

What is Inflammatory Bowel Disease?

Inflammatory Bowel Disease (IBD) is a chronic (ongoing) illness in which the wall of the bowel becomes swollen, inflamed and ulcerated. Symptoms can include severe pain in the abdomen, weight loss, diarrhoea (sometimes with blood or mucus) and continuing tiredness and lack of energy. Some people with IBD also have swollen joints, inflamed eyes or skin rashes.

The two most common forms of IBD are Crohn's Disease and Ulcerative Colitis (UC). About 180,000 people in the UK have been diagnosed as having IBD. The illness can affect people of all ages, but most often starts between the ages of 10 and 40.

There is no cure for Crohn's and UC at present and most people with IBD experience occasional and unpredictable flare-ups of the symptoms with periods of better health in between. Treatment with drugs or surgery will usually control or reduce most of the symptoms, but many find that their general well-being and daily activities are affected to some extent, even when the disease is not active.

Research into the cause of IBD

It is not known what causes Crohn's Disease and Ulcerative Colitis. Recent research has identified particular genes which are more often found in people who have Crohn's or UC and it is clear that some families are more likely to suffer from IBD than others. While for the general population 1 in 400 people might have one of the diseases, there is a chance of about 1 in 50 that someone will develop IBD if they have a close relative who has the condition. This is usually described as a genetic or family

predisposition to the illness, but there still needs to be some other cause to trigger the illness.

At different times, research has focused on viruses, deficiencies in the body's immune system, hereditary factors, mycobacteria in water or milk, diet and lifestyle. In the 1940s and 50s stress was sometimes thought to be a primary cause of IBD. It is now accepted as a factor which may make symptoms worse, rather than cause the illness.

Current ideas about the causes of IBD are mainly focusing on the immune response to intestinal bacteria combined with predisposing genetic factors. Having particular genes make some individuals susceptible to reacting with their own bacteria, normally found in the gut, which could explain why only a few people develop the disease and why there is an increased risk in close relatives who will obviously share some of the genes.

The evidence for measles virus as a possible cause of IBD

From 1990 researchers considered the measles virus as one of the possible triggers for IBD and more particularly for Crohn's Disease. Surveys in Sweden suggested that children who were born at times of measles epidemics, and who were likely to have been exposed to measles virus close to the time of their birth, seemed to have a greater likelihood of developing Crohn's. Another Swedish study looked at the medical records of 25,000 women who gave birth between 1940 and 1949. Four women had measles whilst they were pregnant and three of the children who were subsequently born developed Crohn's Disease in their teens. However, similar

UK studies did not show the same pattern.

In the laboratory, using a number of different techniques, researchers at the Royal Free Hospital, London, identified certain virus particles in the areas of the bowel damaged by Crohn's Disease which they believed to be evidence of measles virus. It is known that measles virus can persist inside the body long after the actual measles infection and this has been shown to cause one or two other very rare illnesses. The Royal Free researchers suggested that the measles virus damages the blood vessels supplying the intestine and that this is then causing the damage and symptoms which we call Crohn's Disease. However, just finding measles-like particles in areas of the bowel affected by Crohn's Disease does not by itself prove that the virus must therefore have a role in causing the Crohn's.

It is important to seek independent confirmation of research and other researchers have tried to confirm the Swedish and Royal Free work. Two other surveys looked at whether children developed Crohn's Disease if their mother was exposed to measles during pregnancy. A UK survey (Lancet 1997) and a Danish one (British Medical Journal, 1998) both found no increased risk of developing Crohn's in these children. In laboratory work, a Japanese research team failed to find evidence of measles virus in their laboratory tests, but an Italian one did report doing so. This illustrates the fact that these types of laboratory techniques are very complex and sensitive, so that there is often debate about whose results are acceptable and whose are not. However, three separate groups of researchers reported over the following three years that they could not find measles virus genetic material in tissue affected by Crohn's Disease or by Ulcerative Colitis.

The evidence for measles vaccination or the MMR vaccination as a possible cause of IBD

Immunisation is the process of increasing the body's ability to resist infection. This is done by adding a vaccine (consisting of dead or weakened bacteria or viruses) to the human body, which stimulates the person's own protective antibodies (and in turn protects against future attacks by the relevant disease).

The vaccine used to immunise children against measles is a weaker form of the live measles virus. The researchers who were looking at whether measles virus itself could be causing Crohn's Disease, also looked at the possibility of the vaccine having the same effect. They undertook an epidemiological survey to compare how many people seemed to have Inflammatory Bowel Disease among three different groups. The three groups were (a) people vaccinated for measles in 1964, (b) people born several years earlier who were probably not vaccinated for measles and (c) partners of the vaccinated people.

The results of their questionnaires were published in The Lancet in 1995 and suggested that the rate of Crohn's Disease and Ulcerative Colitis among those who were vaccinated in 1964 was almost three times higher than among the unvaccinated group, and almost twice as high as in the partner group. These results have been treated with caution because the information collected had significant limitations. It was also surprising that the survey found higher levels of UC as well as Crohn's, although laboratory research had not shown evidence of measles virus particles being present in areas of the bowel damaged by Ulcerative Colitis. The research therefore suggested a possible link, but did not prove either that measles itself causes IBD or that vaccination against measles does so.

A paper published in the Lancet in September 1997 reported research from East Dorset. They looked at the records of 140 patients with IBD who were born in or after 1968, the year in which the measles vaccination was introduced. They were compared to 280 patients who matched them in age, sex and GP, but who did not have IBD. They found no evidence to support the idea that measles vaccination in childhood seems likely to lead to the development of Crohn's or UC at a later date.

The measles vaccine is usually given in combination with the vaccines for mumps and rubella. This is called the MMR vaccine. Subsequent to research at the Royal Free Hospital in the late nineties, there was media coverage of some children who were reported to have developed autistic behaviour followed by the symptoms of Crohn's Disease after receiving the MMR vaccine. This research published in the Lancet medical journal on 28th February 1998 stated that there was no proof of a link between the MMR and the children's symptoms and medical history, but this was not how much of the media reported the findings. Most doctors have not been convinced by this publication that there is any link between the MMR vaccination and the children's autism and subsequent gastrointestinal symptoms.

In May 1998, in another paper in the Lancet, researchers from Finland reported finding no evidence for Inflammatory Bowel Disease or autism associated with MMR vaccine over a 14 year period in which all children were vaccinated at age 14-18 months and again at 6 years old.

Summary of the current research position

Since the publication some years ago of the Swedish and UK surveys suggesting a link between measles virus and Crohn's and between measles vaccination and Crohn's, most of the published research from other researchers in the UK and

from other countries has not found evidence of any such link. It is a similar case with the laboratory research; the most recent research does not support measles virus as causing Crohn's or UC.

On 23rd March 1998, the UK Medical Research Council arranged a meeting of about 50 experts from relevant areas of expertise in vaccinations, gastroenterology and child health to review all the evidence currently available and to express an opinion about whether they felt there was a case for measles virus and the MMR vaccination causing either Crohn's or the reported symptoms of autism. The conclusions of the expert group, as reported in a Press Release by the Department of Health, were that:

- The available virological and epidemiological evidence does not support a causal role for persistent measles infection in Crohn's Disease.
- There is no evidence to indicate any link between MMR vaccination and bowel disease or autism.
- There is therefore no reason for a change in the current MMR vaccination policy.

However, in view of the ongoing controversy over the MMR vaccination, the Scottish Executive agreed to set up an Expert Group on MMR in August 2001 to review the evidence and to look into the consequences of pursuing an alternative policy to MMR. It considered five possible alternatives:

- No immunisation
- Compulsory immunisation
- Deferral of MMR
- A choice between either MMR or single vaccines
- Single vaccines

The Group found that these options could not be supported on the basis of the available scientific evidence and consequently no change was made to their current vaccination policy. These findings were published on 30th April

2002, together with a number of recommendations, which included that the Scottish Executive and the Medical Research Council should work together to drive forward and fund, as appropriate, epidemiological research into Inflammatory Bowel Disease in children. The full report can be viewed at www.show.scot.nhs.uk/mmrexpertgroup/.

In 2005 a study published in the British Medical Journal analysed hospital admissions of children and adolescents with Crohn's over a 12 year period from 1991 to 2002. They compared those born before and after the introduction of the MMR vaccine and found there was no increased risk of Crohn's from the vaccine.

Further evidence against a link between measles virus and IBD has been found in two Canadian studies published in 2007. The laboratory tests in the first used more refined and sensitive techniques than the studies that had found a link. In the second investigation, 235 people with Crohn's and 137 with UC were studied. Significantly fewer with Crohn's and UC had the measles virus compared with those without IBD. This might suggest that having measles may even have some protective effect against getting IBD. However, this was a relatively small study and further research is needed.

Why does the Department of Health believe that the MMR vaccination programme is essential?

Measles can be a serious illness for young children and a small number of those who catch measles will develop serious complications and a few may die. Mumps and rubella can also have serious long-term consequences for a proportion of children. The Department of Health believes that the MMR programme of vaccinating children at a young age and again at school is a highly effective way of ensuring that the majority of children have immunity against these infections.

NACC's national Medical Advisers regularly review the current published research findings and express their views to the Association's Trustees. NACC's present view is that the Government programme for vaccinating young children against measles, mumps and rubella and for the re-vaccination of older children is a sensible policy to reduce the possibility of an epidemic of any of these infections.

Special considerations for people who have a close relative who has Crohn's Disease or Ulcerative Colitis

Research has shown that some families have a greater likelihood of Inflammatory Bowel Disease than others. If your child has a close member of the family who has Crohn's or UC - a parent, brother or sister - you will probably be particularly concerned by the research hypothesis that measles virus could cause IBD and may wish to seek advice on whether it is right for your child to have the MMR vaccination or booster. NACC cannot give specific individual advice on this point. We can say that the balance of research and expert opinion at present suggests that measles virus, measles vaccination and the MMR combined vaccine do not cause either Crohn's or Ulcerative Colitis, whereas the serious effects of measles that can sometimes occur are a known risk. So far as we are aware, there are no published research findings which indicate that the situation might be any different for people who have a family history of IBD. The Department of Health recommends the two doses of MMR for children even if they have a close relative who has Crohn's or UC.

Some people have suggested trying to obtain the mumps and rubella vaccines separately and not having (or postponing) the measles vaccination. The Department of Health advise against this practice because they believe it unnecessarily leaves a child vulnerable to one or more of the three infections. If you

decide that this is an approach that you prefer, you will need to get the agreement of your GP to try and obtain the vaccines separately. This may be difficult and there may be some supply difficulties.

Some people have asked whether a blood test can be taken before their child is due to have the MMR booster to determine whether they already have immunity to the infections. Again this is a matter for your GP, but we have been advised by the Department of Health that such a test is not 100% reliable.

Further help

If you have any further queries, please contact the **NACC Information Line: 0845 130 2233.**

© **NACC February 2008**

This document has been prepared by NACC as general information on the subject and is not intended to replace specific advice about your treatment from your own doctor.

The National Association for Colitis and Crohn's Disease (NACC) is a voluntary Association, established in 1979, which has 30,000 members and 70 Groups throughout the United Kingdom. The Association also provides a supportive listening service called NACC-in-Contact which is available to anyone affected by Inflammatory Bowel Disease.

Membership of the Association costs £12 for the first year and £10 subsequently. Additional donations to help the work of the Association are always welcomed.