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Alkalotic Disequilibrium in Patients with Solid Tumors: Rediscovery of an Old Finding

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Abstract—*Acid-base equilibrium in two groups of cancer patients, one with newly diagnosed bronchogenic cancer and one with various solid tumors, was compared to that of a group of normal volunteers and a group of hospitalized patients with diverse diseases. A consistent tendency toward alkalosis was found in both groups of cancer patients. Similar findings reported in the literature of 40–70 years ago are discussed and the possible biochemical implications of these findings considered. It is our hope that this report of findings obtained with modern technology will encourage studies of the effects of alkalinity in the pathogenesis and progression of cancer.*

INTRODUCTION

THERE are a number of reports in the medical literature of the first half of the twentieth century concerning an apparent association of malignant tumors with systemic alkalosis [1–5]. Furthermore, a few controversial reports suggest the possibility of inhibition of cancer growth by induced systemic acidosis [5–7, 8]. In 1906, Moore and Wilson [4] noted an increase in blood alkalinity in a large series of cancer patients as measured by titration techniques. They suggested that alkalinity was a cause rather than an effect of cancer because of its presence early in the course of the neoplastic process and its persistence after surgical removal of malignant tumors. Similar findings were reported in 1929 by Reding and Slosse [5, 9] using colorimetric methods and once again the suggestion was made that alkalosis might play an etiologic role in cancer. Interpretation of such findings is difficult nowadays not only because of the relatively crude laboratory methodology employed, but also because there is little information on the clinical condition of the patients studied, and no assurance that other causes of alkalosis had been considered.

In addition to studies alluding to systemic alterations in acid-base balance, there have been a wide variety of observations over the years suggesting an association between abnormalities of local pH and the development of cancer. Some gastrointestinal tumors appear to be both preceded and accompanied by micro-environmental conditions in which the local acid-base equilibrium has been temporarily shifted in the alkaline direction. Deficiencies of gastric acid secretion are associated with carcinoma of the stomach and also with other tumors [3, 10]. In the more distal parts of the gastrointestinal tract, cancers have developed at sites at which local alkalinity may have been induced by an excessive elimination of cations [11, 12]. In the Plummer–Vinson syndrome, development of esophageal cancer may be prevented by the administration of iron and hydrochloric acid [13]; although it is not known if hydrochloric acid alone would have the same preventive effect.

The present study was undertaken using current methods of determining clinical acid-base status to determine whether a tendency to systemic alkalosis is present in patients with solid tumors.

MATERIAL AND METHODS

Patient selection

Arterial blood gas analyses (ABG) were performed on 18 normal volunteers and on

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126 patients, hospitalized between 1970 and 1975 at the Medical College of Georgia.

Group 1 consisted of 18 healthy volunteers—eleven females and seven males (ages 21–34, mean 26). These individuals were on no medication, with the exception of five women who were taking oral contraceptive preparations. In this group of volunteers we were unable to detect sex related variations in arterial blood gas values.

Group 2 consisted of 83 consecutive patients studied regarding ABG who were hospitalized with a variety of acute and chronic medical and surgical problems. This group was divided into three subgroups: A, B and C, according to their age on admission: 2A: range 19–34, mean 26; 2B: range 35–53, mean 46; 2C: range 54–77, mean 61. Subgroups A and C were of approximately the same mean age as Groups 1 and 3 respectively. No separation was made regarding sex, diagnosis, severity of the patient's disease process, or medications.

Group 3 consisted of 32 patients—30 males and two females (ages 45–74, mean 61) in whom a diagnosis of lung cancer was clinically suspected and subsequently confirmed. The cell types and frequency of these tumors were as follows: squamous 19, bronchogenic 11, alveolar 1 and clear cell 1. Two patients in this group (Nos. 15 and 18)* complained of chest pain. Three patients (Nos. 17, 20, 26) had severe obstructive ventilatory impairment.

Three patients (Nos. 6, 10, 12) had mild to moderate obstructive ventilatory impairment. One patient (No. 31) had severe restrictive ventilatory impairment. Two patients (Nos. 9 and 15) had mild restrictive ventilatory impairment. Three patients (Nos. 13, 18, 24) had mild to moderate obstructive and restrictive ventilatory impairment. One patient (No. 21) had lobar atelectasis. The predicted normal values for pulmonary function tests were calculated from standard nomograms [14].

Group 4 consisted of 11 hospitalized patients with histologically diagnosed solid tumors of different tissue origin: 7 female and 4 males (ages 25–73, mean 53). Nine of the eleven fell into the age range of Groups 2C and 3, (ie., 48–73). Hospitalization was at various times after the initial diagnosis (0–6 years, mean 2·3 years). The original sites of the tumors are given in the appendix. Only one patient (No. 9) had recently received a course of chemotherapy (vincristine and cyclophosphamide). None of the other patients were receiving drugs. Two patients (Nos. 6, 9) complained of mild to moderate intermittent pain during the time of the study. No other conditions known to affect acid base balance were detected in this group. All patients in Groups 3 and 4 were studied during a symptomatic period of their disease. None of the patients in the two cancer groups had clinical or laboratory evidence of abnormal liver or renal function, serum glucose values which were suggestive of diabetes mellitus, hypercalcemia, hypocalcemia, hyper- or hypokalemia. Cancer patients receiving diuretics, corticosteroids, antacids, or other drugs known to affect acid-base balance were excluded from the study. There was no evidence of clinical dehydration, a history of recent vomiting in any of these patients, or suggestion of abnormal hormonal production known to happen with some tumors.

Methods

The collection and analysis of arterial blood samples were performed identically in all groups. Samples were collected in 10 ml heparinized plastic syringes, immediately immersed in ice and transported to the blood gas laboratory. Analysis was performed within ½ hr after collection, using an Instrumentation Laboratories Blood Gas System, Model 213. The measured pH values were tabulated and corrected to a PCO_2 of 40 mm Hg using the Sigaard–Andersen nomogram [15, 16]. This "corrected" pH is designated as the "metabolic" (met.) pH. Hydrogen ion concentrations were calculated from the measured pH by standard methods. Calculated bicarbonate values are listed in Table 1.

Student's "*t*" test was used to determine the significance of differences of group means. Duncan's multiple range test was employed for non-parametric comparisons of groups.

RESULTS

Data from the arterial blood gas studies of Group 1, 2, 3 and 4 are summarized in Table 1. The *P* values listed for each variable in Table 1 represent the results of Student "*t*" test of the differences between the mean value of that group as compared to that for the normal volunteers (Group 1). Figure 1(a) graphically shows the distribution of measured arterial blood gas values between the normal volunteers and the two cancer groups. Figure 1(b) shows the distribution of measured arterial blood gas values between the two cancer groups and the inpatient population. It is worth noting that none of the 144 individuals studied had a

*See Appendix for individual values.

Table 1. *Normal volunteers—group* 1

No. Cases		Ages	pH	$PaCO_2$ mm Hg	HCO_3^- mEq/L	Met. (pH)	H^+ (nmole/L)
18							
	Range	21–34	7·36–7·45	31·7–40·2	21·0–25·5	7·36–7·42	35·5–43·6
	Mean	26	7·41	36·3	23·1	7·39	38·6
	S.D.		0·02	2·8	1·5	0·02	1·8
			Inpatient population—group 2 (Subgroups A, B and C)				
(A) 13							
	Range	19–34	7·41–7·48	29·1–37·4	20·0–24·0	7·38–7·43	33·1–38·9
	Mean	26	7·44	33·2	22·2	7·39	36·0
	S.D.		0·02	2·8	1·3	0·02	1·9
	*P**		+ <0·001	− <0·01	NS	NS	− <0·001
(B) 39							
	Range	35–53	7·36–7·54	28·1–48·7	18·6–30·5	7·33–7·50	28·8–43·6
	Mean	46	7·43	36·4	23·8	7·41	37·0
	S.D.		0·04	4·2	2·4	0·04	3·0
	*P**		+ <0·05	NS	NS	+ <0·05	NS
(C) 31							
	Range	54–77	7·36–7·50	27·5–48·3	18·4–29·8	7·36–7·47	31·6–43·6
	Mean	61	7·43	37·6	24·6	7·42	37·0
	S.D.		0·03	4·5	2·6	0·03	2·7
	*P**		+ <0·05	NS	+ <0·05	+ <0·01	− <0·05
			Lung cancer—group 3				
32							
	Range	45–74	7·40–7·57	27·5–45·0	19·9–34·8	7·36–7·51	26·9–39·8
	Mean	61	7·48	35·7	26·4	7·44	33·5
	S.D.		0·03	4·1	2·9	0·03	2·5
	*P**		+ <0·001	NS	+ <0·001	+ <0·001	− <0·001
			Other solid tumors—group 4				
11							
	Range	25–73	7·45–7·53	32·0–43·0	23·9–33·7	7·42–7·52	29·5–35·5
	Mean	53	7·48	36·5	27·6	7·46	32·9
	S.D.		0·03	3·4	3·0	0·04	2·1
	*P**		+ <0·001	NS	+ <0·001	+ <0·001	− <0·001

Groups 1, 2, 3 and 4: Arterial blood gases (ABG) data.
*P**—Significance of the difference from the mean of Group 1 (Student's "*t*" test).

Table 2.

Groups	1	2A	2B	2C	3	4
Status	Normal	In-patient subgroups			Lung cancer	Other tumors
Number	18	13	39	31	32	11
pH ($\mu \pm$ S.D.)	7·41 ± 0·02	7·44 ± 0·02	7·43 ± 0·04	7·43 ± 0·03	7·48 ± 0·03	7·48 ± 0·03
		N.S.		$P < 0·001$		
		N.S.		$P < 0·001$		
Met. pH ($\mu \pm$ S.D.)	7·39 ± 0·02	7·39 ± 0·02	7·41 ± 0·04	7·42 ± 0·03	7·44 ± 0·03	7·46 ± 0·04
		N.S.		$P < 0·01$		
		$P < 0·05$		$P < 0·01$		

Means, standard deviations and *P* values between the different groups according to the Student's "*t*" test.

Table 3. Duncan's Multiple Range Test. Means of groups that are not significantly different at the 0·01 level are underlined. The non-parametric comparison shows that both groups of cancer patients (3 and 4) are significantly different from the volunteers (1) and hospital patients of different ages (2A, 2B, and 2C)

	1	2A	2B	2C	3	4
pH	7·41	7·44	7·43	7·43	7·48	7·48
Metabolic pH	7·39	7·39	7·41	7·42	7·44	7·46

measured pH below 7·35. Table 2 shows the means, standard deviations and P values among the different groups. Table 3 shows the statistical differences at the 0·01 level according to the Duncan's Multiple Range Test. The measured arterial pH, (hydrogen ion concentration) and the corrected "metabolic" pH in the two groups of patients with solid tumors show a significant shift in the alkaline direction when compared to a control group of normal volunteers and to three subgroups of hospitalized patients with diverse diseases.

Although the differences between the pH values of the older consecutively hospitalized patients of Group 2C and the cancer patients of Groups 3 and 4 do not seem as impressive as those seen with the volunteers or the younger patients, there still is a clear separation between groups. Both pH and metabolic pH values are significantly higher in Groups 3 and 4 according to the Student "t" test ($P < 0·001$ and $P < 0·01$) and Duncan's multiple range test ($P < 0·01$) than in the older inpatient population (2C) (see Tables 2 and 3).

DISCUSSION

Our findings using modern techniques are in agreement with observations made by other investigators in decades past [4, 5, 9] and suggest that there is an unexplained tendency toward alkalosis in cancer patients with solid tumors which have not yet progressed to the terminal stage.

It is well known that pain, fear and anxiety may be accompanied by both acute and chronic hyperventilation with an associated respiratory alkalosis. Metabolic alkalosis in cancer patients has also been reported to be directly related to the severity of pain [17]. Neither of these situations seems to pertain to our study. No significant differences in arterial

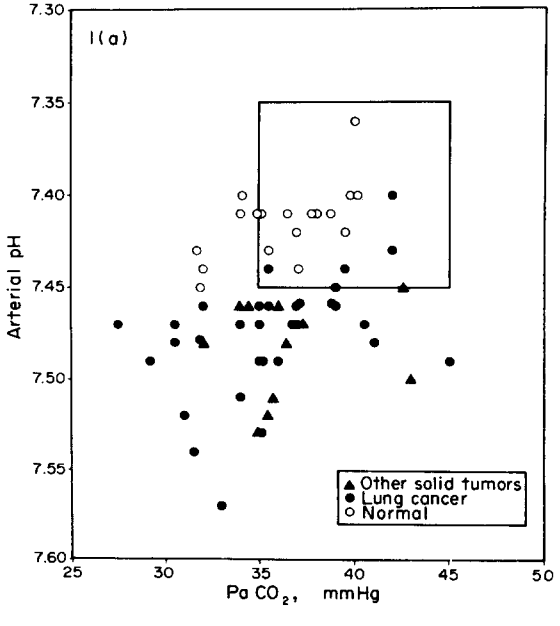

Fig. 1(a). Distribution of measured pH and $PaCO_2$ values in solid tumor groups (3 and 4) and normal volunteers (1). The smaller square indicates the normal range for arterial pH and $PaCO_2$.

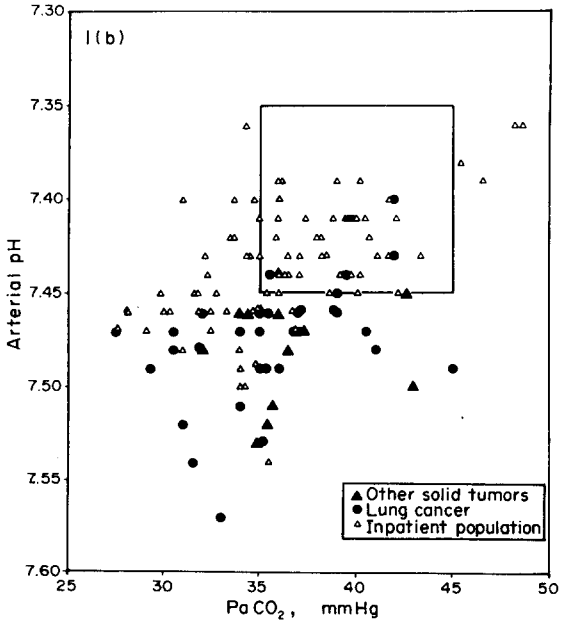

Fig. 1(b). Distribution of measured pH and $PaCO_2$ values in cancer groups (3 and 4) vs the consecutive inpatient population (group 2).

$PaCO_2$ exist between the cancer groups and the older subgroups of inpatients. Indeed a significantly lower mean value for arterial PCO_2 was found in the youngest subgroup of patients.

In addition to the increased rates of anaerobic and aerobic glycolysis and accumulation of lactic acid, a tendency toward decreased glucose levels in the venous effluent of tumors has been reported in association with cancer by some investigators [18–22]. These same three characteristics: an accumulation of lactic acid, increased glycolysis, and decreased glucose levels, can be produced experimentally by increasing the alkalinity of the blood [23–26]. Huckabee has shown in humans that hypoxia is not the only circumstance in which lactate production is increased [27]. He and others have documented that an elevation of pH, of *either* respiratory or metabolic origin accelerates the process of glycolysis and the formation of lactate [27–29]. This alkalosis mediated acceleration of glycolysis has been shown to be induced principally through stimulation of the phosphofructokinase enzyme reaction [29, 30]. Therefore, in many ways alkalosis, independent of the cause, seems to act on the physiology of the organism in a manner similar to hypoxia. It can thus be concluded that many of the abnormal metabolic characteristics of malignant cells and tissues can be induced in normal cells by stimulus of a higher than normal pH.

Reding and Slosse in 1929 [5, 9] reported that a tendency toward alkalinity in the blood exists at the time of the first clinical manifestations of cancer. Our findings, particularly in the lung cancer patients, Group 3, lend support to their contention.

The basis for the association between alkalosis and cancer from the time of its initial clinical manifestations has not been defined, nor obviously has the question of cause and effect been resolved. However, a possible primary role of acidosis in stimulating the immune response has been advanced [31, 32], and a recent report has described tumor inhibition following the induction of systemic acidosis in different animal malignancies [8]. Therefore, the possibility that local and systemic alterations in acid-base balance in the alkalotic direction play an important role in the genesis and/or propagation of cancer remains not only a viable but a vital issue at the present time.

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REFERENCES

1. O. L. E. DeRaadt, Krebserzeugung mittels basischer Nährung. *Z. Krebsforsch.* **32,** 596 (1930).
2. A. Goldfeder, Zur Alkalosefrage in der Krebsforschung. I. Mitteilung. Wie ist die Wirkung der Alkalischen Nahrung auf das Entstehen und Wachstum der Bösartigen Geschwülste. *Z. Krebsforsch.* **38,** 121 (1932).
3. B. Moore, W. Alexander, R. E. Kelly and H. E. Roaf, A study of the pathological variations in the acidity of the gastric contents, especially in relationship to malignant disease. *Biochem. J.* **1,** 274 (1906).
4. B. Moore and F. P. Wilson, A clinical method of haemalkalimetry, with applications to determination of the reactivity of the inorganic salts of the serum in malignant disease and other conditions. *Biochem. J.* **1,** 297 (1906).
5. L. Reding and A. Slosse, Des caractères généraux de l'état cancéreux et précancereux. *Bull. Ass. franc. Cancer* **18,** 122 (1929).
6. A. Goldfeder, Theoretical basis for the acidotic treatment of neoplasia. *Amer. J. Surg.* **19,** 307 (1933).
7. A. Goldfeder, Über den Einfluss der Acidotischwirkenden Chemischen Präparate auf das Wachstum Bzw. Verschwinden der Transplantablen Tiertumore. *Z. Krebsforsch.* **30,** 421 (1933).
8. L. J. Anghileri, Tumor growth inhibition by ammonium chloride-induced acidosis. *Int. J. clin. Pharm.* **12,** 320 (1975).
9. L. Reding, L'équilibre acide-base et l'équilibre ionique dans le cancer et le précancer. *Cancer (Brux.)* **2,** 97 (1928).
10. J. Ewing, *Neoplastic Diseases.* p. 71. W. B. Saunders, Philadelphia (1928).
11. S. Harguindey, R. C. Kolbeck and E. D. Bransome, Ureterosigmoidostomy and cancer: new observations. *Ann. int. Med.* **83,** 833 (1975).

12. M. W. Wheat Jr. and L. V. Ackerman, Villous adenomas of the large intestine: Clinicopathological evaluation of 50 cases of villous adenomas with emphasis on treatment. *Ann. Surg.* **147,** 476 (1958).
13. C. Oberling, *The Riddle of Cancer*. p. 86. Yale University Press, New Haven (1952).
14. R. C. Kory, R. Callahan and H. G. Boren, The Veterans Administration–Army cooperative study on pulmonary function: I. Clinical spirometry in normal men. *Amer. J. Med.* **30,** 243 (1961).
15. O. Sigaard-Andersen and K. Engel, A new acid-base nomogram: An improved method for the calculation of the relevant blood acid-base data. *Scand. J. clin. lab. Invest.* **12,** 177 (1960).
16. O. Sigaard-Andersen, The pH-log PCO_2 blood acid-base nomogram revised. *Scand. J. clin. lab. Invest.* **14,** 598 (1962).
17. R. J. Evans, Acid-base changes in patients with intractable pain and malignancy. *Canad. J. Surg.* **15,** 37 (1972).
18. C. F. Cori and G. T. Cori, The Carbohydrate metabolism of tumors: II. Changes in the sugar, lactic acid and CO_2 combining power of blood passing through a tumor. *J. biol. Chem.* **65,** 397 (1925).
19. J. Gold, Cancer cachexia and gluconeogenesis. *N.Y. Acad. Sci.* **230,** 103 (1974).
20. V. S. Shapot, Some biochemical aspects of the relationship between the tumor and the host. *Advanc. Cancer Res.* **15,** 253 (1972).
21. O. Warburg, On the origin of cancer cells. *Science* **123,** 309 (1956).
22. S. Weinhouse, Glycolysis, respiration, and anomalous gene expression in experimental hepatomas: G. H. A. Flowers Memorial Lecture. *Cancer Res.* **32,** 2007 (1972).
23. G. V. Anrep and R. K. Cannan, The concentration of lactic acid in the blood in experimental alkalaemia and acidaemia. *J. Physiol.* **58,** 244 (1924).
24. J. J. R. Macleod and H. H. Knapp, The influence of alkali administration on the urinary excretion of lactic acid, and the possible significance of the latter in maintaining the neutrality of the body. *Amer. J. Physiol.* **47,** 189 (1918).
25. J. J. R. MacLeod and D. H. Hoover, Studies in experimental glycosuria: Lactic acid production in the blood following the injection of alkaline solutions or dextrose or of alkaline solutions alone. *Amer. J. Physiol.* **42,** 460 (1917).
26. J. J. R. MacLeod and M. E. Fulk, Studies in experimental glycosuria: Retention of dextrose by the liver and muscles and the influence of acids and alkalines on the dextrose concentration of the blood. *Amer. J. Physiol.* **42,** 193 (1917).
27. W. E. Huckabee, Relationships of pyruvate and lactate during anaerobic metabolism: I. Effects of infusion of pyruvate or glucose and of hyperventilation. *J. clin. Invest.* **37,** 244 (1958).
28. W. Gevers and E. Dowdle, The effect of pH on glycolysis *in vitro*. *Clin. Sci.* **24,** 343 (1963).
29. A. S. Relman, Metabolic consequences of acid-base disorders. *Kidney int.* **1,** 347 (1972).
30. M. Ui, A role of phosphofructokinase in pH-dependent regulation of glycolysis. *Biochim. biophys. Acta* **124,** 310 (1966).
31. B. Mookerjee, H. Gault and J. Dossetor, Hyperchloremic acidosis in early diagnosis of renal allograft rejection. *Ann. int. Med.* **71,** 47 (1969).
32. M. Dole and F. R. Wilson, Hyperbaric hydrogen therapy: a possible treatment for cancer. *Science* **190,** 152 (1975).

APPENDIX

Table A1. *Individual data—group* 1

Case	Age–Sex	pH	$PaCO_2$ (mm Hg)	HCO_3^- (mEq/L)	Met. (pH)	H^+ (nmole/L)
1	28 M	7·41	38·0	24·0	7·40	38·9
2	30 F	7·41	35·1	22·1	7·37	38·9
3	34 M	7·40	39·8	24·5	7·40	39·8
4	28 M	7·41	38·7	24·3	7·40	38·9
5	23 F	7·44	32·0	21·5	7·38	36·3
6	21 F	7·42	37·0	24·0	7·40	38·0
7	28 F	7·41	34·0	21·4	7·36	38·9
8	27 F	7·41	34·9	22·0	7·38	38·9
9	22 F	7·40	34·1	21·0	7·36	39·8
10	22 F	7·41	36·5	22·7	7·39	38·9
11	24 F	7·36	40·0	22·3	7·36	43·6
12	26 F	7·45	31·9	22·0	7·39	35·5
13	31 F	7·43	31·7	21·0	7·37	37·1
14	27 M	7·42	39·5	25·5	7·42	38·0
15	28 M	7·44	37·1	25·0	7·41	36·3
16	23 M	7·40	40·2	24·8	7·40	39·8
17	21 F	7·43	35·5	23·4	7·40	37·1
18	28 M	7·41	37·8	23·8	7·39	38·9

Individual data—group 3

Case	Age–Sex	pH	$PaCO_2$ (mm Hg)	HCO_3^- (mEq/L)	Met. (pH)	H^+ (nmole/L)
1	63 M	7·46	39·0	27·6	7·46	34·7
2	63 M	7·46	37·0	26·4	7·44	34·7
3	68 M	7·48	41·0	30·6	7·49	33·1
4	70 M	7·47	34·0	24·8	7·42	33·9
5	58 M	7·54	31·5	27·2	7·47	28·8
6	55 M	7·57	33·0	30·6	7·51	26·9
7	68 M	7·49	45·0	34·8	7·51	32·4
8	64 M	7·49	35·0	26·8	7·45	32·4
9	62 M	7·44	35·5	24·2	7·41	36·3
10	63 M	7·46	32·0	22·8	7·40	34·7
11	66 M	7·53	35·0	29·5	7·49	29·1
12	63 M	7·44	39·5	26·8	7·44	36·3
13	61 M	7·48	30·5	22·4	7·40	33·1
14	64 M	7·49	29·2	22·3	7·40	32·4
15	45 M	7·52	31·0	25·5	7·45	30·2
16	56 M	7·45	39·0	27·0	7·45	35·5
17	62 M	7·47	40·5	29·2	7·48	33·9
18	59 M	7·43	42·0	28·8	7·45	37·1
19	62 F	7·46	35·0	24·8	7·42	34·7
20	62 F	7·47	37·0	27·0	7·45	33·9
21	67 M	7·40	42·0	25·8	7·42	39·8
22	63 M	7·47	35·0	25·4	7·43	33·9
23	74 M	7·47	30·5	22·2	7·39	33·9
24	57 M	7·49	36·0	27·4	7·46	32·4
25	62 M	7·49	35·0	27·0	7·46	32·4
26	48 M	7·47	37·0	27·0	7·45	33·9
27	65 M	7·46	27·5	19·9	7·36	33·9
28	55 M	7·46	35·5	25·7	7·43	34·7
29	69 M	7·51	34·0	27·3	7·46	30·9
30	62 M	7·48	32·0	24·0	7·42	33·1
31	63 M	7·46	39·0	27·8	7·46	34·7
32	63 M	7·46	37·0	26·5	7·44	34·7

Individual data—group 4

Case	Age–Sex	Origin	pH	$PaCO_2$ (mm Hg)	HCO_3^- (mEq/L)	Met. (pH)	H^+ (nmole/L)
1	48 F	Cervix	7·48	32·0	23·9	7·42	33·1
2	73 F	Sigmoid	7·45	42·6	29·4	7·47	35·5
3	63 F	Sigmoid	7·48	36·5	27·5	7·46	33·1
4	25 M	Rectum	7·46	34·5	24·3	7·42	34·7
5	61 F	Rectum	7·50	43·0	33·7	7·52	31·6
6	51 F	Breast	7·46	36·0	25·6	7·43	34·7
7	58 F	Breast	7·52	35·5	28·9	7·48	30·2
8	58 F	Breast	7·46	34·0	24·2	7·42	34·7
9	42 M	Testicle (seminoma)	7·53	35·0	29·5	7·49	29·5
10	60 M	Thyroid (follicular)	7·47	37·3	27·5	7·46	33·9
11	49 M	Neurofibrosarcoma	7·51	35·7	28·7	7·47	30·9