

THE ALL-PARTY PARLIAMENTARY GROUPS ON OBESITY AND DIABETES

Report

Wednesday July 6th 2005

OBESITY AND DISEASE

Obesity and Diabetes

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Introduction

This is the report of a joint meeting of the All Party Parliamentary Groups on Obesity and Diabetes, held at the House of Commons on Wednesday July 6th 2005.

Throughout 2005, the All Party Parliamentary Obesity Group has been holding a series of meetings around the common theme of obesity and disease. Wherever possible, the group will be collaborating with other relevant All Party Groups and involving as wide a range of speakers from advocacy, research and professional organisations as possible. At the end of the series of meetings, the APPG will publish a report of the presentations and discussions that have taken place.

The first three meetings in the series looked respectively at cholesterol/stroke, cancer and heart disease. This meeting was the fourth in the series. The meeting considered the relationship between obesity and the development of type 2 diabetes and, in particular, predisposition and genetic susceptibility to adiposity and insulin resistance.

Over 30 people attended the meeting, representing a wide range of commercial and public sector organisations, government agencies, MPs, academics and healthcare professionals. A list of the organisations represented is appended.

Summary

Chair of the Diabetes APPG, Adrian Sanders MP, welcomed the opportunity to join forces with a sister APPG to push the same message home. He urged those present at the meeting to “make obesity history” before the Olympic games comes to the UK in 2012. Dr Howard Stoate MP, chair of the Obesity APPG, stressed the need to involve more young people in sport and encourage them to follow a healthy lifestyle.

Two eminent professors addressed the meeting. Professor Terrence Wilkin of the Peninsula Medical School, Plymouth described the “Early Bird” study, a clinical study designed to look at what factors, if any, predispose some children to diabetes and other health problems. Professor Stephen O’Rahilly, from the University of Cambridge, talked about genetic susceptibility to adiposity and insulin resistance.

Meeting speakers

Terrence Wilkin, world renowned for his work in the fields of obesity and insulin resistance, is Professor of Endocrinology and Metabolism, Peninsula Medical School, Plymouth Campus, UK. Professor Wilkin is Director of the Early bird study, which is looking at Preventable factors in childhood that lead to insulin resistance, Type 2 diabetes and the metabolic syndrome.

Professor Steve O’Rahilly (MD FRCP FRS) is Professor of Clinical Biochemistry and Medicine and Head of the University of Cambridge Department of Clinical Biochemistry; he is also a principal investigator at the Cambridge Institute for Medical Research (CIMR) and an honorary consultant physician at Addenbrooke’s Hospital. He works on the genetics and molecular mechanisms of obesity and insulin resistance, the major components of type 2 diabetes.

Professor Steve O’Rahilly’s obesity projects include research into molecular mechanisms in human obesity and insulin resistance to understand the molecular mechanisms underlying human obesity and insulin resistance with the ultimate goal of improvement, prevention and treatment of these common human disorders.

Professor Terrence Wilkin

Professor Wilkin described how human genes had gradually evolved over thousands of years, adapting so as to ensure human survival as conditions changed. As a result, man entered the twentieth century as a robust species. However, the pace of change in the broader environment within which we live has really accelerated over the last 50 years. This environmental change really started with the end of the Second World War and a period of unprecedented prosperity and affluence, and culminating in what Professor Wilkin described as the “coca-colonisation” of the Western world. In evolutionary terms, 50 years is a very short space of time and a completely insufficient period of time in which to change one’s genetic make-up!

As a result, the environment in which we live now is maladapted to the genes we possess. What’s clear is that these evolutionary pressures are affecting all of us. It is not just the fat who are getting fatter. The whole population is getting fatter. Thirty years ago, the median Body Mass Index (BMI) for a British male adult was 23. Today, the median BMI is 26.3 Kg/m².

The connection between obesity and diabetes can be summed up in two words: insulin resistance. Insulin is produced in the pancreas and circulated around the body, acting in the muscles, adipose tissue (fat) and liver to regulate the amount of glucose (or energy). When the body becomes overweight, it becomes less responsive to the action of the insulin (i.e. it becomes insulin-resistant). So, for every stepwise increase in weight, we see a stepwise reduction in efficiency. As a result, the pancreas produces more and more insulin and the body finds it more and more difficult to cope. Once a body has lost the ability to control the amount of glucose in the blood, that person is, by definition, diabetic.

Unfortunately, the effects of high insulin go far beyond the effects of simply having high levels of glucose in the blood. There is a whole raft of metabolic disorders associated with high levels of insulin, including hypertension and an increase in blood viscosity (or ‘stickiness’). More recently, researchers discovered a link between insulin resistance and polycystic ovarian syndrome.

The Early Bird Study is a non-intervention prospective cohort study of healthy schoolchildren designed to identify the earliest changes that lead to type 2 diabetes. If the day that diabetes strikes is the explosion, Early Bird is concerned to understand what ignited the fuse, what keeps it alight and, most importantly, how best to extinguish it before detonation occurs. The fuse is a state of insulin resistance which is known to precede diabetes, and the study asks the question: Which children develop insulin resistance, and why?

At the outset, the study took a cohort of 300 healthy five-year olds with the aim of studying them over a period of 11 years when they reach 16. Every six months, the study investigators take a snapshot of all of the kids. The 'snapshots' are detailed studies of body composition, dietary composition, metabolic rate, physical activity and anthropometry. Uniquely, blood samples are taken on each occasion to measure insulin resistance and the metabolic changes with which it is associated.

The Early Bird study started in January 2000 and is programmed to continue for 12 years. Although the study is still ongoing, the interim findings have led to some fascinating interim conclusions:

- Girls as young as five years old already show signs of being predisposed to developing diabetes in later life. The same is not true for boys. Girls have a 35% greater insulin resistance than boys, even when all other factors were controlled for i.e. this is an intrinsic difference between little boys and little girls.
- The level of adiposity (or percentage of the body that is fat) rises year on year and it is increasing at a much faster rate - in both boys and girls - than was seen in the 1990s.
- Bizarrely, however, there is a correlating year on year decrease in levels of insulin resistance. Essentially, then, these children appear to be getting healthier, metabolically speaking, as their fat percentage increases!
- Looking at levels of physical activity, the study found that the activity cost of being driven to school was 16%, compared to children who walked to school. However, the loss of activity is recouped during the week so that, by the end of the week, there was no difference in activity between children who were driven to school and those who weren't. Girls overall are less active than boys.
- Children who were very active at school were less active out of school, and vice versa. Overall, therefore, there was no difference in activity in the group of children over the course of the whole week.
- Fathers are very bad at estimating their own weight and that of their children
Of the very overweight kids, 60% of their fathers thought that they were of a normal weight and 35% of their mothers thought so too.

Professor Stephen O'Rahilly

Professor O'Rahilly then considered the extent to which genetic susceptibility is a factor in obesity, insulin resistance and type 2 diabetes.

Obesity has both mechanical and metabolic effects. When it comes to obesity, everyone is well aware that it is the energy imbalance that does the damage; too many calories in, too few out, causes individuals to put on weight over time. In truth, however, we do not know which side of the equation causes the most difficulties. And when one considers the link between obesity and developing type 2 diabetes, this simple fact of an energy imbalance does not explain why plenty of people of normal weight develop diabetes and yet plenty of fat people do not get diabetes.

The obvious - and scientific - explanation is that there is a huge variation in people's susceptibility to developing certain conditions and diseases. In the case of obesity, individuals vary hugely in their ability to store any additional energy (calories) consumed in our adipose tissue. This variability usually has a genetic or congenital cause.

Professor O'Rahilly described the case of a 6-year old boy who had already developed type 2 diabetes. However, he had been born with a genetic disorder that prevented him from producing

fat cells. As a result, the boy was unable to store any excess energy whatsoever. He was not overweight but his inability to store fat resulted in him developing diabetes at a young age. Similarly, he described a lady whose genetic abnormality enabled her to store fat only in certain places. A genetic mutation in the receptors meant that she could not store fat in the hips and buttocks. As a result, she developed type 2 diabetes in her teens, despite not being overweight.

Professor O’Rahilly suggested that we are not entirely powerless in the face of the current obesogenic environment – there are biological controls in place.

For example, leptin is a biologically active human hormone. Without it, the appetite goes haywire and the brain tells the individual that they are starving hungry. A group of children were developmentally normal but extremely obese. They had intense hunger and appetite. In all cases the children were found to have inadequate natural levels of leptin. Once the children were treated with leptin, their weight came down and their insulin resistance and other metabolic variables began to improve as well.

In short then, there are three potential causes of obesity. “Gluttony and sloth” are two of them, but genetic factors can play a key role in the development of obesity. Unfortunately, many commentators – including the Commons Health Committee – have chosen to overlook or ignore that obesity can have a genetic cause. As much as 70% of the variation in individual BMI measurements could be attributable to genetic factors. It is vital that we start to communicate this information out to parents, school teachers, healthcare professionals and the media.

Ten years ago, researchers knew of no obesity-related genes. Four are now known to exist and all of them have the effect of stimulating the appetite. The newspapers were full recently of the story of a three-year old girl, who had allegedly died “from obesity”. Technically, there was some truth in that; the child was grossly overweight at the time she died. However, what the media chose to disregard or overlook was that this particular child had a genetic abnormality, which meant that she had two mutant leptin receptors. Therefore, she would have been obese in any society, not just in the UK. Unfortunately, ignorance of the role that genetic factors can play in causing obesity and associated conditions resulted in a miscarriage of justice and a gross misrepresentation of the true facts of this particular case.

Audience Discussion

The following key points came out of the audience question and answer session:

- Although the Prentice/Jebb paper in the early 1990’s suggested that people’s calorific intake was not increasing, it is actually very difficult – if not impossible – to accurately measure the dietary intake of children in a free living state. As a result, researchers are missing data on one side of the energy equation.
- It is relatively easy to measure insulin levels, but it is only possible to measure insulin *resistance* by putting values for insulin and glucose through a complex mathematical model, from which it is possible to derive an index. Researchers have found that a Hober index is perfectly valid and reliable for these research purposes. Unfortunately, there is no practical means of measuring Insulin resistance in a GP’s surgery.
- Insulin resistance is a continuum, so it is not possible to state that someone is or is not insulin resistant.

Appendix

The following organisations were represented at the meeting:

- British Medical Association
- Dairy Council
- Diabetes UK
- Fitness Industry Association
- Fuel PR
- House of Commons members
- House of Lords members
- National Obesity Forum
- Peninsula Medical School
- sanofi-aventis Limited
- TOAST
- University of Cambridge
- Weight Concern