The recent substitution of the gamma-camera for the scintiscanner has the advantage of allowing continuous observations to be made. The mean half emptying time for our control subjects agrees closely with that in other series.^{9 15 16} Although the method is associated with a high degree of reproducibility, two of the six diabetics in whom duplicate studies were carried out (cases 7 and 12) showed poor reproducibility. This might imply a greater variation in the rate of gastric emptying in diabetics and means that it is difficult to interpret single observations.

Measuring gastric emptying by this technique has not been described before in diabetics. Our results indicate no significant difference in the rate of emptying between diabetics, with or without autonomic neuropathy, and controls. These results disagree with reports of barium studies in which gastric emptying was delayed.³⁻⁵ Barium is non-physiological, however, and it is possible to measure only the total time taken for barium to leave the stomach. Furthermore, observations of the emptying pattern are not obtained.

Delayed gastric emptying of a solid meal seems to be uncommon in stable diabetics, even those with well-established autonomic neuropathy. Only two diabetics had prolonged emptying times and it was not possible to repeat these studies. One other diabetic had a grossly delayed emptying time on the second but not the first test (table I). Seven of the diabetics with autonomic neuropathy had troublesome gastrointestinal symptoms, including recurrent vomiting in one patient, but their emptying rates could not be distinguished from those without such symptoms.

Gastric acid secretion in response to insulin-induced hypoglycaemia is decreased in diabetics with autonomic neuropathy,¹⁷ which suggests impaired vagal innervation of the stomach. Possibly this test is unreliable in diabetics, who have wider fluctuations in blood glucose levels than controls. If the

stomach is commonly denervated in diabetics, however, our results suggest that there is some compensatory mechanism whereby normal rates of gastric emptying can be maintained. Acute gastric dilatation is well recognised in diabetic ketoacidosis. This is probably the result of acute metabolic and hormonal disturbances, although an acute reversible autonomic disturbance has been suggested.¹⁸

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Request for reprints should be addressed to JHBS.

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The ¹⁴C-glycocholate test in diabetic diarrhoea

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Summary

Twenty-four insulin-dependent diabetics, including seven with diabetic diarrhoea, were studied by means of the ¹⁴C-glycocholate (¹⁴C-GCA) test and various tests for autonomic dysfunction. The breath component of the test was abnormal in four of the seven patients with diarrhoea and one of the other diabetics. Three patients with diarrhoea and a positive breath test result responded to antibiotics, whereas two with diarrhoea and a negative test result did not. High faecal ¹⁴C, suggesting bile acid malabsorption, was found in only one patient with diarrhoea and he had previously failed to respond to cholestyramine.

These results suggest that bacterial overgrowth in the

small intestine does occur in some but not all patients with diabetic diarrhoea and that the ¹⁴C-GCA test can predict the response to antibiotics. All the patients with diabetic diarrhoea had good evidence of autonomic dysfunction.

Introduction

The syndrome of diabetic diarrhoea was first described by Bargen *et al.*¹ It consists of chronic intermittent episodes of watery diarrhoea that are often worse at night and occasionally accompanied by faecal incontinence. The aetiology remains undefined although the clinical association with diabetic neuropathy is well described.²⁻⁴

Clinical improvement has been reported with oral antibiotics in some cases,^{5 6} and bacterial intestinal overgrowth has therefore been implicated. Nevertheless, pathological numbers of organisms have only occasionally been shown in the upper small intestine in such cases.^{4 7 8}

It has recently been suggested that bile acid malabsorption may be implicated and that bile acid sequestering agents, such as cholestyramine, may have useful therapeutic benefit.⁹

Abnormalities of bile acid metabolism may result in diarrhoea in two ways.¹⁰ In conditions of small intestinal bacterial overgrowth, such as occurs in stasis syndromes, diarrhoea may result

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TABLE I—Details of diabetic subjects

Case No	Sex	Duration of diabetes (years)	Proteinuria	Retinopathy	Peripheral neuropathy	Autonomic neuropathy*	Diarrhoea†	Cumulative 6-hourly ¹⁴ CO ₂ output (‰)‡	24-Hour faecal weight (g)	Corrected faecal ¹⁴ C output (‰)‡
<i>Group 1</i>										
1	F	<1	—	—	—	—	—	2.1	85	5.3
2	F	15	—	—	—	—	—	0.8	0	
3	F	5	—	—	—	—	—	0.6	45	
4	F	<1	—	—	—	—	—	1.6	25	
5	F	2	—	—	—	—	—	2.4	0	
6	F	15	—	—	—	—	—	0.7	30	
7	M	8	+	+	+	—	—	3.6	65	0.4
8	M	26	—	—	—	—	—	1.5	60	0.5
<i>Group 2</i>										
9	M	13	+	+	+	+(2)	—	6.5	110	4.0
10	M	26	+	+	+	+(5)	—	0.4	0	
11	M	9	—	—	+	+(1)	—	1.0	0	
12	M	25	+	+	+	+(1)	—	0.3	40	
13	M	14	—	+	+	+(2)	—	1.0	0	
14	M	<1	—	+	+	+(4)	—	0.6	320	5.5
15	M	25	+	+	+	+(1)	—	0.7	150	3.4
16	F	14	—	—	+	+(2)	—	2.6	0	
17	M	25	+	+	+	+(1)	—	1.4	0	
<i>Group 3</i>										
18	M	22	+	+	+	+(2)	+C	2.1	400	2.4
19	M	10	+	+	+	+(4)	+C	0.1	830	65.0
20	M	27	+	+	+	+(2)	+I	0.6	0	
21	M	12	+	+	+	+(2)	+I	10.5	25	0.1
22	M	20	+	+	+	+(2)	+I	9.0	30	
23	M	13	+	+	+	+(4)	+C	4.1	0	
24	F	13	+	+	+	+(2)	+I	5.9	250	7.2

*Number in parentheses indicates number of abnormal function test results (see text).

†I = Intermittent diarrhoea. C = Continuous diarrhoea.

‡Normal range: ¹⁴CO₂ output <4% of ingested dose; faecal ¹⁴C output <10‰ of ingested dose.

from bile acid deconjugation. Diarrhoea may also result from bile acid malabsorption, which can occur in distal ileal disease or malfunction. The ¹⁴C-glycocholate (¹⁴C-GCA) test, including measurement of faecal ¹⁴C excretion,¹¹ may be used to distinguish these conditions.

We used the ¹⁴C-GCA test to evaluate the role of changed bile acid metabolism in diabetic diarrhoea.

Patients and methods

Twenty-four insulin-dependent patients, including seven with a history of diabetic diarrhoea, were studied. Other causes of chronic diarrhoea were excluded by full investigation, which included complete gastrointestinal radiology, small intestinal biopsy, and pancreatic exocrine function studies.

Patients were examined for proteinuria (Albustix sensitive to 0.3 g/l); retinopathy, defined by the usual clinical criteria; and peripheral neuropathy, judged to be present by the absence of knee or ankle reflexes and evidence of sensory impairment. The methods used to assess autonomic function¹²⁻¹⁵ and our criteria of autonomic dysfunction are described in the accompanying paper.¹⁶

The ¹⁴C-GCA test was performed on each patient. After an overnight fast an oral dose of 5 µCi of ¹⁴C-glycocholic acid and 0.1 mmol of unlabelled glycocholate as carrier¹⁷ was given with a standard liquid test meal (corn oil 18 g, glucose 80 g, casilan 15 g, water to 300 ml). Copper thiocyanate (2.5 mmol) was also given as a non-absorbed marker. Expired ¹⁴CO₂ was trapped in counting phials containing methylbenzethonium hydroxide. Samples were obtained in duplicate every hour for six hours and counted for ¹⁴C activity (Intertechnique SL 30). The cumulative output of ¹⁴CO₂ was ex-

pressed as a percentage of the given dose.¹¹ The total 24-hour stool output was collected and weighed. This was homogenised in a liquidiser with a known volume of water. An aliquot was analysed for copper.¹⁸ A further aliquot was oxidised (Packard Oxidiser) and the ¹⁴CO₂ trapped and counted. Faecal ¹⁴C output was corrected for incomplete recovery of copper. Faecal ¹⁴C activity was not measured if the total 24-hour stool output was less than 50 g.

We based our normal results for the ¹⁴C-GCA test on a study of 15 normal controls (mean age 44 years) and 15 non-diabetic patients with diarrhoea for which no cause was found after full investigation (mean age 46 years). Cumulative six-hour breath output of ¹⁴CO₂ was less than 4% of the administered dose and 24-hour faecal recovery, after marker correction, less than 10%.

Results

The subjects studied were divided into three groups (table I). The first group (cases 1-8) had no history of diarrhoea or other gastrointestinal symptoms and on examination showed no evidence of autonomic neuropathy. The second group (cases 9-17) also had no history of diarrhoea but did have diabetic complications and were found to have autonomic neuropathy. Among the patients in this group with only one abnormal test result, the response to the Valsalva manoeuvre was the most common single abnormality. Nevertheless, all these patients had other suggestive clinical features of autonomic dysfunction. The third group (cases 18-24) consisted of patients with diarrhoea. All patients with diabetic diarrhoea had autonomic neuropathy with at least two function study results being abnormal.

Only one (case 9) of the patients in groups 1 and 2 had a raised ¹⁴CO₂ output in the breath. Further studies in this patient, especially small bowel radiology, were not considered justified in the absence of symptoms. Faecal ¹⁴C output was normal in all patients in groups 1 and 2 who passed greater than 50 g of faeces.

Of the seven patients with diabetic diarrhoea the ¹⁴C-GCA test was abnormal in five cases. In four (cases 21-24) ¹⁴CO₂ breath output was raised while faecal ¹⁴C output was normal. In one subject (case 19) the faecal ¹⁴C output was raised, whereas breath excretion was normal.

Five of the patients with a history of diarrhoea were symptomatic at the time of study and all were given a four-week trial of antibiotics (metronidazole 200 mg three times a day or tetracycline 250 mg four times a day). Three of these (cases 21-23) had an increased ¹⁴CO₂ breath output. One further patient (case 24), who was asymptomatic when studied but in whom ¹⁴CO₂ breath output was raised, was also given antibiotics.

After treatment symptoms completely resolved in those patients previously found to have a high ¹⁴CO₂ excretion in the breath, while

TABLE II—Effects of antibiotic treatment

Case No	Before treatment		After treatment	
	Symptoms	% Cumulative 6-hourly ¹⁴ CO ₂ output (normal <4%)	Symptoms	% Cumulative 6-hourly ¹⁴ CO ₂ output (normal <4%)
18	Diarrhoea	2.1	No change	Not repeated
19	Diarrhoea	0.1	No change	Not repeated
21	Diarrhoea	10.5	Stools formed	0.3
22	Diarrhoea	9.0	Stools formed	1.1
23	Diarrhoea	4.1	Stools formed	2.3
24	None	5.9	None (no change)	2.5

no improvement was observed in the other two patients in whom the $^{14}\text{CO}_2$ breath output was normal. The response to ^{14}C -GCA became normal after antibiotics (table II).

The one patient (case 19) in whom faecal ^{14}C output was raised had failed to respond to an earlier course of cholestyramine.

Discussion

The only other report of the ^{14}C -GCA test in diabetic diarrhoea is in a brief letter by Low Beer.¹⁹ He found normal results in six patients, but no details of other gastrointestinal investigations were given and the effect of antibiotics was not described.

Our findings indicate that a positive breath component of the ^{14}C -GCA test is found in some but not all patients with diabetic diarrhoea and no other recognised gastrointestinal disorders. The low faecal excretion of ^{14}C in all but one patient and the satisfactory response to antibiotics suggest that there is bacterial overgrowth and excess bile acid deconjugation in the small gut, rather than bile acid malabsorption.

Evidence for bile acid malabsorption was found only in case 19. This patient had the most severe diarrhoea but had not responded to previous courses of cholestyramine. Condon *et al*⁹ briefly described some patients with this syndrome who did respond to cholestyramine, but this treatment has not been evaluated in a controlled fashion; nor was it tried in our other patients with diarrhoea. Our findings suggest that cholestyramine is unlikely to benefit most patients with diabetic diarrhoea if its action is confined to binding bile acids in the gut lumen.

In the absence of other aetiological factors bacterial overgrowth may result from a change in small intestinal motility. The strong association of autonomic neuropathy with diabetic diarrhoea described by others was confirmed in this series. Our patients with a history of diarrhoea were found to have more widespread evidence of autonomic malfunction than most of the

other subjects. Therefore disturbances of intestinal motility probably result from autonomic damage, and because of the patchy distribution of autonomic neuropathy only a few patients are affected.

The ^{14}C -GCA test, which is simple and well tolerated, may be used to rationalise treatment in diabetic diarrhoea by indicating those patients in whom antibiotic treatment is likely to prove beneficial.

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SHORT REPORTS

Marcus Gunn phenomenon associated with synkinetic oculopalpebral movements

The Marcus Gunn jaw winking phenomenon is characterised by abnormal palpebral movement associated with movements of the jaw. We report the second case, in which an associated concomitant convergence strabismus corrected itself automatically with the elevation of the ipsilateral ptotic lid when the jaw was opened or when ptosis was passively corrected.

Case report

A 17-year-old woman had congenital ptosis of the left upper lid with concomitant convergent strabismus of about 20° on the same side (see figure, *a*). She had always been healthy and she had no history of trauma to the head. On examination movements of the eyes were normal. On opening the jaw or twisting the mouth to the opposite side, either passively or actively, the ptosis and the strabismus corrected spontaneously (see figure, *b*). In contrast, twisting the mouth to the ipsilateral side—that is, to the left—did not correct these. On lifting the left upper lid passively, the strabismus also disappeared. She seemed to be otherwise normal. She was offered a Blaskovics operation, but did not accept and discharged herself.

Discussion

The first case of Marcus Gunn phenomenon associated with synkinetic oculopalpebral movements was described by Garkal.¹ This

is the second case. The phenomenon is produced as the result of congenital misdirection of the motor division of the fifth cranial nerve. The pathways responsible for the clinical findings are afferent ones, beginning with the external pterygoid muscle supplied by the motor division of the fifth cranial nerve. The mesencephalic root of the

Congenital ptosis of left upper lid with concomitant convergent strabismus (*a*). Ptosis and strabismus were spontaneously corrected when jaw was opened (*b*).