253 The shape and relevance of the oral glucose tolerance test (OGTT) curve in CF

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Objectives: In normal individuals, the shape of the OGTT curve (monophasic or biphasic) is influenced not only by the glucose load but also the patient's metabolic response. This has not been studied in CF and may give an insight into the abnormal glucose handling even in those without CFRD.

Method: We compared the area under the curve (AUC) for glucose, insulin, C-Peptide and glucagon following a 2-hour OGTT in 13 pancreatic insufficient adult CF (without known CFRD) and 10 healthy subjects, classified according to the OGTT curve shape.

Results: See table. Biphasic curves were more common in CF ($Chi^2 = 4.97$, $p < 0.03$), and these patients also had higher glucagon levels ($p = 0.01$) compared to their healthy counterparts, whilst CF patients with monophasic curves had reduced C-peptide levels ($p = 0.04$).

Conclusions: This study shows that the shape of the OGTT curve in CF is related to pancreatic alpha and beta-cell function, as well as glucose load. The OGTT shape index may be a useful screening tool to make an early diagnosis of diabetes in CF.

Table: OGTT curve shape

	Controls			CF		
	Monophasic (n = 7)	Biphasic (n = 3)	p	Monophasic (n = 2)	Biphasic (n = 11)	p
$AUC_{glucose}$ (mmol/L)	605 (107)	851 (137)	**0.009**	590 (40)	935 (135)	**0.005**
$AUC_{insulin}$ (μU/ml)	4394 (1864)	5502 (1379)	0.85	2537 (1965)	3962 (1543)	0.48
$AUC_{C–Peptide}$ (ng/ml)	1017 (242)	1146 (258)	0.41	493 (291)	974 (421)	0.19
$AUC_{glucagon}$ (pg/ml)	7782 (1408)	6373 (182)	0.06	8967 (1608)	7868 (1678)	0.56

Results are mean (SD).

Reference(s)

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254 The prognostic significance of hypoglycaemia on oral glucose tolerance tests in adults with cystic fibrosis (CF): A prospective clinical study

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Objectives: Current guidelines recommend an annual oral 75 g glucose tolerance test (OGTT) to screen for Cystic Fibrosis-Related Diabetes (CFRD). Hypoglycaemia during an OGTT is common, but the relevance of this phenomenon is unclear. This study aims to determine the prognostic significance associated with hypoglycaemia on OGTT with regards to CFRD and clinical outcomes.

Methods: Patients attending the Cork Adult CF Centre were recruited over a one-year period during 2006/07, and were followed for five years with annual OGTT and pulmonary function testing.

Conclusion: 76 participants were included. The mean age was 26±8 years. 54 (62%) of the cohort were male. 48 (63%) had normal glucose tolerance on OGTT at entry. A further 12 (16%) had impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), and 16 (21%) had hypoglycaemia on OGTT. The hypoglycaemic cohort had a lower rate of progression to CFRD over 5 years as compared to the normal OGTT group (6% vs 28%, $p < 0.001$), and had a higher rate of pancreatic insufficiency (PI) (87% vs 77%, $p < 0.001$). They had a significantly greater FEV_1 on entry to the study than the IFG/IGT group (74±17 vs 59±22% predicted, $p = 0.04$) and the difference in FEV_1 persisted over the five-year follow-up (79±16 vs 59±21% predicted, $p = 0.003$).

This study highlights that hypoglycaemia on OGTT may be associated with a lower risk of progression to CFRD in adult CF. Hypoglycaemia on OGTT is associated with PI when compared to those with a normal OGTT, and a higher FEV_1 when compared to those with IFG/IGT. Further studies are required to determine the mechanism of hypoglycaemia, and its potential role as a prognostic indicator in CF.

255 Screening glucose disorders in cystic fibrosis: Continuous subcutaneous glucose monitoring compared to oral glucose tolerance test

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Introduction: Diabetes is an important complication of cystic fibrosis (CF). It is associated with increased morbidity and, if left untreated, can lead to deterioration of nutritional and pulmonary status.

Objectives and Methods: The aim of this study was to evaluate the glycemic profile with continuous glucose monitoring system (CGMS) in patients with CF followed in a terciary pediatric center, and compare these results with oral glucose tolerance test (OGTT) and HbA1c. Patients younger than 10 years, with current corticosteroids or immunosuppressive treatment, those who were transplanted or who already had the diagnosis of diabetes were excluded.

Results: Nine patients were included, five males, with a mean age of 17.8 years. Three patients had homozygous ΔF508 CF-mutation. All patients had normal OGTT and a median HbA1c value of 5.4±0.29% [5.1–5.9%]. Mean CGMS glucose was 102.7±8.2 mg/dl and mean glucose lowest and highest values were 63.2±13.7 mg/dl [47–87 mg/dl] and 164.5±27 mg/dl [132–218 mg/dl], respectively. In seven patients CGMS showed peaks of glucose higher than 140 mg/dl at least once after a meal and one individual had values above 200 mg/dl despite normal OGTT. We also found asymptomatic hypoglycemias in five patients during CGMS

Conclusion: Most patients had a glucose profile during CGMS with values below 200 mg/dl. However, we observed abnormal glucose values in more than half of the patients. Asymptomatic hypoglycemias found in this study may reflect an inadequate insulin secretion.

The authors believe that CGMS allows a better diagnosis of glucose disorders in patients with CF compared to OGTT.

256 The diagnostic utility of continuous glucose monitoring (CGM) in cystic fibrosis related diabetes (CFRD)

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The oral glucose tolerance test (OGTT) defines diabetes based on glucose thresholds derived from a non-CF population to prevent micro-vascular complications and may mislead in CF, where glucose handling is variable and clinical deterioration is associated with lower levels of hyperglycaemia. CGM, validated for use in CF, allows the evaluation of a glycaemic profile, and is a stronger predictor for the development of CFRD than an OGTT. To look at this further, we explored the utility of CGM in CFRD diagnosis and management at our large adult CF centre (n = 282; 40% CFRD) in 40 patients over 20 months, comparing it with changes in weight, pulmonary function, HBA_1C and antibiotic treatment. Food and exercise diaries completed during CGM were also evaluated.

The results are summarised in the table. 55% were diagnosed with CFRD (glucose ⩾7.8 mmol/L >4.5% of the time) despite previous normal HBA_1C and serial glucose monitoring. Following insulin therapy, weight improved in 77%, lung function in 50%, HBA_1C in 56%; 64% required less IV antibiotic therapy and 55% fewer oral antibiotics.

Food and exercise diaries were interrogated and adjustments were made for 83% of the group not commenced on insulin and 59% of the insulin commenced group. This study demonstrates the utility of CGM as a diagnostic tool, especially since HBA_1C, OGTT and serial glucose monitoring have significant limitations. The guidance for the diagnosis of CFRD should be updated to include this more physiological test.

Group	FEV$_1$ (%) [SD]		Weight (kg) [SD]		HbA$_1$C (IFCC mmol/mol) [SD]	
	Pre	Post	Pre	Post	Pre	Post
Insulin therapy (n = 22)	59 [24]	62 [25]	55 [8]	56 [8]	41 [4]	40 [4]
Dietary advice only (n = 18)	72 [18]	74 [17]	68 [18]	68 [19]	37 [6]	38 [4]