Electrochemical detector for breath hydrogen determination: measurement of small bowel transit time in normal subjects and patients with the irritable bowel syndrome

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SUMMARY A method is described for the measurement of hydrogen in expired air, using an electrochemical detector. The apparatus is simple to use and sensitive. Its application is illustrated by studies of small bowel transit time made by measuring the time between oral ingestion of the unabsorbable carbohydrate lactulose and a rise in the concentration of hydrogen in expired air. In 20 control subjects transit time was 93.0±6.6 minutes, while in 16 patients with diarrhoea due to the irritable bowel syndrome it was 54.1±6.3 minutes (p<0.001), suggesting an abnormality in small intestinal motility in these patients. Loperamide, a potent antidiarrhoeal agent, increased transit time in 12 of these patients from 56.3±6.7 to 100.0±10.2 minutes (p<0.001).

The measurement of hydrogen in expired air has found an increasing number of applications, including the detection of small bowel bacterial colonisation and disaccharidase deficiency, the detection and quantification of carbohydrate malabsorption, and the measurement of small bowel transit time. The concentration of hydrogen in expired air is conventionally measured by gas chromatography using a thermal conductivity detector. Such apparatus is expensive and not universally available. This report describes the use of an electrochemical detector, which, when combined with a simple chromatographic system, allows rapid and sensitive measurement of breath hydrogen. We report its application to the measurement of small bowel transit time in normal control subjects and in patients with diarrhoea attributed to the irritable bowel syndrome.

Methods

HYDROGEN MEASUREMENTS
The apparatus consists of an electrochemical detector and a simple chromatographic system. The detector uses a metallised membrane electrode which is a non-porous but gas-permeable membrane of polytetrafluoroethylene metallised with a thin layer of platinum. This functions as one electrode of a polarographic electrochemical cell. The gas under test diffuses through the membrane and takes up electrons from, or yields electrons to, the electrode. The magnitude of the resultant electric current is determined by the partial pressure of the gas. Such electrodes are flexible and sensitive, and can be used to detect a number of gases. Oxygen sensors of this type have been described and have been commercially available for some time.

The detector used here is sensitive to hydrogen, carbon monoxide, and also to variations in oxygen concentration. Separation of detector responses is achieved by means of a chromatographic column, 460×6 mm, packed with 13X molecular sieve (Hopkin and Williams, Chadwell Heath, Essex, England), sieved to between 60 and 85 British Standard sieve, and activated by heating to 300°C for two hours. After activation the column can be used at room temperature for several months.

The apparatus used in clinical studies is shown in Fig. 1. A reference carrier-gas, usually air, flows continuously through the column and de-
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Fig. 1  Apparatus for breath hydrogen measurement used in clinical studies. The carrier-gas (A) flows continuously through the system at a rate of approximately 40 ml/min, monitored by a flowmeter (E). The sample to be analysed is injected through a drying tube to fill the sample loop (C). Filling of the loop is indicated by a flowmeter (D). When the arm of the ganged pneumatic valve (B) is depressed the carrier-gas flows through the sample loop, carrying the sample through the chromatographic column (F) to the detector (G). The current produced is shown on a chart-recorder (H). For use outside the laboratory room-air provided by a simple diaphragm pump can be used as the carrier-gas.

...ector and minimises zero-drift of the electrode; this can be a problem when very small concentrations of hydrogen are present. Before use the detector is calibrated using a standard gas mixture containing 25 parts per million (ppm) of hydrogen. The linearity of response of the detector at low concentrations of hydrogen was assessed by measuring detector responses to serial dilutions of the standard gas with air.

PATIENTS
Ten male and 10 female control subjects were studied, mean age 35.1 years (range 15–75 years). They were medical and laboratory staff, medical students, and ambulant patients with non-gastrointestinal illnesses. Eight male and eight female patients with diarrhoea due to the irritable bowel syndrome were also studied, mean age 42.9 years (range 19–65 years). The diagnosis in these patients was based on a compatible history, normal physical examination and sigmoidoscopy, and negative investigations. In all patients the haemoglobin, white cell count, platelet count, sedimentation rate, serum calcium, phosphate, cholesterol, uric acid, glucose, albumin, globulin, bilirubin, urea, alkaline phosphatase, and aspartate aminotransferase were normal. In five patients under the age of 27 years, no other investigations were carried out. In the remaining 11 patients the following tests were performed where considered appropriate, and all were normal: barium enema (11); serum vitamin B₁₂, folate and red-cell folate (nine); barium meal and follow-through (seven); faecal fat estimation (seven); thyroid function
Fig. 2 Drawing from a chart record of detector response to low hydrogen concentrations. Two responses are shown for each hydrogen sample and demonstrate good reproducibility. Each response consists of three peaks, the largest corresponding to hydrogen, the next to the difference in oxygen concentration between the sample and the carrier-gas, and the smallest to carbon monoxide (also present in the standard gas mixture). The linearity of detector response to decreasing hydrogen concentrations is also demonstrated.

Tests (seven); jejunal biopsy (five); lactose tolerance test (three).

All patients had diarrhoea at the time of study, their daily stool frequency being 4.3±0.6 (mean±SEM), and none was taking antidiarrhoeal drugs. In 12 of these patients transit time measurements were repeated after control of diarrhoea with the antidiarrhoeal agent loperamide. The dose required to control diarrhoea varied from one capsule (2 mg) to six capsules (12 mg) daily.

PROCEDURES
Patients were studied seated after an overnight fast, and smoking was prohibited during the test. End-expiratory breath samples were collected via a modified Haldane-Priestley tube.1 The concentration of hydrogen in expired air was measured before and at five or 10 minute intervals after the ingestion of an isotonic solution of lactulose (10 g in 100 ml water). The time elapsing between ingestion of lactulose and the first detectable rise in breath hydrogen concentration was taken as the small bowel transit time.

Breath hydrogen concentrations were measured in ppm. Statistical comparisons were made using Student’s t test.

RESULTS

DETECTOR CHARACTERISTICS
The detector response to low concentrations of hydrogen is shown in Fig. 2. By reducing carrier-gas flow rate and resetting the sensitivity of the chart recorder concentrations of hydrogen as small as 0.25 ppm could be detected.

TRANSIT TIME MEASUREMENTS
The mean transit time in control subjects, 93.0±6.6 minutes, was significantly greater than that in patients with the irritable bowel syndrome, 54.1±
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Fig. 3 Small bowel transit time (SBTT) in 20 control subjects and 16 patients with diarrhoea due to the irritable bowel syndrome (IBS). Bars represent the mean values for each group±standard error.

6-3 minutes (p<0.001; Fig. 3). A double peak in hydrogen excretion, as occurs in small bowel bacterial overgrowth,15 was not observed, although hydrogen measurements were continued after the initial rise in breath hydrogen excretion to exclude this possibility, particularly in those patients with short transit times.

Reproducibility of transit time measurements in patients with diarrhoea was assessed by repeat testing in eight patients after an interval of three to 90 days (Fig. 4). The mean variation of the second from the first measurements was ±16.1%.

Fig. 4 Reproducibility of small bowel transit times (SBTT) done on two occasions in eight patients with diarrhoea.

In 12 of the patients with the irritable bowel syndrome, mean transit time was increased by treatment with loperamide from 56.3±6.7 to 100.0±10.2 minutes (p<0.001). Mean daily stool frequency was reduced from 3.7±0.3 to 1.9±0.3 (p<0.05).

Discussion

Conventional gas chromatographic apparatus is relatively expensive and requires trained personnel for its use, and some systems are too insensitive to measure the low hydrogen concentrations in expired air, necessitating the use of rebreathing techniques.10 More recent systems have increased sensitivity, thus allowing the use of end-expiratory breath sampling, but still need argon as a carrier-gas.11,16

The apparatus described in this paper appears to provide a satisfactory alternative method. It is very simple to use, and more sensitive than reported conventional gas chromatographic systems10,11,16 concentrations of hydrogen as low as 0.25 ppm being detectable. The detector response also shows good linearity at low hydrogen concentrations. A special carrier-gas is not required, air either from a cylinder, or room-air supplied by a simple diaphragm-pump being suitable.

The apparatus described is a prototype, developed at the Health and Safety Executive Laboratories, Sheffield. It is small and easily transportable. Developmental work is under way to produce a commercially available model, which should be substantially cheaper than conventional gas chromatographic apparatus, although the final cost is not yet known. Modification may be possible to eliminate the sensitivity to carbon monoxide and oxygen, which would remove the need for the chromatographic column, although the capacity to determine carbon monoxide concentration could be useful for other purposes.

Determination of small bowel transit time by measuring the rise in breath hydrogen excretion after ingestion of lactulose was first reported and validated by Bond and Levitt,7 and it remains the only available non-invasive, non-radiological method. Bond and Levitt have shown that this method gives reproducible results in normal subjects,7 and the present studies confirm this in patients with chronic diarrhoea. It provides a reproducible index of small intestinal propulsive activity, enabling the transit time of normal subjects and patients with gastrointestinal disorders to be compared.

The irritable bowel syndrome is usually considered to be a colonic disorder, but abnormalities of small bowel motility have been implicated.17, 18 Our observation that mean transit time is shorter
in patients with diarrhoea due to this syndrome than in normal subjects is additional evidence that the small bowel is frequently abnormal in these patients, and is likely to be one factor in the production of their frequent bowel actions. Similarly, the prolongation of small intestinal transit time by loperamide is likely to contribute to the antidiarrhoeal action of this drug.

References