

A MODERN DAY PLAGUE?

Mike Cawthorne, Director of the Clore Laboratory for Translational Metabolic Research at the University of Buckingham, on the need for better and more cost effective treatments for diabetes and obesity

The Clore Laboratory was developed as a diabetes and obesity research centre and has been involved in the discovery and development of every promising drug class in diabetes and obesity. It undertakes both basic and applied preclinical research with other universities worldwide and with major pharmaceutical and biotech companies.

The International Diabetes Federation estimated in 2012 that more than 371 million people had diabetes, with half of them undiagnosed. Expenditure on healthcare of diabetes is more than \$471bn (~€357bn), which is more than 10% of the total healthcare costs of adults aged 20-79 years.

In Europe, there are approximately 55 million people with diabetes, of which 38% are unaware that they have the disease. However, 80% of sufferers live in low or middle income countries, with half the number of people (4.8 million in 2012) who die from diabetes being under 60.

Types of diabetes

There are three main types of diabetes:

- Type 1 diabetes is an autoimmune disorder, which requires insulin injections to treat;
- Type 2 diabetes affects more than 90% of all people with the disease. It usually occurs in adults, although with the high prevalence of childhood obesity it is becoming more common in children. There are two separate lesions in Type 2 diabetes – insulin resistance, which is a failure of tissues to respond adequately to the subject's own insulin, and defective insulin secretion. These two lesions interact. Patients can be controlled with oral therapy but over time they are likely to require exogenous insulin following pancreatic islet failure; and
- The third form of diabetes is gestational diabetes. Failure to control blood glucose during pregnancy predisposes the mother

to develop diabetes in later life. It also programmes the offspring to have a higher risk of becoming obese and diabetic and, in particular, be prone to gestational diabetes. Therefore, the condition is a multi-generational programming mechanism.

Treatment of Type 2 diabetes

People with diabetes have an increased risk of diseases affecting the heart and blood vessels, kidneys, eyes, nerves, teeth and skin. The main oral drug used for treating Type 2 diabetes is metformin. Generally an algorithmic approach is used with drugs being added as patients fail to maintain control. There is a growing realisation that this staging methodology is inadequate and if one attempts to both control glucose (and lipids) and prevent (or at least delay) pancreatic islet cell failure, then multiple treatments are needed that fully address the pathophysiology of the disease. Potentially, this requires drugs to improve insulin sensitivity in liver and skeletal muscle, slow the absorption of nutrients from the gut and provide islet cell protection.

The Clore Laboratory staff have a wealth of background knowledge and experience in undertaking preclinical studies that allow positioning of drugs into the therapeutic regimes of today and tomorrow.

Prevention of Type 2 diabetes

There is a growing recognition for the need to prevent the development of Type 2 diabetes. A major factor is obesity, which results in insulin resistance and compensatory hyperinsulinaemia leading ultimately to islet cell exhaustion. All anti-obesity drugs to

Validated expertise

- More than 500 peer reviewed publications by Clore Laboratory staff in the area of diabetes and obesity;
- Clore Laboratory staff have made major contributions to the development of insulin sensitiser drugs;
- Clore Laboratory staff pioneered brown adipose tissue research and the development of thermogenic drugs; and
- More than 100 man years of pharmaceutical industry research.



