Cystic fibrosis related diabetes – causes, impact on health and management of patients

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Summary
Cystic fibrosis is the commonest, life-threatening recessively inherited disease in the Caucasian population. The disease process which primarily affects the lungs also damages both exocrine and endocrine pancreatic function. With increasing survival, cystic fibrosis-related diabetes is becoming more prevalent increasing from 15% of adolescents with cystic fibrosis to 50% of adults. Impaired glucose tolerance is also common. Insulin secretion gradually decreases over time. Insulin resistance also occurs and can vary dramatically with intercurrent illness. Even mild degrees of hyperglycaemia adversely affect nutritional status and lung function. Good blood glucose control improves nutritional status and lung function. Cystic fibrosis-related diabetes develops insidiously, so that annual screening is recommended, ideally by oral glucose tolerance testing. HbA1c is not sufficiently sensitive to identify early abnormalities in glucose tolerance. Aims of managing cystic fibrosis-related diabetes are to relieve symptoms, maintain normal body weight and growth, improve lung function and improve life expectancy. Insulin is the treatment of choice and the regimen should be tailored to the individual. Initially, only rapid-acting insulin with the main meal may be necessary, but as insulin secretion diminishes, a full basal-bolus regimen becomes necessary. Individuals with cystic fibrosis struggle to consume sufficient calories, so that a high calorie, high fat diet is usually appropriate. Supplemental enteral nutrition, with matching insulin administration, is frequently required. Special situations, including pregnancy, require specific management. The psychological impact of cystic fibrosis-related diabetes on the individual is enormous. Successful management requires support from a multi-disciplinary team with the necessary specialist knowledge and skills.

Eur Diabetes Nursing 2014; 11(3): 85–91

Key words
cystic fibrosis; cystic-fibrosis-related diabetes (CFRD); cystic fibrosis transmembrane conductance regulator protein (CFTR)

Background
Cystic fibrosis is the most common, life-threatening recessively inherited disease in the Caucasian population. One in 25 individuals is a carrier and one in 2500 live-born infants has the disease. A large number of mutations can affect the cystic fibrosis transmembrane conductance regulator (CFTR) on chromosome 7. The protein product of this gene, the CFTR protein, controls movement of salt and water across the cell membrane. In cystic fibrosis, the protein does not function normally and the passage of salt and water is abnormal. The resultant disease affects many organs. Decreased loss of salt and water from cells leads to the presence of salty sweat and to thick mucous secretions in the lungs, pancreas and other organs. In the lungs, there is recurrent infection and chronic inflammation, leading eventually to obstruction of the bronchi and alveolae, fibrosis and bronchiectasis. In the pancreas, there is obstruction of the pancreatic ducts, chronic inflammation, fibrosis and fatty infiltration. This leads to impaired pancreatic exocrine function, with decreasing secretion of digestive juices and malabsorption. Damage to the endocrine pancreas, islets of Langerhans, also occurs. Cystic fibrosis-related diabetes (CFRD) develops when the pancreatic beta-cells fail to make sufficient insulin to control the blood glucose.

Pathophysiology of CFRD
CFRD is a unique form of diabetes, although it has features of both type 1 and type 2 diabetes.[1] It is associated with the more severe cystic fibrosis gene mutations.[2,3] Both insulin deficiency and insulin resistance are present. Accumulation of thick, viscous secretions in the pancreatic ducts leads to progressive obstruction and scarring, with eventual beta-cell damage and insulin deficiency. Deposition of amyloid protein also causes physical damage. Insulin secretion falls gradually and progressively as beta-cell damage increases. Thus CFRD develops slowly over time. Abnormalities in insulin secretion are probably present from a young age, before hyperglycaemia develops.[4]

Recently, new data suggest that the cystic fibrosis disease process is not the only explanation for declining insulin secretion in individuals who develop CFRD. Genes which increase susceptibility to type 2 diabetes are more common in patients with CFRD compared to individuals with cystic fibrosis who do not develop diabetes.[5] In addition, CFRD is expressed on islet alpha- and beta-cells, so that the CFTR defect itself may play a role in

failing insulin secretion. Genetic variants in genes coding for other ion channels which interact with the cystic fibrosis transmembrane regulator are also associated with increased risk of diabetes in cystic fibrosis.[6]

Insulin resistance is also present and can vary widely depending on the health of the individual. Factors driving insulin resistance include infection, courses of steroid therapy and cystic fibrosis relate liver dysfunction. Thus glucose tolerance may fluctuate over time, primarily due to changes in insulin resistance.

Other endocrine cells of the islets of Langerhans are also affected by the disease process, so that secretion of glucagon and pancreatic polypeptide are also abnormal. Decreased glucagon secretion may predispose the individual to hypoglycaemia.

Presentation of CFRD

CFRD develops slowly over time, with progression from normal glucose tolerance to impaired first phase insulin secretion and eventually more severe loss of insulin secretion (case study 1). With the loss of first phase insulin secretion, post-prandial hyperglycaemia develops, but fasting glucose remains normal. This stage is called CFRD without fasting hyperglycaemia. As insulin secretion falls further, fasting glucose rises and CFRD with fasting hyperglycaemia develops. At any time during this process, severe insulin resistance may develop temporarily and lead to transient but sometimes severe hyperglycaemia.

CFRD may present with the classic symptoms of hyperglycaemia of polyuria and polydipsia, but these occur very late in the disease process. A more insidious onset is usual. Often, an adult may struggle to maintain or gain weight, or a child have poor growth velocity or delayed puberty. There may be an unexplained decline in pulmonary function. The decline in nutritional status and pulmonary function may begin at the very early stages of glucose intolerance, in those with minimal hyperglycaemia,[7–11] With greater post-prandial hyperglycaemia, an individual may complain of tiredness and general lethargy after food. Diabetic ketoacidosis is rare, presumably because of continuing endogenous insulin secretion.[12]

Screening for, and diagnosis of, CFRD

Because CFRD is so common, has an insidious onset and important consequences, guidelines recommend annual screening for everyone with cystic fibrosis, when they are in stable, baseline health.[13–16] Current UK guidelines suggest that screening should start at 12 years of age,[13] whereas the European and US guides suggest 10 years.[14,15] The oral glucose tolerance test is the 'gold standard' but because of variable intestinal transit times, results may vary from day to day. It is also unpleasant and time consuming for the individual and labour-intensive for the healthcare system. Measurement of random clinic glucose is not recommended for screening, but a value greater than 8mmol/l should prompt further investigation, as a Cochrane review has concluded that the risk of accelerated lung damage increases at this level.[17] HbA1c will probably only be in the 'diabetes range' (>48mmol/mol [6.5 %]) when fasting hyperglycaemia has developed, so is not sufficiently sensitive to use as a screening tool. If there is doubt about the diagnosis, self capillary blood glucose monitoring may be useful, particularly if the person is willing to make measurements 60–120 min after their main meal.

- Attain and maintain normal body weight
- Maintain optimal growth in children
- Avoid symptoms of hyperglycaemia
- Avoid acute complications of diabetes (hypoglycaemia and diabetic ketoacidosis)
- Slow loss of lung function
- Improve life expectancy
- Delay tissue complications of diabetes (retinopathy, neuropathy, nephropathy)

Table 1 Aims of management of cystic fibrosis-related diabetes

Continuous glucose monitoring may provide additional information, but experience with this in CFRD is limited, so it is currently not recommended for screening.[17,18] Glucose values diagnostic of CFRD are as in the general population: fasting glucose ≥7.0mmol/l and post-prandial / 2h OGTT value > or ≥11.0mmol/l, or HbA1c ≥48mmol/mol. It is also important to identify individuals with impaired glucose tolerance (2h glucose 7.8–10.9 mmol/l).

Prevalence of CFRD

Decades ago, people with cystic fibrosis died early in life because of respiratory complications of the disease, and few lived long enough to develop CFRD. With improved treatment of the chest disease, the average life span is now approximately 52 years, and a significant proportion develop CFRD. The prevalence of CFRD increases with age, from approximately 15% in adolescents to 50% in adults.[2,19] Impaired glucose tolerance is also common, one series reporting that 20% of children with cystic fibrosis had impaired glucose tolerance.[20]

Aims of management of CFRD

Individuals with CFRD have poorer nutritional status, more severe lung disease and greater mortality than

individuals with cystic fibrosis who do not have diabetes.[21] Individuals with cystic fibrosis and HbA1c ≥48mmol/mol are at three times the risk of death compared to individuals with HbA1c <48mmol/mol.[22] However, mortality in CFRD is improving over time, presumably because of improved care.[2] The aims of management are shown in table 1. Maintaining optimal nutritional status is important to allow normal growth and development. Avoidance of symptoms secondary to hyperglycaemia and the acute complications of diabetes (diabetic ketoacidosis and hyperosmolar hyperglycaemia syndrome) are clearly important. CFRD increases the risk of end-stage pulmonary disease in cystic fibrosis,[23] and accelerates decline in lung function.[24,25] There is some evidence that insulin therapy improves these outcomes. One trial has shown an increase in body mass index with mealtime rapid-acting insulin analogues in adults with CFRD without fasting hyperglycaemia.[26]

Other small, uncontrolled studies in individuals with cystic fibrosis and impaired glucose tolerance suggest that insulin improves weight and lung function.[27,28] Recently, as individuals survive longer with cystic fibrosis and CFRD, we have learned that they may develop the chronic complications of diabetes.[29,30] Thus, good glycaemia control is essential.

For many individuals, the addition of the tasks associated with the self-management of diabetes to an already complex and time-consuming treatment regimen is a huge burden. Thus it is important to keep diabetes treatment regimens as simple and flexible as possible.

Aims of treatment include achieving and maintaining normal weight, growth and development. Targets for glucose and HbA1c are as for any type of diabetes.

Management of CFRD

A multi-disciplinary team, with specialist knowledge of CFRD, is the key in successful management. Specialist dietetic and nursing skills are paramount. It is important to remember that people with cystic fibrosis should not be in contact with each other in groups or clinic because of the risk of cross infection. This is very important as infection with certain bacteria will mean they are not eligible for lung transplantation.

Nutritional status

It has long been established that resting energy expenditure increases as lung function declines. Calorific requirements are estimated to increase by 120–150% of normal.[31] Poor nutritional intake is well documented, so that actual intake is frequently less than recommended.[32] The reasons for the increased demand for energy and poor intake are multifactorial: increased demand from catabolic lungs and reduced intake due to infection, coughing, malabsorption, anorexia, depression and psycho-social factors.

People with cystic fibrosis require a high calorie, high fat diet. Fat is the most energy dense nutrient and individuals with cystic fibrosis are encouraged to consume it. To prevent malabsorption, Pancreatic Enzyme Replacement Therapy (PERT) is required to be taken with fat. Individuals with cystic fibrosis become adept at adjusting the quantity of PERT to be taken with each meal/snack/drink, depending on the fat content. At present there is no evidence of increased macrovascular disease when CFRD is present.

Case study 1

The slow progression of cystic fibrosis

At the age of 19 years, David had cystic fibrosis but normal glucose tolerance. He had his first holiday in Spain with friends, where he played football in the heat (temperature 35ºC). As they flew home the next day, his friends noticed that David was a little confused and drowsy. He was admitted to hospital directly from the airport. He was dehydrated, with a low serum sodium and capillary blood glucose of 25.4mmol/l. He was rehydrated with saline and received insulin by intravenous infusion for 48 hours. He recovered quickly and when able to eat, was commenced on subcutaneous insulin in the form of a basal bolus regimen, with 12 units long-acting analogue insulin initially, and 6 units rapid-acting insulin analogue with meals. Over the next week, the dose of rapid-acting analogue was gradually reduced and then stopped. In the second week, the long-acting analogue dose was then also reduced and stopped. Capillary blood glucose monitoring demonstrated persistently normal fasting glucose values (4–5mmol/l) and values 90min post main meal of 5.7–7.9mmol/l. Insulin was withheld and weight and lung function held steady over the next three years.

Glucose levels then rose after the main meal to 8–12mmol/l, so that rapid-acting insulin analogue, initially 4 units, was introduced. David learned to adjust this dose depending on the amount and type of food he ate. Three years later, capillary glucose monitoring showed hyperglycaemia 90 min after lunch, and David introduced a second dose of rapid-acting insulin with lunch. A year later, David also required rapid-acting insulin with breakfast.

Five years later, David noticed that capillary blood glucose levels before breakfast were slowly rising and were usually 7-8mmol/l. Long-acting insulin analogue at bedtime was commenced and the dose titrated to keep fasting glucose levels 4–5mmol/l. David is now 30 years old. His body mass index is 23.8kg/m2, HbA1c 52mmol/mol and lung function is stable.

Carbohydrate foods and drinks such as lemonade and jelly sweets do not contain any fat and therefore PERT are not required to be taken with them. People with cystic fibrosis often regard these foods as 'free foods,' and some consume these in large amounts. At the diagnosis of CFRD, if these items are limited, the calories must be replaced by other foods to prevent weight loss.

To support nutritional status, oral supplements are frequently used by people with cystic fibrosis. Individuals may consume on average 2–3 portions per day. The most common type used contains a mixture of protein, carbohydrate, fat and vitamins. Each 200ml carton/bottle contains approximately 40g carbohydrate, hence insulin maybe required with each supplement. The type of supplement may change due to taste fatigue.

Enteral tube feeding either as nasogastric or Percutaneous Endoscopic Gastrostomy is advised when dietary manipulation and supplements have not achieved appropriate nutritional status.[33,34] White reported in her study that almost one third of people with cystic fibrosis who had enteral feeding had co-existing CFRD at the start of treatment, indicating the more advanced stage of disease.[35] The prevalence of CFRD in this cohort increased to 53% during the following three year period.

Generally enteral feeds are given overnight in 8–10 hours. Most people with cystic fibrosis have 'nights off' the feed, depending on their nutritional requirements and social life. When prescribing insulin, this variability in nutrient intake should be considered. The aim of the feeds is to give between 1500–2000kcal/night, that is approximately 200–250g of carbohydrate per night. Individuals having enteral feeding at night are encouraged to continue to eat during the day although many find it difficult to achieve this in the early part of the day.

Nutritional education in CFRD

The dietary advice offered to individuals with CFRD differs from that recommended to other people with diabetes, in that they are encouraged to consume a high fat intake. Carbohydrate portions are taught and, for those who are willing to learn, carbohydrate counting is also used. Due to the complexity of their nutritional needs it is recommended that people with cystic fibrosis should be reviewed by a dietitian experienced in this area.

Drug management

Insulin deficiency is the primary pathophysiological mechanism so that insulin replacement is probably the most effective therapy. Most individuals with CFRD are in a catabolic state and are underweight, so that the anabolic effects of insulin are important. Metformin, the thiazolidenediones and incretins are inappropriate. Sulphonylureas and prandial glucose regulators are used occasionally, but there is no good data. There are no good trials to guide us in the choice of insulin regimen. A recent Cochrane review found only three randomised controlled trials, two comparing insulin with oral repaglinide and one comparing insulin glargine with neutral protamine Hagedorn insulin.[36] No convincing evidence was found for one regimen over any other.

The choice of insulin regimen depends on the stage of CFRD and the patient's wishes. Initially, if the person has CFRD or impaired glucose tolerance without fasting hyperglycaemia, then rapid-acting insulin with the main meal may be all that is required. The rapid-acting insulin analogues can be given before or immediately at the end of the meal. This is helpful if the person is unsure how much they will be able to eat. The initial dose should be small, perhaps 4 units, and then titrated up depending on blood glucose 60–120min post-prandially. With time and experience, the person can learn about carbohydrate counting and develop confidence in insulin dosage adjustment.

As CFRD progresses, rapid-acting insulin may be required with smaller meals and some larger snacks. For those having food supplements, rapid-acting insulin (4–8 units) may be required with each portion. Eventually, when CFRD with fasting hyperglycaemia develops, basal insulin should be introduced, usually in the form of once-daily basal insulin analogue. The long-acting insulin can be given at any time in the 24 hours, but is best agreed with the person as a time they will remember to give the insulin and can keep relatively constant. Again, the initial dose should be small. Titration upwards depends on fasting glucose levels.

Some individuals with CFRD find multiple injection therapy too intrusive and elect for a twice-daily regimen, using pre-mixed insulin. Some, presumably those with substantial residual pancreatic insulin secretion, gain good control on this, but other do not. In addition, the necessities of eating fixed amounts of food at fixed times place additional restrictions on their lifestyle. Alternatively, once-daily long-acting analogue insulin may be effective, at least in some individuals with early CFRD.[37]

There are a few case reports of individuals with CFRD who have undergone whole-organ pancreas transplantation or islet cell transplantation,[38] in combination with lung or liver transplantation,[39] but these are clearly not options for the majority of individuals.

Hypoglycaemia

Hypoglycaemia may occur in individuals with insulin treated CFRD, as in any person taking insulin. Awareness of hypoglycaemia is usually good. However, glucagon secretion is impaired in CFRD.[40] People with cystic fibrosis commencing insulin should therefore be fully informed about hypoglycaemia.

Education

Individuals with CFRD should have full access to relevant education programmes so that they can attain the knowledge and skills necessary for effective self-management of CFRD.

Screening for the chronic complications of diabetes

Individuals with cystic fibrosis and fasting hyperglycaemia are at risk of the specific chronic tissue complications of diabetes: retinopathy, nephropathy and neuropathy. As in all forms of diabetes, the prevalence of complications increases with duration of diabetes and HbA1c. Data is limited, but in one series 16% had retinopathy and 14% microalbuminuria.[30] Renal biopsy studies have confirmed diabetic nephropathy.[41] Thus, people with CFRD, particularly those with fasting hyperglycaemia, should be offered annual screening for these complications, as in any individual with diabetes of any cause.

Case Study 2

Teenage tantrums

Mary was aged 18 years when her diabetes care was transferred to the adult diabetes clinic. She had developed cystic fibrosis-related diabetes at the age of 13 years and was prescribed a basal bolus insulin regimen. HbA1c was 112mmol/mol and body mass index 17.4kg/m2. On her third visit to the diabetes clinic, Mary confessed that she hated given insulin injections and missed many. After discussion, she agreed to switch to twice daily injections of pre-mixed insulins, saying that she felt she would manage to give two injections of insulin a day. Over the next six months, HbA1c fell to 76mmol/mol and body mass index increased to 19.4kg/m2. Over the next seven years, Mary managed to maintain this level of control, but declined to try a basal bolus regimen again.

However, at the age of 26 years, Mary announced that she would like to have a child. She was aware of the need to have good glucose control pre-conception and asked to try a basal-bolus insulin regimen again. She felt that she would be able to manage a more complex regimen and that her glucose control would improve on it. With education and support from the specialist cystic fibrosis dietitian and diabetes nurse, Mary became adept at using rapid-acting insulin analogue with meals and once daily long acting insulin analogue. HbA1c fell to 52mmol/mol within six months. Mary managed to maintain very good glucose control for 18 months, before finally undergoing successful in vitro fertilisation treatment. She worked hard during the pregnancy to maintain good control and was delivered of a healthy baby boy. Two years later, Mary and her son continue to thrive.

Special situations

Acute illness

With the development of an intercurrent illness, such as a chest infection, an individual with cystic fibrosis may develop very marked insulin resistance. Blood glucose and ketone levels should be monitored carefully. For those who already have CFRD, rapid and substantial increases in insulin doses may be required. It is not uncommon for doses to double or even treble. If the person is very unwell, intravenous insulin may be required, administered according to local protocols for hyperglycaemia emergencies. Those able to eat and drink normally should continue subcutaneous insulin but at doses titrated according to blood glucose concentrations. Individuals who usually only have prandial insulin may require basal insulin temporarily. Even individuals who usually have normal glucose tolerance may develop significant hyperglycaemia and require insulin temporarily. In this situation, a basal bolus regimen provides the most flexibility.

As the acute illness improves, insulin resistance falls and the doses of insulin can be gradually reduced or stopped over the following days or weeks. All of this requires very careful blood glucose monitoring and close collaboration between the individual and the diabetes and cystic fibrosis teams.

Supplemental nutrition

Most food supplements contain significant amounts of carbohydrate which may precipitate hyperglycaemia and failure of the body to optimally utilise the nutrition. Thus it is worthwhile asking the person with CFRD to monitor capillary blood glucose 60–120 min after intake. If glucose is >9mmol/l, a small dose of rapid-acting insulin (~6 units) may be needed with the supplement.

Nasogastric or PEG feeding may cause hyperglycaemia which is difficult to control and may need high doses of insulin. Most individuals have supplemental feeding overnight, and eat normally by day. Overnight intake is varied, but typically around 1500 calories. Thus insulin requirements are higher overnight, and lower by day. Long-acting insulin analogues may not be ideal in this situation, as doses sufficient to control overnight hyperglycaemia may cause hypoglycaemia during the day. Thus isophane

insulins may be more appropriate, with a bigger dose at night and a smaller dose in the morning. Quick-acting insulin as the feed starts may be necessary to prevent rapid hyperglycaemia at onset of feeding. This can be given as quick-acting analogue separately to the isophane insulin or as a mixed preparation. The dose of insulin with the feed should be adjusted to obtain glucose levels at the end of the feed of approximately 9mmol/l. Care should be taken to avoid hypoglycaemia in the hour or two after the feed is stopped, when calorie intake falls quickly but subcutaneous insulin may continue to act. Hypoglycaemia immediately post-feed may limit attempts to control overnight hyperglycaemia.

Individuals with normal glucose tolerance may develop hyperglycaemia overnight with supplemental feeding and may require overnight insulin to gain full benefit from the nutrition.

Pre-conception and pregnancy care

It is particularly important for women with CFRD to plan pregnancy and to receive appropriate pre-conception counselling and care.[42] Women with CFRD who may wish to have children should be fully informed of the risks associated with diabetes and the need to optimise management before contraception is stopped. Hyperglycaemia at the time of conception and in the first weeks of pregnancy will increase the risk of congenital malformation, as is the case in any type of pre-pregnancy diabetes. It also seems sensible to assume that good glucose control at the time of conception will reduce these risks, and that continuing good control throughout pregnancy will improve the outcome for mother and baby, as it does in other forms of diabetes.

Strenuous efforts to achieve optimal glucose control should be made, and high dose folic acid (5mg daily) commenced to reduce the risk of neural tube defects in the baby. Careful screening for diabetes complications should be performed, and any risk the complications may pose during pregnancy assessed. Drugs prescribed should also be reviewed and any known to be harmful during pregnancy stopped, if possible. All of this must be done sensitively: many women with cystic fibrosis have subfertility or infertility and may either take a long time to conceive naturally or require in vitro fertilisation. Maintaining tight glucose control throughout a long pre-conception period is exceptionally difficult.

Insulin resistance increases during pregnancy, particularly during weeks 16–36. Women with cystic fibrosis but normal glucose tolerance pre-pregnancy should be aware that they may develop 'gestational CFRD' as their pregnancy progresses. Careful assessment of glucose tolerance as part of pre-conception care is required, best done by oral glucose tolerance test (OGTT). In those women without diabetes pre-pregnancy, the OGTT should be repeated at 16 and 28 weeks. Cut-off glucose levels for the diagnosis of gestational diabetes in women with cystic fibrosis should be as in the general population. Some women will elect to perform self-blood glucose monitoring throughout the pregnancy rather than undergo repeated OGTTs.

Management of gestational diabetes in cystic fibrosis is generally different to the management of gestational diabetes in the general population: given that women with cystic fibrosis are usually underweight or normal weight, calorie restriction and prescription of metformin are inappropriate. If glucose levels remain above target after avoidance of large amounts of refined carbohydrate, then insulin should be prescribed. The insulin regimen chosen should reflect the pattern of hyperglycaemia: mealtime rapid acting analogue insulin for prandial hyperglycaemia and longer acting insulin if there is fasting hyperglycaemia. Post-natally, insulin can generally be stopped and glucose tolerance re-assessed six weeks later.

Transplantation

More and more individuals with cystic fibrosis are undergoing lung transplantation because of end-stage respiratory disease. This can have a variable effect on glucose tolerance. Removal of chronically infected lungs will reduce insulin resistance and improve glucose tolerance.[43] However, immunosuppressive therapies may have deleterious effects: steroids increase insulin resistance while tacrolimus and cyclosporine reduce insulin secretion. In one series, more than 50% of individuals with cystic fibrosis undergoing lung transplantation developed new-onset diabetes after transplantation.[44] Thus, post-transplantation there is an on-going need to continue to monitor glucose levels carefully in those known to have pre-transplant CFRD and to adjust glucose-lowering therapies appropriately. Individuals with cystic fibrosis and normal glucose tolerance pre-transplantation should understand that they are at high risk of developing new onset diabetes after transplantation. Careful screening of glucose tolerance, with appropriate action when results are abnormal, is essential.

Psychological issues

The diagnosis of diabetes on top of the existing cystic fibrosis is undoubtedly the 'straw that broke the camel's back' for many indi-

viduals, particularly teenagers.[45] Thus while not denying the serious implications of the diagnosis, the diabetes team needs to exert even more tact and empathy than usual. Compliance with even the most simple of regimens may be poor. Much support and positive encouragement is needed (case study 2).

Conclusions

CFRD is becoming increasingly common. It has deleterious effects on nutritional status and lung function and should be screened for assiduously. Insulin is the treatment of choice, and should be commenced early. The insulin regimen should be chosen to suit the individual. A multidisciplinary team with specialist knowledge of and training in the management of CFRD is essential. Successful management of CFRD demands a great deal of input from the person with cystic fibrosis, who should have access to appropriate education and support.

Declaration of interests

There are no conflicts of interest declared.

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