

Aetiology

Aetiology

The aetiology of CD remains incompletely understood but is thought to involve a complex interplay of genetic and environmental factors. Although CD shares some features with chronic infections, particularly tuberculosis, no causative organism has ever been demonstrated. There is an intriguing similarity to Johne's disease of cattle, a chronic inflammatory enteropathy resulting from infection with *Mycobacterium paratuberculosis* suggesting that CD may have a related aetiology. Some studies have identified mycobacterial DNA more frequently in tissue from patients with CD than in tissue from controls, but trials have not demonstrated any therapeutic benefit of treating CD with antituberculous drugs. A wide variety of foods and a highly refined diet have been implicated in CD; however, no conclusive link has been proven. There is considerable recent interest in food additives, particularly preservatives that may support a proinflammatory dysbiosis in the gut microbiome. An association with high levels of sanitation in childhood has also been implicated. Smoking increases the relative risk of CD threefold and is an exacerbating factor after diagnosis, contrary to the protective effect seen in UC. Smoking cessation has a beneficial effect on disease activity comparable to that of medical therapies and is therefore an essential component in the effective management of CD. Genetic factors are important in CD. Approximately 10% of patients have a first-degree relative with the disease, and concordance approaches 50% in monozygotic twins. Inheritance is thought to involve multiple genes with low penetrance. Variants of NOD2/CARD15, a gene involved in intracellular recognition of bacteria, have been shown to have a strong association with CD. Recent genome-wide association studies have identified activation of over 200 genes in IBD, some of which are associated with CD and others with UC. Most patients have no identifiable germline mutational signature, and epigenetic mutations are more likely to be involved. Both UC and CD are associated with alterations in the gut microbiome, with generally decreased microbial diversity. New techniques including next-generation 16S ribosomal RNA sequencing allow detailed analysis of individual microbial communities within the gut with sequential studies informing changes that might be associated with disease activity. Despite over a decade of intense study, no definitive signature of either CD or UC has been established, other than reduced microbial diversity, particularly in CD. Heinrich Albert Johne, 1839–1910, pathologist, Dresden, Germany. In both CD and UC increased gut mucosal permeability appears to develop at a relatively early stage and may lead to increased passage of luminal antigens that induce a cell-mediated inflammatory response. Proinflammatory cytokines, such as interleukin-2 and tumour necrosis factor, are then released. It has been suggested that CD is associated with a defect in suppressor T cells. It is unclear whether the proposed increase in intestinal permeability is a cause or consequence of the disease process. Animal studies have suggested that the increase in gut permeability develops because of changes in bacterial recognition proteins and an increase in inflammatory gene activation before macroscopic evidence of inflammation develops. Studies of healthy and apparently unaffected first-degree relatives of patients with CD suggest that gut permeability is increased, which in turn suggests that a genetically determined increase in gut permeability, perhaps combined with an abnormal immune-mediated response to colonisation of the gut with enteric microflora, may initiate the disease.

Revision #1

Created 2025-12-31 15:27:32 UTC by Omar Ayman

Updated 2025-12-31 15:27:32 UTC by Omar Ayman