HOW I WOULD MANAGE A 13-YEAR-OLD GIRL WITH NEWLY DIAGNOSED TYPE 1 DIABETES

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PRESENTATION

An explosion in the incidence of diabetes has occurred worldwide in the last three decades.[1] Both in western countries and in the developing world, Type 2 diabetes is the most prominent form (>80%). A further rise in incidence and prevalence has, however, also occurred in young people. As in most northern European countries, north America and Australia, Type 1 diabetes has increased in Scotland by two- to three-fold (see Figure 1), with a suggestion that Type 1 diabetes is presenting at a younger

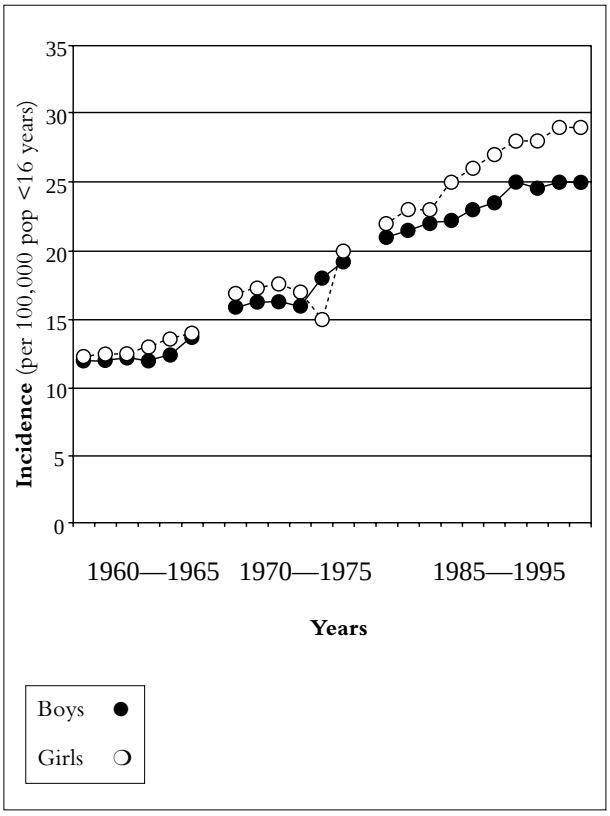

FIGURE 1
Increase in incidence of Type 1 diabetes in young people (<16 years of age) in Scotland (1960–1995).

age more frequently.[2, 3] No specific cause for this autoimmune disease has been found and recent evidence suggests an abnormal immunological response to a non-specific antigen, probably viral in origin.[4]

Recently, an increase in 'other' forms of diabetes has been documented in young people. There has been a categorisation of the syndrome of 'maturity-onset diabetes in the young' (MODY), with the identification of specific enzyme deficiencies and molecular abnormalites,[5] and the isolation of genetic abnormalities which account for the rare syndrome of neonatal diabetes[6] (see Table 1). Of more serious clinical concern is the potential rise of Type 2 diabetes in the adolescent population in Scotland. The significant rise in Type 2 diabetes described in various countries in the world has a link to urban deprivation, ethnicity and obesity. Population studies in Kuwait and Singapore have suggested that Type 2 diabetes in adolescence accounts for up to 50% of new cases at diagnosis, with similar figures observed in large urban centres in the US.[7, 8] It remains to be seen whether a similar increment will occur in Scotland: with a high adult prevalence of Type 2 diabetes (2–3% of the >50 years of age population[9]) and rising obesity in the young age range,[10] it will be of interest if the relatively homogeneous Caucasian population 'resists' the rise in Type 2 diabetes in the next decade.

The classic clinical presentation of young people with Type 1 diabetes is weight loss, polydipsia, polyuria and general malaise, with duration of symptoms varying from six months to as short as one week. In the Tayside region, as in many other parts of Scotland, most children now present with relatively mild symptoms and are identified quickly by the presence of a high concentration of urine glucose and ketones, and a persistently abnormal random (>11·0 mmol/l) or fasting (>7·0 mmol/l) blood glucose.[11] The decline in frequency of diabetic ketoacidosis at presentation is probably related to more rapid diagnosis in the primary setting, with no evidence of a change in the 'metabolic nature' of the diabetes.

INITIAL THERAPY

The mainstay of insulin therapy at the onset of diabetes has been 'conventional insulin', i.e. a twice daily, mixed insulin regimen (either self-titrated soluble insulin with an isophane preparation, or a pre-mixed preparation containing 30–50% soluble insulin). For younger children aged less than three or four years, a once daily insulin (isophane preparation) injection has been the initial therapy. The initial dose is usually <0·5 units per kg body weight per day. Over the next six to 18 months the daily insulin requirement usually rises up to 0·8–1·0 unit per kg body weight per day as the 'honeymoon' period subsides, representing the gradual loss of endogenous insulin secretion as the autoimmune process continues.

For the majority of young patients, this approach is highly successful, with resolution of the presenting symptoms, weight gain and good general health. The twice daily regimen fits well with conventional meal patterns with the injections taken at breakfast and the main evening meal that is usually eaten at around five to six o'clock, after the school day. The diabetes education programme (see Table 2) is conducted through the clinic, and at home, by nurse specialists and dietitians, both preferably with paediatric training.

In some countries, this approach is considered to be suboptimal. A more aggressive intensive insulin regimen is considered appropriate from the onset of therapy: pre-meal rapid insulin with a longer-acting isophane preparation at

TABLE 1
Phenotype and genotype of maturity onset diabetes of the young (MODY*).

Type of MODY	Chromosome and mutated gene	Regulatory function	Diabetes	Therapy	Complications	Other
1	20q; hepatocyte nuclear factor (HNF-4a)	Transcription factor, nuclear hormone receptor family	Severe	Oral hypoglycaemics, insulin	Similar to late onset Type 2 diabetes	
2	7p; Glucokinase	Enzyme	Mild	Diet, oral hypoglycaemics	Rare	Associated with low birth weight
3	12q; hepatocyte nuclear factor (HNF-1a)	Transcription factor, POU homeodomain	Severe	Oral hypoglycaemics, insulin	Similar to late onset Type 2 diabetes	Glycosuria secondary to low renal threshold
4	13q; insulin promoter factor (1 IPF-1)	Transcription factor, Antp homeodomain	Moderate	Diet, oral hypoglycaemics	Unknown	
5	17-cenq; hepatocyte nuclear factor (HNF-1b)	Transcription factor, POU homeodomain	Severe	Insulin	Nephropathy	Renal function abnormality and cysts

* *MODY: Onset of hyperglycaemia under 25 years of age, autosomal dominant inheritance (usually with 3 generations) and usually not treated with insulin for >5 years after initial clinical presentation.*

breakfast and bedtime.[11] The use of an insulin pump has also been employed from diagnosis.[12] The rationale for this latter approach is two-fold. First, it is suggested that a rapid return to normal blood glucose concentration using frequent administration of soluble insulin preparations in low dosage preserves pancreatic beta-cell function; second, the overall improvement in glycaemic control produced by this approach is sustained in the long-term. As yet, no convincing data exist to support this view. While this intensive approach has an appeal in attempting to mimic the physiological replacement of insulin from the outset, an undoubted increase in commitment is required from the family.

Which treatment our teenage girl receives is based on the experience and views of the diabetes team supporting the family. As yet, no evidence exists to support which treatment is the preferred choice – conventional or intensive.

LIFE WITH DIABETES

The burden of the routine of diabetes treatment was described from the early days of insulin use. R.D. Lawrence encouraged the use of frequent doses of soluble insulin and a detailed attention to carbohydrate intake. However, it was appreciated that many found the regimen of injections, diet and monitoring of diabetes difficult to accept. For the majority, this resulted in poor glycaemic control; for some, a small minority, it resulted in severe disruption of their lives with frequent ill-health, episodes of ketoacidosis and hypoglycaemia – so-called brittle diabetes.[13]

The consequence of glucose toxicity over time became apparent with the development of the microvascular complications of diabetes and the heavy burden of macrovascular disease. Improving glycaemic control over time became the target for the health professionals looking after young people with diabetes, and data from the Diabetes Control and Complications Trial (DCCT)[14] confirmed that keeping glycated haemoglobin (a marker of overall glycaemic control) as near to normal as possible limited the development and progression of the long-term vascular complications of Type 1 diabetes, even in the teenage population.

The problem for a newly-diagnosed teenage girl is keeping up with the daily routine of diabetes in a manner to establish 'good control'. The DIABAUD project of the Scottish Study Group for the Care of the Young Diabetic (SSGCYD)[15] has shown that this is a difficult task for the majority of children and teenagers, with over 60% of children <15 years of age having glycaemic control that is outside the accepted range for the prevention of long-term microvascular disease (see Figure 2).

Many factors will influence how our teenager controls her diabetes. Frequent insulin injections, frequent monitoring of blood glucose and strict attention to diet are easy to advise; they are extremely difficult to adhere to on a day-to-day basis, year in year out. In Tayside, using data obtained from encashed prescriptions we have identified poor adherence to insulin therapy. In the course of one year, 25% of older teenagers will fail to collect 28% of their prescribed insulin dose, with poor adherence predicting those young people with Type 1 diabetes who present with ketoacidosis.[16] Similar poor adherence is observed with blood glucose estimations and diet.

Overt social disturbance will obviously influence the ability to 'stick to the diabetes routine' and includes parental separation, alcoholism, unemployment, neglect and abuse. Similarly, psychological disturbance (both in the teenagers themselves and in their parents) affects the concordance with the 'diabetes lifestyle'; eating disorders and anorexia nervosa are significantly increased, especially in young women

TABLE 2
Education and training programme for a new case of a child with diabetes.*

SESSION 1: within first week

Topic	Mother	Father	Child	Comments
	Date	Date	Date	Date
Introduction to diabetes: plan of management and education				
Demonstration of injection techniques				
Demonstration of use of blood glucose meter				
Demonstration of finger pricker				
Demonstration of finger pricking technique and observation of this				
Discuss recording results				
Hypoglycaemic attacks				
Basic dietary advice				

SESSION 2

Topic	Mother	Father	Child	Comments
	Date	Date	Date	Date
Detailed diabetic diet on-going				
Diabetic ketoacidosis (DKA)				
Coping with illness and testing for ketones				
How and when to give glucagon				
Exercise and diabetes				

SESSION 3

Topic	Mother	Father	Child	Comments
	Date	Date	Date	Date
Insulin adjustment programme				
Diabetes and school (give school pack)				
Coping with illness reinforced				
Foot care				
Hypoglycaemic attacks reinforced				
Parent's group				

SESSION 4

Topic	Mother	Father	Child	Comments
	Date	Date	Date	Date
Holiday advice				
What to do if you forget your insulin injection				
Hypoglycaemic attacks reinforced				
DLA Packs				
Diabetes UK				

* *Schedule followed by the DiabNet Project. This programme should be undertaken on diagnosis and completed within a short timescale (maximum of six months).*

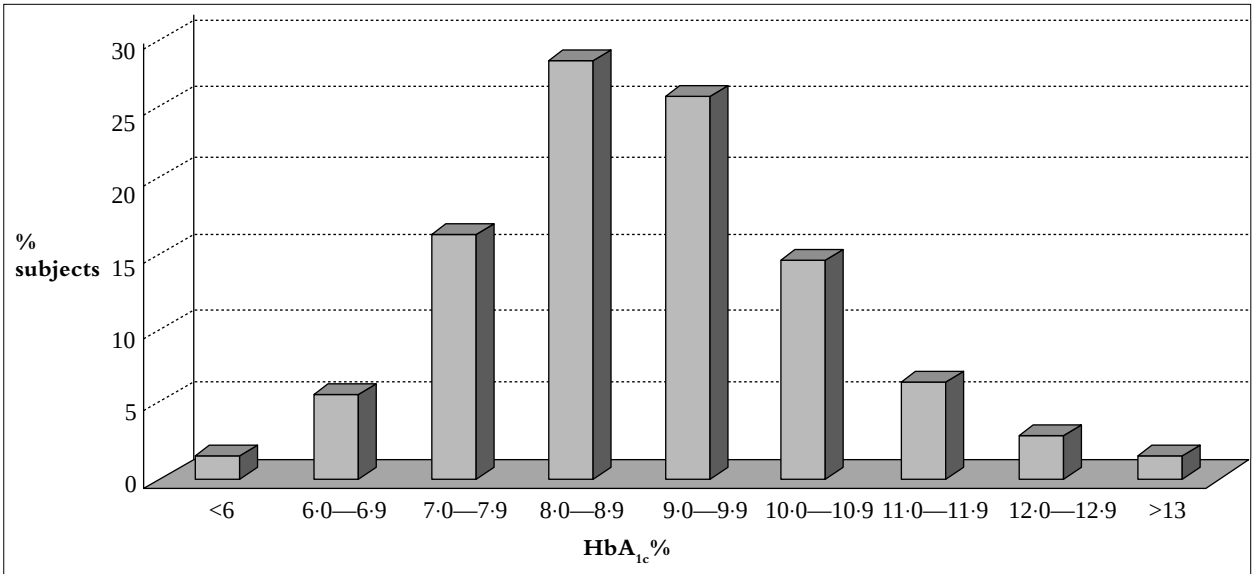

FIGURE 2
Distribution of HbA_{1C}% in 1,609 children and adolescents (<15 years of age) with Type 1 diabetes in Scotland.*

* *Data from DIABAUD Project of the SSGYCD.*

with Type 1 diabetes,[17] and depression is common.

However, in the DIABAUD project of the SSGCYD, while significant associations with glycaemic control were identified (age, sex, insulin regimen, body mass index, season, social circumstances, family history), these associations accounted for <12% of the patient-to-patient variation in glycated haemoglobin concentration.[18] Other factors (not analysed in DIABAUD) appear to influence glycaemic control in the individual patient. In addition, it appeared that there was also an individual effect of the Diabetes Centre where the child or teenager was being supervised. No explanation can be given at the present time for the major factors predicting sustained good glycaemic control. It can be speculated, however, that deployment of resources, organisation of the clinic and strategies of medical care will explain the differences, and operate by supporting the patient and their family over the years of self-care.

OTHER THERAPEUTIC APPROACHES

The cornerstones of therapy remain insulin injections, carbohydrate regulation and monitoring with the following targets:

- daily blood glucose measurements with the majority between 4 and 10 mmol/l;
- glycated haemoglobin – HbA_{1c} <8·0%;
- normal physical growth;
- no life-threatening episodes of diabetic ketoacidosis (DKA) or hypoglycaemia;
- participation in routine school and leisure activities; and
- no restriction on future education or employment.

Data from the DIABAUD study and from other population studies (Denmark[18] and France[19]) indicate that conventional insulin therapy alone (i.e. twice daily insulin injections) is insufficient and that more intensive therapy is required, with the provision of considerable support for the patient and their family. Only one centre in Europe claims that a twice daily regimen is effective, although again this group offer considerable support to their families.[20]

Intensive insulin regimens have been developed over the last 15 years with the use of frequent (usually >4, pre-meal bolus) injections of short-acting insulin. Recently, changes in insulin preparations and delivery methods have made this approach more acceptable.

Insulin pen systems

These are now commonplace and are much preferred by patients. They remove the need for sterilisation and are simple in terms of drawing up the correct insulin dose. They are ideal for giving insulin as a pre-meal injection, with the ability to alter the dose in relation to the carbohydrate content of the meal. While knowledge of the meal content is required, adjustments can be made for the amount of carbohydrate, again reducing restrictions.

Insulin analogues

The production of fast-acting insulin (immediate insulin absorption profile following subcutaneous injection, as against a relatively delayed absorption profile from short-acting soluble insulin) has improved the blood glucose profiles with pre-meal injections.[21] Their immediate onset of action also allows for a more 'social use' and injection can be given at the start of a meal, not some 15 to 20 minutes beforehand, as for the short-acting preparations. In the young child it may be prudent to give the injection, during, or indeed after, the meal, particularly if there is some doubt about how much food will be consumed.

Of potential interest is analogue insulin at the other end of the absorption spectrum. A long-acting insulin analogue has been used in older patients, particularly people with Type 2 diabetes. Clinical research is in progress with these new preparations in Type 1 diabetes, particularly as part of a multiple injection regimen.

Insulin pumps

This form of insulin delivery is now gaining momentum

for use in young people with Type 1 diabetes. Continuous subcutaneous insulin therapy (CSII) has been available using an 'open loop' system from the early 1980s. Improvements in the technical design of the pump and the external delivery cannulae underlie the resurgence in their use, with an apparent expanding use in young people.[22] Pump use in both the adult, and teenage and child populations in the UK appears to have been limited, although recently a national pump interest group has been established and interest is being shown in the support groups, Diabetes UK and the Association of British Clinical Diabetologists.

While considerable effort is required from the patient, with significant technical support from the clinical centres, excellent near-normal glycaemic control can be obtained by most patients who become established on long-term treatment of their diabetes by CSII. Modern pumps cost around £2,000, and the major challenge in the UK for pump therapy is to persuade the financing of this form of therapy, which in current terms costs around £1,000 per annum per patient and is not supported by the NHS. In some centres in Europe and the US pump therapy appears to be the dominant therapy. Continuous subcutaneous insulin therapy may appeal to around 20–30% of a Type 1 clinic population.

Support network

Although not designed to ask this question, the DCCT suggested strongly that specific changes in insulin and diet therapy will fail unless they are accompanied by a major social support network for teenagers with diabetes and their families. Our work within the DIABAUD project in Scotland and the Hvidøre Study Group in Denmark, suggests that the differences that are observed between the average glycaemic control in different clinical centres can be explained to a large extent by clinic structure, utilisation of resources, communication between patients and health carers and a matching of the health beliefs of patients with their health carers.[23] We believe that these factors, while influenced by the macro-cultural characteristics of the society locally and nationally, can be adjusted to the benefit of the patient and their families. Operating outside an extensive social support network (supplied by health carers, family, peer support group and other families with diabetes) is extremely difficult for people with diabetes, especially teenagers. The challenge for all clinical groups is to help in developing and sustaining a support network within the confines of NHS resources.

Immune and molecular therapy

This approach has been boosted with recent developments in islet cell transplantation. In Canada, a trial of treatment using a specific combination of immunosuppressant therapy with specially prepared islet cell preparations has eliminated successfully the need for insulin injections in young people with Type 1 diabetes.[24] Although work in this area has been reported over the last two decades, this is a significant development. However, it still does not address the problem of supply of the large quantity of islet cell tissue that would be required to introduce this therapy into routine practice. Current research is exploring the production of human fetal cell lines, but this has not been tested in clinical trials.

A recent development is the use of 'switching on of insulin genes' in other tissues. A recently published report on work in mice has shown that this is another therapeutic option.[25] Again, a considerable amount of further work is needed to place this into the clinical arena.

SUMMARY

Our teenage girl who has developed diabetes in the new millennium is, therefore, at both a challenging, and potentially very changing, time in terms of diabetes care strategies.

The basic clinical approach of insulin, attention to diet and close monitoring of blood glucose will still form the mainstay of her clinical therapy. For many patients this will give good overall glycaemic control with the anticipated lack of long-term micro- and macrovascular complications of diabetes. For many patients, however, a more 'intensive' approach is required: multiple insulin injection regimens and/or CSII, carbohydrate counting and close blood glucose monitoring. An extensive support network will be required to maintain this intensive approach on a routine basis. It is likely that analogue insulins will play an increasing part in intensive insulin regimens.

While of considerable interest to patients and health carers, the immunological and molecular therapies need considerable development work. They are unlikely to be part of routine clinical strategies for some time but are exciting opportunities that may be available to our young patient in the future.

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