the more lasting effects of pain relief is suggested, even though all sizes of fibres sustain some damage.

Summary and Conclusions

The neurotoxicity of ethoglucid given by arterial perfusion has been investigated in dogs in order to study the histological basis of the various effects noted in clinical practice.

A direct toxic effect on nerve fibres of all types was found, and, in addition, damage to muscle and skin in the infused area was observed. A greater proportion of these effects appears to be reversible.

The results support the hypothesis that relief of pain is primarily the result of damage to pain-nerve fibres, which occurs rapidly after administration of the drug, but they offer no definite explanation why this relief tends to persist while other neurological effects subside, although a theoretical possibility is discussed.

The value of ethoglucid in the treatment of advanced malignant disease depends on its pain-relieving effect as well as its cytotoxic properties.

Our thanks are due to Mr. F. D. Naylor for his assistance with the experiments and to Mr. K. Horton for preparing the histological sections. The ethoglucid used in this study was supplied by I.C.I., to whom we are grateful. The work was carried out while one of us (M. R. B.) was in receipt of a British Empire Cancer Campaign Research Grant, and for this support we are indebted.

REFERENCES

- Baxter, D. W., and Schacherl, U. (1962). *Canad. med. Ass. J.*, **86**, 1200.
 Berry, K., Olszewski, J. (1963). *Neurology (Minneapolis)*, **13**, 152.
 Bond, M. R., Clarke, S. D., and Neal, F. E. (1964). *Brit. med. J.*, **1**, 951.
 Boone, S. C., and Woodhall, B. (1964). *J. surg. Res.*, **4**, 413.
 Hanna, D. C., Gaisford, J. C., and Goldwyn, R. M. (1963). *Amer. J. Surg.*, **106**, 783.
 Mahaley, M. S., and Woodhall, B. (1962). *Cancer Chemother. Rep.*, **16**, 543.
 Sholes, D. M. (1960). *Amer. J. Obstet. Gynec.*, **80**, 481.
 Smith, M. C. (1964). *Brit. J. Anaesth.*, **36**, 387.
 Stewart, W. A., and Lourie, H. (1963). *J. Neurosurg.*, **20**, 64.
 Westbury, G. (1962). *Proc. roy. Soc. Med.*, **55**, 643.
 — (1963). *Ibid.*, **56**, 655.
 Woodhall, B., Mahaley, M. S., jun., Boone, S., and Huneycutt, H. (1962). *J. surg. Res.*, **2**, 373.
 — Pickrell, K. L., Georgiade, N. G., Mahaley, M. S., jun., and Dukes, H. T. (1960). *Ann. Surg.*, **151**, 750.

Improving the Reliability of the Rebreathing Method for Measuring Mixed Venous P_{CO_2}

SIMON GODFREY,* M.B., M.R.C.P.

Brit. med. J., 1965, **1**, 1163–1165

A rebreathing method for measuring mixed venous P_{CO_2} , suitable for clinical use, was described by Campbell and Howell (1960a, 1960b, 1962), employing a principle probably first introduced by Plesch (1909). The present paper is based upon experience gained in the everyday use of the method, and suggests a modification to obtain the maximum accuracy with minimum discomfort to the patient.

Briefly, the standard procedure advised by Campbell and Howell (1962) consists of a first stage of rebreathing from a bag of oxygen of not more than two or three times the tidal volume for a period of 90 seconds. This usually produces a bag P_{CO_2} a little above mixed venous P_{CO_2} (Campbell and Howell, 1960b). After a rest of at least two minutes the second stage consists in rebreathing the prepared mixture for 20 seconds. During this second stage small differences between mixed venous and bag P_{CO_2} are usually eliminated. In their papers Campbell and Howell have commented that various changes in the procedure may be necessary with some patients, but these manoeuvres are rarely employed in normal clinical practice.

The main problems which have been encountered with the standard method are: (1) many subjects become very uncomfortable after 90 seconds of rebreathing from a small bag, however persuasive the operator; and (2) although Campbell and Howell have suggested a checking procedure it is not

routinely performed, and with inexperienced operators gross errors have been found through some fault in technique which has escaped notice.

In order to overcome these difficulties various modifications of the technique have been examined. In particular, the need for an arbitrary time for the first stage has been queried, and a routine checking procedure has been sought.

Personal experience showed that during the first stage a stimulus to breathing was noticed when the bag P_{CO_2} was close to arterial blood P_{CO_2} . It therefore seemed that the discomfort during rebreathing was probably part of a CO_2 response. Preliminary experiments showed that if the rebreathing was terminated about 10 to 15 seconds after the response was noted the bag P_{CO_2} was a little above mixed venous P_{CO_2} .

The second stage of the rebreathing procedure can be regarded as the "fine adjustment" of a bag P_{CO_2} which is already close to mixed venous levels. The gas is rebreathed for 20 seconds, during which time any differences between bag and mixed venous P_{CO_2} should be eliminated, before much blood with an elevated P_{CO_2} has had time to recirculate. In fact, recirculation of blood does mean that the bag P_{CO_2} after 20 seconds is a little too high, but this is of no clinical significance. The only way to obtain a completely accurate result is to scan the record from a rapid CO_2 analyser and look for a plateau in the CO_2 concentrations of gas passing back and forth from mouth to bag (Collier, 1956). A comparison of the P_{CO_2} obtained after 20 seconds of rebreathing from a bag close to

* Medical Unit, Brompton Hospital, London. Present address: Department of Physiology, London Hospital Medical College, London E.1.

mixed venous PCO_2 , with the plateau PCO_2 obtained in this way, shows that the 20-second PCO_2 is about 1 to 2 mm. Hg higher. Both figures are constant with repeated rebreathing periods (personal observations).

Neglecting the small error due to recirculation, if the bag PCO_2 is the same as mixed venous PCO_2 , then no change will occur in its composition during the 20 seconds of rebreathing. This has been found to be true even in subjects with large dead spaces.

Procedure

Applying the principles discussed above, studies were made of 19 patients with various respiratory diseases and one normal subject.

Each subject rebreathed 100% oxygen from a bag containing three times his normal tidal volume. The first stage was continued until about 10 seconds after a definite change in the depth or rate of respiration was noted. The gas in the bag was sampled and its CO_2 content was estimated with a modified Haldane apparatus (Campbell, 1960).

The second stage was begun after a rest of at least two minutes. The subject rebreathed the prepared bag for 20 seconds and its CO_2 content was again determined. After a further two-minute rest, the procedure was repeated. This

TABLE I.—Illustrative Result of Rebreathing Procedure. Arterial PCO_2 Measured Directly is Also Shown

Time	Bag PCO_2 (mm. Hg)
End of 1st stage (80 seconds)	72.5
End of 1st 20-second rebreathing period ..	67.5
" " 2nd " " " " ..	65.5
" " 3rd " " " " ..	65.5
" " 4th " " " " ..	65.5
Arterial PCO_2	60.0

TABLE II.—Clinical Details and Results

Subject	Diagnosis	Age	Time for First Stage (secs.)	No. of 20-sec. Periods	Mixed Venous PCO_2 (mm. Hg)	Arterial PCO_2 (mm. Hg)
1	E.	62	90	3	47.8	—
2	D. I. P. F.	52	60	4	45.5	38.0
3	Bronchiectasis	70	60	2	58.5	—
4	C. B. & A.	57	100	5	49.0	—
5	C. B. & E.	60	80	3	65.6	60.0
6	C. B. & E.	59	75	2	65.7	—
7	E.	48	80	5	58.5	55.0
8	C. B.	69	90	2	57.1	—
9	C. B. & E.	60	100	2	54.2	46.0
10	C. B.	70	65	3	74.3	—
11	E.	42	80	2	44.2	41.0
12	A.	27	55	3	42.8	—
13	Normal	25	40	3	50.7	45.0
14	A.	45	60	3	43.5	—
15	C. B.	63	90	3	57.1	50.0
16	C. B.	64	105	2	80.0	—
17	Sarcoid	46	65	4	52.1	48.0
18	C. B.	70	70	2	67.8	64.0
19	D. I. P. F.	50	50	2	48.5	43.0
20	E.	56	120	4	51.4	—

Note: E. = Emphysema. C. B. = Chronic bronchitis. A. = Asthma. D. I. P. F. = Diffuse interstitial pulmonary fibrosis

second stage of rebreathing periods was continued until the bag PCO_2 remained unchanged by 20 seconds of rebreathing. This constant level was taken as the mixed venous PCO_2 . The level was accepted as constant if readings differed by less than $\pm 0.1\%$ CO_2 (equivalent to a PCO_2 of 0.72 mm. Hg), which has been found to be within the limits of accuracy of the estimation (Campbell, 1960).

In 10 subjects arterial blood was sampled between three and six minutes after the end of the rebreathing procedure. The arterial PCO_2 was measured with a Severinghaus electrode. All subjects were at rest throughout the whole procedure.

Results

In order to illustrate the kind of results obtained, the readings for one patient are shown in Table I. It can be seen that, once the constant PCO_2 level was reached, two further 20-second rebreathing periods did not cause any change. In other subjects as many as five consecutive 20-second periods have not affected the bag PCO_2 .

The clinical details and results in all 20 subjects are shown in Table II. The duration of the first stage varied from 40 to 120 seconds, with an average of 76.8 seconds (S.D. = 20 seconds). In every case the bag PCO_2 at the end of the first stage was a few mm. Hg higher than the constant level obtained in the second stage. This constant level of bag PCO_2 was always obtained after repeated 20-second rebreathing periods, the average number of such periods required being three.

In the 10 subjects upon whom arterial punctures were performed the average difference between arterial and mixed venous PCO_2 was 5.4 mm. Hg (S.D. 1.6, range +3.2 to +8.2 mm. Hg).

Discussion

The object of this investigation was to find a comfortable, accurate, and reliable method for the bedside measurement of mixed venous PCO_2 . By allowing the subject to terminate the first stage at the beginning of the CO_2 response, the dyspnoea of a severe CO_2 stimulus was avoided. It is quite clear from the results that the rebreathing time required in the first stage to reach approximately mixed venous PCO_2 levels varies considerably, and it is therefore better to allow the CO_2 response to signal the end of this stage than to choose an arbitrary time. However, if there is doubt of the patient's ability to increase his ventilation—for example, if the patient is unconscious or paralysed—an arbitrary time of, say, 80 to 90 seconds will be needed for the first stage. Any errors incurred will have to be eliminated in the second stage.

The repetition of the 20-second rebreathing periods of the second stage increases the total duration of the investigation by about five minutes but is a valuable check on the results. If any gross error has occurred in the first stage these periods will eliminate it, and, provided they are repeated until a constant value is obtained, the end-result will be accurate. The fact that results agree also serves as a check on the sampling and analysis procedure.

In the present investigation the average arteriovenous PCO_2 difference was found to be 5.4 mm. Hg. This is a little lower than the 6 mm. Hg found by most investigators (Hackney, Sears, and Collier, 1958; Campbell and Howell, 1960b), but the series is rather small and the difference is probably within the range of experimental error.

During the investigation the possibility of using larger bag volumes was considered. Employing bags of between 5 and 10 times the subject's tidal volume, it was found that the first stage needed to be considerably longer, but the number of 20-second periods required for the second stage was much the same. It was concluded, in agreement with Campbell and Howell (1962), that the smaller bag gave better results.

Proposed Technique

The following method, based upon the work described above, is offered as an accurate bedside procedure for measuring mixed venous PCO_2 , without distressing the patient.

Selection of Bag Volume.—The patient breathes quietly with the mouthpiece tap open to the air and the bag empty. The tap is then switched back and forth to catch three expirations in the bag and its size is noted. The expired air is then emptied out and the bag is filled to the same volume

with oxygen. This can be judged accurately enough if the total bag capacity is not more than about 2 litres.

Stage 1—Preparation of the Bag.—The bag of oxygen is rebreathed until an increase is noted in the depth or rate of respiration. About 10 seconds' more rebreathing is encouraged and the first stage is terminated.

Stage 2—Fine Adjustment.—After at least two minutes the prepared bag is rebreathed for 20 seconds and its PCO_2 is measured. After a further two-minutes rest (about the time required to analyse the previous sample of gas), the 20-second rebreathing period is repeated. This procedure is continued until the bag PCO_2 remains unaltered by the rebreathing. This value is taken as the mixed venous PCO_2 .

Summary

The problems encountered in the measurement of mixed venous PCO_2 by the rebreathing method are discussed. An adaptation of the method is described which allows the use of small-bag volumes without distressing the patient. The time for the initial preparation of the bag is not fixed but depends

upon the observation of a change in ventilation which is thought to be a CO_2 response. The subsequent 20-second rebreathing periods are repeated to ensure more accurate results. The application of the method to a group of patients is described and the findings are discussed.

I am extremely grateful to Dr. E. J. M. Campbell for introducing me to the study of PCO_2 and for his helpful criticism and advice during this investigation. Professor J. G. Scadding, Dr. J. R. Bignall, and Dr. K. M. Citron kindly allowed me to study patients under their care and read the manuscript. Dr. L. H. Capel provided facilities for studies with a rapid CO_2 analyser and Dr. E. N. O'Brien for estimation of arterial PCO_2 .

REFERENCES

- Campbell, E. J. M. (1960). *Brit. med. J.*, 1, 457.
 — and Howell, J. B. L. (1960a). *pH and Blood Gas Measurements: Methods and Interpretations*, edited by R. Woolmer. Churchill, London.
 — (1960b). *Brit. med. J.*, 1, 458.
 — (1962). *Ibid.*, 2, 630.
 Collier, C. R. (1956). *J. appl. Physiol.*, 9, 25.
 Hackney, J. D., Sears, C. H., and Collier, C. R. (1958). *Ibid.*, 12, 425.
 Plesch, J. (1909). *Z. exp. Path. Ther.*, 6, 484.

Dissection of the Aorta with Pericardial Tamponade: Successful Relief of Tamponade

PETER SLEIGHT,* M.D., M.R.C.P.

Brit. med. J., 1965, 1, 1165–1167

Dissection of the aorta is fatal in over 75% of cases (De Bakey, Henly, Cooley, Crawford, and Morris, 1961). Rupture of the aorta is the commonest cause of death, and the usual site of rupture is into the pericardium. This caused death by cardiac tamponade in 86% of Hirst, Johns, and Kine's (1958) collected series of 505 cases, and in 89% of the 106 cases in Shennan's (1934) classic report. It was the cause of post-operative death in 3 out of 72 cases of aortic dissection treated surgically by De Bakey *et al.* (1961). Tamponade has usually been a rapidly fatal catastrophe revealed only at post-mortem examination; occasionally this has been diagnosed before death (Lownsbury, 1935; Lowell, 1940; Ellis, 1947), but relief of tamponade by aspiration has seldom been reported.

Campbell (1946) described survival for three months after aspiration of a haemothorax following rupture of a dissecting aneurysm into the left pleura. The following case is reported as the diagnosis of cardiac tamponade due to haemopericardium was made clinically, and the patient was relieved surgically, with dramatic improvement in her condition.

Case Report

A 79-year-old woman was on her way to play bridge when she developed severe central chest pain while struggling to open a lift door. She collapsed and was taken to the casualty department of this hospital. The pain was very severe and was also felt in the left side of the abdomen. Later she gave a history of a previous attack of severe chest pain one week earlier; this earlier chest

pain had been situated behind the xiphisternum and through to the back, but not below the diaphragm.

On first examination in the casualty department she was in severe pain and complaining of thirst; she was shocked and sweating, but had a blood-pressure of 110/70. The pulse rate was 96. The jugular venous pressure (J.V.P.) was raised to the angle of the jaw. The heart sounds were normal; no murmurs were heard. The arterial pulses were all present and equal. The liver was palpable with an enlarged right lobe, but the abdomen was soft and normal bowel sounds were heard. Neurological examination was negative.

An electrocardiogram (E.C.G.) (Fig. 1) showed minimal ST segment depression and T-wave inversion in leads I, II, AVL, V4–V7, but was otherwise normal. The systolic blood-pressure rapidly fell to 40–50 mm. Hg, but the pulse rate remained inappropriately low with a sinus rate of 80/min. The J.V.P. was measured (with an intravenous catheter) at +8 cm. of saline above the sternal angle.

She was given morphine (15 mg.) intravenously and continuous oxygen by mask. She became stuporous, with Cheyne-Stokes

FIG 1.—E.C.G. showing non-specific T inversion V4–V6.

* From the Cardiac Department, St. George's Hospital, London. Present address: Department of the Regius Professor of Medicine, Radcliffe Infirmary, Oxford.