Effect of gaseous anaesthesia on blood carbon dioxide measurements

R. R. OGILVIE AND G. F. A. HOWIE

From the Departments of Surgery and Radiology, University of St. Andrews, and Royal Infirmary, Dundee

SYNOPSIS The present study of the effect of two common anaesthetic gases on blood acid-base parameters shows that the micro-Astrup measurement of carbon dioxide tension is not invalidated by the presence of nitrous oxide. This result was anticipated from the theoretical aspect of this technique. The mean error involved in estimating plasma carbon dioxide content in the presence of nitrous oxide using the volumetric Van Slyke apparatus without absorption of carbon dioxide by sodium hydroxide can be of the order of 25%. No such effect was measurable in estimating carbon dioxide contents in the presence of halothane.

The degree of respiratory alkalosis during anaesthesia reported in earlier papers (Walker, Morgan, Breckenridge, Watt, Ogilvie, and Douglas, 1963; Morgan, Ogilvie, and Walker, 1963) was greater than had been originally appreciated.

A 'false' increase in carbon dioxide content will also falsely increase buffer base or 'base excess' as calculated from standard nomograms (Singer and Hastings, 1948; Davenport, 1958; Siggaard-Andersen, 1963).

The measurement of blood acid-base parameters is becoming increasingly useful clinically, but in patients exposed to open-heart surgery certain routine methods may lead to considerable errors at the times when the patient is receiving a volatile anaesthetic. If the carbon dioxide content of plasma is estimated in the volumetric Van Slyke apparatus, volatile anaesthetic gases will cause falsely high results if, as is usual in routine practice, specific absorption by sodium hydroxide is not employed. The key factors then derived from the blood pH and carbon dioxide content, *viz.*, $p\text{CO}_2$ and base excess (or buffer base), will necessarily be in error, causing possible false interpretations of respiratory and metabolic changes.

Such discrepancies were found on reviewing our earlier work (Walker *et al.*, 1963; Morgan *et al.*, 1963) and led to a systematic study of the degree of error involved.

METHODS

Acid-base parameters were derived by coincidental use of the volumetric Van Slyke (Peters and Van Slyke, 1932) and micro-Astrup (Siggaard-Andersen, Engel, Jørgensen,

and Astrup, 1960) techniques on arterial blood from 20 patients undergoing routine bilateral femoral arteriography for peripheral vascular disease. Equal numbers had nitrous oxide or halothane as the gaseous anaesthetic.

Blood was withdrawn from the femoral artery into a siliconed, heparinized syringe after non-gaseous anaesthesia was induced with succinylcholine chloride (Scoline) and sodium thiopentone (Pentothal) or sodium methohexatone (Brietal) and before the injection of the radio-opaque contrast medium (Hypaque 45%). This sample was then divided into two main aliquots, one for plasma carbon dioxide content measured by the volumetric Van Slyke apparatus without the addition of sodium hydroxide, the other for pH measurements before and after equilibration with gases of known $p\text{CO}_2$ values in the Astrup apparatus. In the case of the Van Slyke estimations, the $p\text{CO}_2$ values were calculated (Milch, Bane, and Roberts, 1957) from the measured blood pH values and carbon dioxide contents. In the micro-Astrup technique, blood carbon dioxide content and $p\text{CO}_2$ values were calculated using the Siggaard-Andersen (1962) curve nomogram (Cartesian nomogram).

Anaesthesia was maintained with nitrous oxide/oxygen in the normal proportion of 3:1 or halothane 1 to 1½ in oxygen, and after 15 to 30 minutes another arterial blood sample was taken and treated similarly. Two blood samples were thus obtained from each patient, one

before and one during the period of gaseous anaesthesia. In 14 patients the carbon dioxide content was also measured with the Natelson microgasometer (which is a modified manometric Van Slyke technique with sodium hydroxide used as a carbon dioxide absorbent; Natelson and Menning, 1955; Holaday and Verosky, 1956; Natelson, 1961) and in two by the colorimetric procedure in the Technicon AutoAnalyzer, in which evolved carbon dioxide acts on buffered phenolphthalein (Skeggs, 1960).

RESULTS

Discrepancies observed between the $p\text{CO}_2$ values obtained by the micro-Astrup carbon dioxide equilibration technique and those derived from the blood pH values and carbon dioxide contents estimated by the volumetric Van Slyke apparatus in three patients undergoing open-heart surgery are shown in Table I. Serious discrepancies only occurred when the patient was anaesthetized, the Astrup $p\text{CO}_2$ values during this period being lower than the corresponding Van Slyke values, on average by 25%. However, estimations carried out by the two methods during the post-operative period generally agreed within reasonable limits of experimental error (Fig. 1).

TABLE I

pCO_2 VALUES CALCULATED USING THE VOLUMETRIC VAN SLYKE AND MICRO-ASTRUP TECHNIQUES SIMULTANEOUSLY DURING AND AFTER ANAESTHESIA IN THREE PATIENTS UNDERGOING OPEN-HEART SURGERY

Case	In Theatre and during N_2O Anaesthesia		Post-Operative after Anaesthesia	
	Van Slyke	Astrup	Van Slyke	Astrup
I.K.	30.4	22.0	46.9	47.8
	39.9	31.8		
	67.7	54.8		
N.I.	37.5	24.5	43.3	46.5
	50.4	38.0		
	48.6	35.0		
Mean	45.8	34.5	47.4	49.4

In the patients undergoing routine bilateral femoral arteriography, the values derived for carbon dioxide tensions before nitrous oxide anaesthesia by either the Astrup method or the Van Slyke technique agree on average within 5% (Tables II and III). However, the 'carbon dioxide contents' and consequently the derived $p\text{CO}_2$ values of the blood samples removed during nitrous oxide anaesthesia were greatly different, the Astrup results being about 25% lower (Fig. 2).

The relative accuracy of the two methods used was compared with two others in routine work, the Natelson microgasometer and the AutoAnalyzer colorimetric procedure (Table III). Under conditions

FIG. 1. Average $p\text{CO}_2$ values calculated using the volumetric Van Slyke and micro-Astrup techniques simultaneously during and after anaesthesia in three patients undergoing open-heart surgery. Good agreement in the results obtained by the two methods is seen after but not during anaesthesia.

FIG. 2. Average carbon dioxide content and $p\text{CO}_2$ results measured or calculated simultaneously by the volumetric Van Slyke and micro-Astrup techniques before and during nitrous oxide anaesthesia in 10 patients undergoing routine arteriography. Results from the two methods agree before anaesthesia but not during it.

of nitrous oxide anaesthesia the volumetric Van Slyke estimations were at variance with an error of about 25%.

When halothane was used as the gaseous anaesthetic there was no appreciable difference in the carbon dioxide content and the derived $p\text{CO}_2$ using the Astrup, Van Slyke, and micro-Natelson techniques (Fig. 3).

TABLE II

BLOOD CARBON DIOXIDE RESULTS MEASURED OR CALCULATED SIMULTANEOUSLY BY THE VOLUMETRIC VAN SLYKE AND MICRO-ASTRUP TECHNIQUES BEFORE AND DURING NITROUS OXIDE ANAESTHESIA IN 10 PATIENTS UNDERGOING ARTERIOGRAPHY

Case No.	Before N ₂ O Anaesthesia					During N ₂ O Anaesthesia				
	pH	CO ₂ Content (m.mol./l.)		pCO ₂ (mm.Hg)		pH	CO ₂ Content (m.mol./l.)		pCO ₂ (mm.Hg)	
		Van Slyke	Astrup	Van Slyke	Astrup		Van Slyke	Astrup	Van Slyke	Astrup
1	7.459	22.2	25.8	31.0	36.0	7.443	29.9	19.7	43.2	27.4
2	7.315	26.7	26.7	51.1	51.3	7.420	29.5	24.1	44.9	36.8
3	7.487	22.2	21.9	29.1	28.7	7.494	27.1	20.5	35.0	26.5
4	7.382	22.5	20.6	37.2	34.0	7.618	26.0	12.2	25.5	12.0
5	7.410	22.2	20.3	34.6	32.3	7.360	29.8	22.3	51.7	40.5
6	7.412	23.6	23.1	36.6	35.8	7.498	27.5	22.4	35.3	29.0
7	7.412	25.4	24.6	39.3	38.3	7.412	30.7	23.2	47.6	36.0
8	7.520	20.6	20.5	25.2	25.0	7.560	27.5	20.2	30.8	22.5
9	7.475	23.0	20.8	31.0	27.7	7.605	28.2	18.5	28.4	18.5
10	7.410	24.7	25.0	38.5	41.0	7.420	29.5	24.8	44.9	39.5
Average	7.428	23.3	22.9	35.4	35.0	7.483	28.6	20.8	38.7	28.9

TABLE III

pCO₂ VALUES CALCULATED BEFORE AND DURING NITROUS OXIDE ANAESTHESIA USING THE MICRO-NATELSON AND/OR TECHNICON AUTOANALYZER TECHNIQUES SIMULTANEOUSLY WITH THE VOLUMETRIC VAN SLYKE AND MICRO-ASTRUP METHODS IN SEVERAL OF THE PATIENTS UNDERGOING ARTERIOGRAPHY

Case No.	Before N ₂ O Anaesthesia			During N ₂ O Anaesthesia		
	Van Slyke	Astrup	Micro-Natelson	Van Slyke	Astrup	Micro-Natelson
2	51.1	51.3	52.7	44.9	36.8	36.3
4	37.2	34.0	34.9	25.5	12.0	13.9
5	34.6	32.3	32.2	51.7	40.5	39.9
7	39.3	38.3	39.5	47.6	36.0	35.7
Average	40.6	39.0	39.8	42.4	31.3	31.5

Case No.	Before N ₂ O Anaesthesia			During N ₂ O Anaesthesia		
	Van Slyke	Astrup	AutoAnalyzer	Van Slyke	Astrup	AutoAnalyzer
3	29.1	28.7	30.1	35.0	26.5	27.1
5	34.6	32.3	34.3	51.7	40.5	36.5
Average	31.9	30.5	32.2	43.4	33.5	31.8

FIG. 3. Average carbon dioxide content and pCO₂ results measured or calculated simultaneously by the volumetric Van Slyke, micro-Astrup, and micro-Natelson techniques before and during halothane anaesthesia in 10 patients undergoing routine arteriography. Reasonable agreement of the results obtained by all three methods, both before and during halothane anaesthesia, suggest that the volumetric Van Slyke carbon dioxide estimation is not affected by this gaseous anaesthetic.

DISCUSSION

The effect of volatile anaesthetic gases on the carbon dioxide content of serum measured by the Van Slyke technique was noted by Austin in 1924. When ether was added to dogs' blood *in vitro* such that the concentration was 1.0 to 1.8 mg./ml., which is that associated with deep anaesthesia (White, 1923; Ronzoni, 1923), a considerable error was found to be produced in the volumetric and manometric Van Slyke carbon dioxide estimations. This error was due to the anaesthetic gas vapourizing in the vacuum chamber of the Van Slyke apparatus and thus adding to the volume of the extracted gases. To attempt to overcome this error, Austin developed a method which employed an empirical correction. This method subsequently gave way to the methods of Orcutt and Waters (1937) and Goldstein (1950), but the technical difficulties in estimating blood carbon dioxide accurately in the presence of different anaesthetic gases using a Van Slyke-Neill apparatus is emphasized in the paper by Holaday and Verosky (1955) when they compare these latter two methods.

Sodium or potassium hydroxide is often added to the Van Slyke apparatus as a 'specific' absorbent of carbon dioxide. Unfortunately, ether is highly soluble in both these absorbing agents whilst potassium hydroxide has a high affinity for nitrous oxide. However, Nunn (1958) has shown that nitrous oxide is not appreciably absorbed by sodium hydroxide. Thus in the presence of anaesthetic gases, strong alkali cannot always be safely assumed to be a specific absorbent of carbon dioxide. Furthermore, the added complication of adding sodium hydroxide is very often omitted quite validly in routine clinical estimations since the majority of estimations are carried out on blood from non-anaesthetized patients.

The difficulties and errors arising when the methods are used to study patients under anaesthesia are evident, with an error of about 25% in measured 'carbon dioxide content' and calculated $p\text{CO}_2$ when the 'routine' volumetric Van Slyke procedure is used. In studies on cyanosis in nitrous oxide/oxygen anaesthesia in man (Raginsky and Bourne, 1934), the nitrous oxide content of the blood ranged from 16.8 to 21.7 vol. % with an average of 18.8 vol. % (about 8.4 mmol./l.). The presence of this amount of nitrous oxide in the average 'carbon dioxide content' of 28.6 mmol./l. (as measured by the volumetric Van Slyke technique in the patients undergoing arteriography during the period of nitrous oxide anaesthesia) produces an error of about 29% in the measured 'carbon dioxide content', a difference of the same degree as our experimental findings. The $p\text{CO}_2$ is, of course, a derived value and the large positive

FIG. 4. Average 'base excess' before and during nitrous oxide anaesthesia for the 10 patients undergoing arteriography, calculated using the respective volumetric Van Slyke and micro-Astrup values in conjunction with the alignment nomogram of Siggaard-Andersen (1963). There is reasonable agreement in the results before anaesthesia, but a difference of almost 4 mEq/l. in those during anaesthesia.

errors possible in the derivation of such values are obvious. When the 'base excess' is calculated using such data falsely positive results are again obtained (Fig. 4), the average variation in the normal patients being of the order of 4 mEq./l. Thus, for example, in states of mild metabolic acidosis the degree would be minimized and decisions on treatment often modified. No such errors were found when halothane was used as the gaseous anaesthetic, probably due to its much smaller effective concentration in blood.

We wish to thank the various anaesthetists for their kind cooperation; Miss P. Mathers, B.Sc., for the micro-Natelson analyses and the staff of the Clinical Chemistry section for the AutoAnalyzer measurements. We are also indebted to Dr. H. G. Morgan and Mr. W. F. Walker for their valuable advice and encouragement in preparing this script.

REFERENCES

- Austin, J. H. (1924). *J. biol. Chem.*, **61**, 345.
- Davenport, H. W. (1958). *The ABC of Acid-Base Chemistry*, 4th ed. University of Chicago Press, Chicago.
- Goldstein, F., Gibbon, J. H. Jr., Allbritton, F. F. Jr., and Stayman, J. W. Jr. (1950). *J. biol. Chem.*, **182**, 815.
- Holaday, D. A., and Verosky, M. (1955). *J. Lab. clin. Med.*, **45**, 149.
- (1956). *Ibid.*, **47**, 634.
- Milch, R. A., Bane, H. N., and Roberts, K. E. (1957). *J. appl. Physiol.*, **10**, 151.
- Morgan, H. G., Ogilvie, R. R., and Walker, W. F. (1963). *J. clin. Path.*, **16**, 545.
- Natelson, S. (1961). *Microtechniques of Clinical Chemistry*, 2nd ed., p. 152. Thomas, Springfield, Illinois.
- , and Menning, C. M. (1955). *Clin. Chem.*, **1**, 165.

- Nunn, J. F. (1958). *Brit. J. Anaesth.*, **30**, 254.
 Orcutt, F. S., and Waters, R. M. (1937). *J. biol. Chem.*, **117**, 509.
 Peters, J. P., and Van Slyke, D. D. (1932). *Quantitative Clinical Chemistry*, vol. 2, (Methods), p. 229. Baillière, Tindall, and Cox, London.
 Raginsky, B. B., and Bourne, W. (1934). *Canad. med. Ass. J.*, **30**, 518.
 Ronzoni, E. (1923). *J. biol. Chem.*, **57**, 761.
 Siggaard-Andersen, O. (1962). *Scand. J. clin. Lab. Invest.*, **14**, 598.
 — (1963). *Ibid.*, **15**, 211.
 —, Engel, K., Jørgensen, K., and Astrup, P. (1960). *Ibid.*, **12**, 172.
 Singer, R. B., and Hastings, A. B. (1948). *Medicine (Baltimore)*, **27**, 223.
 Skeggs, L. T. (1960). *Amer. J. clin. Path.*, **33**, 181.
 Walker, W. F., Morgan, H. G., Breckenridge, I. M., Watt, Arleen Ogilvie, R. R., and Douglas, D. M. (1963). *Scot. med. J.*, **8**, 14.
 White, J. C. (1923). *Arch. Surg.*, **7**, 347.

Broadsheets prepared by the Association of Clinical Pathologists

The following broadsheets (new series) are published by the Association of Clinical Pathologists. They may be obtained from **Dr. R. B. H. Tierney, Pathological Laboratory, Boutport Street, Barnstaple, N. Devon**. The prices include postage, but airmail will be charged extra.

3 The Detection of Barbiturates in Blood, Cerebrospinal Fluid, Urine, and Stomach Contents. 1953. L. C. NICKOLLS. 1s. 13 The Identification of Serotypes of <i>Escherichia coli</i> Associated with Infantile Gastro-enteritis. 1956. JOAN TAYLOR. 1s. 16 Preservation of Pathological Museum Specimens. 1957. L. W. PROGER. 1s. 17 Cultural Diagnosis of Whooping-cough. 1957. B. W. LACEY. 1s. 20 Investigation of Porphyrin/Porphyria. 1958 (reprinted 1962). C. RIMINGTON. 2s. 23 The Dried Disc Technique for Bacterial Sensitivity Tests. 1959. R. W. FAIRBROTHER and J. C. SHERRIS. 1s. 24 Safe Handling of Radioactive Tissues in the Laboratory and Post-mortem Room. 1959. R. C. CURRAN. 1s. 26 The Periodic Acid-Schiff Reaction. 1959. A. G. E. PEARSE. 1s. 28 Daily Fatty Acid Excretion. 1960. A. C. FRAZER. 2s. 29 The Preparation of Bone for Diagnostic Histology. 1960. D. H. COLLINS. 2s. 30 Control of Accuracy in Chemical Pathology. 1961. G. H. GRANT. 4s. 31 Investigation of Haemorrhagic States with Special Reference to Defects of Coagulation of the Blood. 1961. E. K. BLACKBURN. 4s. 32 Detection of Resistance to Streptomycin, P.A.S., and Isoniazid in Tubercle Bacilli. 1961. R. CRUICKSHANK and S. M. STEWART. 2s. 33 The Laboratory Detection of Abnormal Haemoglobins. 1961. (reprinted 1965). H. LEHMANN and J. A. M. AGER. 4s.	34 Titration of Antistreptolysin O. 1961. H. GOODE and R. E. O. WILLIAMS. 2s. 35 The Estimation of Faecal 'Urobilinogen'. 1961. C. H. GRAY. 2s. 36 Quantitative Determination of Porphobilinogen and Porphyrins in Urine and Faeces. 1961. C. RIMINGTON. 3s. 6d. 37 The Paper Electrophoresis of Serum and Urinary Proteins. 1961. G. FRANGLEN and N. H. MARTIN. 4s. 38 The Augmented Histamine Gastric Function Test. 1961. M. LUBRAN. 2s. 39 Investigation of Haemolytic Anaemia. 1961. J. C. SELWYN. 2s. 40 Short-term Preservation of Bacterial Cultures. 1962. E. JOAN STOKES. 2s. 41 Serological Tests for Syphilis. 1962. A. E. WILKINSON. 6s. 42 The Determination of Glucose 6-Phosphate Dehydrogenase in Red Cells. 1962. T. A. J. PRANKERD. 2s. 43 Mycological Techniques. 1962. R. W. RIDDELL. 3s. 6d. 44 The Laboratory Investigation of Catecholamine Secreting Tumours. 1963. M. SANDLER and C. R. RUTHVEN. 2s. 45 Diagnostic Test for Hereditary Galactosaemia. 1963. V. SCHWARTZ. 2s. 46 The Determination of Serum Iron and Total Iron Binding Capacity. 1963. A. JORDAN and D. PODMORE. 2s. 47 Nuclear Sexing. 1964. B. LENNOX and W. DAVIDSON. 2s. 48 The Laboratory Investigation and Control of the Defibrination Syndrome. 1964. R. M. HARDISTY, G. I. C. INGRAM, and A. A. SHARP. 3s. 6d.