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Link shown between Crohn's disease and virus

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A new study reveals that all children with Crohn's disease that were examined had a commonly occurring virus – an enterovirus – in their intestines. This link has previously not been shown for this chronic inflammatory intestinal disorder. The findings are being published today in the latest issue of the international journal *Clinical and Translational Gastroenterology*.

These findings need to be confirmed in larger studies, but they are important, as this connection has never been pointed out before. This paves the way for a better understanding of what might be involved in causing the disease, says Alkwin Wanders, one of the scientists behind the study at Uppsala University and Uppsala University Hospital.

In Sweden several thousand adults live with Crohn's disease, and each year about 100 children and adolescents develop the disorder. The disease affects various parts of the gastrointestinal system and causes symptoms such as stomach aches, diarrhoea, and weight loss – in severe cases fistulas, or strictures in the intestines.

The cause of Crohn's disease is not known. Mutations in more than 140 genes have been shown to be associated with the disorder, but this genetic connection is not a sufficient explanation. Many of these genes play key roles in the immune defence, which has prompted theories that the disease might be caused by impaired immune defence against various microorganisms. In that case, the disease would be a consequence of interplay between heredity and environment.

Recent research has shown that some of the genes that are strongly linked to the disorder are important for the immune defence against a certain type of viruses that have their genetic material in the form of RNA, so-called RNA viruses. Using this as a point of departure, an interdisciplinary research team was established in Sweden to investigate what role this type of virus plays in the disease.

The research team includes the paediatrician Niklas Nyström, the pathologist Alkwin Wanders, virus researchers Gun Frisk and Oskar Skog, the molecular biologist Mats Nilsson, and the geneticist Ulf Gyllensten at Uppsala University and Uppsala University Hospital, along with cell biologists Jonas Fuxe and Tove Berg the paediatrician Yigael Finkel at Karolinska Institutet in Stockholm.

This unique composition, with complementary clinical and scientific expertise, has been extremely fruitful for our studies, says Alkwin Wanders.

In the present study the researchers investigated whether the RNA virus were present in children with Crohn´s disease. They focused in particular on the prevalence of enteroviruses, a group of RNA viruses that are known to infect the intestinal mucous lining.

The results showed significant amounts of enteroviruses in the intestines of all of the children with Crohn´s disease, whereas the control group had no or only minimal amounts of enteroviruses in their intestines. Similar results were obtained using two different methods. Enteroviruses were found not only in intestinal mucous linings but also in so-called nerve cell ganglia in deeper segments of the intestinal wall. Receptors for a group of enteroviruses were also found in both the intestinal mucous linings and nerve cell ganglia, which may explain how the virus can make its way into the nerve system in the intestine.

Another interesting finding is that the enterovirus could be thought to be stored in nerve cells in the intestine and to spread to different parts of the intestine via nerve fibres. This would explain both the fact that the disease is periodic (comes and goes) and the fact that it often affects multiple segments of the intestines, says Alkwin Wanders.

The present study comprises nine children with advanced Crohn's disease and fifteen children with incipient Crohn's disease symptoms. The research now wants to go on to examine larger groups of patients and more control individuals. They also want to pursue experimental research to investigate the link further.

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