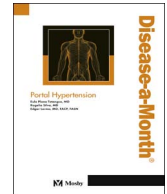


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## A comprehensive review and update on Crohn's disease

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## ABSTRACT

The term inflammatory bowel disease (IBD) refers principally to two major categories of chronic relapsing inflammatory intestinal disorders: Crohn's disease (CD) and ulcerative colitis (UC). In the United States, it is currently estimated that about 1.5 million people suffer from IBD, causing considerable suffering, mortality and economic loss every year. Yet the cause of IBD is unknown, and until we understand more, prevention or cure will not be possible. There is a lot of variation in the incidence and prevalence of CD based on geographic region, environment, immigrant population, and ethnic groups. The annual incidence of CD in North America is reported to be 3.1–20.2 per 100,000 with a prevalence of 201 per 100,000 population. Based on the epidemiological, genetic and immunological data, CD is considered to be a heterogeneous disorder with multifactorial etiology in which genetics and environment interact to manifest the disease. Several genes have been studied so far with respect to CD, but thus far the strong and replicated associations have been identified with NOD2, IL23R and ATG16L1 genes. The risk factors implicated with CD include smoking, low fiber- high carbohydrate diet, altered microbiome and medications such as non-steroidal anti-inflammatory drugs.

CD is typically characterized by transmural inflammation of the intestine and could affect any part of the gastrointestinal tract from mouth to perianal area. In terms of distribution of the disease 25% of the patients have colitis only, 25% is ileitis only and 50% have ileocolitis. The Montreal classification is based on the age at diagnosis (< 16, 17–40, > 40), disease location (Ileal, colonic, Ileocolonic) and the disease behavior (nonstricturing/nonpenetrating, stricturing, penetrating). The key features for diagnosing CD comprises a combination of radiographic, endoscopic and pathological findings demonstrating focal, asymmetric, transmural or granulomatous features. Abdominal Computed tomography (CT) enterography is the most preferred first-line radiologic study used in the assessment of small bowel CD. The diagnostic accuracy of magnetic resonance enterography/enteroclysis is similar to that of CT scans and also prevents exposure to ionizing radiation. Endoscopic scores are considered to be the gold standard tool to measure the activity of CD and they are used more commonly in the clinical trials to measure the efficacy of various drugs on inducing and maintaining mucosal healing. The most common scoring systems used to measure clinical disease activity include Crohn's Disease Activity Index (CDAI), HBI- Harvey-Bradshaw index (HBI), short inflammatory bowel disease questionnaire (SIBDQ) and Lehmann score.

Management of Crohn's disease has been seen as an evolving challenge owing to its widely

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heterogeneous manifestations, overlapping characteristics with other inflammatory disorders, often elusive extraintestinal manifestations and uncertain etiology. Therapeutic interventions are tailored to address symptomatic response and subsequent tolerance of the intervention. Chronology of treatment should favor treatment dose acute disease or “induction therapy”, followed by maintenance of adequate response or remission, i.e. “maintenance therapy”. The medications which are highly effective in inducing remission include steroids and Tumor Necrosis Factor (TNF) inhibitors. Medications used to maintain remission include 5-aminosalicylic acid products, immunomodulators (Azathioprine, 6-mercaptopurine, methotrexate) and TNF inhibitors (infliximab, adalimumab, certolizumab and golimumab). Surgical interventions like bowel resection, stricturoplasty or drainage of abscess is required in up to two thirds of CD patients during their lifetime. The most common indications for surgical resection are medically refractory disease, perforation, persisting or recurrent obstruction, abscess not amenable to percutaneous drainage, intractable hemorrhage, dysplasia or cancer. Endoscopic recurrence in postoperative CD patients, as defined by Rutgeers score i2-i4 occur in 30–90% of the patients at the neoterminal ileum within 12 months of surgery and almost universally by 5 years. Treating CD requires a comprehensive care team including the patient, primary care provider, and gastroenterologist. In summary CD is a chronic inflammatory condition with a remitting and relapsing course primarily affecting relatively younger population with significant socioeconomic effects.

## Introduction

The term inflammatory bowel disease (IBD) refers principally to two major categories of chronic relapsing inflammatory intestinal disorders: Crohn disease (CD) and ulcerative colitis (UC). A subset of patients have indeterminate colitis, characterized by clinical features and test results that do not allow a definitive classification. In the United States, it is currently estimated that about 1.5 million people suffer from IBD, causing considerable suffering, mortality and economic loss every year.<sup>1</sup> Yet the cause of IBD is unknown, and until we understand more, prevention or cure will not be possible. This review specifically focusses on CD discussing the epidemiology, risk factors, clinical features, natural history of the disease, diagnosis, management and other aspects of CD.

## Epidemiology and risk factors

Until the second half of the 20th century, IBD was considered to be a rare disease in North America and Europe.<sup>2</sup> Fig. 1 depicts an historical perspective of CD from its inception to the discovery of the treatment. Industrialized countries in Northern Europe and North America experienced a steady rise in the incidence of CD after World War II.<sup>2,3</sup> There is a lot of variation in the incidence and prevalence of CD based on geographic region, environment, immigrant population, and ethnic groups. Although UC was considered to be more prevalent in the past, with increasing incidence of CD in the past few decades, both UC and CD may be equally prevalent in North America.<sup>4</sup> The annual incidence of CD in North America is reported to be 3.1–20.2 per 100,000 with a prevalence of 201 per 100,000 population.<sup>1</sup> The incidence of CD has been increasing during the last century, however the rate of increase have stabilized now.<sup>5,6</sup>

The incidence of CD is higher in Ashkenazi Jews, urban population and in northern latitudes.<sup>14</sup> The peak incidence of CD is

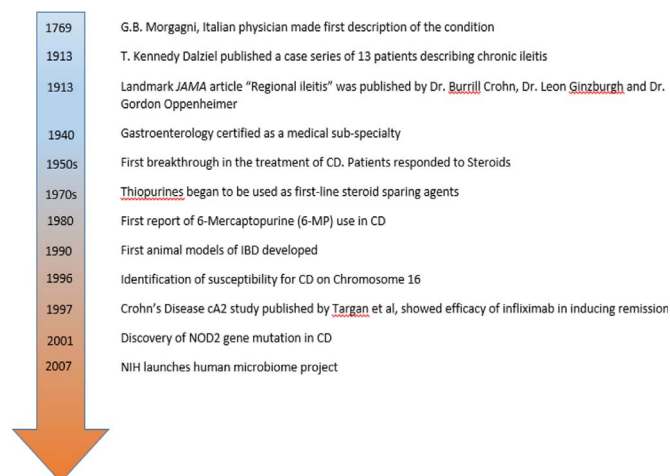


Fig. 1. Historical perspectives.<sup>3,7–13</sup>

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