



Crohn's disease and ulcerative colitis (UC) are described as complex or multifactorial diseases in which a number of factors are thought to contribute to the development of the disease. These include both genetic and environmental influences. There is no single explanation for why one person is affected and another is not. Understanding the causes of these diseases is a major area of research for doctors and scientists. It is generally accepted that the diseases develop due to an abnormal response of the immune system to bacteria in the gut in genetically susceptible individuals exposed to environmental triggers.

The immune system is the mechanism by which the body defends itself against foreign invaders. In early life, the body learns how to recognise its own cells and molecules and tell these apart from foreign ones. This system enables the body to rapidly identify and destroy foreign cells and molecules when they enter the body, to prevent infection. The gastrointestinal tract is in contact with very large numbers of bacteria, viruses and fungi (the gut flora or microbiome). The majority of the gut flora is in the large bowel and exist without causing any problems. Indeed, it beneficially contributes to digestion and preventing the growth of dangerous bacteria. It is thought that in patients with Crohn's or UC, the interaction between the normal healthy gut flora and the body's immune system is abnormal. Either the immune system inadequately responds to bacteria entering through the bowel wall or it becomes overactive, the result of both of these responses, being inappropriate inflammation.

It has been recognised for many years that both Crohn's and UC sometimes occur in multiple individuals in the same family, suggesting a possible shared genetic cause. The role of genetics in a complex disease like Crohn's and UC can be investigated by studying identical and non-identical twins. In about 15-30% of identical twins with Crohn's or UC, both twins will be affected as compared with about 5% of non-identical twins. The fact that the disease is more common in both twins when they are identical confirms there is a genetic basis but in most cases only one twin will be affected demonstrating that additional non-genetic factors are required. Inside

each of our cells in our body, is a substance called DNA which acts as a code book telling our cells how to construct themselves and behave. The exact lettering of this code book differs between individuals and this partly explains why people look and behave differently. The code book is passed from parents to children, with some changes. Studies have shown that there are a number of genetic variants (changes to the lettering of the code book) that are more common in patients with Crohn's or UC than those without. The way in which these changes work to make the diseases more likely is still under investigation but many are thought to influence the behaviour of the immune system. The majority of these changes only increase the risk of disease by a small amount and it is not possible to predict on the basis of these changes who will and who will not develop the disease.

In addition to inherited genetic factors, exposure to certain environmental risk factors have been shown to alter the risk of developing Crohn's or UC. Both diseases are more common in countries in the Western world as compared with developing countries; it is thought that increased hygiene and the modern diet may be responsible for this. One of the most strongly characterised risk factors is cigarette smoking which increases the risk and severity of Crohn's but unusually decreases the risk of UC. Having your appendix removed is associated with a decreased risk of developing UC. Use of antibiotics early in life has been associated with an increased risk of Crohn's. For all

of these risk factors, the mechanism by which they act to alter disease risk and how they combine with each other, as well as the genetic factors remains poorly understood.

The causes of Crohn's and UC are multifactorial and complex. Developing knowledge of the contributing factors is necessary to understand the mechanisms by which the diseases develop to permit new treatment strategies to be devised. Over the last few decades there have been significant advancements in this field but much research is still required for the causes of these diseases to be definitively established.

This article is for information only and should not be used in place of seeing a medical professional. If you have any questions regarding your own health, please see your doctor. This article has been written by Dr Adam Levine MBBS, PhD (doctor and researcher) and Dr Elena Schiff PhD (geneticist and researcher) at University College London

“ What are the causes of Crohn's disease and ulcerative colitis? ”



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02035196515



info@theccr.co.uk

