Methanol in Normal Human Breath

Abstract. *Free methanol has been detected and measured, by gas-liquid chromatography, in the breath of several normal, healthy humans. It is suggested that this is a metabolic product rather than the result of diet or intestinal bacterial decomposition although there seems to be no biochemical reason for its presence.*

In the process of developing a gas chromatographic system for studying the minor organic components of expired human breath, we have observed that the breath of every person tested contained methanol in its free form (Fig. 1). Most of the substances identified in the chromatogram were expected, either because they had already been observed, or because an enzymatic pathway which produced or used them had already been described. The presence of methanol, however, cannot be rationalized in this way. That it is methanol has been shown on three separate column substrates of quite different physical properties; however, the ubiquitousness, amount, and biochemical origin are puzzling.

The apparently universal, but overlooked, presence of methanol in breath is strange, especially since the study of alcohols in the blood has become quite popular. Possibly, however, the chemical methods available for breath and blood analysis do not differentiate between methanol and ethanol at low concentrations, without special care. The latest gas chromatographic methods have apparently been used to identify alcohol in the blood and the breath (*1*) chiefly for legal purposes rather than to establish "normal levels." Only two other groups have reported methanol in normal blood (*2*) and urine (*3*). In each case the assertion appears without data, method, or followup; and in one case (*2*) there is an apparently unsupported conclusion concerning the source of the alcohol. One other report, implying its presence in breath, has appeared (*4*), but whether synthetic mixtures or actual breath samples were being studied at that place in the report is unclear.

We collected breath samples at liquid-air temperatures in siliconed, all glass apparatus. Five microliters of the water condensate thus obtained was analyzed by gas-liquid partition chromatography, by direct injection into an Aerograph Hy-Fi model A 600 B gas chromatograph with a hydrogen-flame detector (*5*). All separations were made on columns (0.3 cm × 1.52 m) filled with Anakrom ABS 70 to 80 mesh support coated with 2-percent *N-,N-,N'-,N'-*, tetramethylazeleamide and 8-percent behenyl alcohol (amide alcohol) at 86°C. Identification of the compounds shown was made by comparison of retention volumes with known standards in dilute water solution. Comparisons of retention volumes for the standards and unknowns on three different columns (amide alcohol, 40-percent diglycerol at 130°C, and 10-percent cetyl alcohol at 85°C on the same support material) proved the identity of methanol, ethanol, and acetone in our samples. The amount and the ratio of ethanol to methanol vary widely from person to person as shown in Table 1. The exact amounts of the three substances shown are not calculated from any internal standard; in order to preserve the high sensitivity of the method no dilution was made and reproducible saturation of the breath was assumed; the usual errors of Hamilton-syringe injection are therefore present in the data. However the values for breath acetone reported are within the "normal" limits determined chemically (*6*), although near the low side of their reported range (0.063 to 144 μg/liter of expired air). The earlier values of Henderson and co-workers (*7*), that is, 4.01 ± 0.28 μg/g of condensate per m^2 of body surface or 0.34 ± 0.02 μg/liter of expired air for the average subject studied, are less than, but of the same order of magnitude as, the data in Table 1.

The ethanol values for normal blood shown in Table 1 are in good agreement with those obtained by Lester (*4*), who used a different gas chromatographic separation method, and they support his contention that normal blood concentrations are in the range ⩽ 1.5 mg per liter, calculated from Harger's partition ratio data on ethanol (*8*) for the conversion of breath to blood values, and that chemical analysis of blood alcohol apparently produces high values (*9*).

Western and Osburn (*2*) have suggested that all "normal" methanol results from dietary sources and they were thus concerned with the health problems ensuing from the slow intake of a poison over long periods of time. Some support may be found for this point of view since some foods, particularly pectin-containing fruits, contain or produce methanol during growth or processing (*2, 10*). Tobacco also contains methanol (*11*) although in the work of Western and Osburn, as in ours, the methanol content of breath seemed not related either to smoking or recent diet. In a representative subject, the methanol concentration in the breath after fasting for 3 to 5, 15, 16, and 17 hours was 0.54, 0.18, 0.45, and 0.35 μg/liter, respectively. In the same subject, 0.5, 1.0, 1.5, 2.0, and 3.0 hrs after eating the methanol concentration in the breath was 0.28, 0.72, 1.95, 0.44, and 0.64 μg per liter, respectively. In other similar subjects, as well as in this one, the methanol in the breath rose to a peak

Table 1. Methanol, ethanol, and acetone in the breath of humans.

Subject	Concentration (μg/liter) expired air		
	Acetone	Methanol	Ethanol
1	0.99	0.06	0.011
2	.82	.078	0.045
3	.59	.074	0.027
4	.66	.206	0.094
5	*	.32	0.37
6	*	.49	0.20
7	*	.35	1.11
8	*	.35	0.17
9	*	.32	0.83

* Not determined.

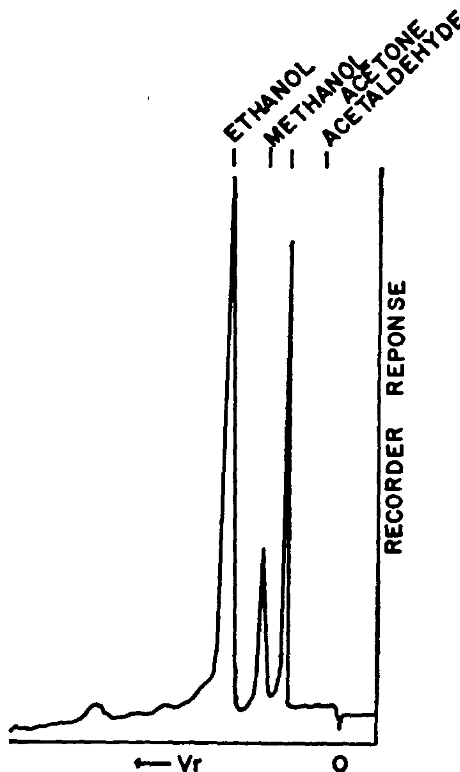

Fig. 1. Chromatogram of 5 μl of condensate of human breath.

1½ to 2 hours after eating. The complete absorption of a small, orally ingested dose of methanol requires about 2 hours in man (*12*) and 4 to 6 hours in rabbits (*13*). In view of this absorption pattern a dietary source of the concentrations in breath is possible.

According to the available biologic half-life data, which is 10 to 13 hours in rabbits and 2 hours in man, the peak observed after eating would drop to one half its value in about 2 hours for a living person. Thus a peak of about 6×10^3 μg/liter of expired air would be required to produce 0.1 μg per liter in the breath after 16 hours; this is quite unreasonable in view of the data presented.

That intestinal bacteria may be the source for the observed methanol is not ruled out from the human data presented. We did not attempt to sterilize the gut to study this point as has been done in other studies (*14*). The wide racial, age, and dietary differences presented by the subjects, who were Indian, Iranian, Iraqi, Egyptian, American, and German, and the differences observed (less than one order of magnitude) suggest strongly, however, that diet is only a minor contributor of variations, not a source.

Although the presence of methanol might be explained from a bacteriologic standpoint, it is more likely that it is the result of some metabolic process. There seems to be, however, no currently available explanation how any carbon metabolic degradation process would produce methanol (*15*) so that its rather universal presence seems to be somewhat of a mystery (*16*).

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Iodine-131 in Utah during July and August 1962

Abstract. *Nuclear explosions in Nevada in July 1962 caused an average intake of about 58,000 picocuries of I^{131} and a peak intake of 800,000 picocuries of I^{131} by Utah residents consuming one liter of milk per day. Corresponding infant thyroid doses were about 1 rad (average) and 14 rad (peak).*

Fallout from nuclear tests in Nevada during July 1962, deposited iodine-131 in Utah. Published meteorological trajectories suggest that fallout from the tests on 7 July, 11 July, and 17 July went west of the main Utah milkshed (*1*), while peak gross beta activities in the air at Salt Lake City of 900 picocuries per cubic meter on 7 to 8 July and 450 pc per m³ on 15 to 16 July implicate the "Sedan" Plowshare test of 6 July and the "Small Boy" weapons test of 14 July (*2*). Much of the high Sedan activity was due to neutron-activated tungsten (*3*). Our measurements of I^{131} in milk collected between Sedan and Small Boy indicate that Sedan contributed 10 to 30 percent of the total I^{131} intake in Utah resulting from these tests.

On 7 July 1962, the day after the 100-kiloton Sedan nuclear test in Nevada, one of us (R.C.P.) was measuring background radiation 20 miles southeast of Salt Lake City. I observed the approach of a large dusty cloud which increased the γ-ray intensity to about 100 times that of normal background. Because of this, we counted the milk scheduled for collection from several farms near Salt Lake City on 12 and 13 July. The radioiodine in this milk ranged from 10 to 2600 pc of I^{131} per liter. At the request of the Utah State Department of Health, we then collected milk from each of our 39 stations located throughout the state in order to measure the extent and degree of the I^{131} contamination. Each station was an individual farm already participating in our study of the ecological factors affecting Cs^{137} uptake in milk and man.

Iodine-131 was evaluated by means of its 364-kev γ-ray detected by a sodium iodide crystal (20 × 10 cm) and recorded on a 400-channel pulse-height analyzer. The accuracy (S.D.) of a measurement was about ± 10 percent or ± 20 pc of I^{131} per liter, whichever was larger. All measured activities of I^{131} in milk were adjusted to the day of sampling.

The buildup and subsequent decrease of I^{131} in milk taken from several individual farms is shown in Fig. 1. Because of the limited data during the period of buildup, we assumed that the concentrations of I^{131} in milk increased in linear fashion from negligible values on 11 July to peak values on 20 July. In equation form:

$$C_1 = C_p \, 0.111 \text{ day}^{-1} t_1 \qquad (1)$$

where C_1 = I^{131} concentration during buildup phase, C_p = peak I^{131} concentration on 20 July 1962, and t_1 = time after 11 July 1962. It will be shown later that a moderate error in Eq. 1 will cause only a small error in computing the total I^{131} intake.

After 20 July 1962, the concentration of I^{131} in milk was evaluated serially for seven separate farms. The concentrations (from the dates of collection) decreased exponentially with effective half-periods ranging from 3.8 to 9.8 days and averaging 5.8 days. Thus, after 20 July, the concentration of I^{131} in milk could be expressed as:

$$C_2 = C_p \exp(-0.12 \text{ day}^{-1} t_2) \qquad (2)$$

where C_2 = I^{131} concentration during decreasing phase, C_p = peak I^{131} concentration on 20 July 1962, and t_2 = time after 20 July 1962.

The daily intake of I^{131} was obtained by multiplying Eqs. 1 and 2 by the volume of milk consumed per day. Then the total I^{131} intake was calculated by integrating the daily intake over the buildup and decreasing phases and is

$$\text{total } I^{131} \text{ intake} = 12.8 \, VC_p \qquad (3)$$

where V = volume of milk consumed per day, and C_p = peak I^{131} concentration in milk.

About one-third of the calculated total intake occurred during the buildup