New study of human pancreases links virus to cause of type 1 diabetes

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A team of researchers from the Peninsula Medical School in the South West of England, the University of Brighton and the Department of Pathology at Glasgow Royal Infirmary, has found that a common family of viruses (enteroviruses) may play an important role in triggering the development of diabetes, particularly in children. These viruses usually cause symptoms similar to the common cold, or vomiting and diarrhoea. However, the team has now provided clear evidence that they are also found frequently in the pancreas of people who develop diabetes.

The research, which was carried out at Peninsula Medical School and funded by Juvenile Diabetes Research Foundation (JDRF), is published today, 6th March 2009, in the leading European diabetes journal, *Diabetologia*. It involved the detailed study of a unique collection of pancreases from 72 young people who died less than a year after the diagnosis of type 1 diabetes.

Type 1 diabetes usually starts in young people and results from the destruction of the insulin-producing beta cells in the pancreas. Patients who develop type 1 diabetes have to take multiple daily injections of insulin for the rest of their lives, and the condition affects around 300,000 people in the UK , including 20,000 children under the age of 15. There are a further estimated 440,000 cases of type 1 diabetes in children worldwide, with more than a fifth living in Europe.

It is accepted that children who develop type 1 diabetes inherit a genetic susceptibility to the disease, but studies of identical twins have shown

that when one twin has the disease, the other twin will only have approximately a 40 per cent chance of developing diabetes - suggesting that factors additional to inheritance are also involved.

It has long been speculated that viruses might play a role in causing type 1 diabetes by infecting the beta cells of the pancreas. This new research, which has made use of unique source material collected in Glasgow, is the first to provide evidence supporting this theory in such a large number of pancreases from young people recently diagnosed with the disease. It has revealed that more than 60 per cent of the organs contained evidence of enteroviral infection of the beta cells. By contrast, infected beta cells were hardly ever seen in tissue samples from 50 children without the condition.

The new research suggests that enteroviral infection of the beta cells in children with a genetic disposition to type 1 diabetes may initiate a process whereby the body's immune system identifies beta cells as 'foreign' and rejects them, as it would a transplanted organ.

An extension of the study to adults with type 2 diabetes showed that a large proportion (40 per cent) of these patients also had enteroviral infection in their beta cells. This compared with only 13 percent of non-diabetic adults of the same age group. Unlike type 1 diabetes, type 2 diabetes usually starts in adults and is associated with obesity. The beta cells are not destroyed in this disease but their ability to make insulin is compromised. The way that enteroviruses might contribute to the development of type 2 diabetes has not been established but it is known from laboratory studies that an enteroviral infection of beta cells reduces their ability to release insulin. It is possible that in people who are obese (where there is a greatly increased demand for insulin secretion) a reduction of beta cell function, secondary to enteroviral infection, may be sufficient to trigger type 2 diabetes - although more research is required to confirm this.

Overall, the findings of this new study suggest that vaccination in childhood to prevent enteroviral infections of beta cells might be an attractive means to reduce the incidence of both common forms of diabetes. However, there are up to 100 different strains of enterovirus and more research will be needed to identify which particular enteroviruses are associated with the development of diabetes, and whether vaccines could be developed to prevent their spread.

Professor Noel Morgan from the Peninsula Medical School commented: "We are genuinely excited by the findings of our study. This is the first time that scientists have been able to provide such extensive evidence for the relationship between enteroviral infection of the beta cells and the development of type 1 diabetes. This is due in large part to the unique availability of such a large number of pancreases from young people who had died of type 1 diabetes soon after becoming ill. Not only did this give us access to extremely important research material, but it also underlines the importance of continued organ donation to the development of medical research in the UK. "

He added: "The next stages of research - to identify which enteroviruses are involved, how the beta-cells are changed by infection and the ultimate goal to develop an effective vaccine - will lead to findings which we hope will drastically reduce the number of people around the world who develop type 1 diabetes, and potentially type 2 diabetes as well."

Professor Adrian Bone from the University of Brighton said: "It is a real privilege to be part of this work which sheds light on how targeted beta-cell destruction may be triggered in individuals at risk of developing diabetes. Whilst experimental studies from many laboratories, including my own, have been able to document the "natural history" of the disease processes culminating in overt diabetes, the role of viral infections in initiating these events is still unproven and controversial.

"Indeed," he added, "viruses have been shown to be capable of both inducing and preventing the development of diabetes. The true importance of our present study lies in the translation of these earlier experimental findings into meaningful observations in children and young people with diabetes."

Pathologist, Dr Alan Foulis of the Royal Infirmary in Glasgow, observed: "It is 25 years since I started assembling this collection of pancreases from patients with recent onset type 1 diabetes, with the express purpose of looking for the presence of enterovirus. It is only very recently that techniques of sufficient sensitivity to detect the virus in such specimens have been developed. The success of this study is largely down to the excellent scientific collaboration we have enjoyed".

Karen Addington, Chief Executive of JDRF, said: "Type 1 diabetes is a life- threatening condition that requires a life-time of painful finger prick blood testing and insulin injections. Incidences are increasing by four per cent each year and there is currently no way to prevent it. We are proud to have funded this crucial piece of research, which helps shed light on the causes of this serious condition. JDRF passionately believes that research such as this brings us a step closer to improving treatment and eventually curing this condition."

Source: The Peninsula College of Medicine and Dentistry