

# Tackling the dragon:

## The Welsh approach to addressing type 2 diabetes

A report from the 2<sup>nd</sup> Welsh Conference of the Primary Care Diabetes Society, which took place on 10 May 2011 at the Parc Hotel by Thistle, Cardiff. This meeting report was generated independently by the publisher and conference speakers, with whom editorial control rests.

The Primary Care Diabetes Society (PCDS) was set up 7 years ago to improve the care of people with diabetes in primary care. The PCDS now runs annual meetings in England, Ireland and Scotland, and the second PCDS meeting in Wales is reported here. This conference examined diabetes care from a Welsh perspective and looked at diagnosing, preventing and screening for diabetes as well as weight management and new diabetes therapies in development. The talks and discussions provided practical guidance to healthcare professionals for confronting current and future therapeutic and political issues that impact directly on everyday practice in Wales, as well as presenting a vision for Welsh diabetes care in the future.

Conference Chairs David Millar-Jones (GP, Cwmbran and PCDS committee member) and Pam Brown (GP, Swansea and PCDS committee member) welcomed over 200 attendees to the event from all over Wales.

### Diagnosing type 2 diabetes: HbA<sub>1c</sub> versus oral glucose tolerance test

*Steve Bain (Professor of Medicine [Diabetes], Swansea)*

Professor Bain began by looking at the history of diabetes diagnosis. "Diabetes was first diagnosed about 2500 years ago on the basis of glycosuria" he said, and commented that 100 years ago, people were still tasting urine to make a diagnosis. In 1979, the National Diabetes Group published

guidance for diagnosing diabetes based on the ability to predict specific diabetes complications, in this case retinopathy (National Diabetes Group, 1979).

Professor Bain pointed out that the recommendation that was made by the group – to conduct an oral glucose tolerance test, which is now seen as the gold standard diagnostic test – was originally only based on 1213 people who were followed up for 3 or 8 years. "It's not quite as 'gold standard' as you might imagine" he said.

A major development was made in 1997 when the American Diabetes Association made the oral glucose tolerance test equivalent to the 2-hour fasting test, meaning that fewer people needed to undergo an oral glucose

tolerance test (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997). "The recommendations that were made in 1997 by the American Diabetes Association no longer used glucose tolerance testing (except in certain circumstances) and relied on fasting plasma glucose levels", said Professor Bain.

In 2009, the International Expert Committee published a report recommending that HbA<sub>1c</sub> be used for diagnosis in type 2 diabetes. "An HbA<sub>1c</sub> level  $\geq 6.5\%$  ( $\geq 48$  mmol/mol) would be regarded as the diagnostic criteria for type 2 diabetes" he said.

Professor Bain then looked at the pros and cons of each diagnostic test. He said "the advantages for using

fasting plasma glucose is that everybody can do it, it doesn't cost very much and it's a single sample (as opposed to a glucose tolerance test)".

Biological variability, diurnal variation, and inconvenience are the disadvantages of fasting plasma glucose testing.

"The gold standard oral glucose tolerance test is a good indication of the risk of developing diabetes, because it tests beta-cell function in response to a glucose challenge" said Professor Bain. However, he also explained how inconvenience, expense and variability were the main disadvantages to this approach.

Professor Bain then moved on to the advantages of using HbA<sub>1c</sub> as a diagnostic test

## MEETING REPORT

including not needing to fast, the results not being affected by stress or exercise, little biological variability and the use of a single sample. He identified that the disadvantages were that HbA<sub>1c</sub> can vary in people with haemoglobinopathies, and between different ethnicities, it may not be available in some areas of the world and the test costs more. “The cost does need to be seen in light of the costs associated with the other tests, not just the cost of the test itself” he emphasised.

In Wales, a meeting has been planned to discuss whether diagnosis using an HbA<sub>1c</sub> cut point of <6.5% (<48 mmol/mol) should be recommended. Professor Bain also reminded delegates that

HbA<sub>1c</sub> laboratory reporting changed to mmol/mol without the percent value in June 2011.

### **Preventing diabetes – the Welsh agenda**

*Dai Williams (National Director for Diabetes UK Cymru, Cardiff)*

“Diabetes is not a traditional epidemic,” said Dai, referring to the standard response to an influenza epidemic. “It has crept up on us and the Welsh Assembly Government has not taken measures to protect the public.” He then introduced a typical person with type 2 diabetes – Ray – who was diagnosed with diabetes 7 years ago, weighs 22 stone and is due to start insulin but is afraid of needles. Dai described how Ray’s treatment would be

intensified to control future complications. He looked at the costs of medication and the resulting reduction in HbA<sub>1c</sub> level: “Prescribing costs for type 2 diabetes have increased by 89% and mean HbA<sub>1c</sub> level has decreased by 0.1 percentage points” he said (Currie et al, 2010).

“But are people actually taking their medications properly and do they understand why they need them?” asked Dai. He reminded delegates that NICE (2003) technology guidelines, which are mandatory, state that all people with diabetes should have structured education, and moved on to discuss how it can be delivered in Wales. Research from Diabetes UK shows that in Wales on average only 2% of people with type 2 diabetes

have attended structured education. The reasons for this appeared to be a lack of awareness of the existence of structured education programmes such as DAFNE (Dose Adjustment For Normal Eating) and DESMOND (Diabetes Education and Self Management for Ongoing and Diagnosed). “GPs don’t know about them, health board managers don’t know about them, so people with diabetes aren’t informed about the benefits of such education” said Dai. He recommended more publicity to raise awareness of structured education programmes.

Data from the National Diabetes Prevention Programme showed that a change in lifestyle reduces the incidence of diabetes in

## Masterclasses

### **Masterclass 1: Do you know your patient’s VIP status?**

*Scott Cawley, Professional Lead for Diabetic Foot Services, Cardiff*

Scott looked at the key aspects of screening and foot ulcer management in primary care. He explained each aspect of the pneumonic VIP: Vascular state will determine the potential to heal; Infection, if not controlled, can lead to limb loss; and Pressure needs to be removed for the wound to heal. Scott emphasised the importance of managing all three aspects of VIP and used interactive case studies to illustrate each point.

### **Masterclass 2: Safe glycaemic targets: A balancing act**

*Julia Platts, Consultant Diabetologist and Endocrinologist, Cardiff*

Target HbA<sub>1c</sub> level has been a topic of much debate over the past 10 years. NICE, professional diabetes societies and the Government have set targets but, as Dr Platts explained, setting the right target for an individual can be challenging.

She presented the evidence for benefit if HbA<sub>1c</sub> targets are achieved and the risk of harm when aiming for tight glycaemic control in particular individuals.

### **Masterclass 3: Dyslipidaemia in people with type 2 diabetes**

*Alan Rees, Consultant Physician in Endocrinology, Diabetes and Metabolism, Cardiff*

Dr Rees explored the reasons for the dyslipidaemia experienced by people with diabetes, which is characterised by mild hypertriglyceridaemia, lowered levels of HDL-cholesterol and an LDL-cholesterol particle that is more atherogenic.

He also explained the evidence for the efficacy of various pharmacotherapies indicated for the treatment of dyslipidaemia.

### **Masterclass 4: Insulin therapy and the new antidiabetes agents**

*Jeff Stephens, Reader in Diabetic Medicine and Consultant Physician, Swansea*

Newer therapies, such as dipeptidyl peptidase-4 inhibitors and glucagon-like peptide-1 receptor agonists were discussed in this interactive masterclass.

Dr Stephens discussed the mode of action and guidance for these therapies and also looked at drugs in these classes that are in development. He presented some clinical case studies to help the delegates use these newer therapies in context.

## MEETING REPORT

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high-risk individuals by 58% compared with 31% with metformin (Knowler et al, 2002). “Ann Albright, the Director of the Division of Diabetes Translation in the USA, is working on translating research like this into real-life scenarios” said Dai, who then looked at data from the DEPLOY study, which also took place in the USA. The authors of this study used local YMCAs to deliver health education to people at risk of developing diabetes, and compared it with standard health counselling. Body weight decreased by 6% in the intervention group compared with 2% in the control group (Ackermann et al, 2008), and differences persisted 12 months after the intervention. The intervention group also experienced a greater change in total cholesterol (–1.2 mmol/L versus +0.3 mmol/L). “We need to identify people at the prediabetes stage to prevent them getting to the diabetes stage” said Dai.

To conclude his presentation, Dai returned to telling delegates about Ray. “He really didn’t want to go on insulin so he asked if he could have 6 months to turn things around” he explained. “Ray lost 7 stone in 6 months and felt better than ever – we need to publicise these real-life stories so people know that it is achievable” said Dai.

### **Vascular screening in Wales**

*Julian Halcox (Professor of Cardiology and Consultant Cardiologist, Cardiff)*

“Vascular screening is important” said Professor Halcox as he highlighted

the high prevalence of death from cardiovascular causes. He looked at the INTERHEART study (Yusuf et al, 2004), which identified nine major modifiable risk factors, six of which increased the risk of cardiovascular disease (smoking, HDL-cholesterol:LDL-cholesterol ratio, diabetes, stress, blood pressure and obesity) and three of which decrease the risk (higher fruit and vegetable consumption, more physical activity and moderate alcohol intake).

Commenting on the differences in risk between different ethnic groups, he said that in this study “the prevalence of risk factors drove the difference rather than the fact that they operate in a different way in certain individuals”, suggesting that it is environmental factors (rather than genetic) that determine cardiovascular risk. “We can potentially do a huge amount to modify these risk factors” said Professor Halcox, emphasising that the risk factors need to be addressed early enough to make a difference to the progression of disease.

Professor Halcox advocated targeting more than one risk factor in an individual: “we have changed over the past 20 years from targeting a single risk factor to taking a more globally integrated risk factor approach, and nowhere is that more important than in managing the person with diabetes”.

The vascular checks programme is underway in England and Professor Halcox identified the strengths and

weaknesses of the approach. The programme prioritises those who are at greatest risk of atherosclerosis including smokers, people with a family history of cardiovascular disease, obese people and people from certain ethnic groups.

One challenge Professor Halcox highlighted was the use of the Framingham risk calculator. He explained that it does not take into account some risk factors such as existing heart disease and diabetes. “When risk is calculated in people with existing coronary heart disease, only a third of them would be considered to be at high risk even though they have developed the disease” said Professor Halcox referring to a study by Ajani and Ford (2006). “So at a population level there are failings as far as the risk factor assessment is concerned”.

He recommended the use of the QRISK 2 risk calculator (<http://qrisk.org>), although due to the amount of laboratory information required, it is best used in a primary care setting, where such information is stored in databases.

Professor Halcox concluded that the key to preventing cardiovascular disease is “catching it at a young age” with readily available healthy options and improved education.

### **Complexities of weight management**

*David Millar-Jones (GP and Welsh Representative on the PCDS, Cwmbran)*

Dr Millar-Jones emphasised the complexity of weight

management and encouraged delegates to therefore be more sympathetic to people having difficulty losing weight.

“Weight gain is a psychosocial condition” he said, “and I would argue that obesity is a medical condition”. It is estimated that the number of bariatric operations will increase in response to the obesity epidemic from 500 now to 4000 in 8 years time (NICE, 2002). However, as Dr Millar-Jones explained, bariatric surgery is not appropriate for everyone. “Weight loss can unearth underlying psychological disorders” he said. “There are a large proportion of people who become overweight and suffer from an underlying mental illness, either as a cause or a consequence of the weight gain”. Counselling is an important part of managing obesity, as well as diet, exercise, education and pharmacological therapy.

Dr Millar-Jones then looked at all the reasons why people are obese. “People often like to apportion blame and will tell you it’s their glands, or their tablets or their genes or that they haven’t got time to exercise” he said. However, weight loss is a complex process and “we’ve got to start respecting that some people are being honest when they state that they are exercising and eating very little”. He explained that “glands” could relate to hypothyroidism, Cushing’s or polycystic ovary syndrome, lots of tablets do indeed cause weight gain and there are

some genetic factors related to weight gain.

Dr Millar-Jones looked at the cycle that occurs through dieting, resulting in net weight gain. The body's physiological response to starvation is to slow down metabolism, which can result in a weight loss plateau. "People can feel very discouraged at this point, give up the diet and binge eat" said Dr Millar-Jones. This results in a low self-esteem and the start of another diet.

The endocannabinoid system plays a part in this cycle. Activation of the system increases food consumption and promotes weight gain. It has been shown to be more active in obese people, and receptors for endocannabinoids are expressed in the brain, gastrointestinal organs and adipose tissue (Engeli et al, 2005).

"Ghrelin is another hormone that influences eating patterns" said Dr Millar-Jones. "When you eat a Chinese take-away, you feel full, but a few hours later you are hungry again" he went on, describing the effect of eating a meal high in carbohydrate and fat on levels of ghrelin. "Protein helps to suppress ghrelin, so when a high protein meal is eaten, hunger will be kept under control".

Dr Millar-Jones finished his talk by advocating a combined approach to managing obesity, with diet, exercise, counselling, pharmacotherapies, and the option of surgery. He said "even with pharmacotherapy

and surgery options, the only way people are going to lose weight is by hard work and active counselling".

### New developments in diabetes – a practical approach

*Marc Evans (Consultant Diabetologist, Cardiff)*

"Newer agents: are they really jumping into the unknown or are they re-inventing the wheel?" asked Dr Evans as he began his talk on new agents for diabetes therapies. "The key with new treatments for diabetes is that they control blood glucose levels without hypoglycaemia and weight gain" he said.

Type 2 diabetes has a complex pathophysiology with many different factors influencing the condition including decreased incretin effect, increased lipolysis, increased glucose reabsorption and neurotransmitter dysfunction.

Dr Evans showed how therapies are being developed to work on every aspect of the pathophysiology of type 2 diabetes, beginning with increased glucose reabsorption in the kidney. "Sodium glucose co-transporter-2 inhibitors work by blocking the reabsorption of glucose by the kidneys so more glucose is passed in the urine" he said. Participants trialling this therapy also experienced weight loss due to the excretion of glucose, but with increased genital infections (Rosenstock et al, 2010). "Importantly, this side-effect did not cause people to drop out of the

study, so it appears that it would not affect adherence" said Dr Evans.

New insulin delivery systems were also discussed by Dr Evans. "Inhaled prandial insulin has been developed and has a much smaller delivery device than previous inhaled insulins" he said, and explained that because inhaled insulin goes straight to the liver, it reduced hypoglycaemia by suppressing hepatic glucose production (Rossiter et al, 2010). However, inhaled insulin does also have side-effects such as a cough. "Safety has always been a problem with inhaled insulin, and lung function will need to be monitored" he said.

Insulin degludec is a novel insulin with an ultra-long-acting profile. "It has comparable glycaemic control to treatment with insulin glargine when used three-times-weekly or once-daily but a lower rate of hypoglycaemia when used once-daily" said Dr Evans citing data from Zinman et al (2010).

Dr Evans also discussed linagliptin, a new agent in the dipeptidyl peptidase-4 inhibitor class, and exenatide once-weekly, a long-acting version of exenatide.

"The use of bile acid sequestrants to lower blood glucose is a novel approach" said Dr Evans. Colesevelam is a bile acid sequestrant that lowers blood glucose and increases GLP-1 secretion in rats (Shang et al, 2010).

Dr Evans concluded by saying "there are multiple new therapies in development and they all target the treatment of blood

glucose levels with a low risk of hypoglycaemia and a beneficial effect on weight gain". ■

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