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Crohn's Disease

Crohn's disease (also known as **Crohn-Leśniowski Disease**, or **morbus Leśniowski-Crohn**, **granulomatous colitis** and **regional enteritis**) is an inflammatory disease of the intestines that may affect any part of the gastrointestinal tract from mouth to anus, causing a wide variety of symptoms. It primarily causes abdominal pain, diarrhea (which may be bloody), vomiting, or weight loss, [1][2][3] but may also cause complications outside of the gastrointestinal tract such as skin rashes, arthritis, inflammation of the eye, tiredness, and lack of concentration. [1]

Crohn's disease is an autoimmune disease, in which the body's immune system attacks the gastrointestinal tract, causing inflammation; it is classified as a type of inflammatory bowel disease. There has been evidence of a genetic link to Crohn's disease, putting individuals with siblings afflicted with the disease at higher risk. [4] It is understood to have a large environmental component as evidenced by the higher number of cases in western industrialized nations. Males and females are equally affected. Smokers are three times more likely to develop Crohn's disease. [5] Crohn's disease affects between 400,000 and 600,000 people in North America. [6] Prevalence estimates for Northern Europe have ranged from 27–48 per 100,000. [7] Crohn's disease tends to present initially in the teens and twenties, with another peak incidence in the fifties to seventies, although the disease can occur at any age. [1][8]

There is no known pharmaceutical or surgical cure for Crohn's disease. [9] Treatment options are restricted to controlling symptoms, maintaining remission and preventing relapse.

The disease was named for American gastroenterologist Burrill Bernard Crohn, who in 1932, along with two colleagues, described a series of patients with inflammation of the terminal ileum, the area most commonly affected by the illness. [10] For this reason, the disease has also been called **regional ileitis** [10] or regional enteritis. The condition, however, has been independently identified by others in the literature prior, most notably in 1904 by Polish surgeon Antoni Leśniowski for whom the condition is additionally named (Leśniowski-Crohn's disease) in the Polish literature.

Classification

Crohn's disease is one type of inflammatory bowel disease (IBD). It affects the gastrointestinal tract and can be categorized by the area of the gastrointestinal tract which it affects. *Ileocolic Crohn's disease*, which affects both the ileum (the last part of the small intestine that connects to the large intestine) and the large intestine, accounts for fifty percent of cases. *Crohn's ileitis*, affecting the ileum only, accounts for thirty percent of cases, and *Crohn's colitis*, affecting the large intestine, accounts for the remaining twenty percent of cases and may be particularly difficult to distinguish from ulcerative colitis. Gastroduodenal Crohn's disease causes inflammation in the stomach and first part of the small intestine, called the duodenum. Jejunoileitis causes spotty patches of inflammation in the top half of the small intestine, called the jejunum (MedlinePlus 2010). The disease can attack any part of the digestive tract, from mouth to anus. However, individuals affected by the disease rarely fall outside these three classifications, being affected in other parts of the gastrointestinal tract such as the stomach and esophagus. [1]

Crohn's disease may also be categorized by the behavior of disease as it progresses. This was formalized in the Vienna classification of Crohn's disease.[11] There are three categories of disease presentation in Crohn's disease: stricturing, penetrating, and inflammatory. *Stricturing disease* causes narrowing of the bowel which may lead to bowel obstruction or changes in the caliber of the feces. *Penetrating disease* creates abnormal passageways (fistulae) between the bowel and other structures such as the skin. *Inflammatory disease* (or non-stricturing, non-penetrating disease) causes inflammation without causing strictures or fistulae.[11][12]

Symptoms

Many people with Crohn's disease have symptoms for years prior to the diagnosis.[13] The usual onset is between 15 and 30 years of age but can occur at any age.[14] Because of the 'patchy' nature of the gastrointestinal disease and the depth of tissue involvement, initial symptoms can be more vague than with ulcerative colitis. People with Crohn's disease will go through periods of flare-ups and remission.

Gastrointestinal symptoms

Abdominal pain may be the initial symptom of Crohn's disease. It is often accompanied by diarrhea, especially in those who have had surgery. The diarrhea may or may not be bloody. People who have had surgery or multiple surgeries often end up with short bowel syndrome of the gastrointestinal tract. The nature of the diarrhea in Crohn's disease depends on the part of the small intestine or colon that is involved. Ileitis typically results in large-volume watery feces. Colitis may result in a smaller volume of feces of higher frequency. Fecal consistency may range from solid to watery. In severe cases, an individual may have more than 20 bowel movements per day and may need to awaken at night to defecate.[1][8][15][16] Visible bleeding in the feces is less common in Crohn's disease than in ulcerative colitis, but may be seen in the setting of Crohn's colitis.[1] Bloody bowel movements are typically intermittent, and may be bright or dark red in colour. In the setting of severe Crohn's colitis, bleeding may be copious.[8] Flatulence and bloating may also add to the intestinal discomfort.[8]

Symptoms caused by intestinal stenosis are also common in Crohn's disease. Abdominal pain is often most severe in areas of the bowel with stenoses. In the setting of severe stenosis, vomiting and nausea may indicate the beginnings of small bowel obstruction.[8] Although the association is greater in the context of ulcerative colitis, Crohn's disease may also be associated with primary sclerosing cholangitis, a type of inflammation of the bile ducts.[17]

Perianal discomfort may also be prominent in Crohn's disease. Itchiness or pain around the anus may be suggestive of inflammation, fistulization or abscess around the anal area[1] or anal fissure. Perianal skin tags are also common in Crohn's disease.[18] Fecal incontinence may accompany peri-anal Crohn's disease. At the opposite end of the gastrointestinal tract, the mouth may be affected by non-healing sores (aphthous ulcers). Rarely, the esophagus, and stomach may be involved in Crohn's disease. These can cause symptoms including difficulty swallowing (dysphagia), upper abdominal pain, and vomiting.[19]

Systemic symptoms

Crohn's disease, like many other chronic, inflammatory diseases, can cause a variety of systemic symptoms.[1]

Among children, growth failure is common. Many children are first diagnosed with Crohn's disease based on inability to maintain growth.[20] As Crohn's disease may manifest at the time of the growth spurt in puberty, up to 30% of children with Crohn's disease may have retardation of growth.[21] Fever may also be present, though fevers greater than 38.5 ˚C (101.3 ˚F) are uncommon unless there is a complication such as an abscess.[1] Among older individuals, Crohn's disease may manifest as weight loss. This is usually related to decreased food intake, since individuals with intestinal symptoms from Crohn's disease often feel better when they do not eat and might lose their appetite.[20]

People with extensive small intestine disease may also have malabsorption of carbohydrates or lipids, which can further exacerbate weight loss.[22]

Extraintestinal symptoms

In addition to systemic and gastrointestinal involvement, Crohn's disease can affect many other organ systems.[23]

Inflammation of the interior portion of the eye, known as uveitis, can cause eye pain, especially when exposed to light (photophobia). Inflammation may also involve the white part of the eye (sclera), a condition called episcleritis. Both episcleritis and uveitis can lead to loss of vision if untreated.

Crohn's disease is associated with a type of rheumatologic disease known as seronegative spondyloarthropathy. This group of diseases is characterized by inflammation of one or more joints (arthritis) or muscle insertions (enthesitis). The arthritis can affect larger joints such as the knee or shoulder or may exclusively involve the small joints of the hand and feet. The arthritis may also involve the spine, leading to ankylosing spondylitis if the entire spine is involved or simply sacroiliitis if only the lower spine is involved. The symptoms of arthritis include painful, warm, swollen, stiff joints and loss of joint mobility or function.

Crohn's disease may also involve the skin, blood, and endocrine system. One type of skin manifestation, erythema nodosum, presents as red nodules usually appearing on the shins. Erythema nodosum is due to inflammation of the underlying subcutaneous tissue and is characterized by septal panniculitis. Another skin lesion, pyoderma gangrenosum, is typically a painful ulcerating nodule. Crohn's disease also increases the risk of blood clots; painful swelling of the lower legs can be a sign of deep venous thrombosis, while difficulty breathing may be a result of pulmonary embolism. Autoimmune hemolytic anemia, a condition in which the immune system attacks the red blood cells, is also more common in Crohn's disease and may cause fatigue, pallor, and other symptoms common in anemia. Clubbing, a deformity of the ends of the fingers, may also be a result of Crohn's disease. Finally, Crohn's disease may cause osteoporosis, or thinning of the bones. Individuals with osteoporosis are at increased risk of bone fractures.[7]

Crohn's disease can also cause neurological complications (reportedly in up to 15% of patients).[24] The most common of these are seizures, stroke, myopathy, peripheral neuropathy, headache and depression.[24]

Crohn's patients often also have issues with small bowel bacterial overgrowth syndrome, which has similar symptoms.[25]

Complications

Crohn's disease can lead to several mechanical complications within the intestines, including obstruction, fistulae, and abscesses. Obstruction typically occurs from strictures or adhesions which narrow the lumen, blocking the passage of the intestinal contents. Fistulae can develop between two loops of bowel, between the bowel and bladder, between the bowel and vagina, and between the bowel and skin. Abscesses are walled off collections of infection, which can occur in the abdomen or in the perianal area in Crohn's disease sufferers.

Crohn's disease also increases the risk of cancer in the area of inflammation. For example, individuals with Crohn's disease involving the small bowel are at higher risk for small intestinal cancer. Similarly, people with Crohn's colitis have a relative risk of 5.6 for developing colon cancer.[26] Screening for colon cancer with colonoscopy is recommended for anyone who has had Crohn's colitis for at least eight years.[27] Some studies suggest that there is a role for chemoprotection in the prevention of colorectal cancer in Crohn's involving the colon; two agents have been suggested, folate and mesalamine preparations.[28]

Individuals with Crohn's disease are at risk of malnutrition for many reasons, including decreased food intake and malabsorption. The risk increases following resection of the small bowel. Such individuals may require oral supplements to increase their caloric intake, or in severe cases, total parenteral nutrition (TPN). Most people with moderate or severe Crohn's disease are referred to a dietitian for assistance in nutrition.[29]

Crohn's disease can cause significant complications including bowel obstruction, abscesses, free perforation and hemorrhage.[30]

Crohn's disease can be problematic during pregnancy, and some medications can cause adverse outcomes for the fetus or mother. Consultation with an obstetrician and gastroenterologist about Crohn's disease and all medications allows preventative measures to be taken. In some cases, remission can occur during pregnancy. Certain medications can also impact sperm count or may otherwise adversely affect a man's ability to conceive.[31]

Cause

Although the exact cause of Crohn's disease is still unknown, a combination of environmental factors and genetic predisposition seems to cause the disease.[32] The genetic risk factors have now more or less been comprehensively elucidated, making Crohn's disease the first genetically complex disease of which the genetic background has been resolved.[33] The relative risks of contracting the disease when one has a mutation in one of the risk genes, however, are actually very low (approximately 1:200). Broadly speaking, the genetic data indicate that innate immune systems in patients with Crohn's disease malfunction, and direct assessment of patient immunity confirms this notion.[34] This had led to the notion that Crohn's disease should be viewed as innate immune deficiency, chronic inflammation being caused by adaptive immunity trying to compensate for the reduced function of the innate immune system.[35]

Genetics

Some research has indicated that Crohn's disease may have a genetic link.[36] The disease runs in families and those with a sibling with the disease are 30 times more likely to develop it than the general population.

Mutations in the CARD15 gene (also known as the NOD2 gene) are associated with Crohn's disease [37] and with susceptibility to certain phenotypes of disease location and activity. [38] In earlier studies, only two genes were linked to Crohn's, but scientists now believe there are over thirty genes that show genetics play a role in the disease, either directly through causation or indirectly as with a mediator variable. Anomalies in the XBP1 gene have recently been identified as a factor, pointing towards a role for the unfolded protein response pathway of the endoplasmatic reticulum in inflammatory bowel diseases. [39][40]

Environmental factors

Diet is believed to be linked to its higher prevalence in industrialized parts of the world. Smoking has been shown to increase the risk of the return of active disease, or "flares". [5] The introduction of hormonal contraception in the United States in the 1960s is linked with a dramatic increase in the incidence rate of Crohn's disease. Although a causal linkage has not been effectively shown, there remain fears that these drugs work on the digestive system in ways similar to smoking. [41]

Immune system

Abnormalities in the immune system have often been invoked as being causes of Crohn's disease. Crohn's disease is thought to be an autoimmune disease, with inflammation stimulated by an over-active T_h1 cytokine response. [42] However, more recent evidence has shown that T_h17 is of greater importance in the disease. [43] The most recent gene to be implicated in Crohn's disease is ATG16L1, which may induce autophagy and hinder the body's ability to attack invasive bacteria. [44]

Contrary to the prevailing view that Crohn's disease is a primary T cell autoimmune disorder, there is an increasing body of evidence in favour of the hypothesis that Crohn's disease results from an impaired innate immunity. [45] The immunodeficiency, which has been shown to be due to (at least in part) impaired cytokine secretion by macrophages, is thought to lead to a sustained microbial-induced inflammatory response, particularly in the colon where the bacterial load is especially high. [34][46]

Microbes

A variety of pathogenic bacteria were initially suspected of being causative agents of Crohn's disease. [47] However, most health care professionals now believe that a variety of microorganisms are taking advantage of their host's weakened mucosal layer and inability to clear bacteria from the intestinal walls, both symptoms of the disease. [48]

Some studies have suggested that *Mycobacterium avium subspecies paratuberculosis* plays a role in Crohn's disease, in part because it causes a very similar disease, Johne's disease, in cattle. [49] The mannose bearing antigens (mannins) from yeast may also elicit an antibody response. [50] Other studies have linked specific strains of enteroadherent *E. coli* to the disease. [51] Still, this relationship between specific types of bacteria and Crohn's disease remains unclear. [52][53]

Some studies have suggested that some symptoms of Crohn's disease, ulcerative colitis and irritable bowel syndrome have the same underlying cause. Biopsy samples taken from the colons of all three patient groups were found to produce elevated levels of a serine protease.[54] Experimental introduction of the serine protease into mice has been found to produce widespread pain associated with irritable bowel syndrome as well as colitis, which is associated with all three diseases.[55] The authors of that study were unable to identify the source of the protease, but a separate review noted that regional and temporal variations in those illnesses follow those associated with infection with a poorly understood protozoan, Blastocystis.[56]

A study in 2003 put forth the "cold-chain" hypothesis, that psychrotrophic bacteria such as Yersinia spp and Listeria spp contribute to the disease. A statistical correlation was found between the advent of the use of refrigeration in the United States and various parts of Europe and the rise of the disease.[57][58] Later studies have provided support for this hypothesis.[59]

Studies done at the University of Liverpool have offered ideas that would explain the apparent connection between Crohn's disease, Mycobacterium, other pathogenic bacteria, and genetic markers.[60][61] In many individuals genetic factors predispose individuals to Mycobacterium avium subsp. paratuberculosis infection. This bacteria then produce mannins which protect both itself and various bacteria from phagocytosis, which causes a variety of secondary infections.[62] Other mycobacterial diseases, such as leprosy and Tuberculosis could be considered similar in that they have strong genetic components, but are not genetic per se.

Pathophysiology

During a colonoscopy, biopsies of the colon are often taken in order to confirm the diagnosis. There are certain characteristic features of the pathology seen that point toward Crohn's disease. Crohn's disease shows a transmural pattern of inflammation, meaning that the inflammation may span the entire depth of the intestinal wall.[1] Grossly, ulceration is an outcome seen in highly active disease. There is usually an abrupt transition between unaffected tissue and the ulcer. Under a microscope, biopsies of the affected colon may show mucosal inflammation. This inflammation is characterized by focal infiltration of neutrophils, a type of inflammatory cell, into the epithelium. This typically occurs in the area overlying lymphoid aggregates. These neutrophils, along with mononuclear cells, may infiltrate into the crypts leading to inflammation (crypititis) or abscess (crypt abscess). Granulomas, aggregates of macrophage derivatives known as giant cells, are found in 50% of cases and are most specific for Crohn's disease. The granulomas of Crohn's disease do not show "caseation", a cheese-like appearance on microscopic examination that is characteristic of granulomas associated with infections such as tuberculosis. Biopsies may also show chronic mucosal damage as evidenced by blunting of the intestinal villi, atypical branching of the crypts, and change in the tissue type (metaplasia). One example of such metaplasia, *Paneth cell metaplasia*, involves development of Paneth cells (typically found in the small intestine) in other parts of the gastrointestinal system.[63]

Diagnosis

The diagnosis of Crohn's disease can sometimes be challenging,[13] and a number of tests are often required to assist the physician in making the diagnosis.[8] Even with a full battery of tests it may not be possible to diagnose Crohn's with complete certainty; a colonoscopy is approximately 70% effective in diagnosing the disease with further tests being less effective. Disease in the small bowel is particularly difficult to diagnose as a traditional colonoscopy only allows access to the colon and lower portions of the small intestines; introduction of the capsule endoscopy[64] aids in endoscopic diagnosis.

Endoscopy

A colonoscopy is the best test for making the diagnosis of Crohn's disease as it allows direct visualization of the colon and the terminal ileum, identifying the pattern of disease involvement. Occasionally, the colonoscope can travel past the terminal ileum but it varies from patient to patient. During the procedure, the gastroenterologist can also perform a biopsy, taking small samples of tissue for laboratory analysis which may help confirm a diagnosis. As 30% of Crohn's disease involves only the ileum,[1] cannulation of the terminal ileum is required in making the diagnosis. Finding a patchy distribution of disease, with involvement of the colon or ileum but not the rectum, is suggestive of Crohn's disease, as are other endoscopic stigmata.[65] The utility of capsule endoscopy for this, however, is still uncertain.[66]

Radiologic tests

A small bowel follow-through may suggest the diagnosis of Crohn's disease and is useful when the disease involves only the small intestine. Because colonoscopy and gastroscopy allow direct visualization of only the terminal ileum and beginning of the duodenum, they cannot be used to evaluate the remainder of the small intestine. As a result, a barium follow-through x-ray, wherein barium sulfate suspension is ingested and fluoroscopic images of the bowel are taken over time, is useful for looking for inflammation and narrowing of the small bowel.[65][67] Barium enemas, in which barium is inserted into the rectum and fluoroscopy used to image the bowel, are rarely used in the work-up of Crohn's disease due to the advent of colonoscopy. They remain useful for identifying anatomical abnormalities when strictures of the colon are too small for a colonoscope to pass through, or in the detection of colonic fistulae.[68]

CT and MRI scans are useful for evaluating the small bowel with enteroclysis protocols.[69] They are additionally useful for looking for intra-abdominal complications of Crohn's disease such as abscesses, small bowel obstruction, or fistulae.[70] Magnetic resonance imaging (MRI) are another option for imaging the small bowel as well as looking for complications, though it is more expensive and less readily available[71]

Blood tests

A complete blood count may reveal anemia, which may be caused either by blood loss or vitamin B_{12} deficiency. The latter may be seen with ileitis because vitamin B_{12} is absorbed in the ileum.[72] Erythrocyte sedimentation rate, or ESR, and C-reactive protein measurements can also be useful to gauge the degree of inflammation.[73] It is also true in patient with ilectomy done in response to the complication. Another cause of anaemia is anaemia of chronic disease, characterized by its microcytic and hypochromic anaemia. There can be various reasons for anaemia, including

medication used in treatment of inflammatory bowel disease like azathioprine which can lead to cytopenia and sulfasalazine which can also result in folate malabsorption, etc. Testing for anti-*Saccharomyces cerevisiae* antibodies (ASCA) and anti-neutrophil cytoplasmic antibodies (ANCA) has been evaluated to identify inflammatory diseases of the intestine [74] and to differentiate Crohn's disease from ulcerative colitis. [75] Furthermore, increasing amounts and levels of serological antibodies such as ASCA, anti-laminaribioside [Glc(β1,3)Glb(β); ALCA], anti-chitobioside (GlcNAc(β1,4)GlcNAc(β); ACCA], anti-mannobioside [Man(α1,3)Man(α)AMCA], anti-Laminarin [Glc(β1,3))3n(Glc(β1,6))n; anti-L] and anti-Chitin [(GlcNAc(β1,4)n; anti-C] associate with disease behavior and surgery, and may aid in the prognosis of Crohn's disease. [76][77][78][79]

Comparison with ulcerative colitis

The most common disease that mimics the symptoms of Crohn's disease is ulcerative colitis, as both are inflammatory bowel diseases that can affect the colon with similar symptoms. It is important to differentiate these diseases, since the course of the diseases and treatments may be different. In some cases, however, it may not be possible to tell the difference, in which case the disease is classified as **indeterminate colitis**. [1][8][15]

Treatment

Main articles: Treatment of Crohn's disease and Biological therapy for inflammatory bowel disease

Currently there is no cure for Crohn's disease and remission may not be possible or prolonged if achieved. [85] In cases where remission is possible, relapse can be prevented and symptoms controlled with medication, lifestyle changes and in some cases, surgery. Adequately controlled, Crohn's disease may not significantly restrict daily living. [86] Treatment for Crohn's disease is only when symptoms are active and involve first treating the acute problem, then maintaining remission.

Medication

Acute treatment uses medications to treat any infection (normally antibiotics) and to reduce inflammation (normally aminosalicylate anti-inflammatory drugs and corticosteroids). When symptoms are in remission, treatment enters maintenance with a goal of avoiding the recurrence of symptoms. Prolonged use of corticosteroids has significant side-effects; as a result they are generally not used for long-term treatment. Alternatives include aminosalicylates alone, though only a minority are able to maintain the treatment, and many require immunosuppressive drugs. [81]

Medications used to treat the symptoms of Crohn's disease include 5-aminosalicylic acid (5-ASA) formulations, prednisone, immunomodulators such as azathioprine, mercaptopurine, methotrexate, infliximab, adalimumab [15], certolizumab [87] and natalizumab. [88][89] Hydrocortisone should be used in severe attacks of Crohn's disease. [90]

Low doses of the opiate receptor antagonist Naltrexone (also Low dose naltrexone) have been found to be effective in inducing remission in 67% of patients with Crohn's disease in a small study conducted at Pennsylvania State University. Dr. Jill Smith, Professor of Gastroenterology at Pennsylvania State University's College of Medicine concluded that "LDN therapy appears effective and safe in subjects with active Crohn's disease." [91] Smith and her colleagues have since received a NIH grant and are proceeding with a definitive Phase II placebo-controlled clinical trial.

Lifestyle changes

Certain lifestyle changes can reduce symptoms, including dietary adjustments, proper hydration and smoking cessation. Eating small meals frequently instead of big meals may also help with a low appetite. To manage symptoms have a balanced diet with proper portion control. Fatigue can be helped with regular exercise, a healthy diet and enough sleep. A food diary may help with identifying foods that trigger symptoms. Some patients should follow a low dietary fiber diet to control symptoms especially if fiberous foods cause symptoms.[86]

Surgery

Crohn's cannot be cured by surgery, though it is used when partial or a full blockage of the intestine occurs. Surgery may also be required for complications such as obstructions, fistulas and/or abscesses, or if the disease does not respond to drugs. After the first surgery, Crohn's usually shows up at the site of the resection though it can appear in other locations. After a resection, scar tissue builds up which can cause strictures. A stricture is when the intestines become too small to allow excrement to pass through easily which can lead to a blockage. After the first resection, another resection may be necessary within five years.[92] For patients with an obstruction due to a stricture, two options for treatment are strictureplasty and resection of that portion of bowel. There is no statistical significance between strictureplasty alone versus strictureplasty and resection in cases of duodenal involvement. In these cases, re-operation rates were 31% and 27%, respectively, indicating that strictureplasty is a safe and effective treatment for selected patients with duodenal involvement.[93]

Short bowel syndrome (SBS, also short gut syndrome or simply short gut) can be caused by the surgical removal of the small intestines. It usually develops if a person has had half or more of their small intestines removed.[94] Diarrhea is the main symptom of short bowel syndrome though other symptoms may include cramping, bloating and heartburn. Short bowel syndrome is treated with changes in diet, intravenous feeding, vitamin and mineral supplements and treatment with medications. Another complication following surgery for Crohn's disease where the terminal ileum has been removed is the development of excessive watery diarrhea. This is due to an inability to reabsorb bile acids after resection of the terminal ileum.

In some cases of SBS, intestinal transplant surgery may be considered; though the number of transplant centres offering this procedure is quite small and it comes with a high risk due to the chance of infection and rejection of the transplanted intestine.[95]

Prospective treatments

Researchers at University College London have questioned the wisdom of suppressing the immune system in Crohn's, as the problem may be an under-active rather than an over-active immune system: their study found that Crohn's patients showed an abnormally low response to an introduced infection, marked by a poor flow of blood to the wound, and the response improved when the patients were given sildenafil citrate.[34]

Recent studies using helminthic therapy or hookworms to treat Crohn's Disease and other (non-viral) auto-immune diseases seem to yield promising results.[96]

Complementary and alternative medicine

More than half of Crohn's disease sufferers have tried complementary or alternative therapy.[97] These include diets, probiotics, fish oil and other herbal and nutritional supplements. The benefit of these medications is uncertain.

Acupuncture is used to treat inflammatory bowel disease in China, and is being used more frequently in Western society.[98] However, there is no evidence that acupuncture has benefits beyond the placebo effect.[98]

Methotrexate is a folate anti-metabolite drug which is also used for chemotherapy. It is useful in maintenance of remission for those no longer taking corticosteroids.[99]

Metronidazole and ciprofloxacin are antibiotics which are used to treat Crohn's that have colonic or perianal involvement, although, in the United States, this use has not been approved by the Food and Drug Administration.[100] They are also used for treatment of complications, including abscesses and other infections accompanying Crohn's disease.[8]

Thalidomide has shown response in reversing endoscopic evidence of disease.[101]

Cannabis-derived drugs may be used to treat Crohn's Disease with its anti-inflammatory properties. Cannabis-derived drugs may also help to heal the gut lining.[102]

Soluble Fiber has been used by some to treat symptoms.^ a b c Tungland BC, Meyer D, Nondigestible oligo- and polysaccharides (dietary fiber): their physiology and role in human health and food, Comp Rev Food Sci Food Safety, 3:73-92, 2002 (Table 3)[1]

Probiotics include Sacchromyces boulardii[103] and E. coli Nissle 1917.[104]

Boswellia is an ayurvedic (Indian traditional medicine) herb, used as a natural alternative to drugs. One study has found that the effectiveness of H-15 extract is not inferior to mesalazine, and suggests it that its safety makes it superior in benefit-risk evaluations.[105]

Prognosis

Crohn's disease is a chronic condition for which there is currently no cure. It is characterised by periods of improvement followed by episodes when symptoms flare up. With treatment, most people achieve a healthy height and weight, and the mortality rate for the disease is relatively low. However, Crohn's disease is associated with an increased risk of small bowel and colorectal carcinoma, including bowel cancer.[106]

Epidemiology

The incidence of Crohn's disease has been ascertained from population studies in Norway and the United States and is similar at 6 to 7.1:100,000.[107][108] Crohn's disease is more common in northern countries, and shows a higher preponderance in northern areas of the same country.[109] The incidence of Crohn's disease is thought to be similar in Europe but lower in Asia and Africa.[107] It also has a higher incidence in Ashkenazi Jews.[15]

Crohn's disease has a bimodal distribution in incidence as a function of age: the disease tends to strike people in their teens and 20s, and people in their 50s through to their 70s, and ages in between due to not being diagnosed with Crohn's and being diagnosed instead with irritable bowel syndrome (IBS).[1][8] It is rarely diagnosed in early childhood. It usually strikes females who are pediatric patients more severely than males.[110] However, only slightly more women than men have Crohn's disease.[111] Parents, siblings or children of people with Crohn's disease are 3 to 20

times more likely to develop the disease.[112] Twin studies show a concordance of greater than 55% for Crohn's disease.[113]

History

Inflammatory bowel diseases were described by Giovanni Battista Morgagni (1682–1771), by Polish surgeon Antoni Leśniowski in 1904 (leading to the use of the eponym "**Leśniowski-Crohn disease**" in Poland) and by Scottish physician T. Kennedy Dalziel in 1913.[114]

Burrill Bernard Crohn, an American gastroenterologist at New York City's Mount Sinai Hospital, described fourteen cases in 1932, and submitted them to the American Medical Association under the rubric of "Terminal ileitis: A new clinical entity". Later that year, he, along with colleagues Leon Ginzburg and Gordon Oppenheimer published the case series as "Regional ileitis: a pathologic and clinical entity".[10]

References

1. ^ [a b c d e f g h i j k l m n o] Baumgart DC, Sandborn WJ (12 May 2007). "Inflammatory bowel disease: clinical aspects and established and evolving therapies.". *The Lancet* **369** (9573): 1641–57. doi:10.1016/S0140-6736(07)60751-X. PMID 17499606.
2. **^** Mayo Clinic: Crohn's Disease
3. **^** National Digestive Diseases Information Clearinghouse
4. **^** Barrett, JC; Hansoul, S; Nicolae, DL; Cho, JH; Duerr, RH; Rioux, JD; Brant, SR; Silverberg, MS *et al*. (August 2008). "Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease". *Nature Genetics* **40** (8): 955–962. doi:10.1038/ng.175. PMID 18587394.
5. ^ [a b] Cosnes J (June 2004). "Tobacco and IBD: relevance in the understanding of disease mechanisms and clinical practice". *Best Pract Res Clin Gastroenterol* **18** (3): 481–96. doi:10.1016/j.bpg.2003.12.003. PMID 15157822.
6. **^** Loftus, E.V.; P. Schoenfeld, W. J. Sandborn (January 2002). "The epidemiology and natural history of Crohn's disease in population-based patient cohorts from North America: a systematic review". *Alimentary Pharmacology & Therapeutics* **16** (1): 51–60. doi:10.1046/j.1365-2036.2002.01140.x. PMID 11856078.
7. ^ [a b] Bernstein, Charles N.; Wajda, A; Svenson, LW; Mackenzie, A; Koehoorn, M; Jackson, M; Fedorak, R; Israel, D *et al*. (July 2006). "The epidemiology of inflammatory bowel disease in Canada: a population-based study". *The American Journal of Gastroenterology* **101** (7): 1559–68. doi:10.1111/j.1572-0241.2006.00603.x. PMID 16863561.
8. ^ [a b c d e f g h i] Wu, George Y; Marcy L Coash, Senthil Nachimuthu (Jan 20, 2009). [emedicine.medscape.com/article/172940-overview "Crohn Disease"]. eMedicine. emedicine.medscape.com/article/172940-overview. Retrieved 2009-11-04.
9. **^** Le, Tri H (Aug 7, 2008). [emedicine.medscape.com/article/183084-overview "Ulcerative colitis"]. eMedicine. emedicine.medscape.com/article/183084-overview. Retrieved 2009-11-04.
10. ^ [a b c] Crohn BB, Ginzburg L, Oppenheimer GD (2000). "Regional ileitis: a pathologic and clinical entity. 1932". *Mt. Sinai J. Med.* **67** (3): 263–8. PMID 10828911.

11. ^ [a] [b] Gasche C, Scholmerich J, Brynskov J, D'Haens G, Hanauer S, Irvine E, Jewell D, Rachmilewitz D, Sachar D, Sandborn W, Sutherland L (2000). "A simple classification of Crohn's disease: report of the Working Party for the World Congresses of Gastroenterology, Vienna 1998". *Inflamm Bowel Dis* **6** (1): 8–15. PMID 10701144.
12. **^** Dubinsky MC, Fleshner PP. (2003). "Treatment of Crohn's Disease of Inflammatory, Stenotic, and Fistulizing Phenotypes". *Curr Treat Options Gastroenterol* **6** (3): 183–200. doi:10.1007/s11938-003-0001-1. PMID 12744819.
13. ^ [a] [b] Pimentel, Mark; Michael Chang, Evelyn J. Chow, Siamak Tabibzadeh, Viorelia Kirit-Kiriak, Stephan R. Targan, Henry C. Lin (2000). "Identification of a prodromal period in Crohn's disease but not ulcerative colitis". *American Journal of Gastroenterology* **95** (12): 3458–62. doi:10.1111/j.1572-0241.2000.03361.x. PMID 11151877.
14. **^** Crohn's Disease Overview
15. ^ [a] [b] [c] [d] Podolsky, Daniel K. (2002). "Inflammatory bowel disease". *New England Journal of Medicine* **346** (6): 417–29. doi:10.1056/NEJMra020831. PMID 12167685. http://content.nejm.org/cgi/content/extract/347/6/417. Retrieved 2006-07-02.
16. **^** Mueller, M. H.; M. E. Kreis, M. L. Gross, H. D. Becker, T. T. Zittel & E. C. Jehle (2002). "Anorectal functional disorders in the absence of anorectal inflammation in patients with Crohn's disease". *British Journal of Surgery* **89** (8): 1027–31. doi:10.1046/j.1365-2168.2002.02173.x. PMID 12153630.
17. **^** Kumar, Vinay; Abul K. Abbas, Nelson Fausto (July 30, 2004). "Ch 17: The Gastrointestinal Tract". *Robbins and Cotran: Pathologic Basis of Disease* (7th ed.). Philadelphia, Pennsylvania: Elsevier Saunders. pp. 847. ISBN 0-7216-0187-1.
18. **^** Taylor B, Williams G, Hughes L, Rhodes J (1989). "The histology of anal skin tags in Crohn's disease: an aid to confirmation of the diagnosis". *Int J Colorectal Dis* **4** (3): 197–9. doi:10.1007/BF01649703. PMID 2769004.
19. **^** Fix, Oren K.; Jorge A. Soto, Charles W. Andrews and Francis A. Farraye (2004). "Gastroduodenal Crohn's disease". *Gastrointestinel Endoscopy* **60** (6): 985. doi:10.1016/S0016-5107(04)02200-X. PMID 15605018.
20. ^ [a] [b] Beattie, R.M.; N. M. Croft, J. M. Fell, N. A. Afzal and R. B. Heuschkel (2006). "Inflammatory bowel disease". *Archives of Disease in Childhood* **91** (5): 426–32. doi:10.1136/adc.2005.080481. PMID 16632672.
21. **^** Büller, H.A. (1997). "Problems in diagnosis of IBD in children". *The Netherlands Journal of Medicine* **50** (2): S8–S11. doi:10.1016/S0300-2977(96)00064-2. PMID 9050326.
22. **^** O'Keefe, S. J. (1996). "Nutrition and gastrointestinal disease". *Scandinavian Journal of Gastroenterology Supplement* **31** (220): 52–9. doi:10.3109/00365529609094750. PMID 8898436.
23. **^** Danese, Silvio; Stefano Semeraro, Alfredo Papa, Italia Roberto, Franco Scaldaferri, Giuseppe Fedeli, Giovanni Gasbarrini, Antonio Gasbarrini (2005). "Extraintestinal manifestations in inflammatory bowel disease". *World Journal of Gastroenterology* **11** (46): 7227–36. PMID 16437620. http://www.wjgnet.com/1007-9327/11/7227.asp. Retrieved 2009-11-07.
24. ^ [a] [b] Crohn's disease. professionals.epilepsy.com. Retrieved on July 13, 2007.
25. **^** MedlinePlus Encyclopedia *Small bowel bacterial overgrowth*
26. **^** Ekbom A, Helmick C, Zack M, Adami H (1990). "Increased risk of large-bowel cancer in Crohn's disease with colonic involvement". *Lancet* **336** (8711): 357–9. doi:10.1016/0140-6736(90)91889-I. PMID 1975343.

27. ^ Collins P, Mpofu C, Watson A, Rhodes J (2006). "Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease". *Cochrane Database Syst Rev* (2): CD000279. doi:10.1002/14651858.CD000279.pub3. PMID 16625534.
28. ^ Lynne V McFarland (2008). "Colorectal cancer and dysplasia in inflammatory bowel disease". *World Journal of Gastroenterology*: 2665.
29. ^ Evans J, Steinhart A, Cohen Z, McLeod R (2003). "Home total parenteral nutrition: an alternative to early surgery for complicated inflammatory bowel disease". *J Gastrointest Surg* **7** (4): 562–6. doi:10.1016/S1091-255X(02)00132-4. PMID 12763417.
30. ^ "Complications of Crohn's Disease". https://www.livingwithcrohnsdisease.com/livingwithcrohnsdisease/crohns_disease/complications_of_crohns.html. Retrieved 2009-11-07.
31. ^ Kaplan, C (2005-10-21). "IBD and Pregnancy: What You Need to Know". Crohn's and Colitis Foundation of America. http://www.ccfa.org/about/news/pregnancy. Retrieved 2009-11-07.
32. ^ Braat H, Peppelenbosch MP, Hommes DW (August 2006). "Immunology of Crohn's disease". *Ann. N. Y. Acad. Sci.* **1072**: 135–54. doi:10.1196/annals.1326.039. PMID 17057196.
33. ^ Henckaerts L, Figueroa C, Vermeire S, Sans M (May 2008). "The role of genetics in inflammatory bowel disease". *Curr Drug Targets* **9** (5): 361–8. doi:10.2174/138945008784221161. PMID 18473763.
34. ^ [a] [b] [c] Marks DJ, Harbord MW, MacAllister R, Rahman FZ, Young J, Al-Lazikani B, Lees W, Novelli M, Bloom S, Segal AW (2006). "Defective acute inflammation in Crohn's disease: a clinical investigation". *Lancet* **367** (9511): 668–78. doi:10.1016/S0140-6736(06)68265-2. PMID 16503465.
35. ^ Comalada M, Peppelenbosch MP (September 2006). "Impaired innate immunity in Crohn's disease". *Trends Mol Med* **12** (9): 397–9. doi:10.1016/j.molmed.2006.07.005. PMID 16890491.
36. ^ "Crohn's disease has strong genetic link: study". Crohn's and Colitis Foundation of America. 2007-04-16. http://www.ccfa.org/reuters/geneticlink. Retrieved 2009-11-07.
37. ^ Ogura Y, Bonen DK, Inohara N, *et al.* (2001). "A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease". *Nature* **411** (6837): 603–6. doi:10.1038/35079114. PMID 11385577.
38. ^ Cuthbert A, Fisher S, Mirza M, *et al.* (2002). "The contribution of NOD2 gene mutations to the risk and site of disease in inflammatory bowel disease". *Gastroenterology* **122** (4): 867–74. doi:10.1053/gast.2002.32415. PMID 11910337.
39. ^ Kaser, A; Lee, AH; Franke, A; Glickman, JN; Zeissig, S; Tilg, H; Nieuwenhuis, EE; Higgins, DE *et al*. (5 September 2008). "XBP1 Links ER Stress to Intestinal Inflammation and Confers Genetic Risk for Human Inflammatory Bowel Disease". *Cell* (Cell Press) **134** (5): 743–756. doi:10.1016/j.cell.2008.07.021. PMID 18775308. PMC 2586148. http://www.cell.com/content/article/abstract?uid=PIIS0092867408009410.
40. ^ Clevers, H (2009). "Inflammatory Bowel Disease, Stress, and the Endoplasmic Reticulum". *N Engl J Med* **360** (7): 726–727. doi:10.1056/NEJMcibr0809591. PMID 19213688. http://content.nejm.org/cgi/content/full/360/7/726.
41. ^ Lesko S, Kaufman D, Rosenberg L, *et al.* (1985). "Evidence for an increased risk of Crohn's disease in oral contraceptive users". *Gastroenterology* **89** (5): 1046–9. PMID 4043662.

42. **^** Cobrin GM, Abreu MT (2005). "Defects in mucosal immunity leading to Crohn's disease". *Immunol. Rev.* **206**: 277–95. doi:10.1111/j.0105-2896.2005.00293.x. PMID 16048555.
43. ^ [a] [b] Elson, CO; Cong, Y; Weaver, CT; Schoeb, TR; Mcclanahan, TK; Fick, RB; Kastelein, RA (2007). "Monoclonal Anti–Interleukin 23 Reverses Active Colitis in a T Cell–Mediated Model in Mice". *Gastroenterology* **132** (7): 2359. doi:10.1053/j.gastro.2007.03.104. PMID 17570211.
44. **^** Prescott NJ, Fisher SA, Franke A, *et al.* (2007). "A nonsynonymous SNP in ATG16L1 predisposes to ileal Crohn's disease and is independent of CARD15 and IBD5". *Gastroenterology* **132** (5): 1665–71. doi:10.1053/j.gastro.2007.03.034. PMID 17484864.
45. **^** Marks DJ, Segal AW. (January 2008). "Innate immunity in inflammatory bowel disease: a disease hypothesis". *J Pathol.* **214** (2): 260–6. doi:10.1002/path.2291. PMID 18161747.
46. **^** Dessein R, Chamaillard M, Danese S (September 2008). "Innate immunity in Crohn's disease: the reverse side of the medal". *J Clin Gastroenterol* **42** (Suppl 3 Pt 1): S144–7. doi:10.1097/MCG.0b013e3181662c90. PMID 18806708.
47. **^** "OVERVIEW: MAP and Crohn's Disease Research". http://www.crohns.org/research/index.htm. Retrieved 2009-11-07.
48. **^** Sartor, R. (July 2006). [www.nature.com/nrgastro/journal/v3/n7/full/ncpgasthep0528.html "Mechanisms of Disease: pathogenesis of Crohn's disease and ulcerative colitis"]. *Nature Clinical Practice Gastroenterology & Hepatology* **3** (7): 390–407. doi:10.1038/ncpgasthep0528. www.nature.com/nrgastro/journal/v3/n7/full/ncpgasthep0528.html. PMID 16819502
49. **^** Naser SA, Collins MT (2005). "Debate on the lack of evidence of Mycobacterium avium subsp. paratuberculosis in Crohn's disease". *Inflamm. Bowel Dis.* **11** (12): 1123. doi:10.1097/01.MIB.0000191609.20713.ea. PMID 16306778.
50. **^** Giaffer MH, Clark A, Holdsworth CD (1992). "Antibodies to Saccharomyces cerevisiae in patients with Crohn's disease and their possible pathogenic importance". *Gut* **33** (8): 1071–5. doi:10.1136/gut.33.8.1071. PMID 1398231.
51. **^** Baumgart M *et al.* (2007). "Culture independent analysis of ileal mucosa reveals a selective increase in invasive Escherichia coli of novel phylogeny relative to depletion of Clostridiales in Crohn's disease involving the ileum". *The ISME Journal* **1** (5): 403. doi:10.1038/ismej.2007.52. PMID 18043660. http://www.nature.com/ismej/journal/v1/n5/full/ismej200752a.html.
52. **^** "Possible links between Crohn's disease and Paratuberculosis" (PDF). *EUROPEAN COMMISSION DIRECTORATE-GENERAL HEALTH & CONSUMER PROTECTION*. http://ec.europa.eu/food/fs/sc/scah/out38_en.pdf. Retrieved 2009-11-07.
53. **^** Gui GP, Thomas PR, Tizard ML, Lake J, Sanderson JD, Hermon-Taylor J (March 1997). "Two-year-outcomes analysis of Crohn's disease treated with rifabutin and macrolide antibiotics" (PDF). *J. Antimicrob. Chemother.* **39** (3): 393–400. doi:10.1093/jac/39.3.393. PMID 9096189. http://jac.oxfordjournals.org/cgi/reprint/39/3/393.
54. **^** Cenac N, Andrews CN, Holzhausen M, *et al.* (March 2007). "Role for protease activity in visceral pain in irritable bowel syndrome". *J. Clin. Invest.* **117** (3): 636–47. doi:10.1172/JCI29255. PMID 17304351.

55. ^ Cenac N, Coelho AM, Nguyen C, *et al.* (November 2002). "Induction of intestinal inflammation in mouse by activation of proteinase-activated receptor-2". *Am. J. Pathol.* **161** (5): 1903–15. PMID 12414536. PMC 1850779. http://ajp.amjpathol.org/cgi/pmidlookup?view=long&pmid=12414536.
56. ^ Boorom KF, Smith H, Nimri L, *et al.* (October 2008). "Oh my aching gut: irritable bowel syndrome, Blastocystis, and asymptomatic infection". *Parasit Vectors* **1** (1): 40. doi:10.1186/1756-3305-1-40. PMID 18937874.
57. ^ Hugot, Jean-Pierre; Alberti, Corinne; Berrebi, Dominique; Bingen, Edouard; Cezard, Jean-Pierre (2003-12-13). "Crohn's disease: the cold chain hypothesis". *The Lancet* **362** (9400): 2012–2015. doi:10.1016/S0140-6736(03)15024-6. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(03)15024-6.
58. ^ "Fridges blamed for Crohn's disease rise". *Medical News TODAY*. 2003-12-12. http://www.medicalnewstoday.com/articles/4849.php.
59. ^ Forbes, Alastair; Kalantzis, Tommy (July 2006). [www.springerlink.com/content/p6q21tp76x013u51/ "Crohn's disease : the cold chain hypothesis"]. *International Journal of Colorectal Disease* (Springer Berlin / Heidelberg) **21** (5): 399–401. doi:10.1007/s00384-005-0003-7. ISSN 0179-1958. PMID 16059694. www.springerlink.com/content/p6q21tp76x013u51/. Retrieved 2009-11-04.
60. ^ Subramanian, Sreedhar; Carol, L. Roberts; Hart, C. Anthony; Martin, Helen M.; Edwards, Steve W.; Rhodes, Jonathan M.; Campbell, Barry J. (2008). "Replication of Colonic Crohn's Disease Mucosal Escherichia coli Isolates within Macrophages and Their Susceptibility to Antibiotics". *Antimicrobial Agents and Chemotherapy* **52** (2): 427–434. doi:10.1128/AAC.00375-07. PMID 18070962. PMC 2224732. http://aac.asm.org/cgi/content/abstract/52/2/427.
61. ^ Mpofu, Chiedzo M.; Cambell, Barry J.; Subramanin, Sreedhar; Marshall-Clarke, Stuart; Hart, Anthony C.; Cross, Andy; Roberts, Carol L.; McGoldrick, Adrian *et al*. (2007). "Microbial Mannan Inhibits Bacterial Killing by Macrophages: A Possible Pathogenic Mechanism for Crohn's Disease". *Gastroenterology, the official journal of the AGA Institute* **133** (5): 1487–1498. doi:10.1053/j.gastro.2007.08.004. PMID 17919633. http://www.gastrojournal.org/article/S0016-5085(07)01450-3/abstract.
62. ^ "New insights into Crohn's Disease". http://www.liv.ac.uk/researchintelligence/issue33/crohns.htm.
63. ^ Crawford JM. "The Gastrointestinal tract, Chapter 17". In Cotran RS, Kumar V, Robbins SL. *Robbins Pathologic Basis of Disease: 5th Edition*. W.B. Saunders and Company, Philadelphia, 1994.
64. ^ HCP: Pill Cam, Capsule Endoscopy, Esophageal Endoscopy
65. ^ [a] [b] Hara, Amy K.; Jonathan A. Leighton, Russell I. Heigh, Virender K. Sharma, Alvin C. Silva, Giovanni De Petris, Joseph G. Hentz and David E. Fleischer (January 2006). "Crohn disease of the small bowel: preliminary comparison among CT enterography, capsule endoscopy, small-bowel follow-through, and ileoscopy". *Radiology* **238** (1): 128–34. doi:10.1148/radiol.2381050296. PMID 16373764.
66. ^ Triester, Stuart L.; Jonathan A. Leighton, Grigoris I. Leontiadis, Suryakanth R. Gurudu, David E. Fleischer, Amy K. Hara, Russell I. Heigh, Arthur D. Shiff, and Virender K. Sharma (2006). "A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease". *The American Journal of Gastroenterology* **101** (5): 954–64. doi:10.1111/j.1572-0241.2006.00506.x. PMID 16696781.

67. ^ Dixon, P.M.; M.E. Roulston and D.J. Nolan (1993). "The small bowel enema: a ten year review". *Clinical Radiology* **47** (1): 46–8. doi:10.1016/S0009-9260(05)81213-9. PMID 8428417.
68. ^ Carucci, L. R.; M. S. Levine (2002). "Radiographic imaging of inflammatory bowel disease". *Gastroenterology Clinics of North America* **31** (1): 93–117. doi:10.1016/S0889-8553(01)00007-3. PMID 12122746.
69. ^ Rajesh, A.; D.D.T. Maglinte (2006). "Multislice CT enteroclysis: technique and clinical applications". *Clinical Radiology* **61** (1): 31–9. doi:10.1016/j.crad.2005.08.006. PMID 16356814.
70. ^ Zissin, Rivka; Marjorie Hertz, Alexandra Osadchy, Ben Novis and Gabriela Gayer (2005). "Computed Tomographic Findings of Abdominal Complications of Crohn's Disease—Pictorial Essay" (PDF). *Canadian Association of Radiologists Journal* **56** (1): 25–35. PMID 15835588. http://www.carj.ca/issues/2005-Feb/25/pg25.pdf. Retrieved 2009-11-07.
71. ^ MacKalski, B. A.; C. N. Bernstein (2005). "New diagnostic imaging tools for inflammatory bowel disease". *Gut* **55** (5): 733–41. doi:10.1136/gut.2005.076612. PMID 16609136.
72. ^ Goh, Jason; C. A. O'Morain (2003). "Review article: nutrition and adult inflammatory bowel disease". *Alimentary Pharmacology & Therapeutics* **17** (3): 307–20. doi:10.1046/j.1365-2036.2003.01482.x. PMID 12562443.
73. ^ Chamouard, Patrick; Zoe Richert, Nicolas Meyer, Gabriel Rahmi, René Baumann (2006). "Diagnostic Value of C-Reactive Protein for Predicting Activity Level of Crohn's Disease". *Clinical Gastroenterology and Hepatology* **4** (7): 882. doi:10.1016/j.cgh.2006.02.003. PMID 16630759. Epub ahead of print
74. ^ Kaila, B; K Orr and C N Bernstein (2005). [www.pulsus.com/journals/abstract.jsp?sCurrPg=journal&jnlKy=2&atlKy=743&isuKy=263&isArt=t "The anti-Saccharomyces cerevisiae antibody assay in a province-wide practice: accurate in identifying cases of Crohn's disease and predicting inflammatory disease"]. *The Canadian Journal of Gastroenterology* **19** (12): 717–21. PMID 16341311. www.pulsus.com/journals/abstract.jsp?sCurrPg=journal&jnlKy=2&atlKy=743&isuKy=263&isArt=t. Retrieved 2006-07-02.
75. ^ Israeli, E.; I. Grotto, B. Gilburd, R. D. Balicer, E. Goldin, A. Wiik and Y. Shoenfeld (2005). "Anti-Saccharomyces cerevisiae and antineutrophil cytoplasmic antibodies as predictors of inflammatory bowel disease". *Gut* **54** (9): 1232–6. doi:10.1136/gut.2004.060228. PMID 16099791.
76. ^ Ferrante, M.; L. Henckaerts, M. Joossens, M. Pierik, S. Joossens, N. Dotan, G.L. Norman , R.T. Altstock , K. Van Steen , P. Rutgeerts , G. Van Assche and S.Vermeire (2007). "New serological markers in inflammatory bowel disease are associated with complicated disease behaviour". *Gut* **56** (10): 1394–403. doi:10.1136/gut.2006.108043. PMID 17456509.
77. ^ Papp, M.; I. Altorjay, N. Dotan, K. Palatka, I. Foldi, J. Tumpek, S. Sipka, M. Udvardy, T. Dinya, L. Lakatos, A. Kovacs, T. Molnar, Z. Tulassay, P. Mihelle, G.L. Norman, T. Szamosi , J. Papp; Hungarian IBD Study Group and P.L. Lakatos (2008). "New serological markers for inflammatory bowel disease are associated with earlier age at onset, complicated disease behavior, risk for surgery, and NOD2/CARD15 genotype in a Hungarian IBD cohort". *Am J Gastroenterol* **104** (6): 1426–34. doi:10.1111/j.1572-0241.2007.01652.x. PMID 18047543.

78. **^** Seow, C.H.; J.M. Stempak, W. Xu, H. Lan, A.M. Griffiths, G.R. Greenberg, A.H. Steinhart, N. Dotan and M.S. Silverberg (2009). "Novel anti-glycan antibodies related to inflammatory bowel disease diagnosis and phenotype". *Am J Gastroenterol* **104** (6): 1426–34. doi:10.1038/ajg.2009.79. PMID 19491856.
79. **^** Dotan, I. (2007). "Serologic markers in inflammatory bowel disease: tools for better diagnosis and disease stratification". *Expert Rev Gastroenterol Hepatol* **1** (2): 265–74. doi:10.1586/17474124.1.2.265. PMID 19072419.
80. ^ [a] [b] [c] [d] Kornbluth, Asher; David B. Sachar (July 2004). "Ulcerative colitis practice guidelines in adults (update): American College of Gastroenterology, Practice Parameters Committee" (PDF). *American Journal of Gastroenterology* **99** (7): 1371–85. doi:10.1111/j.1572-0241.2004.40036.x. PMID 15233681. http://www.acg.gi.org/physicians/guidelines/UlcerativeColitisUpdate.pdf. Retrieved 2009-11-07.
81. ^ [a] [b] [c] [d] [e] Hanauer, Stephen B.; William Sandborn (2001-03-01). "Management of Crohn's disease in adults" (PDF). *American Journal of Gastroenterology* **96** (3): 635–43. doi:10.1111/j.1572-0241.2001.03671.x. PMID 11280528. http://www.acg.gi.org/physicians/guidelines/CrohnsDiseaseinAdults.pdf. Retrieved 2009-11-07.
82. **^** Broomé, Ulrika; Annika Bergquist (February 2006). "Primary sclerosing cholangitis, inflammatory bowel disease, and colon cancer". *Seminars in Liver Disease* **26** (1): 31–41. doi:10.1055/s-2006-933561. PMID 16496231.
83. **^** Shepherd, NA. (Aug 2002). "Granulomas in the diagnosis of intestinal Crohn's disease: a myth exploded?". *Histopathology* **41** (2): 166–8. doi:10.1046/j.1365-2559.2002.01441.x. PMID 12147095.
84. **^** Mahadeva, U.; Martin, JP.; Patel, NK.; Price, AB. (Jul 2002). "Granulomatous ulcerative colitis: a re-appraisal of the mucosal granuloma in the distinction of Crohn's disease from ulcerative colitis.". *Histopathology* **41** (1): 50–5. doi:10.1046/j.1365-2559.2002.01416.x. PMID 12121237.
85. **^** "Clinical Research Alliance Update" (PDF). Crohn's and Colitis Foundation of America. 2007-05-01. http://www.ccfa.org/ccfaprof/research-grant-opps/documents/May-2007-Newsletter.pdf. Retrieved 2008-02-14.
86. ^ [a] [b] Fries, WS (2007-05-16). "Crohn's Disease: 54 Tips to Help You Manage". WebMD. http://www.webmd.com/digestive-disorders/features/crohns-disease-54-tips-to-help-you-manage?ecd=wnl_gid_120607. Retrieved 2008-02-14.
87. **^** Food and Drug Administration (April 22, 2008). [www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116882.htm "FDA Approves Cimzia to Treat Crohn's Disease"]. Press release. www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116882.htm. Retrieved 2009-11-04.
88. **^** Sandborn, W.J.; Colombel, J.F.; Enns, R.; Feagan, B.G.; Hanauer, S.B.; Lawrance, I.C.; Panaccione, R.; Sanders, M.; Schreiber, S.; Targan, S.; Others, (2005). "Natalizumab Induction and Maintenance Therapy for Crohn's Disease". *New England Journal of Medicine* **353** (18): 1912. doi:10.1056/NEJMoa043335. PMID 16267322.
89. **^** Macdonald, JK; Mcdonald, JW (2006). "Natalizumab for induction of remission in Crohn's disease (Cochrane Review)". *The Cochrane Database of Systematic Reviews* **3**: 1465–858. doi:10.1002/14651858.CD006097. PMID 16856112. http://dellboy.update-software.com/abstracts/AB006097.htm. Retrieved 2008-02-15.
90. **^** Longmore, Murray; Ian Wilkinson, Tom Turmezei, Chee Kay Cheung (2007). *Oxford Handbook of Clinicial Medicine, 7th edition*. Oxford University Press. pp. 266–7. ISBN 0-19-856837-1.

91. ^ *Smith JP, Stock H, Bingaman S, Mauger D, Rogosnitzky M, Zagon IS (April 2007). "Low-dose naltrexone therapy improves active Crohn's disease.". *Am J Gastroenterol* **102** (4): 820–8. doi:10.1111/j.1572-0241.2007.01045.x. PMID 17222320.
92. ^ Tresca, AJ (2007-01-12). "Resection Surgery for Crohn's Disease". About.com. http://ibdcrohns.about.com/od/surgeryprocedures/a/resectioncrohns.htm. Retrieved 2008-02-14.
93. ^ Ozuner G, Fazio VW, Lavery IC, Milsom JW, Strong SA (1996). "Reoperative rates for Crohn's disease following strictureplasty. Long-term analysis". *Dis. Colon Rectum* **39** (11): 1199–203. doi:10.1007/BF02055108. PMID 8918424.
94. ^ Short Bowel Syndrome as defined by the National Institute of Diabetes and Digestive and Kidney Diseases
95. ^ Rhodes, M (2006-10-24). "Intestinal transplant for Crohn's disease". revolutionhealth.com. http://www.revolutionhealth.com/conditions/digestive/crohns-disease/surgery/intestinal-transplant. Retrieved 2009-03-22.
96. ^ Croese J, O'neil J, Masson J, *et al.* (2006). "A proof of concept study establishing Necator americanus in Crohn's patients and reservoir donors". *Gut* **55** (1): 136–7. doi:10.1136/gut.2005.079129. PMID 16344586.
97. ^ Caprilli R, Gassull M, Escher J *et al.* (2006). "European evidence based consensus on the diagnosis and management of Crohn's disease: special situations". *Gut* **55 Suppl 1**: i36–58. doi:10.1136/gut.2005.081950c. PMID 16481630.
98. ^ [a] [b] Joos S, Brinkhaus B, Maluche C, *et al.* (2004). "Acupuncture and moxibustion in the treatment of active Crohn's disease: a randomized controlled study". *Digestion* **69** (3): 131–9. doi:10.1159/000078151. PMID 15114043.
99. ^ Feagan BG, Fedorak RN, Irvine EJ, *et al.* (2000). "A comparison of methotrexate with placebo for the maintenance of remission in Crohn's disease. North American Crohn's Study Group Investigators". *N. Engl. J. Med.* **342** (22): 1627–32. doi:10.1056/NEJM200006013422202. PMID 10833208.
100. ^ Ursing B, Alm T, Bárány F, *et al.* (1982). "A comparative study of metronidazole and sulfasalazine for active Crohn's disease: the cooperative Crohn's disease study in Sweden. II. Result". *Gastroenterology* **83** (3): 550–62. PMID 6124474.
101. ^ Cohen LB (2004). "Re: Disappearance of Crohn's ulcers in the terminal ileum after thalidomide therapy. Can J Gastroenterol 2004; 18(2): 101-104". *Can. J. Gastroenterol.* **18** (6): 419; author reply 419. PMID 15230268.
102. ^ Cannabis-based drugs could offer new hope for inflammatory bowel disease patients
103. ^ Saccharomyces boulardii in maintenance treatment of Crohn's disease. Guslandi M, Mezzi G, Sorghi M, Testoni PA. Dig Dis Sci 2000;45:1462-1464.
104. ^ Malchow HA. Crohn's disease and Escherichia coli. A new approach in therapy to maintain remission of colonic Crohn's disease? J Clin Gastroenterol 1997;25:653-658
105. ^ Gerhardt, H; Seifert, F; Buvari, P; Vogelsang, H; Repges, R (2001). "Therapy of active Crohn disease with Boswellia serrata extract H 15". *Zeitschrift fur Gastroenterologie* **39** (1): 11–7. doi:10.1055/s-2001-10708. PMID 11215357.

106. ^ Canavan, C; Abrams, KR; Mayberry, J (2006). "Meta-analysis : colorectal and small bowel cancer risk in patients with Crohn's disease". *Alimentary pharmacology & therapeutics* **23** (8): 1097–104. doi:10.1111/j.1365-2036.2006.02854.x. ISSN 0269-2813. PMID 16611269. http://cat.inist.fr/?aModele=afficheN&cpsidt=17660183. Retrieved 2007-05-23.

107. ^ [a] [b] Hiatt, Robert A.; Leon Kaufman (1988). "Epidemiology of inflammatory bowel disease in a defined northern California population". *Western Journal of Medicine* **149** (5): 541–6. PMID 3250100.

108. ^ Moum, B.; M. H. Vatn, A. Ekbom, E. Aadland, O. Fausa, I. Lygren, N. Stray, J. Sauar, T. Schulz (1996). "Incidence of Crohn's disease in four counties in southeastern Norway, 1990-93. A prospective population-based study. The Inflammatory Bowel South-Eastern Norway (IBSEN) Study Group of Gastroenterologists". *Scandinavian Journal of Gastroenterology* **31** (4): 355–61. doi:10.3109/00365529609006410. PMID 8726303.

109. ^ Shivananda, S.; J. Lennard-Jones, R. Logan, N. Fear, A. Price, L. Carpenter and M. van Blankenstein (1996). "Incidence of inflammatory bowel disease across Europe: is there a difference between north and south? Results of the European Collaborative Study on Inflammatory Bowel Disease (EC-IBD)". *Gut* **39** (5): 690–7. doi:10.1136/gut.39.5.690. PMID 9014768.

110. ^ "Crohn's disease manifests differently in boys and girls". *CCFA.org*. http://www.ccfa.org/reuters/ibdboysgirls.

111. ^ "Who is affected by Crohn's disease". *WebMD.com*. http://www.webmd.com/hw-popup/who-is-affected-by-crohns-disease.

112. ^ Satsangi J, Jewell DP, Bell JI (1997). "The genetics of inflammatory bowel disease". *Gut* **40** (5): 572–4. PMID 9203931. PMC 1027155. http://gut.bmj.com/cgi/pmidlookup?view=long&pmid=9203931.

113. ^ Tysk C, Lindberg E, Järnerot G, Flodérus-Myrhed B (1988). "Ulcerative colitis and Crohn's disease in an unselected population of monozygotic and dizygotic twins. A study of heritability and the influence of smoking". *Gut* **29** (7): 990–6. doi:10.1136/gut.29.7.990. PMID 3396969. PMC 1433769. http://gut.bmj.com/cgi/pmidlookup?view=long&pmid=3396969.

114. ^ Kirsner JB (1988). "Historical aspects of inflammatory bowel disease". *J. Clin. Gastroenterol.* **10** (3): 286–97. doi:10.1097/00004836-198806000-00012. PMID 2980764.

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