THE ARTERIAL–ALVEOLAR INERT GAS ("N_2") DIFFERENCE IN NORMAL AND EMPHYSEMATOUS SUBJECTS, AS INDICATED BY THE ANALYSIS OF URINE *

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Canfield and Rahn (2) have theorized that an arterial-alveolar difference in inert gas pressure is established whenever various units of the lung have unequal ventilation-perfusion ratios, even though the net inert gas exchange is zero.[1] The magnitude of this difference is expected to serve as an index of the variance of ventilation-perfusion ratios among the alveoli. The existence of such a difference has been shown in anesthetized dogs (2, 3). Similar measurements have not yet been made on man. The major difficulty in these determinations is the lack of a sufficiently accurate and reproducible method for measuring the partial pressure of inert gas in the arterial blood. It can be argued (see below) that urine inert gas tension reflects arterial inert gas tension. With this in mind, a method for determining the inert gas content of urine (4) has been applied to human urine in a manner believed to enable the calculation of the arterial inert gas tension within ± 2 mm Hg. Since the inert gas tension of mean alveolar air can be calculated with similar accuracy, a study of the arterial-alveolar inert gas pressure difference has been possible. This difference is $+3$ mm Hg in normal laboratory personnel and can be over $+20$ mm in patients with diffuse, obstructive emphysema.

METHODS

Seven male laboratory personnel and seven male subjects with severe, diffuse, obstructive emphysema were studied. After emptying the bladder, each subject slowly drank 0.5 to 1 L of water. Approximately one-half hour later the barometric pressure was read and the rectal temperature taken 7 to 8 cm from the external sphincter. After accumulating a sufficient amount of urine, the subject voided into the apparatus shown in Figure 1. This apparatus was designed to obtain anaerobic urine samples and was maintained at 36.5° C by a constant temperature water bath. Suspended in the bath were a long, thin separatory funnel (A) and a larger glass container (B). A three-way stopcock, which could be controlled from outside the water bath, enabled incoming urine to be directed to A or B. A was open to the atmosphere just above the surface of the water. The glans penis was pressed into a receptacle (C) just outside the water bath, and a thin, easily distensible rubber tube covering the receptacle was pulled over the distal penis to ensure a tight seal. During the first part of the voiding, urine was directed into B. After the dead space of the system had been flushed and no air bubbles remained, the stream was diverted into A. Immediately after voiding, two Ostwald-Van Slyke pipets with rubber tip and stopcock and custom-built to deliver 25 ml were inserted (in an "inverted" fashion) to the bottom of A and filled. These aliquots were used for the duplicate Van Slyke manometric analysis of the inert gas content of the bladder urine. The remaining urine was equilibrated in a tonometer with air at 37° C and also analyzed in duplicate for inert gas content, using the same Van Slyke apparatus. The detailed procedures for analysis and tonometry have been described previously (4).

A temperature slightly below body temperature (36.5° C) was chosen for the collection apparatus to avoid any change in the inert gas content of the urine between the time of voiding and the time of sampling. Since the urine could cool only slightly, its inert gas tension had to remain near that of atmospheric air. Any gas exchange that still occurred across its upper surface was not important, since pipets were filled from the lowermost part of the sample immediately after voiding. Keeping the water bath below body temperature also prevented any loss of gas because of supersaturation. It is possible that in practice a less elaborate collection apparatus may serve equally well.

Anaerobically collected urine aliquots were introduced into a Van Slyke apparatus within 5 to 30 minutes after filling of the pipets. In actual experiments, no change in inert gas content could be detected after a filled pipet had stood at room temperature for as long as 8 hours. Alcohol was prohibited for 36 hours before the experiment, since small amounts of it appear unchanged in the urine for 8 hours or more after ingestion (5). Such traces of alcohol can be measured as "inert gas" with the method of analysis

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[1] Since the inert gas of arterial blood and alveolar air is often treated as being entirely N_2, the arterial-alveolar inert gas pressure difference has also been referred to as the arterial-alveolar "N_2" difference.

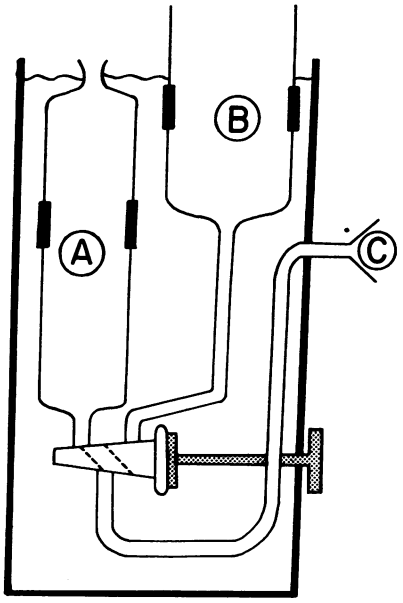

FIG. 1. APPARATUS FOR COLLECTING ANAEROBIC BLADDER URINE SAMPLES. For description, see text.

used (6). No restrictions were imposed during the period of urine formation.

Rectal temperatures were between 36.9 and 37.7° C and averaged 37.2° C. PB ranged from 737.1 to 752.0 mm Hg. Analysis temperatures were between 23.3 and 32.0° C. Ammonia concentration of the bladder urine (7) varied from 1 to 28 mmoles per L (with one exception, which was 68 mmoles per L). Specific gravities were between 1.0045 and 1.0160, and osmolalities between 137 and 580 mOsm per kg.

CALCULATIONS

Partial pressure of inert gas in arterial blood (P_a). No method for the direct determination of inert gas tension is available. We originally hoped to calculate the inert gas tension of arterial blood by measuring its inert gas content before and after tonometry with a known inert gas tension at body temperature. Early attempts at this analysis were unsatisfactory, and we turned our attention to urine. Since one may assume no net inert gas exchange in the tissues, it might be argued that inert gas tension is the same throughout the body, i.e., $Pa_{N_2} \doteq Pv_{N_2} = P_{tissues_{N_2}} = P_{urine_{N_2}}$. Applying considerations similar to those above, the inert gas tension of bladder urine can be obtained from this proportion:

$$\frac{P_{N_2} \text{ of bladder urine}}{P_{N_2} \text{ of tonometered urine}} = \frac{\text{inert gas content of bladder urine}}{\text{inert gas content of tonometered urine}}.$$

This is the general approach we have used. However, certain refinements, which will be discussed below, are necessitated by temperature variation within the body.

For the development of the final equation for determining the inert gas tension of arterial blood, four assumptions are necessary: *1*) The partial pressure of inert gas (N_2-A) in the urine is the same as that in the blood perfusing the urinary system. *2*) The inert gas measured in bladder urine is entirely N_2 and A, in the ratio expected after equilibration with air. *3*) The alteration in blood inert gas solubility caused by any change in blood temperature between the lung and the urinary system results in an inverse alteration of blood inert gas tension, of the same percentage magnitude. That is, $\frac{\alpha_1}{\alpha_2} = \frac{P_2}{P_1}$, where 1 and 2 represent different temperatures. *4*) Over a small temperature range, the relative change in inert gas solubility in water is the same as that in blood or urine. That is, $\frac{\Delta\alpha/\alpha}{^\circ C}$ is a constant for water, urine and blood. Near 37° C this constant is −1.2 per cent per degree C increase. (This assumption is necessitated by the lack of inert gas solubility data for blood and urine at different temperatures.)

The following symbols will be used. In order to simplify the nomenclature, the usual subscript N_2 (designating the N_2-A mixture that is the inert gas of air) will be omitted.

V_u = inert gas content (volumes per cent, STPD) of anaerobically collected bladder urine; V_e = inert gas content (volumes per cent, STPD) of urine equilibrated in a tonometer with air at 37° C; t_k = temperature (° C) at which blood and urine equilibrate within the urinary tract; t_l = temperature (° C) at which alveolar air and blood equilibrate within the lung (referred to as "lung temperature"); PB = ambient pressure (mm Hg) during tonometry of urine; FI = inert gas fraction of air; α_{b_k} and α_{b_l} = Bunsen coefficients of the inert gas of air for blood at t_k and t_l. Bunsen coefficients are defined as the volume of gas (STP) absorbed by 1 vol of fluid when the dry pressure of the gas is 760 mm Hg. α_{u_k} and $\alpha_{u_{37}}$ = Bunsen coefficients of the inert gas of air for urine at t_k and 37° C; p_k = partial pressure of inert gas (mm Hg) in blood perfusing the urinary system; P_a = partial

pressure of inert gas (mm Hg) in blood leaving the lungs (referred to as "arterial blood").

V_u and V_e are both the result of particular inert gas partial pressures and solubilities. If assumptions *1* and *2* are correct, V_u is given by this equation:

$$V_u = \frac{P_k}{760} \times \alpha_{u_k} \times 100. \quad [1]$$

V_e is given by this equation:

$$V_e = \frac{F_I(P_B - 47.1)}{760} \times \alpha_{u_{37}} \times 100. \quad [2]$$

Dividing V_u (Equation 1) by V_e (Equation 2) and solving for P_k, we obtain:

$$P_k = \frac{V_u}{V_e} \times F_I(P_B - 47.1) \times \frac{\alpha_{u_{37}}}{\alpha_{u_k}}. \quad [3]$$

If assumption *3* is correct, we may also say:

$$\frac{\alpha_{b_k}}{\alpha_{b_1}} = \frac{P_a}{P_k}. \quad [4]$$

Solving Equation 4 for P_a and substituting for P_k from Equation 3, we obtain:

$$P_a = \frac{V_u}{V_e} \times F_I(P_B - 47.1) \times \frac{\alpha_{u_{37}}}{\alpha_{u_k}} \times \frac{\alpha_{b_k}}{\alpha_{b_1}}. \quad [5]$$

The last two factors in Equation 5 have arisen because of slight differences among t_k, t_1 and 37° C. If assumption *4* is correct, $\frac{\alpha_{u_{37}}}{\alpha_{u_k}} = 1 - 0.012(37 - t_k)$ and $\frac{\alpha_{b_k}}{\alpha_{b_1}} = 1 - 0.012(t_k - t_1)$. When these two factors are multiplied, t_k becomes insignificant and the product is $1 - 0.012(37 - t_1)$. Equation 5 therefore becomes:

$$P_a = \frac{V_u}{V_e} \times F_I(P_B - 47.1) \times [1 - 0.012(37 - t_1)]. \quad [6]$$

The similarity of Equation 6 to the proportion mentioned at the beginning of this section is to be noted. Only a single correction factor for temperature variation within the body has been added. However, this correction factor is significant.

The description of the method used for determining the inert gas content of urine (4) includes a discussion of extraction chamber correction factors for accuracy. Since P_a depends only on the ratio of V_u to V_e, these factors are not necessary if V_u and V_e are determined by the same analyst on the same extraction chamber. In other words, if one ignores the absolute values of V_u and V_e and calculates only P_a, "standardization" of extraction chambers is unnecessary. The actual pressure and temperature readings needed for the Van Slyke manometric determination of V_u and V_e by the method used (4) may now be substituted directly into Equation 6:

$$P_a = \frac{\left[\frac{P_1 - P_2}{1 + 0.00384\ t}\right]_u}{\left[\frac{P_1 - P_2}{1 + 0.00384\ t}\right]_e} \times F_I(P_B - 47.1) \times [1 - 0.012(37 - t_1)]. \quad [7]$$

Definitions of P_1, P_2 and t have been given with the description of the method. F_I has been checked on a Scholander gas analyzer (8) and was always taken to be 0.7903 (9).

Partial pressure of inert gas in mean alveolar air (P_A). P_a has been determined from urine formed over a 0.5 to 1.5 hour period. The respiratory exchange ratio may vary from moment to moment, especially in emphysematous patients. It is therefore preferable to determine the inert gas tension of mean alveolar air over the entire period of urine formation rather than at any particular instant. We therefore believe (see below) that the average alveolar inert gas tension during the period of urine formation can be calculated as accurately as it can be measured. In addition, it is difficult to determine the "ideal" method of sampling alveolar air, particularly in emphysematous patients.

Using standard respiratory physiology symbols and treating all inert gas as N_2, this equation for alveolar inert gas tension may be developed when CO_2 is absent from the inspired gas (10):

$$P_{A_{N_2}} = F_{I_{N_2}}\left[\frac{P_{A_{CO_2}}(1 - R)}{R} + (P_B - P_{H_2O})\right]. \quad [8]$$

Implicit in this equation are two assumptions: *1*) mean intra-alveolar pressure = P_B; and *2*) alveolar air is 100 per cent saturated with water

vapor. We have made two additional assumptions: *3*) R = 0.85 (in all experiments); and *4*) $P_{A_{CO_2}}$ = 40 mm Hg (in all experiments). (The reasonableness of this assumption even in the case of emphysematous patients will be pointed out below.) With these assumptions, Equation 8 may be rewritten as follows. The subscript N_2 is again omitted.

$$P_A = F_I[7.1 + (P_B - P_{H_2O})] \quad [9]$$

where P_A = average partial pressure of inert gas (mm Hg) in mean alveolar air during period of urine formation; F_I = inert gas fraction in inspired air; P_B = ambient pressure (mm Hg) during the period of urine formation;[2] P_{H_2O} = vapor pressure of water (mm Hg) at t_1. The latter has been described previously. F_I has been checked on a Scholander gas analyzer (8) and always taken to be 0.7903 (9). Vapor pressures of water at t_1 have been obtained by interpolating values in standard tables (11).

Lung temperature. The calculations of P_a and P_A both involve t_1, the temperature at which alveolar air and blood equilibrate within the lung. We are aware of three studies that discuss the relationship of lung temperature to rectal temperature (12–14). All agree that lung temperature is slightly below rectal temperature. In the experiments reported, t_1 has always been assumed to be 0.5° C below the measured rectal temperature. This is the maximum difference observed and is least favorable from the viewpoint of demonstrating an arterial-alveolar inert gas tension difference. Rectal temperature was always measured 7 to 8 cm from the external sphincter because it gradually increases for the first 6 cm from the sphincter (15).

RESULTS

P_A and duplicate values of P_a were calculated for each experiment from Equations 9 and 7. The arterial-alveolar difference in inert gas pressure, which will be designated henceforth as aAD, was obtained by subtracting each P_A from the average P_a. Values for all experiments appear in Table I. In 18 experiments on 7 normal subjects, aAD ranged from −1.1 to +6.0 mm Hg and averaged 3.4 mm Hg. In eight experiments on seven emphysematous patients, aAD ranged from +14.3 to +29.5 mm Hg and averaged 22.2 mm Hg.

TABLE I

*The arterial-alveolar inert gas difference (aAD) in normal laboratory personnel and in patients with severe, diffuse, obstructive emphysema**

Normal subjects	aAD
	mm Hg
F.K.	0.5
F.K.	4.1
F.K.	4.3
R.K.	1.6
R.K.	5.2
R.K.	6.0
H.H.	5.2
H.H.	5.7
H.H.	0.1
J.P.	−1.1
J.P.	3.3
J.P.	−1.1
L.M.	5.0
L.M.	5.6
J.C.	5.8
J.C.	5.6
P.H.	1.7
P.H.	3.8
Emphysematous patients	
E.C.	28.0
E.S.	26.3
M.L.	20.9
P.S.	29.5
L.K.	17.7
F.Z.	15.7
A.P.	24.9
A.P.	14.3

* For calculation of aAD, see text.

DISCUSSION

Reliability of observed aAD values. To evaluate the aAD values observed, the reliability of our analytical method and the reliability of our assumptions must be considered. Our analytical method is used to determine V_u/V_e. This ratio has been determined twice in each experiment. The average difference between duplicate determinations was 0.3 per cent. For any individual experiment, it may be shown that the mean of duplicate determinations has a 95 per cent chance of being within 0.3 per cent of the true V_u/V_e. Thus, if our assumptions are correct, 95 per cent of our aAD values should be within 1.7 mm Hg (0.3 per cent)of the true aAD.

In evaluating our various assumptions, it is important to consider the errors they may cause in terms of their final influence on the aAD. The underestimation of t_1 by 0.1° C causes aAD

[2] It is to be noted that the barometric pressure has been read twice in each experiment—during the period of urine formation and during the period of urine tonometry.

TABLE II

*Mass spectrometer analyses of inert gas of bladder urine and tonometered urine**

	Specimen	N_2	A	CO_2	O_2	"Hydrocarbon"
		%	%	%	%	%
Normal subject F.K. aAD = 4.3	Bladder urine	97.7	2.0	0.05		0.25
	Tonometered urine	98.0	1.9	0.04		0.03
Emphysematous patient A.P. aAD = 14.3	Bladder urine	97.0	2.5	0.24	0.10	0.24
	Tonometered urine	97.1	2.4	0.33	0.06	0.06

* The inert gas of bladder and tonometered aliquots from single urine samples of a normal subject and an emphysematous patient were collected, as described elsewhere (4). For discussion of this table, see text. Results have been calculated on a water-free basis.

to be underestimated by 0.9 mm Hg. The overestimation of R by 0.05 causes aAD to be overestimated by 2.3 mm. The underestimation of $P_{A_{CO_2}}$ by 5 mm Hg causes aAD to be overestimated by only 0.7 mm. Every 1 per cent unsaturation of alveolar air with water vapor causes aAD to be overestimated by 0.4 mm. If $\frac{\Delta\alpha/\alpha}{^\circ C}$ of blood or urine differs by 50 per cent from the corresponding value for water, aAD will change by only 0.6 mm in a typical case.

The aAD values observed in emphysematous patients are even larger than might theoretically have been proposed. In attempting to account for them, we have also considered that the mean intra-alveolar pressure throughout the respiratory cycle may be greater than atmospheric in emphysematous patients. Our analyses of typical mouth-to-esophagus pressure difference tracings in quietly breathing emphysematous patients (16, 17) indicate a mean positive intra-alveolar pressure of 1 to 2 mm Hg. This would cause our emphysematous aAD values to be overestimated by approximately the same amount.

The assumption that the inert gas measured in bladder urine is entirely N_2 and A, in the ratio expected after equilibration with air, deserves particular attention. If some gas other than N_2 or A were measured in bladder urine but not in equilibrated urine, it would be incorrectly interpreted as an aAD. The evidence that this situation did not obtain in the experiments reported will now be discussed. This evidence is direct and indirect.

The direct evidence consists of the mass spectrometer analyses shown in Table II. The inert gas of bladder and tonometered aliquots from single urine samples of a normal subject and an emphysematous patient were collected, as described elsewhere (4). aAD was 4.3 and 14.3 mm Hg, respectively. The percentage of the inert gas which was N_2 and A was 99.5 to 99.9, in the ratio expected if the relative solubilities of N_2 and A are the same in urine as in water. There was never a mass 12 peak to indicate that some of the "N_2" measured was CO. The small "hydrocarbon" fraction has not been identified specifically. The trace of "O_2" (mass 32 peak) reported in the emphysematous urine may represent O_2 "carry-over" from a previous mass spectrometer analysis rather than incomplete O_2 absorption. Comparing corresponding bladder and tonometered urine analyses, there is no obvious difference between the inert gas of bladder and tonometered urine.[3] There is also no obvious difference between the inert gas of a normal subject's bladder urine and an emphysematous patient's bladder urine.

The indirect evidence lies in two areas. If ammonia occurs as part of the "inert gas" of bladder urine, aAD, as measured by our method, should increase with ammonia concentration. No relationship between the ammonia concentration of bladder urine and aAD could be found in normal subjects or in emphysematous patients. The ranges of ammonia concentration in the two groups were similar (1 to 28 mmoles per L). If some volatile substance were being excreted preferentially in the urine in significant amounts, its concentration (and therefore aAD) might be

[3] There was 0.2 per cent less "hydrocarbon" reported in each tonometered aliquot than in the corresponding bladder aliquot. If this were a true, consistent difference, it would reduce each aAD calculated by 1 mm Hg.

expected to increase with urinary solute concentration. No relationship between osmolality or specific gravity and aAD could be found in normal subjects or in emphysematous patients. The ranges of osmolality and specific gravity in the two groups were similar (137 to 580 mOsm per kg and 1.0045 to 1.0160). Unlike mass spectrometer analysis, this last evidence does not rule out the presence of some gas or other volatile substance which re-equilibrates with urinary tract capillary blood after the solute concentration of forming urine has become constant.

Evidence that gas other than N_2 and A can at times be measured in bladder urine but not in equilibrated urine is provided by the study of Van Der Aue, Brinton and Kellar (6). Bladder urine gave positive chemical tests for ethanol for 1 to 2 hours after drinking alcohol (rum). Significant increases in the differences in inert gas content between bladder and tonometered urine occurred during the same period. Such increases would account for a 10 to 15 mm Hg overestimation of aAD. When a few drops of ethanol were added to a urine just before analysis, even more striking increases in inert gas content occurred (6).

We believe that we have occasionally measured gas other than N_2 and A in bladder urine, but not in equilibrated urine in experiments performed without diuresis. The more concentrated urines obtained have had specific gravities as high as 1.0340. In eight experiments on four normal subjects, aAD ranged from -3 to $+8$ and averaged 4 mm Hg. In additional experiments on one of the same subjects (J.P.) and another normal subject (J.C.), aAD was 18 and 19 mm Hg, respectively. In one experiment on an emphysematous patient, aAD was 38 mm Hg. Specific gravities in these last three cases were 1.0270, 1.0240 and 1.0285. The inert gas contents of the tonometered aliquots were not remarkable for these solute concentrations. The cause of these occasional marked increases in aAD has not been identified. Diet preceding collection of the samples may be of interest. All samples not produced during diuresis were tested for "acetone bodies" with sodium nitroprusside-ammonium sulfate-sodium carbonate powder, and were negative. aAD values determined from diuresis urines of J.P. and J.C. have been given in Table I. The emphysematous patient was not studied during diuresis.

Interpretation of results. There is an obvious difference between the aAD values observed in normal subjects and emphysematous patients. Even the highest value in a normal subject and the lowest value in an emphysematous patient are widely separated. The aAD values observed in normal subjects suggest a small positive aAD in normal man. However, we cannot rule out the possibility of a constant error in one or more of our assumptions. aAD values nearly identical to those reported here have recently been obtained by Briscoe and Gurtner (18), using a similar experimental approach.

The possible existence of an aAD was suggested by Canfield and Rahn (2), who theorized that such a difference must be established whenever various units of the lung have unequal ventilation-perfusion ratios. The inert gas tension of alveolar gas and pulmonary capillary blood varies in such units of the lung. (This variation is a consequence of the variation in CO_2 and O_2 tension resulting from unequal ventilation-perfusion ratios.) Indeed, inert gas tension can theoretically differ by as much as 70 mm Hg in various units of the normal lung. In units of the lung with high ventilation-perfusion ratios, inert gas tension is relatively low; these units contribute more heavily to mean alveolar air than to arterial blood. In units of the lung with low ventilation-perfusion ratios, inert gas tension is relatively high; these units contribute more heavily to arterial blood than to mean alveolar air. Thus, alveolar gas and pulmonary capillary blood with different inert gas tensions contribute unequally to mean alveolar air and arterial blood, resulting in an aAD for inert gas. It is therefore suggested that the magnitude of aAD is an index of the variance of ventilation-perfusion ratios among the alveoli. The aAD values observed in normal subjects suggest that such variance exists in the healthy lung, but is small. The aAD values observed in patients indicate that a large variance exists in the emphysematous lung. Using a different experimental approach, West, Fowler, Hugh-Jones and O'Donnell (19, 20) have reached similar conclusions.

At this point it might be worthwhile to consider a brief comparison between the aAD for N_2

and the opposite gradient, the AaD for O_2. If *only* unequal ventilation-perfusion ratios exist in the lung (i.e., no diffusion barriers or shunts), then it can be shown that the O_2 difference should be equal to the sum of the N_2 difference plus CO_2 difference, provided the O_2 and CO_2 dissociation curves are linear (2). Since the O_2 dissociation curve is not linear between the venous and arterial P_{O_2}, the aAD for O_2 must always be somewhat larger than the sum of the aAD for N_2 and CO_2.

In addition we must consider the effects of diffusion barriers and shunts. These cannot, by themselves, produce a N_2 difference (2), but can have a profound effect upon the AaD for O_2. Thus an observed AaD for O_2 while breathing air provides no information as to its specific source in the pulmonary system, be it a shunt, diffusion limitation, unequal ventilation-perfusion ratio, or any combination of these factors. On the the other hand, the N_2 difference provides specific information in terms of variance of ventilation-perfusion ratio. An observed N_2 difference of 20 mm Hg, for example, indicates that the O_2 difference is likely to be considerably larger. At least 20 mm of O_2 difference must result from ventilation-perfusion ratio inequalities, while all additional differences (i.e., greater than 20 mm) are due to shunts and diffusion limitations.

Wide variance in the hematocrit of blood in the pulmonary capillaries may theoretically alter a pre-existing aAD for inert gas, but by a negligible amount. It is also of interest to consider that our emphysematous patients with arterial inert gas tension 20 to 35 mm Hg above ambient inert gas tension must consistently lose inert gas to the atmosphere through the skin. From the study of Behnke and Willmon (21), we would expect the amount of this inert gas exchange to be negligible.

In a preliminary report (1), an average aAD of 10 mm Hg was reported in normal subjects. All aAD values did not take into account the difference in temperature between the lung and rectum. When this is done, all values become similar to those reported here. This emphasizes the importance of temperature variation within the body in the calculation of the aAD.

Comparison of P_a calculated from simultaneously sampled urine and venous blood. To test further the assumption that the inert gas content of bladder urine accurately reflects P_a, we have attempted to apply our method of determining inert gas content to blood, as described elsewhere (4). This has made possible the calculation of P_a from urine and simultaneously sampled blood.

TABLE III

*Comparison of arterial inert gas tensions (P_a) calculated from simultaneously sampled urine and venous blood**

	P_a calculated from urine	P_a calculated from blood
	mm Hg	*mm Hg*
Normal subjects		
R.K. (aAD = 6.0)	566.1	563.7
P.H.	558.7	560.6
Emphysema patient		
A.P. (aAD = 14.3)	571.1	571.1

* For details of these calculations, see text.

Venous blood of two normal subjects and one emphysematous patient has been analyzed. Antecubital[4] blood, 60 to 70 ml, was drawn anaerobically in a single venipuncture near the end of the period of urine formation. The dead space of each syringe had been filled with sterile heparin. After a syringe had been filled, a small amount of Hg was introduced to facilitate thorough mixing of the blood and heparin and remixing of the blood before filling of the Ostwald-Van Slyke pipet. The latter was necessary to ensure even distribution of erythrocytes throughout the syringe, since N_2 and A are more soluble in erythrocytes than in plasma (22). The inert gas content of the blood was determined before and after tonometry with a known inert gas tension at 37° C, in the usual fashion. P_a was then calculated from Equation 7.

A comparison of the P_a values determined from urine and venous blood appears in Table III. In normal subjects, P_a calculated from venous blood was 2.4 mm Hg below and 1.9 mm Hg above P_a calculated from duplicate urine analyses. In the emphysematous patient, P_a values determined from urine and venous blood coincided within 0.1 mm Hg. aAD in this patient was 14.3 mm Hg, and, as previously de-

[4] The use of an antecubital vein assumes no significant inert gas exchange across the skin drained by the vein during the drawing of the blood sample (21).

scribed, bladder and tonometered aliquots of the same urine sample were subjected to mass spectrometer analysis.

It is interesting that Hill, Twort and Walker (23) recognized as early as 1910 that urine should reflect blood inert gas tension. In 1939, Behnke and Yarbrough (24) began to measure the inert gas content of urine as a test for bubble formation in the blood stream after exposure to increased barometric pressures. Van Der Aue and associates (6) extended this work in 1945.

SUMMARY

An arterial-alveolar difference in inert gas pressure is theoretically established whenever various units of the lung have unequal ventilation-perfusion ratios. A recent method for determining the inert gas content of a fluid has been applied to human bladder urine in a manner believed to enable the calculation of the inert gas tension of arterial blood within ±2 mm Hg (0.3 per cent). The inert gas tension of mean alveolar air can be calculated with similar accuracy and the arterial-alveolar inert gas pressure difference determined. This difference ranged from −1.1 to +6.0 mm Hg in normal subjects and averaged 3.4 mm. In patients with diffuse, obstructive emphysema, it ranged from +14.3 to +29.5 mm Hg and averaged 22.2 mm. These findings are believed to indicate a small variance of ventilation-perfusion ratios in the healthy lung and a wide variance of ventilation-perfusion ratios in the emphysematous lung.

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