

## CF Guidelines - Cystic Fibrosis Related Diabetes

### C.F.R.D is characterised by:

- Impaired and delayed insulin secretion, due to destruction of pancreatic islet cells.
- Peripheral insulin resistance (exacerbated by infection and use of glucocorticoids)
- Glucagon and pancreatic polypeptide production are also impaired. Insulin clearance rate is increased.

The mean age of onset of C.F.R.D is 20 years, with prevalence of 1.5% at 10 years, 13% at 20 years and 50% at 30 years in the Danish study. The onset of diabetes is often insidious and in some patients is heralded with weight loss, fatigue & poor appetite. A decline in lung function may be noticed in the 2 years preceding a diagnosis of diabetes. Polyuria, nocturia and polydypsia are unusual but should still be asked about in clinic. Precipitating factors can be oral steroids, respiratory exacerbations, supplemental feed (eg gastrostomy night feeds). Ketoacidosis is rare in CF at diagnosis or in the course of the disease due to some residual islet cell function but may occur.

### Diagnosis:

Initially patients develop post-prandial hyperglycaemia before progressing to insulin deficiency and C.F.R.D. However, the delayed insulin secretion seen in CF, together with delay gastric emptying may result some pre-diabetic patients experiencing post-prandial hypoglycaemia. The gold standard in diagnosis of diabetes mellitus is the oral glucose tolerance test (OGTT) - protocol at end of this document. The diagnosis of C.F.R.D is complicated by the fact that the OGTT may not accurately reflect glucose handling by those with CF. HbA1C may be falsely low due to increased RBC turnover (due to chronic infection and hypoxaemia) or abnormal glycosylation. It is still worth measuring HbA1C to identify those with high levels. Where there are clinical suspicions of C.F.R.D, the patient should be advised to keep a food diary and check blood glucose (BMs) pre- and 2 hours post meals for 3 days. Urine dipstick for glucose and ketones may be useful in those who cannot be persuaded to check their BMs. However, a lack of glycosuria and a normal fasting BM do not exclude C.F.R.D. Pregnant ladies with CF should be asked to monitor their BMs regularly.

### Treatment:

- Patients with C.F.R.D lack insulin - close liaison with diabetes team is required.
- Oral hypoglycaemics should only be used with care. Poor glucose control should not be tolerated so that starting insulin should not be delayed. There is no trial evidence of benefit from this form of C.F.R.D management.
- Dietetic involvement is vital. The nutritional status is usually more impaired by CF than by C.F.R.D. Continued high calorie/high fat diets are encouraged however older children and adults should have low sugar drinks (ie diet coca-cola). Calorie and salt intake should not be restricted.
- Insulin regimen is tailored to individual patient's requirements and lifestyle. Often in C.F.R.D, insulin requirement is lower than in standard DM. Adolescent patients are often difficult to manage as compliance with the insulin and glucose monitoring can be sporadic. Close liaison with the diabetic team is vital.

Potential insulin regimes -  
3-4 times daily regimen:

- Good control and flexible but only the motivated will cope with number

of injections. Some patients may only require short-acting insulin for meals, others may need some intermediate or long-acting cover as well, especially if on overnight feeds. Patients with fasting hyperglycaemia will require a long acting insulin (Insulatard/Humalin I). Use of ultra-long acting analogues (levemis/glargine) is generally less recommended.

2 times daily regimen:

- Use Mixtard / Humulin preparations, M3 = 30% short acting insulin and 70% isophane (intermediate) acting insulin. Easier to use, control may not be so good. Very occasionally, patients may required insulin pumps. If there are problems, discuss with a senior doctor, do not attempt to program or alter them in any way.

Stage of Disease	Pre-meal Sugars	Post-meal Sugars	Symptoms	Complication Risk	Treatment
<b>Hypoglycaemia</b>	Normal	Low	Hypoglycaemia after meals.	Unknown, likely to be very low.	Dietician
<b>Impaired glucose tolerance</b>	Normal	Intermittently raised	None/weight loss? Clinical decline?	Unknown, likely to be very low.	Dietician. Insulin when exacerbates?
<b>C.F.R.D without fasting hypoglycaemia</b>	Normal	Mostly raised	Potentially none. Thirst, polyuria, weight loss, clinical decline.	Unknown, likely to duration, control and risk factors.	Dietician. Insulin with meals if symptomatic or clinical decline.
<b>C.F.R.D with fasting hypoglycaemia</b>	Mostly raised	Mostly raised	Thirst, ployuria, weight loss, clinical decline.	Unknown, likely to duration, control and risk factors.	Dietician. Insulin with meals. Basal insulin

### Other issues at time of diagnosis:

- Initially finger prick BMS should be checked 4-5 a day. When adequate control is established, patients should be encouraged to monitor their BMs at least daily.
- More intensive monitoring will be required during periods of illness or steroid use when insulin requirement will increase (during admissions, patient should check pre and 2 hour post meal BMs)
- Patients should aim for a blood glucose of no less than 4 mmol/l and no more than 10 mmol/l before meals, although individual targets may differ (see below).
- It is vital that patients are taught how to recognise the symptoms of hypoglycaemia and learn how to deal with it ie glucose rich snack followed by complex carbohydrate food.

### Potential changes to insulin regime during exacerbations - check pre and 2 hour post meal BMs:

- Raised BMs after meals - Start/increase short acting insulin with meal by 2 units - (or 10% if greater.)
- Fasting glucose raised in mornings - add/increase intermediate acting insulin (4-8 units) at bedtime.
- 6pm BM raised when patient takes prednisolone in morning - add/increase intermediate acting insulin (4-8 units) at 9am.

### On going monitoring:

- Initially finger prick BMS should be checked 4-5 a day. When adequate control is established, patients should be encouraged to monitor their BMs at least daily.

- More intensive monitoring will be required during periods of illness or steroid use when insulin requirement will increase during admissions, patient should check pre and 2 hour post meal BMs.
- Patients should aim for a blood glucose of no less than 4 mmol/l and no more than 10 mmol/l before meals, although individual targets may differ - (see below).
- It is vital that patients are taught how to recognise the symptoms of hypoglycaemia and learn how to deal with it ie glucose rich snack followed by complex carbohydrate food.

### Examples of treatment targets for individuals with C.F.R.D:

	Tight Control	Modified Control	Symptomatic Control
<b>Fasting Glucose</b>	4 - 6 mmol/L	4 - 10 mmol/L	<10 mmol/L unless Pulmonary function tests stable and weight loss not problem.
<b>2 hr post meal glucose</b>	4 - 7 mmol/L	4 - 10 mmol/L	<10 mmol/L unless Pulmonary function tests stable and weight loss not problem.
<b>Hypoglycaemia</b>	Mild daytime hypo's only	Aim for none	Aim for none
<b>HbA1c</b>	<7.0%	8.0%	Irrelevant

### Long term management:

- As life expectancy improves with CF, patients are beginning to show microvascular complications. This means tight control is essential.
- The prevalence of retinopathy is 16% at 5 years and 23% at 10 years following diagnosis. Ophthalmology review (retinal photography) should be performed yearly in those >12 years old.
- The prevalence of nephropathy is 5-21%. Alb/creatinine ratio from early morning urine at annual assessment. However, intermittent microalbuminuria may occur when patients are pyrexial, so should not immediately be ascribed to diabetes. It is important to monitor renal function closely if patients are on other nephrotoxic drugs especially aminoglycosides.
- HbA1C should be checked every 3 months.
- Blood pressure should be measured at every clinic.
- It is important to monitor injection sites and to rotate sites used.
- Foot examination should occur annually.
- Annual review should also specifically consider frequency of Hypoglycaemia and sexual dysfunction.

### Oral glucose tolerance Test - CF patients only:

- Patients should be starved from midnight before the test, (unless an evening test has specifically requested in which they should have their evening meal around 5pm) they can have a small sip of water only when they wake.
- Patients to be given an early appointment i.e : 8.30 – 9.00 (unless attending for an evening test in which an appointment for 17.30 – 18.00 should be given) Evening tests are requested if IGT is suspected even if morning fasted OGTT is normal, it is like doing post-prandial measurements after a large meal.
- Patient should be weighed on arrival and Ametop/Emla applied on appropriate vein or portacath - if not done so already prior to arrival.
- Insert cannula (or access portacath as per protocol) and take baseline blood for glucose (yellow top bottle) and a sample for HbA1C (brown top) along with any other bloods that have been requested.
- Label, time and mark yellow bottle "baseline" or "0 minutes".
- Give Glucose drink 1.75g/kg up to a maximum of 75g. This can either be in

the form of oral glucose solution 75g in 150ml (ordered from pharmacy), give the required dose/amount diluted with the same amount of water and flavoured if necessary. Lucozade sparkling energy drink 70kcal/100ml formulation (Not the diet variety) can be used as an alternative, give 9.2ml/kg up to a maximum of 394mls. The glucose drink should be consumed within 5 minutes and note the time.

- Take further blood samples for glucose (yellow top) at -
  - + 30 minutes - label, time, and mark this sample + 30 minutes.
  - + 60 minutes - label, time, and mark this sample + 60 minutes.
  - + 90 minutes - label, time, and mark this sample + 90 minutes.
  - + 120 minutes - label, time, and mark this sample + 120 minutes.Blood samples are usually withdrawn from the cannula or portacath - as per protocol, ensure that the 1st 2-3ml from cannula or 5ml from portacath is discarded before taking the sample.
- Send all samples together with a biochemistry form requesting glucose tolerance test, glucose levels at baseline, + 30,+ 60, + 90 and + 120 minutes.
- The test is now complete, remove cannula or de-access portacath as per protocol and discharge patient.
- Document in notes and await results.

Document approved - December 2011  
Document due for review - December 2013

***Acknowledgements:*** *The Peninsula CF team acknowledges the use of guidelines produced by The CF Trust, Manchester, Papworth, Leeds and Brompton CF teams during development of these local Peninsula protocols and guidelines.*