Determination of Acetone Concentration in Arterial Blood by Vapor Phase Chromatography of Alveolar Gas

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SUMMARY

The concentration of acetone in arterial blood may be determined by vapor phase chromatographic analysis of alveolar gas. Alveolar gas may be considered as a biological specimen preferable to blood. It is easily obtained, does not require anticoagulant or refrigeration for storage, and analysis by vapor phase chromatography is speedily and easily achieved. DIABETES *14*:663-65, October 1965.

It is generally recognized that treatment of diabetic coma is facilitated by observing the variations in acetonemia accompanying metabolic acidosis.[1] A popular clinical method employs Acetest Tablets* and serial dilutions of plasma.[2-4] Other investigators have related severity of coma to the concentration of acetone in expired air as measured by the mass spectrometer or vapor phase chromatograph.[5,6]

The arterial blood concentration of any volatile liquid can be calculated from the concentration in alveolar gas and the gas-blood partition coefficient.[7,8] Although acetonemia may be expressed as concentration of acetone in expired or alveolar gas, more meaningful figures for the clinician may be obtained by the calculation of its concentration in blood. The purpose of this investigation is to demonstrate the feasibility of determining blood concentration of acetone by vapor chromatographic analysis of alveolar gas samples.

METHODS

Observations were made upon dogs. Following induction of anesthesia with 20 mg./kg. of intravenously administered Nembutal, a cuffed orotracheal tube was inserted and the cuff was inflated. A catheter was placed in the femoral artery. A solution of 10 per cent chemically pure acetone in 5 per cent glucose and water was prepared and attached to an intravenously placed needle. Quantities of this solution varying from 20 to 50 cc. were administered intermittently by drip to the dogs.

Periods of administration of acetone were alternated with ten to fifteen-minute intervals in which the drip was discontinued in order to allow distribution of the acetone. Samples of alveolar gas and arterial blood were then obtained for analysis. Following sampling, the intravenous drip of acetone was restarted and another quantity was administered. The intravenous administration of acetone was adjusted so that blood concentrations of acetone ranged from about 5 mg. per cent to 130 mg. per cent and the concentration at each sampling period was approximately twice the value of the preceding period.

Alveolar samples were withdrawn in 10 ml. Hamilton syringes. An 18-gauge needle was attached to the syringe and inserted through the wall of the endotracheal tube. At end-expiration the opening of the tube was obstructed with the operator's thumb and 10 ml. of gas were withdrawn. Three such samples, taken within a three-minute interval of time, were obtained following each period of administration of acetone. The alveolar samples were then analyzed immediately on the vapor chromatograph.

A Perkin Elmer 154L vapor fractometer with a 1 cc. gas injection chamber and catherometer detection cell was employed for alveolar gas analysis. A 10'-column, one-quarter inch in diameter, packed with 10 per cent polyethylene glycol on Teflon, was employed. At a column temperature of 70° C. and pressure of 5 lb./sq. in., acetone eludes from this column in two minutes and fifty-seven seconds (figure 1).

The chromatograph was calibrated with seven samples of acetone in air, the concentrations ranging from 0.004 per cent to 0.175 per cent. The vapor samples were prepared by evaporating a known quantity of acetone in a fixed volume of air (figure 2). The peak area was

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* Acetest Tablets, Ames Company, Elkhart, Indiana.

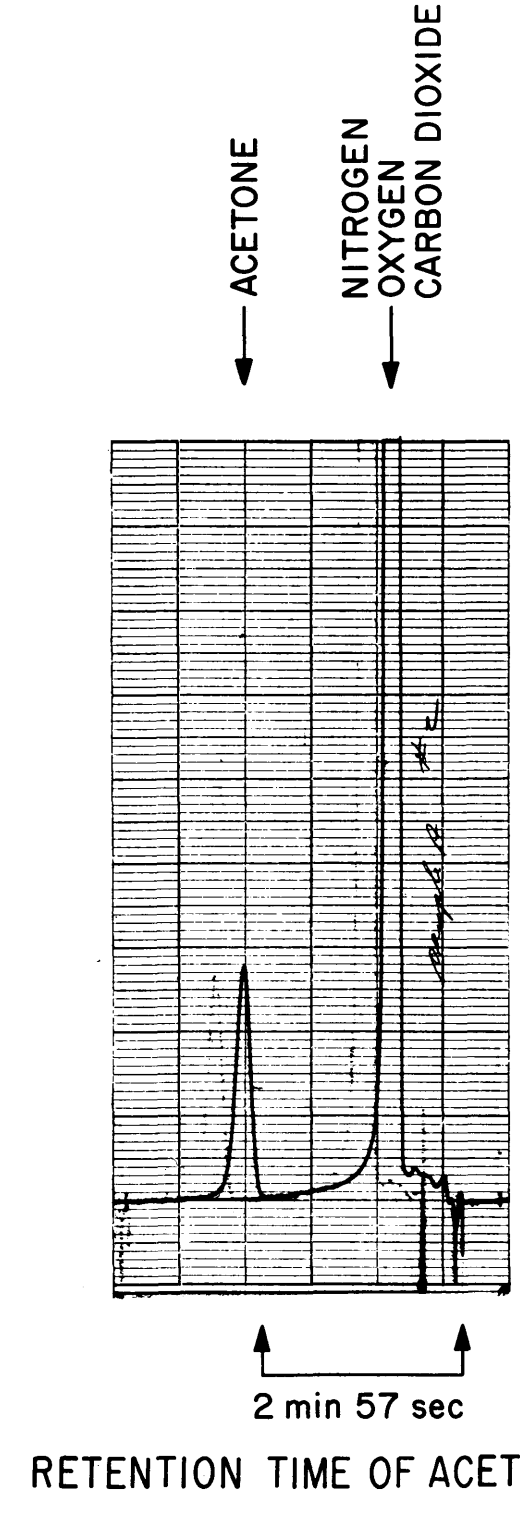

FIG. 1. Acetone read-out two minutes and fifty-seven seconds following injection.

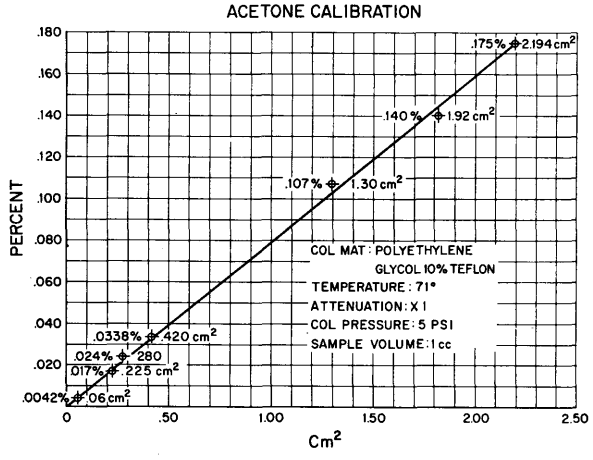

FIG. 2. Calibration of acetone vapor concentration vs. peak area.

calculated by multiplying the peak height by the peak width at one half the peak height.

The concentration of acetone in alveolar gas was determined from the calibration graph, relating peak area to percentage concentration by volume. This was converted to concentration in milligrams per 100 cc. of arterial blood by means of the following formula:

$$\text{Mg. \% art. blood} = \text{\% conc. alv. gas} \times \text{vap. dens.} \times \frac{273 + 38}{273} \times \frac{\text{gas}}{\text{blood}} \text{ solub. coef.}^{7}$$

The figure 333 was accepted as the gas/blood partition coefficient and 2.59 as the vapor density.[8]

Blood specimens (20 cc.) were withdrawn slowly from the endarterial catheter during the three-minute period of alveolar sampling. Each blood specimen was then divided into three equal parts, placed in oxalated test tubes, labeled and iced. Determinations of acetone concentration in the blood were then completed by a private laboratory employing the method of Nadeau modified by Procos.[9,10]

RESULTS

Results from experiments on two dogs are recorded in table I. Average deviation was smaller for the data derived from chromatographic analysis of alveolar gas than from direct analysis of blood, and values from direct measurement were consistently higher than concentrations derived from chromatographic measurement.

The data were analyzed by multiple regression technic on the basis of arithmetic, logarithmic and square root scales. The results were that: (1) The relations were the same for each of the two dogs. (2) The form of the relation can be expressed as $y = ax$, when y is blood concentration determined by direct measurement and x denotes either the area described by the chroma-

TABLE 1

	Sample period	Curve area	Mean curve area	Per cent alveolar acetone	Mean alveolar acetone	Blood acetone calculated from alveolar acetone: Mg. per cent	Mean	Average deviation	Blood acetone as determined by direct analysis of blood: Mg. per cent	Mean	Average deviation
DOG A	(1)	0.075	0.072	0.0055	0.0053	4.1	4.0	0.13	5.0	4.5	0.50
		0.067		0.0050		3.8			4.0		
		0.075		0.0055		4.1			—		
	(2)	0.166	0.163	0.013	0.012	9.8	9.3	0.66	11.0	11.5	0.50
		0.157		0.011		8.3			—		
		0.166		0.013		9.8			12.0		
	(3)	0.028	0.028	0.022	0.022	16.5	16.5	0	17.0	17.0	0
		0.028		0.022		16.5			17.0		
		0.028		0.022		16.5			—		
	(4)	0.789	0.776	0.063	0.062	47.4	46.4	0.66	50.0	50.7	1.56
		0.770		0.061		45.9			53.0		
		0.770		0.061		45.9			49.0		
	(5)	1.08	1.08	0.086	0.086	64.7	64.5	0.30	68.0	65.7	1.76
		1.07		0.085		64.0			66.0		
		1.08		0.086		64.7			63.0		
DOG B	(6)	1.60	1.60	0.128	0.128	96.5	95.7	0.75	104.0	111.0	7.00
		1.60		0.128		95.0			118.0		
	(7)	2.02	2.00	0.160	0.158	120.5	119.7	0.75	128.0	130.0	2.00
		1.98		0.157		119.0			132.0		

tographic read-out curve, or the alveolar gas concentration of acetone determined chromatographically. (3) On the square root scale, the value of the standard error of estimate is .20 (mg. per 100 cc.)$^{1/2}$ by either method; (4) the prediction equations obtained were:

$y = (65.32) \times$ **area of chromatographic read-out curve**

or

$y = (825.3) \times$ **concentration acetone in alveolar gas by chromatographic analysis.**

The regression curves expressed by these two equations are presented in figure 3.

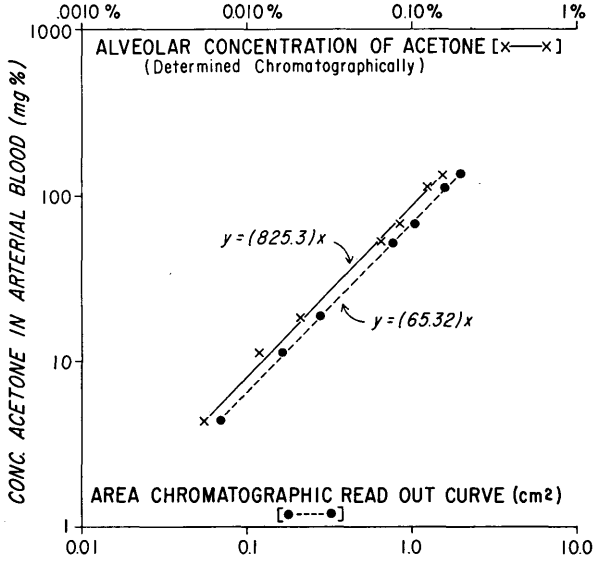

FIG. 3. Relation of blood acetone measured directly by method of Nadeau (ordinate) to alveolar concentration of acetone calculated from gas chromatograph and to area of acetone read-out curve (abscissa).

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