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My46 Trait Profile

Crohn's disease

Crohn's disease is a chronic illness characterized by inflammation within the gastrointestinal tract. It is caused by a combination of genetic and environmental factors.

Characteristics of Crohn's disease

Crohn's disease (CD) is a chronic, recurring inflammation of the digestive system. CD is part of a group of complex disorders named Inflammatory Bowel Diseases (IBD). CD commonly affects the lower part of the small intestine (the ileum) and portions of the large intestine (the colon), but it can involve any area of the digestive system, from the mouth to the anus.

The symptoms of CD may vary over time and from person to person depending on which part of the digestive system is involved. The most common symptoms are abdominal pain, diarrhea, fever, and weight loss. Other symptoms may include bleeding, anemia, loss of appetite, and the inability to absorb certain vitamins and nutrients. Other symptoms may include pain in the joints, inflammation of the eyes, and skin lesions. Complications of CD include obstruction or blockage of the intestines, localized infections or collection of pus, fissures or tears in the skin surrounding the anus, and abnormal connections (or fistulas) between the intestine and other organs such as bladder or skin. It is thought that individuals with CD have an increased risk to develop colorectal cancer.

The severity of CD ranges from mild to severe. Individuals with CD generally experience unpredictable peaks of disease activity and remissions (periods of disease inactivity). The region of the digestive system affected by CD seems to remain stable or doesn't change, but the severity of the disease often gets worse over time. Individuals with CD often have multiple hospitalizations and surgeries. The debilitating symptoms of CD can interfere with an individual's ability to work and perform daily activities. Several studies have noted that CD may have a negative impact on the quality of life in individuals with the condition.

Diagnosis/Testing

CD is usually diagnosed in early adult life, but it can occur at any age. About 20% of individuals with CD are diagnosed before their 18th birthday. Childhood-onset is most often associated with a severe disease course. Traditionally, the diagnosis of CD is based on physical examination, disease history, laboratory tests, imaging tests of the entire colon (colonoscopy) or the distal part of the colon (sigmoidoscopy) and radiologic studies (e.g., barium contrast X-rays).

Although the exact cause of CD is unknown, it appears to result from an abnormal immune response to intestinal bacteria (microbes) in genetically susceptible individuals. Genetic, microbial and environmental factors are likely to play a role in CD. Changes or variants in more than 30 genetic regions are thought to affect CD risk. In individuals with CD, certain genetic changes may help predict the severity of the disease. For example, three variants in the NOD2 gene may predict an increased risk for surgery or complicated disease in individuals with CD. Having one variant increases the risk for complicated disease course by 8%, and having two variants by 41%. Any NOD2 variant increases the risk of surgery by 58%. Knowing the genetic make-up in individuals could help to predict severity of the disease, response to treatment, and identify unaffected family members at risk of developing CD.

Females may be slightly more predisposed to developing CD than males. CD is seen in all ethnic groups, but it has an increased frequency in European Americans and individuals of Ashkenazi Jewish descent. In the last several decades,

the incidence of CD has been on the rise in countries with historically low rates of the disease, particularly South Asia.

Management/Surveillance

CD can be treated and controlled by medication and surgery. Currently, there is no cure for CD. The traditional treatment includes anti-inflammatory medications, steroids, antibiotics, and immune modulators. Some individuals with CD do not respond to treatment or develop resistance to treatment. About 50% of individuals with CD require surgery during the first 10 years after diagnosis.

The strongest environmental risk factor is smoking. Cigarette smoking is thought to increase the risk of developing CD, as well as increase disease activity and likelihood for complications. Individuals with CD should be encouraged to quit smoking. Other environmental factors include breastfeeding, diet, living in an industrialized nation, domestic hygiene, microbial intestinal infections, and stress. Other lifestyle factors such as high intake of total fat, dairy products and meat are also associated with an increased risk to develop CD; high fiber and fruit intake seems to reduce the risk. High levels of stress, lack of sleep, depression and anxiety are associated with an increase in disease activity. Moderate exercise is typically encouraged to improve quality of life and emotional health.

Mode of inheritance

CD is considered to be a complex disease, which means that it is caused by a combination of many different factors. These factors can be genetic or non-genetic (such as environmental factors and lifestyle choices such as smoking). Complex conditions are inherited in a multifactorial pattern. This means that the chance for an individual to develop CD is influenced by the number and type of genetic and non-genetic factors that occur tougher to which an individual is exposed. In other words, no single gene, and no single environmental factor cause CD. However, not all of these genetic factors and environmental factors are known.

Risk to family members

Although there is no clear pattern of inheritance, CD tends to run in families. Studies have reported that 15% of individuals with CD have an affected family member (parents, child, or sibling) with IBD.

The prevalence of CD in the general population is less than 0.5%. However, the chance of developing CD in an individual who has an affected family member is about 5-15%. Three variants in the NOD2 gene are one the strongest genetic risk factors for CD, but they are neither sufficient nor necessary to develop the disease. About 40% of individuals with CD carry at least one copy of these variants.

Special considerations

None

Resources

Crohn’s and Colitis Foundation of America
http://www.ccfa.org/
Genetics Home Reference: Crohn’s disease
http://ghr.nlm.nih.gov/condition/crohn-disease

References

Dam, AN. et al. (2013).Environmental influences on the onset and clinical course of Crohn's disease-part 1: an overview of external risk factors.” Gastroenterology and Hepatolology 9(11): 711-717.
Erazo, ML. et al. (2012).Evaluation of 22 genetic variants with Crohn's disease risk in the Ashkenazi Jewish population and its implications for genetic counseling.” Mount Sinai School of Medicine.
Hedin, CR. et al. (2012).“Family studies in Crohn's disease: new horizons in understanding disease pathogenesis, risk and prevention.” Gut 61(2): 311-318.
Jostins, L. et al. (2012).Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease.” Nature 491(7422): 119-124.
Sorrentino, D. et al. (2014).Tissue Studies in Screened First-degree Relatives Reveal a Distinct Crohn's Disease Phenotype.” Inflammatory Bowel Diseases 2014 Apr 30. [Epub ahead of print]

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