Society for Endocrinology media release

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Type 1 diabetes may be linked to infectious disease burden

Countries with lower mortality from infectious disease exhibit higher rates of type 1 diabetes, according to a new study by Dr. A. Abela and Professor S. Fava of the University of Malta. The findings, collating data from three major international studies and presented at the Society for Endocrinology annual conference in Harrogate UK, suggest that the as yet unexplained global rise in type 1 diabetes may be linked to reduced exposure to pathogens in early life.

Type 1 diabetes is caused when the immune system destroys the cells of the pancreas that release insulin, leaving the patient unable to control his own blood sugar. It is estimated to affect around half a million children worldwide, increasing in incidence by an estimated 3% every year. This increase is well documented and is linked to the developed world, but is so far unexplained – various theories put forward include the 'hygiene hypothesis', which suggests that encounters between the developing immune system and micro-organisms such as bacteria and parasites are part of human evolution and may therefore protect against the development of auto-immunity.

The researchers investigated whether markers of infectious disease burden could be linked to the local incidence of type 1 diabetes. They used data from the World Health Organisation (WHO) DiaMond Project, WHO global burden of disease: 2004 update, and the Alexander Project, to correlate type 1 diabetes incidence by country with mortality from infectious disease and bacterial antibiotic susceptibility (which indicates antibiotic use and thus exposure to bacterial infection).

Type 1 diabetes rates were highest in countries with low mortality from infectious disease. This was true for total mortality from infectious disease ($r=-0.35$, $p=0.008$), as well as deaths caused specifically by diarrhoea, respiratory disease, tuberculosis, and infections and parasitic disease (all $p<0.05$). They also found type 1 diabetes rates are significantly associated with the local susceptibility of the bacteria *Streptococcus pneumoniae* to all antibiotics studied.

This study suggests that there may be an association between type 1 diabetes rates and infectious disease burden. It is possible that the increasing global incidence of type 1 diabetes may be linked to lack of exposure to pathogens during early life. Whilst the data provide support for the hygiene hypothesis it does not prove it: the rise in type 1 diabetes rates is a complex problem and this study is of association only. Other potential contributing factors may show a similar geographical variation to infectious disease burden, as this is linked to the developed world. The authors are keen to use further studies to identify other environmental factors which may predispose to type 1 diabetes.

Study leader Professor Stephen Fava, Consultant in Diabetes and Endocrinology at Mater Dei Hospital, Malta & Associate Professor of Medicine at the University of Malta, said:

"*The global rise in type 1 diabetes is an unexplained phenomenon. Many suggest that the exposure, or rather the lack of exposure, to infectious disease when young might be linked to the development of autoimmunity.*

"Our data show that type 1 diabetes rates were highest in countries where markers of exposure to infectious disease were lowest. Incidence of type 1 diabetes was significantly linked to mortality from a variety of infectious diseases and to the local susceptibility of a common bacterium to antibiotics.

"These data provide support for the notion that the immune system can somehow become disordered and attack the body's own cells if it is not trained by regular exposure to micro-organisms – the so called hygiene hypothesis. More research is needed to try to identify other environmental factors that may be linked to the continuing conundrum of rising type 1 diabetes rates."

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Notes for Editors:
This research will be presented as a poster (223) at the Society for Endocrinology BES meeting, on Tuesday 19 March 2013. The abstract for this poster is reproduced at *Endocrine Abstracts*.

This study has also been accepted for publication to the peer-reviewed journal *Acta Diabetologica*, DOI: 10.1007/s00592-013-0464-z.

Details on the studies mentioned in this press release can be found by following the links below:

World Health Organization (WHO) Multinational Project for Childhood Diabetes (WHO DIAMOND Project) (for type 1 diabetes rates)

WHO report: global burden of disease: 2004 update (for mortality rates from infectious disease)

The Alexander Project (for bacterial susceptibility to antibiotics)

The Society for Endocrinology BES 2013 conference is Britain's biggest scientific meeting on hormones, and is taking place at the Harrogate International Centre from 18-21 March 2013. For the full programme, please click here.

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For more information: contact the Society for Endocrinology press office

Toby Stead
Public & Media Relations Executive
Mob: +44 (0)7876 823 929
Tel: +44 (0)1454 642 252
Email: toby.stead@endocrinology.org

Paul MacKenzie-Cummins
Communications and Public Relations Manager
Mob: +44(0)7453 755 057
Tel: +44 (0)1454 642 772
Email: paul.mackenzie-cummins@endocrinology.org

The Society for Endocrinology is Britain's national organisation promoting endocrinology and hormone awareness. For general information, please visit our website: http://www.endocrinology.org

For more information on diabetes, endocrinology and hormones please visit You & Your Hormones (www.yourhormones.info), the Society for Endocrinology's public information website.

ABSTRACT

Association of the Incidence of Type 1 diabetes with markers of infection and antibiotic susceptibility at country level

Alexia-Giovanna Abela[1,2], Stephen Fava[1,2]

[1]Diabetes and Endocrine Centre, Mater Dei Hospital, Malta, [2]University of Malta Medical School, Msida, Malta

Aim: To investigate the association between country incidence of type 1 diabetes (T1DM) and mortality from infectious disease as well as to antibiotic susceptibility.

Materials and Methods: An ecological study correlating data from the World Health Organisation (WHO) DiaMond Project for the incidence of T1DM, the WHO estimates of mortality (2004) from communicable diseases and the Alexander Project for bacterial susceptibility to antimicrobial agents.

Results: There were statistically significant negative correlations between the incidence of T1DM and mortality from: infections and parasitic diseases ($r = -0.34$, $p = 0.01$), respiratory infections ($r = -0.29$, $p = 0.03$), tuberculosis ($r = -0.36$, $p = 0.007$), diarrhoeal diseases ($r = -0.32$, $p = 0.02$) and total infectious disease mortality ($r = -0.35$, $p = 0.008$). There was a positive correlation between T1DM incidence and susceptibility of *S. pneumoniae* to penicillin ($r = 0.47$, $p = 0.03$), erythromycin ($r = 0.52$, $p = 0.014$), doxycycline ($r = 0.65$, $p = <0.002$) and co-trimoxazole ($r = 0.58$, $p = 0.007$). We also found a positive correlation between T1DM incidence and the mean susceptibility ($r = 0.62$, $P = 0.004$), and lowest antibiotic susceptibility ($r = 0.73$, $p = <0.0001$) of *S. pneumoniae.*

Conclusion: We found a negative correlation between country incidence of T1DM and its mortality from infectious diseases. Mortality from infectious diseases is a strong marker of the total infective burden. Incidence of T1DM was found to be positively correlated with the susceptibility of *Strep. pneumoniae* to all antibiotics studied. Increased antibiotic susceptibility of a given organism may be an indirect marker of a low degree of exposure of the community to it. Our results provide support for the hygiene hypothesis, namely that diminished bacterial exposure in early post-natal life results in increased risk of developing T1DM.