

Giving hope to CD sufferers

Dr Maria Luisa Mearin, of PreventCD, the project to prevent Coeliac Disease (CD), describes how research into Coeliac Disease is moving from treatment to prevention in Europe



Can you explain a little about the background of your project, its aim and where the concept came from?

The PreventCD project started in January 2007 and it is aimed at reducing the number of people suffering from coeliac disease (CD) in Europe. This is a disorder caused by hypersensitivity to gluten, and it is thought to affect approximately 2.5 million Europeans. We think it is preventable by improving the feeding patterns in infants. Hopefully, this will lead to the development of new European guidelines for early nutrition.

In the 1980s, new advice was given to parents in Sweden about early feeding in young infants; including introduction of gluten not before six months of age. At the same time additional gluten was added to the formula feeding for children from age six months. After that, there was an epidemic of CD in Sweden, which strongly suggested a link between CD and patterns of feeding. The data from the epidemic suggest that introducing small amounts of gluten into the diet during the breast-feeding period may prevent the disease. Therefore, studies in Sweden have become an important part to this project.

PreventCD is divided into two areas: the population study, which is performed in Sweden, and the family study.

Can you tell us more about the family study?

This part of the project includes more than 1,000 children at high risk for developing CD from eight European countries. Since the data from the epidemic in Sweden indicates that half of the CD cases might have been avoided if all of the infants had been introduced to gluten in small amounts while still being breast-fed, we perform a food intervention study to induce tolerance for gluten in these children with high risk for coeliac disease.

How does the population study work?

This study is part of the ETICS study – Exploring the Iceberg of Coeliacs in Sweden. Paediatric departments in six different areas of the country collaborate with schools and the health services. The study invites all children, born during the CD epidemic (1993) and post-epidemic (1997) periods, when they reach 12 years of age. All sixth grade 12 years old children are invited by letter to take part and those who accept have their weight and height measured, fill in questionnaires and blood samples are taken. These samples are stored and analysed for serological markers indicative of CD. Children with suspected CD are referred to a paediatric department for a diagnostic small intestinal biopsy, and thereafter followup according to a standardised protocol.

Approximately 10,000 children were invited to participate in 2005-2006, and 10,000 children born in 1997 will be invited to participate in the study in 2009-2010.

Have you had any results from the studies so far?

Well, it seems that early feeding habits do have an influence on the development of CD. Not only in infancy but also in pre-puberty. The first part of the population study has shown that the children born during the Swedish epidemic of CD also have the highest incidence of CD in Europe at the age of 12 years (three per cent).

Under-diagnosis seems to be a particular problem with CD. How have you approached this?

The population study approaches this by mass screening of CD in children 12 years of age. The study also explores the opinion of the parents and children about mass screening and also around early diagnosis of CD as a form of secondary prevention.

Is there a case for mass screening for CD?

Personally, I would say yes, but we need follow-up studies to assess the long term health gain obtained by screening. What is happening in Sweden is also very important, taking the opportunity to study what is the effect of the screening in the population: What do the children think? What do the parents think?

At what stage is the project now?

In April 2009, the second Annual Progress report was submitted. The project was well received and the reviewers found its progress satisfying and, in many cases, it actually exceeded expectations. We have delivered our planned milestones on schedule and more than 1,000 infants have been recruited for the family intervention study.

We feel this project is already providing vital information for combined epidemiological, genetic and immunological studies. In the project we are trying to prevent CD, but we are also trying to understand how it works. Among the reviewers the effective collaboration between the genetics and immunology leaders was considered a strong feature of PreventCD.



RESEARCH GROUP OF PREVENTCD. PICTURE TAKEN DURING THE 4TH PROGRESS MEETING, JUNE 17-18 2009. UMEÅ, SWEDEN

Studies look for new pathways into prevention of Coeliac Disease



Coeliac disease affects many people and the health burden it imposes is huge. But, according to researchers in the PreventCD project, the road to successful prevention starts at infancy

CONTRARY TO POPULAR opinion, Coeliac Disease (CD) is not a rare food intolerance affecting the small bowel, which is easily explained and just as easily treated. CD is actually a frequent auto-immune disease in which the body's immune system attacks its own tissues in different organs. CD is triggered by gluten, a common name for proteins found in wheat, rye and barley. It is estimated that some 2.5 million people in Europe suffer from CD and yet, only a fraction of these individuals are recognised and properly diagnosed.

The consequences of the high prevalence of CD and its apparent failure to be diagnosed in significant numbers are serious. People with CD have a 20 per cent increased risk of acquiring other autoimmune diseases, which lengthens if the condition remains undiagnosed, and untreated CD may also increase the risk of developing certain types of cancer.

The treatment is a strict, long-life gluten-free diet, that is both expensive and difficult

to follow, with a considerable burden on the individual and family life.

In order to develop prevention strategies, the European Union-funded FP6 project PreventCD is now studying the hypothesis that it is possible to induce gluten tolerance in children genetically predisposed to CD by introducing small quantities of gluten during the breastfeeding period.

A meta-analysis study on research carried out between 1966 and 2004 on breast-feeding and CD has shown that breast-feeding is associated with a reduced risk of developing the disease in childhood. In addition – and very importantly for the PreventCD project – in the mid 1980s to mid 1990s, Sweden experienced nothing less than an epidemic of CD, without comparison in the rest of the world. This has been attributed to changes in feeding advice to Swedish mothers to introduce gluten after the age of six months. At the same time additional gluten was added to the formula feeding for children from age six months. After

re-introduction of the traditional early feeding practices in the mid 1990s the Swedish epidemic of CD disappeared. This 'experiment in nature' has had a positive outcome since Sweden now has birth cohorts that differ with respect to infant feeding practices. These birth cohorts provide researchers with an opportunity to increase the understanding of CD, and to hopefully take steps to prevent its occurrence.

To do this, PreventCD (which comprises 17 partners from across Europe, including researchers in the Netherlands, Italy, Sweden, Poland, Spain, Germany, Norway, Croatia, Hungary, Belgium and Israel) has been working on two distinct strands of research; a family study conducted across Europe and a population study that focuses on Swedish children born during and after the CD epidemic years.

The family study is being held in eight European countries and involves more than 1,000 children from families with a high risk for CD. The children are being followed up for three

PREVENTCD

Influence of the dietary history in the prevention of Coeliac Disease: possibilities of induction of tolerance for gluten in genetic predisposed children

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Luisa Mearin has coordinated several national and international collaborative studies on coeliac disease, among them EU funded projects, the 'European multicentre study on coeliac disease and non-Hodgkin lymphoma', performed in 10 European countries (*Biomed 2 Programme 1996*; BMH4-CT98-3091; DG 12-SSMI) and 'the European platform for research on prevention and treatment of coeliac disease: a multidisciplinary approach to integrate basic scientific knowledge in clinical applications and food industry' (*CDEUSSA*; FP6 - contract FOOD-ct-2005-517787) (2005-2007). This last project has formed a European platform for research on prevention and treatment of coeliac disease with a multidisciplinary approach and has developed evidence based advice for the EU over the aspects of coeliac disease that should be topics of research.

years to track the influence of the dietary history on the possible development of CD. The infants start receiving very small amounts of gluten or placebo when they turn four months.

The mothers are encouraged to breast-feed their infants during the intervention period, which lasts for two months. The theory is that if small amounts of food substances are gradually administered, the immune system 'learns' not to respond to this substance. This is also called 'induction of tolerance'.

The population study, which is part of the Swedish study called ETICS (Exploring the Iceberg of Coeliacs in Sweden), began in 2005 with the invitation for 10,000 children aged 12 years born during the CD epidemic to come forward to be screened for CD. Seventy-five per cent of those invited agreed to participate, and between 2009-2010 another 10,000 children aged 12 years born after the CD epidemic have been invited to take part. The first screening effort revealed the highest prevalence of CD in Europe: three per 100 - with two-thirds of cases undiagnosed prior to the study. These findings indicate that early feeding habits do indeed have an influence on the development of CD, not only in infancy but also at pre-puberty.

The leader of the Swedish research team, Anneli Ivarsson, has suggested, based on an estimate of the attributable fraction, that half of the CD cases during the Swedish epidemic might have been avoided if all infants had been introduced to gluten in small amounts while still being breast-fed. This finding opens the way to possible prevention strategies. However, there is still not enough evidence-based knowledge in this area, thus methodologically correct clinical trials are needed. The results of the PreventCD study, which has been planned especially to address the possibility of reducing the risk of developing CD, shall provide us with such knowledge and possibly with the development of new guidelines for early infant nutrition.

If the hypothesis regarding breast-feeding and the introduction of gluten at an early age is correct, the outcome of the PreventCD project might have a significant impact upon infant feeding advice currently given to mothers across Europe and, in particular, to mothers from high-risk families for CD. In addition, the studies on gluten content in breast-feeding samples from mothers from high-risk families from different countries with children with different feeding practices will offer useful information to the European food industry in its effort to develop food for health.

