A simple method of measuring breath hydrogen in carbohydrate malabsorption by end-expiratory sampling

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Summary
1. A simple method is described for measuring the hydrogen concentration in alveolar air by end-expiratory sampling, by using a modified Haldane–Priestley tube and gas chromatography. Hydrogen was generated in vivo by ingestion of the non-absorbable sugar lactulose.

2. Alveolar hydrogen concentration showed a highly significant correlation with hydrogen production measured either by a rebreathing technique or by a total collection procedure.

3. The coefficient of variation of the end-expiratory method, assessed by comparing sixty-one paired results, was 11·6%. The coefficient of variation in ten measurements in one subject at 1 min intervals was 17·6%.

Key words: alveolar air, carbohydrate malabsorption, end-expiratory sampling, hydrogen.

Introduction
The use of breath-analysis tests for the study of a wide range of gastrointestinal disorders is rapidly increasing in popularity (Newman, 1974; Hepner, 1974). Most tests in current use require radioisotopes and this limits their usefulness considerably (Newman, 1974). Non-isotopic breath tests offer a definite advantage.

Hydrogen is produced in the gastrointestinal tract by certain bacteria from suitable substrates, e.g. non-absorbed sugars (Levitt & Bond, 1970), and can be measured in expired air by gas chromatography (Nielsen, 1961). The amount of hydrogen exhaled in a given time is proportional to intestinal hydrogen production (Levitt, 1969). To date, methods for measuring breath hydrogen have involved either collection of expired air from a single breath or over several minutes (Calloway & Murphy, 1968), or rebreathing techniques in a closed circuit (Levitt, 1969).

In our experience, these methods present problems both in patient acceptability and in technical application in clinical situations. We have therefore turned to the much simpler technique of sampling end-expiratory alveolar breath with a modification of the Haldane–Priestley tube.

Material and methods
The modified Haldane–Priestley tube used in these studies (Fig. 1) was 170 cm long with an internal diameter of 12 mm. This is 50 cm longer, and the internal diameter is 13 mm smaller, than that originally described (Haldane & Priestley, 1905). Samples of expired air (30 ml) were collected at the end of a prolonged expiration by aspiration into a plastic syringe from the side arm of the tube. Two samples were taken 1 min apart and the hydrogen concentration was expressed in μmol/l of expired air.

Rebreathing was carried out with a closed circuit consisting of a mouthpiece and two soda–lime canisters connected by corrugated polyvinyl tubing to a reservoir bag filled with a measured volume of oxygen and a known concentration of helium as a marker. Samples were taken after 1 min and 5 min rebreathing
and the concentrations of hydrogen and helium were measured. Repeated samples were taken in two subjects. There was a near-linear rise in hydrogen concentration with time over the 5 min period. In these two subjects, after extended rebreathing periods of 8 and 10 min, the rate of rise in hydrogen concentration diminished, suggesting that the rise in hydrogen concentration above the initial venous concentration of hydrogen was causing a back-pressure effect. The dilution of the helium marker at 1 min was used to determine the total volume of gas in the system. The amount of hydrogen produced over the 5 min was calculated and hydrogen production expressed as \( \mu \text{mol/min} \).

Timed collections of expired air were made for 4 min into a multilaminated collecting bag and the hydrogen concentration was measured. Hydrogen production was then calculated and expressed in \( \mu \text{mol/min} \).

All helium and hydrogen estimations were made by gas chromatography, a Gow–Mac chromatograph being used, with 1.83 m x 6.3 mm (6 ft x ¼ in) copper columns with molecular sieve 5A 60/80 mesh, operated at 50°C with argon as carrier gas. Each sample was injected via a 10 ml sampling loop and insertion valve. This unit measures hydrogen concentration to an accuracy of 0.09 \( \mu \text{mol/l} \) (1 \( \mu \text{mol/l} = 22 \text{ p.p.m.} \)).

In fifteen subjects, base-line samples were taken after an overnight fast. Each subject then drank 50 ml of unflavoured lactulose (660 g/l) as a non-absorbable sugar and sampling was repeated at 30 min intervals for 180 min. The alveolar hydrogen concentration was measured by the procedure described and compared with hydrogen production measured by the rebreathing technique in eight subjects and by the total collection technique in seven subjects.

Results

Alveolar hydrogen concentration

The mean fasting hydrogen concentration for thirteen of the fifteen subjects was 0.58 ± 0.84 \( \mu \text{mol/l} \); the other two subjects had meals containing beans later on the evening before the test, resulting in fasting levels of 7.41 and 4.55 \( \mu \text{mol/l} \) respectively. After lactulose ingestion, peak hydrogen concentration for these thirteen subjects rose to 5.02 ± 3.46 (sd) \( \mu \text{mol/l} \). The two inadequately fasted subjects showed similar
rises, producing peak hydrogen concentrations of 16:07 and 14:38 \textmu mol/l respectively.

Reproducibility of measuring alveolar hydrogen concentration was examined in two ways. In sixty-one pairs of samples with hydrogen concentrations from 0:22 to 16:07 \textmu mol/l, if the mean of each pair was taken as 100\%, the SD from the mean value for all pairs over this wide range of concentration was 11:6\%. Taking one subject 2 h after lactulose ingestion and sampling repeatedly each minute for 10 min, resulted in a mean hydrogen concentration of 4:09 \textmu mol/l with coefficient of variation of 17:6\%.

The alveolar hydrogen concentration was compared with hydrogen production measured by the re-breathing technique. The correlation coefficients in each of the eight subjects for the six 30 min samples varied from 0:89 to 0:98 (P < 0.01 for each subject). When all the points obtained from each of the eight subjects were considered the correlation coefficient was 0:92 (P < 0.001).

The alveolar hydrogen concentrations were also compared with the hydrogen production measured in 4 min collections of expired air. Six measurements were made in each individual at 30 min intervals. The correlation coefficients in each of the six out of seven subjects varied from 0:93 to 0:997 (P < 0:01 for each subject). In the seventh subject no significant production of hydrogen occurred. Considering all points from these six subjects, there was a highly significant correlation (r = 0:80; P < 0.001; n = 36).

**Discussion**

Much of the basic work in respiratory physiology has been done with the Haldane–Priestley tube (Haldane & Priestley, 1905), a simple piece of equipment which is able to obtain gas samples at concentrations very close to alveolar values in people with good lung function. However, the tube is not widely used in clinical situations because patients with impairment of lung function are frequently incapable of delivering an adequate sample of mixed alveolar gas into the tube. Severe respiratory disease is uncommon in patients being investigated for gastrointestinal disorders, and alternative methods could be employed if hydrogen breath tests were indicated in these patients.

Hydrogen is a rapidly diffusing molecule, and the Haldane–Priestley tube was therefore modified by one of us (D.J.A.J.) to decrease the hydrogen loss by diffusion whilst not greatly increasing the resistance of the tube.

The results in this paper indicate that the much simpler end-expiratory-sample method for measuring breath hydrogen concentration gives reproducible results which correlated highly with hydrogen production values obtained by more elaborate methods previously described.

Applied at 1 min intervals over 10 min, the procedure gave a well-grouped cluster of concentrations with a coefficient of variation of 18\%. Thus there are not wide fluctuations observed over this period and hydrogen appears to be released at a fairly steady rate from the bowel into the splanchnic blood.

Excluding the two subjects who were not adequately fasted, the rise in breath hydrogen after ingestion of non-absorbable carbohydrate is very marked. Thus, in making a diagnosis of carbohydrate malabsorption, the errors of the technique are acceptable since they are small relative to the large rises observed when significant amounts of carbohydrates reach the bacteria in the large bowel.

It has been shown that fermentation of 1 g of different carbohydrates such as glucose, lactose or lactulose, produces the same volume of hydrogen in a given person (Bond & Levitt, 1972). An estimate of the proportion of carbohydrate unabsorbed may therefore be obtained with this technique by comparing the hydrogen produced from a given weight of a test sugar to that from a given weight of a non-absorbable carbohydrate such as lactulose.

We believe this technique to be far simpler, more acceptable for the patient and less time-consuming for the operator than previously described methods. It is easily adaptable to both out-patient and bedside situations (Metz, Jenkins, Peters, Newman & Blendis, 1975) and gives results clearly accurate enough to detect the changes in hydrogen concentration that are found in carbohydrate malabsorption.

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References


