

INDIRECT ESTIMATION OF ARTERIAL CO₂ TENSION IN EMPHYSEMA

BY

L. FEINMANN, D. J. NEWELL, AND G. B. PENDLENTON

From Normans Riding Hospital, Newcastle General Hospital, and the Nuffield Department of Industrial Health, Newcastle upon Tyne

(RECEIVED FOR PUBLICATION AUGUST 15, 1959)

In 1952, Marshall, Bates, and Christie showed by fractional analysis that the pattern of carbon dioxide content of a single expiration was abnormal in emphysema. This abnormal pattern has been suggested as a test for emphysema (Dornhorst, Semple, and Young, 1953). We have described a method of demonstrating the abnormality directly (Feinmann, Leathart, and Pendleton, 1955). A more accepted method of estimating the severity of this aspect of pulmonary insufficiency is by measurement of the arterial carbon dioxide tension (Platts and Greaves, 1957), but this involves arterial puncture and skilled anaerobic blood-gas analysis.

In a normal person, the plateau of "alveolar" carbon dioxide measured in a single expiration at rest is in equilibrium with arterial carbon dioxide, and its tension can be used as an indirect estimate of the latter; but the absence of a plateau in emphysema makes this impossible. Sivertson and Fowler (1956) suggested that the mixed venous carbon dioxide tension should be used as a measurement of pulmonary insufficiency because the level of this can be estimated indirectly by analysis of expired air after 20 to 30 seconds of breath holding, both in normal subjects and those suffering from emphysema. Collier (1956) described a similar technique, using rebreathing rather than breath holding.

This paper describes the application of the single-breath technique to indirect estimation of arterial carbon dioxide tension in emphysema.

METHOD

An infra-red carbon dioxide analyser (type S.C., Infra Red Development Co.) was used for rapid continuous gas analysis as previously described (Feinmann and others, 1955). The machine was calibrated using carbon-dioxide-free air and three suitable mixtures of carbon dioxide and air, made up in polythene Haldane bags and analysed by the

Haldane technique. The calibration was checked frequently during experiments.

After a tidal inspiration, air was expired into a spirometer which has a linear potentiometer attached to its pulley. From a side-piece near the mouth, air was drawn by a pump at 3 litres per minute through the analyser and back to the spirometer. The leads of an oscilloscope were arranged so that the spot was moved horizontally by change in volume recorded from the potentiometer and vertically by a 6 c.p.s. signal from the carbon dioxide analyser. A curve of carbon dioxide content against volume was thus traced on the face of the oscilloscope and photographed on a stationary film. The same manoeuvre was repeated after holding the breath for two and a half seconds and again after five and 10 seconds of breath holding after a tidal inspiration. There is a delay of one-third of a second in the carbon dioxide record and the calibration curve is not linear. Photographs were taken of the readings given by the calibration gas mixtures and of a volume record. The calibration curve was projected on to a large screen and with superimposed transparent graph paper the records obtained of individual expirations were projected and re-calibrated. Using the 6 c.p.s. carbon dioxide signal as a time marker, the record was also corrected approximately for the one-third second delay in the carbon dioxide response.

Immediately after the breath analyses, an arterial blood sample was collected anaerobically into a heparinized syringe and sodium fluoride added to a concentration of 0.06%. The pH was measured at ambient temperature using a Stadie electrode and a Pye pH meter with extended scale. Before and after each measurement the calibration of the machine was checked with phosphate buffers, pH 7.43 and 7.73 at 20° C. prepared according to Van Slyke, Weisiger, and Van Slyke (1949). Duplicate measurements were invariably made. Temperature correction was calculated according to Rosenthal's (1948) formula.

Oxygen saturation and carbon dioxide content were estimated by Van Slyke's manometric technique; haematocrit after 3,000 revolutions per minute for 30 minutes. The arterial carbon dioxide tension was calculated from these figures (Van Slyke and Sendroy, 1928).

RESULTS

Investigations were made on 20 patients, all of whom were thought on clinical grounds to be suffering from emphysema. All showed an

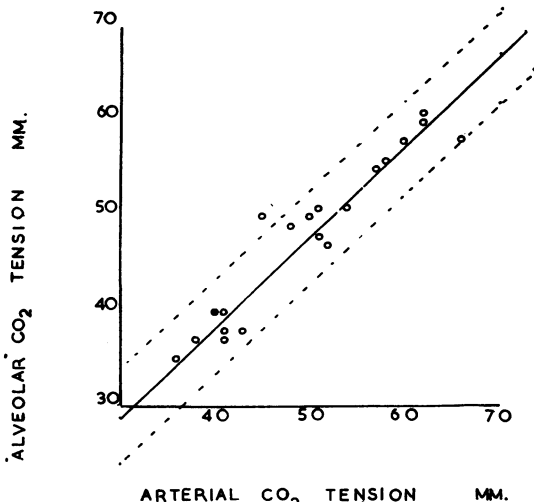


FIG. 1.—Relation between "alveolar" CO₂ tension measured by the method described and arterial CO₂ tension, with regression line ($x=1.04y$) and 95% confidence limits.

abnormal CO₂/volume curve, and the slope and height of this curve were not materially affected by voluntary hyperventilation. In all cases the shape of the curve was altered by a prior period of breath holding, and after either two and a half, five, or 10 seconds of breath holding a plateau of

TABLE I

Subject	Date	Arterial Oxygen Saturation (%)	Arterial CO ₂ Tension (mm. Hg)	"Alveolar" CO ₂ Tension (mm. Hg)	Duration of Breath Holding to Achieve Plateau (seconds)
G.L.	31/5/57	90	45	50	10
J.C.	3/6/57	94	40	40	10
T.K.	13/6/57	91	54	51	10
C.K.	21/6/57	87	38	36	10
J.A.	4/7/57	93	41	38	10
E.P.	4/7/57	85	52	47	10
T.G.	23/9/57	88	51	48	5
T.F.	26/9/57	89	41	37	5
T.C.	26/9/57	91	43	38	10
G.D.	26/9/57	91	36	36	5
T.N.	2/10/57	91	41	40	5
E.W.	18/10/57	74	60	58	5
H.D.	24/10/57	83	58	56	10
T.K.	28/11/57	96	40	40	10
J.P.	18/12/57	91	41	40	10
T.P.	18/12/57	91	51	51	10
A.B.	5/2/58	91	50	50	10
A.B.	11/2/58	70	66	58	10
W.E.	8/4/58	75	57	55	10
W.A.C.	29/4/58	73	57	58	10
G.L.	20/5/58	82	62	61	10
(repeat)			62	60	10
W.B.	17/6/58	90	48	49	10

carbon dioxide was achieved. The first appearance of a plateau was taken to demonstrate an equilibrium representing mixed "alveolar" carbon dioxide, and its height was measured.

Table I shows the figures obtained for mixed "alveolar" carbon dioxide by this method, and for comparison the arterial carbon dioxide tensions measured immediately afterwards. With one exception it can be seen that the level obtained falls at or a few millimetres below the arterial carbon dioxide tension and gives an estimate entirely adequate for clinical purposes. The figures have been analysed with a regression line of $x=1.04y$ and with 95% limits at a distance of ± 5.4 mm. measured in the alveolar direction.

DISCUSSION

We have been impressed by the single-breath technique as a method of demonstrating pulmonary insufficiency in bronchitis and emphysema. The essential physiological defect shown by this test can be stated as follows:

In a healthy subject, after emptying the dead space, a plateau of "alveolar" air is produced (Fig. 2). The level of this plateau is lowered rapidly by voluntary hyperventilation. Changes

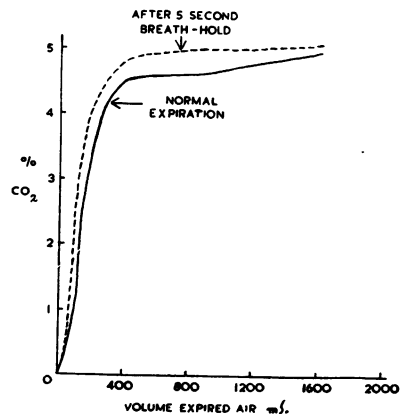


FIG. 2.—Carbon dioxide content of expired air related to volume expired. Normal subject during a normal expiration and after breath holding for five seconds.

in the depth of inspiration and in the rate of expiration materially affect the shape of the curve.

In emphysema those parts of the lung with a high ventilation-perfusion ratio are emptied first and those with more normal ratios later, and this mixing defect produces a sloping curve which fails to reach a plateau (Fig. 3). The shape and height of this curve are not materially affected by voluntary hyperventilation or by a deep inspira-

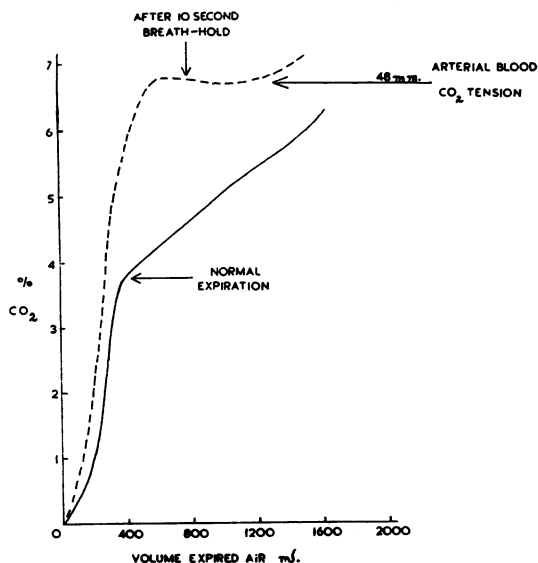


FIG. 3.—Carbon dioxide content of expired air related to volume expired in a patient with emphysema after a normal breath and after breath holding for 10 seconds.

rising part of the curve being represented by an approximate integration. This would tend to mask variation in its shape and in the apparent size of the dead space produced by varying speed and depth of breathing and other factors discussed by Rauwerda (1946), Fowler (1949), Bartels, Severinghaus, Forster, Briscoe, and Bates (1954), and Shephard (1956). The effect of integration is much less on the later, more slowly expired part

tion. One of our laboratory criteria of emphysema is the lack of ability to reduce the level of expired carbon dioxide by voluntary hyperventilation. In both normal people and those with emphysema (Fig. 4), a short period of breath holding produces a plateau about 10 mm. below the mixed venous carbon dioxide tension estimated by the method of Sivertson and Fowler. We have not made any attempt to compare the "alveolar" figures obtained from normal subjects with arterial levels because the resting arterial carbon dioxide can so easily be shifted in a normal subject by overbreathing.

The manœuvre which we have described and which enables us to estimate arterial carbon dioxide tension without complex blood analysis must represent a fairly complex phenomenon in itself. During a short period of breath holding, air from different parts of the lung has the opportunity to mix. At the same time, that part of the lung which is well ventilated but poorly perfused and which is expired first presumably has further opportunity to become perfused and come into equilibrium with arterial blood. The combination of these two factors during a period of breath holding up to 10 seconds by the emphysematous patient brings expired air to a tension which is at or a few millimetres below that of arterial carbon dioxide.

The relatively slow response of our carbon dioxide analyser must result in the first, steeply

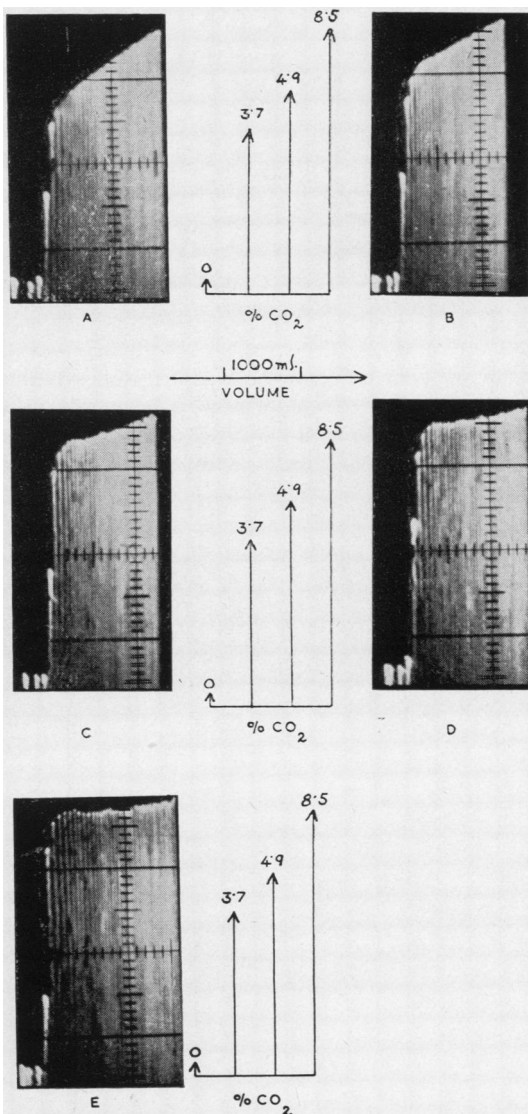


FIG. 4.—Records obtained with the apparatus described in the text in a patient with emphysema. Without breath holding, A. After breath holding: for 2½ seconds, B; for 5 seconds, C; for 10 seconds, D; for 20 seconds, E. Calibration for CO₂ percentage and for volume is indicated centrally.

of the breath and in any case affects equally normal expiration and that after breath holding.

Fenn and Dejours (1954) have described the factors involved in the effect of breath holding on the carbon dioxide level of expired air. We have not discussed them or made any attempt to relate the plateau achieved after breath holding to diminution of physiological dead space on the one hand and more even alveolar ventilation-perfusion ratio on the other. It seems more useful to consider that breath holding results in an equalization of time constants in the emphysematous lung using the conception described by Otis, McKerrow, Bartlett, Mead, McIlroy, Selverstone, and Radford (1956).

The apparatus used is relatively expensive and takes some time to set up and calibrate, but once this has been done a large number of patients can be examined quickly and without discomfort. The investigation is easier to perform than arterial blood-gas analysis and its accuracy is sufficient for clinical purposes, being of the same order as the method suggested by Collier (1956). It has the advantage over other methods that it indicates the mechanism by which arterial carbon dioxide tension is raised, distinguishing hypoventilation from ventilation-perfusion ratio inequality. As observations are bracketed by checks on the calibration of the machine using gas mixtures,

misleading results due to technical failure are not likely to be obtained. The method indicates an abnormal pattern of carbon dioxide expiration in many cases of emphysema in which the arterial carbon dioxide tension is within normal limits.

SUMMARY

An indirect method of estimating the arterial carbon dioxide tension in emphysema is described and discussed. A regression line is given with 95% confidence limits at a distance of ± 5.4 mm

This work was done with the help of a research grant from the Newcastle Regional Hospital Board.

REFERENCES

- Bartels, J., Severinghaus, J. W., Forster, R. E., Briscoe, W. A., and Bates, D. V. (1954). *J. clin. Invest.*, **33**, 41.
 Collier, C. R. (1956). *J. appl. Physiol.*, **9**, 25.
 Dornhorst, A. C., Semple, S. J. G., and Young, I. M. (1953). *Lancet* **1**, 370.
 Feinmann, L., Leathart, G. L., and Pendleton, G. B. (1955). *Nature (Lond.)*, **176**, 739.
 Fenn, W. O., and Dejours, P. (1954). *J. appl. Physiol.*, **7**, 313.
 Fowler, W. S. (1949). *Ibid.*, **2**, 289.
 Marshall, R., Bates, D. V., and Christie, R. V. (1952). *Clin. Sci.* **11**, 297.
 Otis, A. B., McKerrow, C. B., Bartlett, R. A., Mead, J., McIlroy, M. B., Selverstone, N. J., and Radford, E. P. (1956). *J. appl. Physiol.*, **8**, 427.
 Platts, M. M., and Greaves, M. S. (1957). *Thorax*, **12**, 236.
 Rauwerda, P. E. (1946). Thesis. Groningen University.
 Rosenthal, T. B. (1948). *J. biol. Chem.*, **173**, 25.
 Shephard, R. J. (1956). *J. Physiol. (Lond.)*, **134**, 630.
 Sivertson, S. E., and Fowler, W. S. (1956). *J. Lab. clin. Med.*, **47**, 869.
 Van Slyke, D. D., and Sendroy, J. (1928). *J. biol. Chem.*, **79**, 781.
 ——— Weisiger, J. R., and Van Slyke, K. K. (1949). *Ibid.*, **179**, 743.