

# Type 1 Diabetes Mellitus - insulins

## Notes for key slides

### Slide 1

Introduction slide.

### Slide 2

**Type 1 diabetes mellitus** is characterised by pancreatic beta cell destruction leading to an absolute insulin deficiency. It is one of the most common chronic diseases in childhood.<sup>1</sup> Children and young adults with type 1 diabetes have particular needs which differ from adults with type 1 diabetes.<sup>1</sup> Type 1 diabetes has significant short-term impacts on health and lifestyle and is associated with major long-term complications and reduced life expectancy.

Keeping blood glucose concentrations closer to people without diabetes has been shown to prevent or delay the long term vascular complications of diabetes.<sup>2</sup>

By contrast, **type 2 diabetes mellitus** is generally a disease of the middle aged or elderly and usually develops insidiously, although it can begin in childhood. A survey published in 2002 showed some interesting data.<sup>3</sup>

From a cohort of 11,696 children with diabetes (mean age 11.3 years, mean duration of diabetes 4 years and mean age at diagnosis 7.2 years), 97% had type 1 diabetes. However, 0.9% (102 children) were reported to have type 2 diabetes; this increased from 0.6% (75 children) in 2001.<sup>3</sup>

Management of blood glucose is very important in type 1 diabetes. But in type 2 diabetes a broader approach to reducing CV risk is imperative. See the type 2 diabetes materials on NPCi.

#### References

1 Type I diabetes diagnosis and management of type I diabetes in children and young people. Clinical Guideline Sept 2004. National Collaborating Centre for Women's and Children's Health

2 The Diabetes Control and Complications Trial (DCCT). N Engl J Med 1993; 329: 977-86

3 Diabetes UK. The National Paediatric Diabetes Audit, 2002. Accessed from <http://bsped.org.uk/professional/diabetesuk/NationalPaediatricAudit.pdf> on 3/12/06

### Slide 3

**Key messages adults:** The views and preferences of individuals with type 1 diabetes should be integrated into their healthcare. Diabetes services should be organised, and staff trained, to allow and encourage this.<sup>4</sup>

**Young people with type 1 diabetes mellitus** should be offered multiple daily injection regimens to help optimise their glycaemic control, but, this should only be part of a package of care. This should include; continuing education, dietary management, instruction on use of insulin delivery systems and the expertise of a multi-disciplinary team.<sup>4</sup>

This group of patients should be offered the most appropriate insulin regimens with the aims of achieving HbA<sub>1c</sub> levels to less than 7.5%, without frequent disabling hypoglycaemia. Their care package should be tailored to achieve this goal if possible.

If HbA<sub>1c</sub> levels become elevated and are consistently above 9.5%, they should be offered intensive glycaemic control support by their diabetes team. Blood glucose (as opposed to urine testing) is recommended.<sup>4</sup>

**Pre-school** and primary school children with type 1 diabetes should be offered the most appropriate individualised regimens to optimise their glycaemic control.<sup>4</sup>

#### Reference

4 NICE Clinical Guideline No15. Type 1 diabetes: diagnosis and management of type I diabetes in adults 2004

### Slide 4

#### Short acting/mealtime insulins

If you look at the first two insulin profiles on this graph, you can see a difference. The black one shows rapid-acting insulin analogues with a rapid action and a steep peak.

The blue shows soluble insulin, which takes a bit longer to get going, and lasts longer.

N.B. Duration will vary widely between and within people.

**The intermediate and long-acting insulins** are used to fulfil the basal or background insulin requirement and are usually given once or twice a day, depending on the regimen chosen and their duration of action.

**Isophane insulin** is an intermediate-acting insulin (often known as NPH = neutral protamine hagedorn). It is a suspension of insulin with protamine.

**Of the long-acting analogues**, glargine has a longer duration of action than detemir. Glargine is licensed for once daily dosing, whereas detemir is licensed for once daily or twice dosing, depending on the patient.

**Protamine zinc** has a longer duration of action than isophane. It is usually given once daily with short acting soluble insulin. It isn't used much now because it tends to bind with soluble insulin when mixed in the same syringe. There isn't much prescribing of insulin zinc suspension either. Both insulin zinc and protamine zinc suspension are only available in bovine forms.

The main basal insulins prescribed are isophane insulin and the long-acting analogues.

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The regimen chosen is largely based on the individual patient, including choice and cognitive function – because if the patient doesn't adhere to it, it's at best a waste of their time and effort, and of the healthcare professionals looking after them. We also need to consider their age, mealtimes, diet, exercise, other lifestyle things like whether they work shifts, the level of glycaemic control decided for the patient, their risk or experience of hypoglycaemia, etc.

### Multiple daily injections

This involves giving short or rapid acting insulin before each meal, along with one or more separate injections of intermediate or long-acting insulin. This regimen is often known as the 'basal-bolus regimen' or 'intensive' or 'flexible' insulin therapy, because patients can be a bit more flexible with mealtimes.

### Continuous subcutaneous insulin infusion

Or insulin pump therapy is a programmable pump and insulin storage reservoir that gives a continuous supply of insulin subcutaneously. The patient can trigger pulses to cover each meal. This device is suitable for patients when multiple dose insulin therapy has failed and for those who have the competency and motivation to use this device.<sup>5</sup>

In reality, the commonest regimes are either twice daily injections or multiple daily injections.

### Reference

5 Guidance on the use of continuous subcutaneous insulin infusion for diabetes. NICE Technology Appraisal Guidance No 57, February 2003

## Slide 6

### The DCCT

This is the main randomised controlled trial (RCT) that is used to support tight glycaemic control and, therefore, the use of HbA<sub>1c</sub> as a surrogate outcome for reducing complications in type 1 diabetes trials. DCCT was a multicentre RCT in 1,441 young patients with type 1 diabetes, 726 with no retinopathy at baseline (the primary prevention cohort) and 715 with mild to moderate retinopathy (the secondary prevention cohort).

Patients were randomised to intensive insulin treatment (either insulin pump or at least 3 injections a day and guided by frequent blood glucose monitoring) or conventional therapy with one or two daily insulin injections.<sup>2</sup> DCCT was stopped early at 6.5 years after positive results on microvascular complications were seen with intensive treatments.<sup>2</sup>

The EDIC study was started within a year of DCCT stopping and all patients were advised to switch to intensive therapy. During EDIC patients are monitored annually.<sup>6</sup>

### The DCCT main results

Fewer patients developed retinopathy, nephropathy and neuropathy based on disease oriented outcomes (DOOs). No patient oriented outcome data was available at the time of completion of the study.<sup>2</sup>

## Reference

6 The Epidemiology of Diabetes Interventions and Complications (EDIC) study. JAMA 2003; 290: 2159-2167

## Slide 7

### Possible adverse effects?

We need long-term data over many years in order to make an accurate assessment of the safety of the insulin analogues.

### NICE

For the long-acting insulin analogues, NICE recommendations are based on level D evidence. (This relates to expert committee reports or opinions, and/or clinical experience of respected authorities or extrapolated from studies).

### Cochrane review<sup>7</sup>

For the rapid acting analogues, the Cochrane review has been published since the NICE guidelines were published.

## Reference

7 Siebenhofer A, et al. Short acting insulin analogues versus regular human insulin in patients with diabetes mellitus. The Cochrane Database of Systematic Reviews 2006, Issue 2. Art No. CD 003278

## Slide 8

### What does NICE say?

NICE guidance advocated treatment regimens which are very patient-led. The decision to be a bit more flexible over the target HbA<sub>1c</sub> is based on harms, for example, the number of hypoglycaemic episodes. Children and young people are at more risk from episodes of hypoglycaemia.

### The DCCT study

In the DCCT study<sup>2</sup> those receiving more intensive treatment to achieve lower HbA<sub>1c</sub> had a greater risk of episodes of hypoglycaemia.

Three times as many people in the intensive group had severe hypoglycaemia in terms of episodes requiring assistance or episodes causing coma or seizure (P<0.001).

### Episodes of hypoglycaemia<sup>9</sup>

The number of hypoglycaemic episodes requiring assistance was 61 vs. 19 per 100 patient years, in the intensive group compared to the conventional treatment group.

The number of hypoglycaemic episodes causing coma or seizure was 16 vs. 5 per 100 patient years in the intensive group compared to the conventional treatment group.

## Reference

9 The Diabetes Control and Complications Trial Research Group. Adverse events and their associations with treatment regimens in the diabetes control and complications trial. Diabetes Care 1995; 18: 1415-27

## Slide 9

### So what is a NICE regimen?

Well, it depends on the patient. The options are:

Multiple injection regimens in adults who prefer them as part of an integrated package with education, food, skills training and appropriate self-monitoring.

Prescribe twice daily insulin regimens (often biphasic pre-mixes; containing analogues for those prone to hypoglycaemia at night) for those patients: -

- Who want them and/or
- Who find adherence to lunch-time insulin injections difficult
- With learning difficulties, who may require assistance

### Meal time insulin

Use unmodified soluble insulin or rapid-acting insulin analogues.

Use rapid-acting insulin analogues rather than unmodified insulin:

- Where nocturnal or late inter-prandial hypoglycaemia is a problem

- To avoid the need for snacks whilst maintaining equivalent blood glucose control
- Avoid general use of oral glucose-lowering drugs in people with type 1 diabetes.