Society for Endocrinology media release

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Blood endotoxin raised after high fat meals

New research identifies a higher inflammatory response to high fat meals in people with type 2 diabetes, a factor which could contribute to many of the disease's complications. The findings, presented at the Society for Endocrinology annual meeting in Harrogate, show that all people display increased blood levels of endotoxin following a high fat meal, and that those with type 2 diabetes are exposed to over twice as much endotoxin per high fat meal than those without.

Previous research shows people with type 2 diabetes have raised baseline levels of endotoxin, a bacterial fragment which enters the bloodstream from the gut and is associated with inflammation and heart disease. Dr Alison Harte from the University of Warwick, UK, and colleagues from the UK, Spain and Saudi Arabia investigated the effect that a high fat meal might have on endotoxin levels in people with diabetes. The team gave 54 people (15 obese, 12 with impaired glucose tolerance ('pre-diabetes'), 18 with type 2 diabetes and 9 non-obese controls) high fat meals after an overnight fast. They monitored their blood levels of endotoxin for four hours, comparing these to levels before eating (baseline).

Mean circulating endotoxin levels increased significantly after the high fat meal in all participants over the four hour time period compared to baseline values: obese baseline: 5.1±0.94 EU/ml; 4 hr: 7.7±0.58 EU/ml ($p<0.01$), pre-diabetes baseline: 5.7±0.10 EU/ml; 4 hr: 7.5±0.20 EU/ml ($p<0.05$) and type 2 diabetes subjects baseline: 5.3±0.54 EU/ml; 4 hr: 14.2 ±3.0 EU/ml ($p<0.01$). In the non-obese control group, whilst there was a rise in circulating endotoxin (baseline 3.3±0.15 EU/ml; 4hr 6.3±1.4 EU/ml) this did not reach significance past 1hr. Most importantly, these data show a large, long lasting and significant rise in endotoxin levels (to approximately 125.4% of that of controls) amongst subjects with type 2 diabetes.

Inflammation is a reaction mediated by the immune system in response to a physical stressor, for example a wound or infection. In normal circumstances it is a temporary measure which aids healing. However, if inflammation is long-term, it can be damaging. In obesity and type 2 diabetes there is widespread inflammatory damage to blood vessels and other tissues, contributing to many associated conditions such as heart disease (which as many as 80% of type 2 diabetics die from[1]).

This study could explain one mechanism by which obesity can lead to inflammatory damage, and help researchers develop new preventative measures. If confirmed in larger studies, it suggests that the high fat, low carbohydrate diets currently promoted to aid weight loss and control of blood sugar may be harmful to diabetics. Also, altering the size and timing of meals

(i.e. infrequent, large meals versus a continual grazing routine) may help to control the chronic inflammation and resulting damage.

Dr Alison Harte, lead investigator and Post-Doctoral Research Fellow at the University of Warwick said:

"Our study shows for the first time that eating a high fat meal is rapidly followed by an increase in blood endotoxins, which are bacterial fragments that can provoke inflammation. Patients with type 2 diabetes show this response to a greatly enhanced degree, over twice that of controls.

"High fat, low carbohydrate diets are often promoted to patients with type 2 diabetes as they have been suggested to aid weight loss and control blood sugar, but if confirmed in larger studies our data show that being healthy is not just about losing weight, as these particular diets could increase inflammation in some patients and with it the risk of heart disease.

"The next phase of our research is to understand the effects of small, frequent meals versus large, infrequent meals on endotoxin levels in type 2 diabetics. We'd also be interested to find out the effects of meals of different fat and carbohydrate contents."

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Notes for editors:

This research will be presented as a lecture (OC3.2) at the Society for Endocrinology BES meeting, 08:30 on Tuesday 20 March 2012. The abstract for this lecture is reproduced at: http://www.endocrine-abstracts.org/ea/0028/ea0028oc3.2.htm.

[1] *Diabetes Atlas,* third edition, International Diabetes Federation 2006

The Society for Endocrinology BES 2012 conference is Britain's biggest scientific meeting on hormones, and is taking place at the Harrogate International Centre from 19-22 March 2012. For the full programme, please click here.

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Please mention the Society for Endocrinology meeting in any story

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

ABSTRACT

Post-prandial high fat intake leads to acute exposure to circulating endotoxin in type 2 diabetes mellitus subjects.

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Habitual post-prandial absorption of saturated fatty acids (SFAs) increases systemic atherogenic lipoproteins and a pro-inflammatory response, a condition exacerbated by obesity, insulin resistance (IR) and type 2 diabetes mellitus (T2DM). Also, gut derived bacteria (endotoxin) is absorbed coupled to damaging lipoproteins as it crosses the mucosa, which could directly impact on adipose tissue, as our previous studies suggest. The current studies addressed whether a SFA rich meal increases circulating endotoxin absorption and whether this is dependent on disease state. Subjects (n=58) with and without T2DM were given a high-fat meal (meal: 75g fat, 5g carbohydrate, 6g protein) following an over-night fast [non-obese controls (NOC): age: 39.8 (Mean±SEM)11.2yr, BMI: 25.3 (mean±SD)3.3Kg/m^2; n=10; Obese: age: 43.8±9.5yr; BMI: 33.3±2.6Kg/m^2; n=15; impaired glucose tolerance (IGT): age: 41.7±3.3yr; BMI: 32.0±4.5Kg/m^2; n=12; T2DM: age: 46.4±9.6yr; BMI: 30.1±5.2 Kg/m^2; n=21]. Baseline (0 hr) and post-prandial sera (1-4 hr) were taken from subjects and endotoxin, inflammatory cytokines and lipid levels measured. Baseline circulating endotoxin was significantly higher in the T2DM, IGT and obese subjects compared with NOC (Baseline endotoxin: T2DM:5.73(mean±SEM)0.85EU/mL*; Obese:5.75±1.45EU/mL*; IGT:5.83±0.45EU/mL* Vs NOC:3.55±0.50EU/mL; *p<0.05). The high fat meal led to a significant rise in endotoxin levels in T2DM and IGT subjects over the post-prandial time period compared with baseline. The findings also showed that, at 4hr post-feed, T2DM subjects exhibited a mean endotoxin level 118.5% higher than that of the NOC. A strong positive correlation between increasing BMI and log endotoxin was noted in the non-obese and obese cohorts (r value=0.501** and 0.301*, respectively; **p<0.001, *p<0.05). These studies highlight that post-prandial exposure to a high-fat meal elevates circulating endotoxin, with T2DM subjects exposed to as much as 119% more circulating endotoxin post-prandially, per high-fat meal. Therefore a continual grazing routine will cumulatively promote their pathogenic condition more rapidly than other individuals, due to the exposure to elevated endotoxin.

N.B. The data presented in the press release is the most up-to-date data following reanalysis of that submitted in the abstract, and is the data that will be presented at the conference.