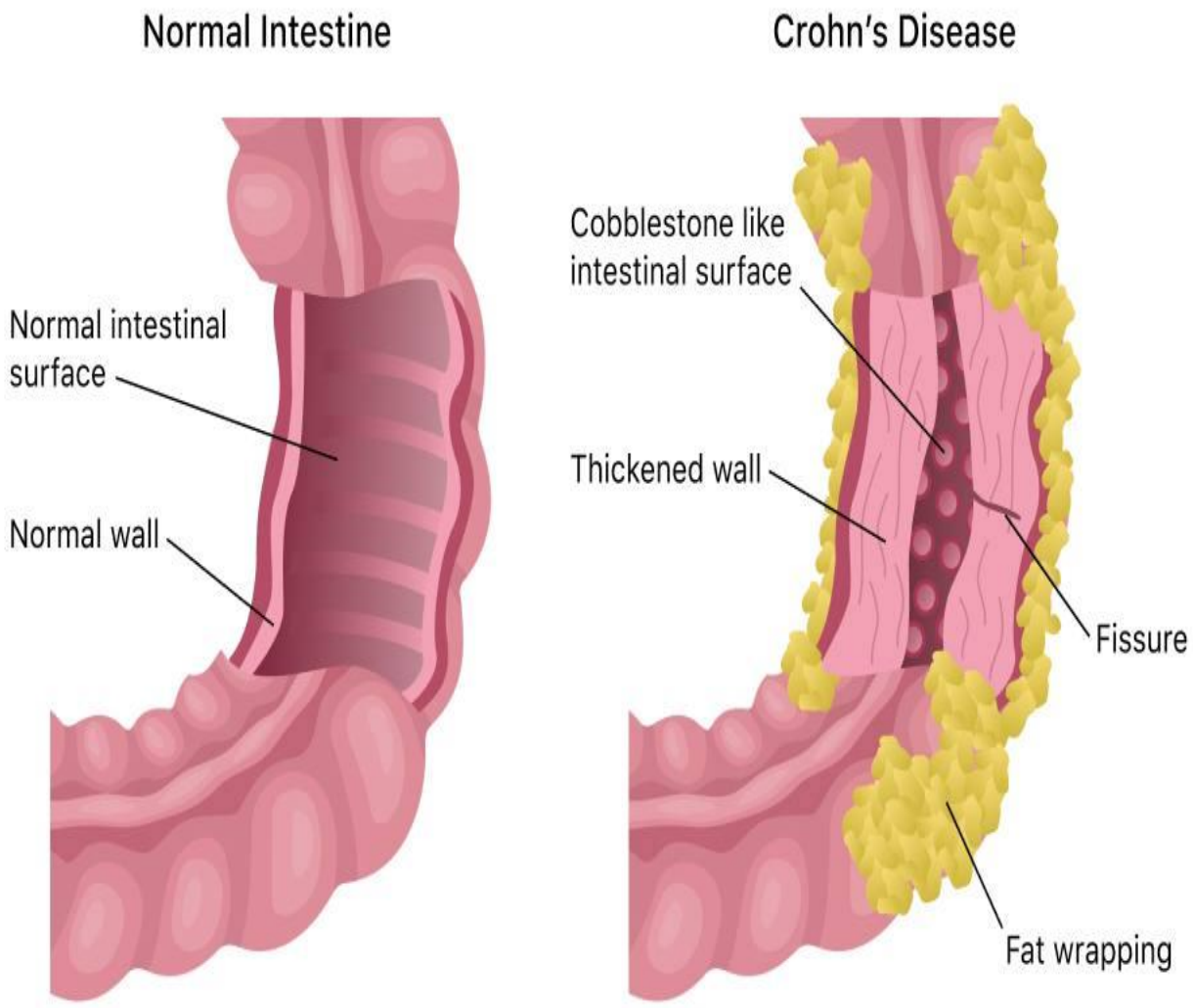

Figure.1 Diferent between Normal Intestine And Crohn's Disease[55]

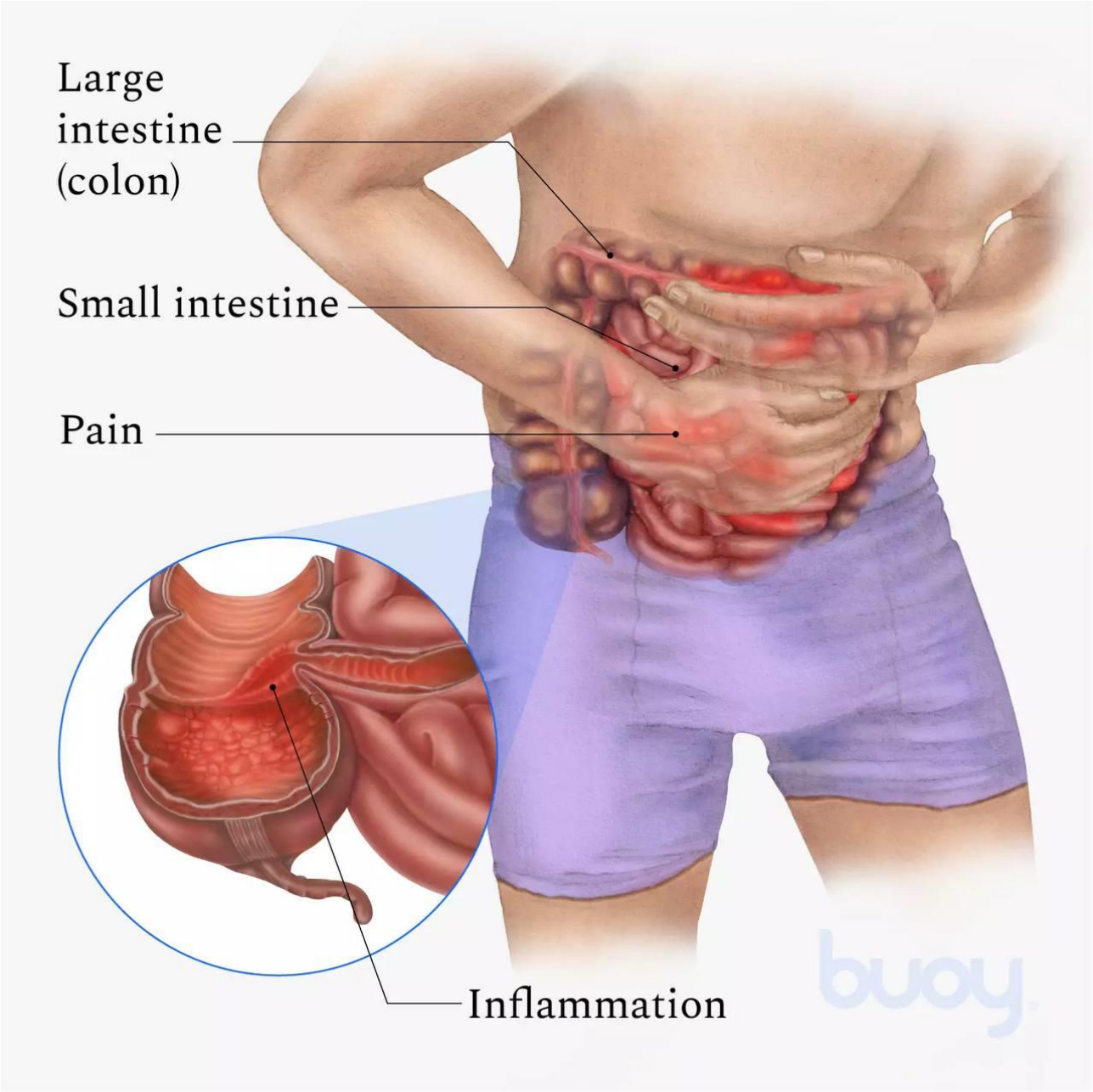

Figure.3 Inflammation of intestine with infection of Crohn's Disease[56]

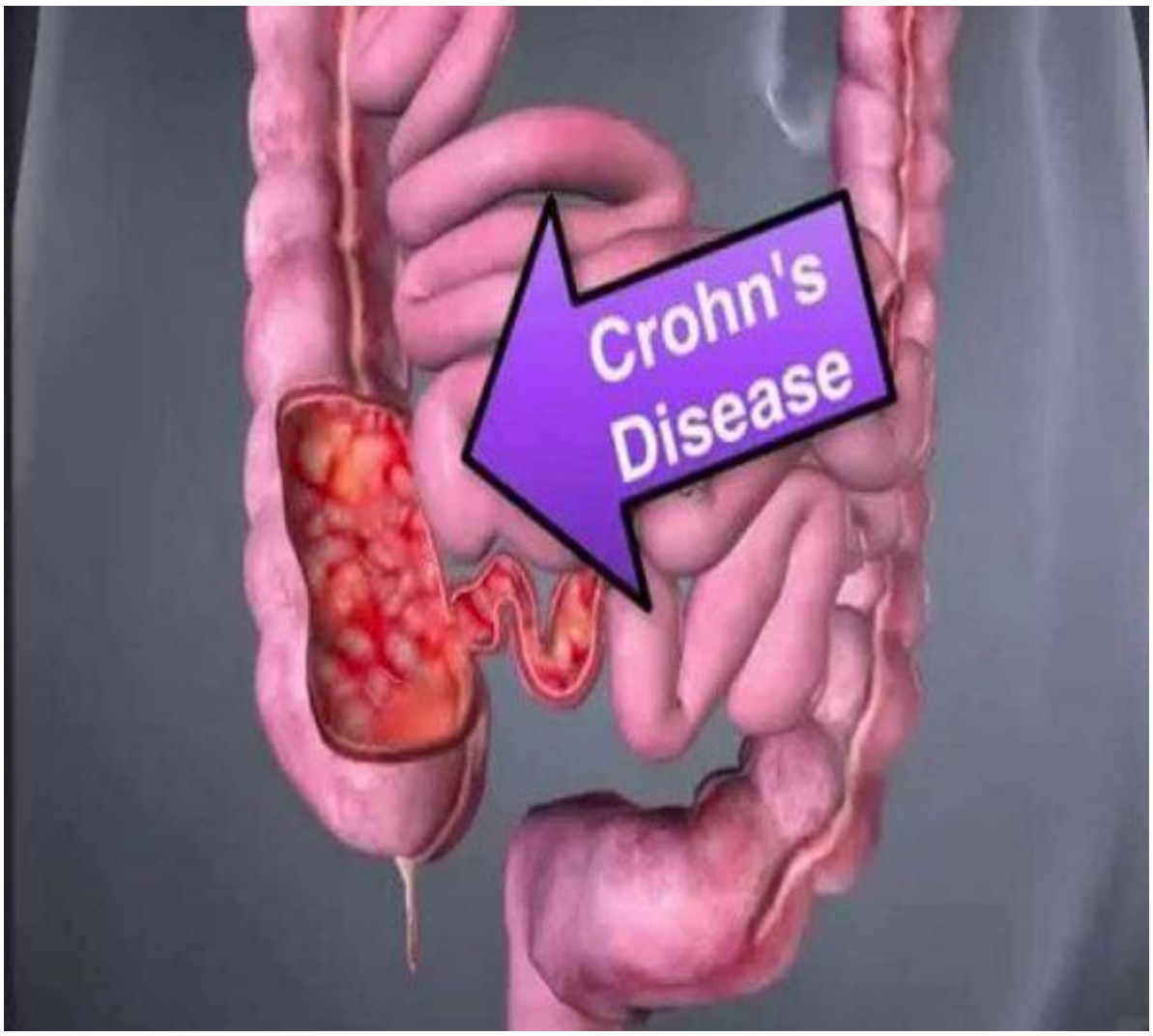

Figure.4 Intestine with infection Crohn's Disease[57]

Signs And Symptoms

Presenting symptoms are quite variable but may correlate with disease phenotype and location to some extent. Some patients may have symptoms for years before the diagnosis of CD,[35] Patients with inflammatory disease often present with abdominal pain and diarrhea, though they may develop more systemic symptoms including weight loss, low-grade fevers, and fatigue. Often patients with stricturing disease develop bowel obstructions (most commonly, small bowel). Bowel obstructions are characterized by lack of flatus and bowel movements, hyperactive bowel sounds, and nausea and vomiting. Patients with penetrating CD can develop fistula or abscesses. When an abscess is present, in addition to abdominal pain, patients can have systemic symptoms such as fever and chills. Patients may also present with signs of acute peritonitis. Penetrating disease may also result in symptoms related to the fistula location: diarrhea in cases of enteroenteric fistula, urinary tract infection from enterovesicular or enterouretheral fistula, or passage of stool from the vagina in cases of enterovaginal fistula, or drainage from the skin in enterocutaneous fistula. In cases of severe CD colitis, bloody stool may be present but classicallyconditions limit spinal flexion and can be very debilitating. Presenting symptoms are morning stiffness and pain, which are relieved with exercise,[36,37]

Diagnosis

The diagnosis of CD is a clinical one and can be quite difficult given that the presenting symptoms can be insidious and nonspecific.5 Red flag symptoms that require further evaluation include weight loss, bloody diarrhea, iron deficiency, and night-time awakenings. Similarly, significant family history of IBD, unexplained elevations in the c-reactive protein level, sedimentation rates, or other acutephase reactants (eg, ferritin and platelets), or low B12 should prompt further investigation for possible CD. The diagnosis of CD is made on the basis of symptoms and endoscopic and radiologic findings,[38,39] Pathology can be confirmatory. In cases of colonic or ileal CD, endoscopic to identify the radiopaque markers on the patency capsule to determine whether it passed through the small bowel. If this passed through, then the regular capsule endoscopy can likely be performed without significant risk of being retained,[40] Imaging can also be used to diagnose CD. Both computed tomography enterography (CTE) and magnetic resonance enterography (MRE) allow for visualization of the bowel wall, mucosa, and extraluminal complications. The CTE and MRE have supplanted small-bowel barium studies as the criterion standard for the diagnosis and assessment of CD,[41] Compared with CTE, MRE is more expensive but importantly, it avoids radiation exposure and does not use iodinated contrast. Although a number of studies have evaluated the use of serologic markers in diagnosing CD,[42,43] no marker or panel of markers is sensitive or specific enough to establish or rule out the diagnosis of CD.

Treatment

The treatment of CD depends on disease severity, location of disease, and subtype of disease (ie, inflammatory, stricturing, or penetrating). We now also attempt to determine who is at risk for aggressive CD and who may require earlier and more aggressive therapies. Risk factors for aggressive disease activity include age of diagnosis less than 30 years, extensive anatomic involvement, perianal disease, deep ulcers, prior surgery, and stricturing and/or penetrating disease,[44] One of the biggest challenges associated with CD is that after 20 years of disease activity 80% of patients will require a surgery and approximately 30% will require surgery within 5 years of diagnosis,[45,46] Although the goal of medical therapy is to maintain remission without the need for surgery, once stricturing and/or fistulizing complications occur, surgery may be required. Unfortunately, because surgery is not curative for CD, many patients will require multiple surgeries over their lifetime,[46] There are a number of different drugs used to treat CD. Mesalamine has been evaluated in a number of studies but has not been shown to effectively induce or maintain remission in CD. The perceived benefit of mesalamine is likely related to its safety profile,[45] Antibiotic are also used in CD, but the evidence supporting their use is also limited ,[47] The main role of antibiotics is to treat the suppurative or perianal complications of CD,[48] The immunosuppressants azathioprine (AZA)/mecaptopurine (MP) and MTX have been used for many years to treat CD but because of slow onset of action they are typically used to maintain remission. However, more recent studies question the overall efficacy of AZA/MP as monotherapy and their use in early CD,[49,50] More recently, these drugs are used in combination with anti-TNF drugs to decrease their immunogenicity and increase anti-TNF drug concentrations. The mainstay of therapy for CD has been anti-TNF agents. More recently approved drugs are monoclonal antibodies directed against certain integrins (a4 or a4b7) or interleukins (IL-12/IL-23). The first antiintegrin approved for CD was natalizumab, but this is associated with progressive multifocal leukoencephalopathy (PML), a fatal brain infection,[51,52] Vedolizumab is a gutselective antiintegrin that has not been associated with PML and is used mostly to maintain remission in moderate to severe CD with only modest effectiveness at induction of remission,[53] In contrast, the most recently approved agent, ustekinumab, an IL-12/IL-23 inhibitor, has been shown to be as effective as anti-TNF therapy at inducing and maintaining remission in moderate to severe CD,[54].

Conclusion

Crohn disease is a chronic IBD that can affect any portion of the gastrointestinal tract. It is typically medically managed, but a significant percentage of patients will require surgery. The goals of care are to induce and maintain a steroid-free remission, decrease the risk of complications and surgery, and also improve the overall quality of life. To this end, patients with CD are best comanaged with primary care physicians to help optimize their primary prevention and reduce their risk of complications. Being aware of the subtypes and natural history of CD as well as the potential complications of the disease and the medication used to treat the disease is critical to optimizing the health care of patients with CD.

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