

3. Robertson WG, Peacock M, Heyburn PJ, et al. Should recurrent calcium oxalate stone formers become vegetarians? *Br J Urol* 51, 427-431 (1979).
4. Galosy R, Clarke L, Ward DI, Pak CYC. Renal oxalate excretion in calcium urolithiasis. *J Urol* 123, 320-323 (1979).
5. Robertson WG, Rutherford A. Aspects of the analysis of oxalate in urine—a review. *Scand J Urol Nephrol* (Suppl) 85-93 (1982).
6. Hodgkinson A, Williams A. An improved colorimetric procedure for urine oxalate. *Clin Chim Acta* 36, 127-132 (1972).
7. Tukey JW. *Exploratory Data Analysis*, Addison-Wesley, Reading, MA, 1977, pp 32-41.
8. Laker MF, Hofmann AF, Meeuse BJD. Spectrophotometric

- determination of urinary oxalate with oxalate oxidase prepared from moss. *Clin Chem* 26, 827-830 (1980).
9. Olthuis FMFG, Markslag AMG, Elhorst JTK, Krugers-Dagneaux PGLC. Urinary oxalate estimation. *Clin Chim Acta* 75, 123-128 (1977).
10. Park KY, Gregory CJ. Gas-chromatographic determination of urinary oxalate. *Clin Chem* 26, 1170-1172 (1980).
11. Menon M, Mahle CJ. Ion-chromatographic measurement of oxalate in unprocessed urine. *Clin Chem* 29, 369-371 (1983).
12. Potenzy N, Bais R, O'Laughlin PD, et al. Urinary oxalate determination by use of immobilized oxalate oxidase in a continuous-flow system. *Clin Chem* 29, 16-20 (1983).

I-1313

CLIN. CHEM. 29/11, 1980-1981 (1983)

## Time-Course of Cigarette Smoke Contamination of Clinical Hydrogen Breath-Analysis Tests

Andrea Rosenthal and Noel W. Solomons<sup>1</sup>

The time-course of the contamination of exogenous hydrogen from cigarette smoke on postprandial breath hydrogen concentration was evaluated in 10 subjects, six regular smokers and four occasional smokers. Breath hydrogen values were determined by gas chromatography 10 min, 5 min, and immediately prior to smoking a filter cigarette; during smoking from a sample of exhaled air containing smoke; and 5, 10, and 15 min after extinguishing the cigarette. A three- to 137-fold increase above basal hydrogen concentrations was produced by exhaled cigarette smoke, but most subjects had re-equilibrated to baseline values within 10 to 15 min after the cigarette. If subjects undergoing clinical hydrogen breath tests cannot refrain from smoking during the duration of the test, one should allow an interval of at least 15 min from the end of smoking to the collection of a breath sample.

**Additional Keyphrases:** *variation, source of · chromatography, gas*

The hydrogen breath-analysis test has been used in gastrointestinal diagnosis for over a decade (1), its primary application being in evaluation of lactose malabsorption (2-4). The technique is based on the principle that hydrogen is produced in the colon by normal fecal bacteria when ingested carbohydrate escapes complete absorption in the small intestine; a fixed fraction of this colonic hydrogen is absorbed into the bloodstream and excreted by the lungs (5).

Although the original test was based on continuous collection of expired air in a closed system (6), subsequent procedures for breath H<sub>2</sub> tests involved sampling the air at fixed periods after the oral carbohydrate load (2, 3, 7).

Tadesse and Eastwood (8) reported a substantial increase in breath H<sub>2</sub> and CH<sub>4</sub> concentrations when cigarettes were smoked during the course of a breath test. Because the contaminant gases in cigarette smoke are of exogenous origin and poorly soluble in blood, they postulated that the interference caused by smoking would be transient. However, they studied only five subjects. In their report, they provide only mean data, no individual data or any expression of variance around the mean, and no indication of whether the subjects were fasting or in the postprandial state at the time of study.

We encountered a subject with unexpectedly high and erratic values for H<sub>2</sub>, unexplained until she was discovered smoking surreptitiously during the course of a lactose absorption test. We then undertook to re-evaluate the issue of cigarette-smoke contamination of expired air in the context of a H<sub>2</sub> breath test.

### Materials and Methods

Ten healthy subjects participated in the study. Six were regular smokers, who consumed at least 20 cigarettes per day; the remaining four were occasional smokers. They ranged in age from 20 to 39 years, and none had obvious clinical manifestations of chronic lung disease. One subject was studied in the fasting state; the remainder were studied at various intervals after meals.

Samples of mixed, expired air were collected by having subjects breathe through a low-resistance, one-way Hans Rudolph valve into a 5-L gas-bag. Breath H<sub>2</sub> concentration was measured in a gas chromatograph (Microlyzer Model 12; Quintron Instruments Co., Milwaukee, WI 53215), calibrated with a standard gas mixture containing 100  $\mu$ L/L of H<sub>2</sub> in N<sub>2</sub> (Scotty Gas II; Supplex Inc., Bellefonte, PA 16823) (9, 10). Samples of air were collected 10 min, 5 min, and immediately before the test (11). A cigarette was lit while smoking; subjects exhaled breath containing cigarette smoke directly into the collection bag after each puff or two puffs of the cigarette. The subject then smoked the cigarette

<sup>1</sup>Department of Nutrition and Food Science, Room 201B-213, 18 Vassar St., Massachusetts Institute of Technology, Cambridge, MA 02139.

Address correspondence to this author.

Received May 20, 1983; accepted July 12, 1983.

to completion, then samples of breath were collected 5, 10, and 15 min later. A total of seven breath samples were collected and analyzed for each subject.

## Results

Table 1 shows the absolute concentrations of breath  $H_2$  before, during, and after smoking. The average breath  $H_2$  concentration from exhaled breath containing cigarette smoke was 123 (SD 44)  $\mu\text{L/L}$ . The three pre-cigarette  $H_2$  concentrations were averaged for each individual, and the increase or decrease in breath  $H_2$  concentration, in terms of percentage of the pre-smoking mean, was computed for the samples collected during and after smoking (Table 2). Mean  $H_2$  concentrations during smoking were twice those reported by Tadesse and Eastwood (8), but the range was broad, probably reflecting the depth of inhaling. Although in eight of 10 subjects values for  $H_2$  were the same or lower than one or more value recorded before smoking, the mean after-smoking values were slightly higher, and the variance was slightly greater.

## Discussion

We confirm the previous observations (8) that cigarette smoke induces a massive increase in breath  $H_2$  concentration due to exogenous contamination of alveolar gas with  $H_2$  from the cigarette. The increase appears to be transient, and  $H_2$  is rapidly washed out of the lungs of young, healthy volunteers. Within 10 or 15 min, most of our subjects seem to have re-equilibrated to their pre-smoking breath- $H_2$  concentrations, or the trend of the data was consistent with a postprandial response to dietary carbohydrate incompletely absorbed from their last meal. Our design simulated actual clinical breath tests by including subjects who had consumed carbohydrates shortly before the test.

Because gas exchange is impaired in individuals with emphysematous changes of their lungs secondary to chronic smoking, a greater persistence of residual cigarette smoke might be seen in patients with chronic lung disease. Poor gas exchange, however, might confound the reliability of any interval-sampling collection procedure for such patients, even in the absence of concurrent smoking.

The  $H_2$  breath-test technique is a simple, non-invasive, inexpensive approach to the diagnosis of some gastrointestinal disorders (1, 11). Our study shows that the contamination of expired air with  $H_2$  produced by tobacco smoking is a transient phenomenon. The  $H_2$  is rapidly washed out of the lungs, and, if there is a sufficient interval before breath collection, smoking should not interfere with a valid recording of the breath  $H_2$  response to an ingested carbohydrate. Tadesse and Eastwood (8) suggested that at least 10 min be

**Table 1. Breath  $H_2$  Concentrations before, during, and after Smoking a Cigarette**

Subjects	$H_2$ concn, $\mu\text{L/L}$						
	10 min prior	5 min prior	Zero time	During smoke	5 min after	10 min after	15 min after
1	1	2	2	95	3	2	2
2	3	2	4	159	4	4	3
3	6	9	9	87	14	9	12
4	24	30	32	120	48	67	67
5	2	2	3	75	6	4	4
6	1	1	1	138	3	1	1
7	13	15	13	163	7	19	19
8	3	6	7	147	7	7	6
9	5	4	5	54	6	5	5
10	8	14	16	188	23	12	20
$\bar{X}$	7	8	9	123	12	13	14
(SD)	(7)	(9)	(9)	(44)	(14)	(20)	(20)

**Table 2. Relative Change in Breath  $H_2$  Concentration during and after Smoking a Cigarette, Compared with Concentration at Zero Time**

Subjects	% change in $H_2$ concn			
	During smoke	5 min after	10 min after	15 min after
1	5588	80	20	20
2	5200	33	33	0
3	988	75	12	50
4	319	67	134	134
5	3119	158	72	72
6	13700	200	0	0
7	1092	-49	39	39
8	2658	31	31	13
9	1056	28	7	7
10	1383	82	-5	58

allowed between the end of cigarette smoking and collection of a breath sample; our data are consistent with that recommendation.

We do not advocate smoking during the  $H_2$  breath-analysis test, and feel that efforts to encourage subjects to refrain from this practice during the entire duration of a study should be made. However, in community-level surveys of lactose absorption, in which minute-to-minute control of each subject is difficult and in which initial cooperation is dependent upon the acceptability of the restrictions and inconveniences imposed, allowing an insistent subject to smoke—except within 10 to 15 min of collection—might facilitate his or her participation. Moreover, in the occasional patient in the clinic who is made unbearably uncomfortable by prolonged abstinence from smoking, the use of cigarettes away from the collection intervals should not interfere with the validity of the results. The effect of cigarette smoke contamination in tests on individuals with severe lung disease remains to be evaluated.

## References

- Solomons NW. The hydrogen breath test and gastrointestinal disorders. *Compr Ther* 7 (8), 7-15 (1981).
- Bond JH, Levitt MD. Quantitative measurement of lactose absorption. *Gastroenterology* 70, 1058-1061 (1976).
- Newcomer AD, McGill DB, Thomas PJ, Hofmann AF. Prospective comparison of indirect methods for detecting lactase deficiency. *N Engl J Med* 293, 1232-1236 (1975).
- Solomons NW. Diagnosis and screening techniques for lactose maldigestion: Advantages of the hydrogen breath test. In *Lactose Digestion: Clinical and Nutritional Implications*, DM Paige, TM Bayless, Eds., Johns Hopkins Univ Press, Baltimore, MD, 1981, pp 91-109.
- Levitt MD. Production and excretion of hydrogen gas in man. *N Engl J Med* 281, 122-127 (1969).
- Bond JH, Levitt MD. Use of pulmonary hydrogen ( $H_2$ ) measurements to quantitate carbohydrate malabsorption: Study of partially gastrectomized patients. *J Clin Invest* 51, 1219-1225 (1972).
- Solomons NW, Viteri F, Rosenberg IH. Development of an interval sampling hydrogen ( $H_2$ ) breath test for carbohydrate malabsorption in children: Evidence for a circadian pattern of breath  $H_2$  concentration. *Pediatr Res* 12, 816-823 (1978).
- Tadesse K, Eastwood M. Breath-hydrogen test and smoking. *Lancet* ii, 91-92 (1977).
- Christman NT, Hamilton LH. A new chromatographic instrument for measuring trace concentrations of breath hydrogen. *J Chromatogr* 229, 259-265 (1982).
- Solomons NW, Hamilton LH, Christman NT, Rothman D. Evaluation of a rapid breath-hydrogen analyzer for clinical studies of carbohydrate absorption. *Dig Dis Sci* 28, 397-404 (1983).
- Rosado JL, Solomons NW. Sensitivity of the hydrogen breath-analysis test for detecting malabsorption of physiological doses of lactose. *Clin Chem* 29, 545-548 (1983).