VARIATION IN PERFORMANCE OF OXYGEN THERAPY DEVICES

TOWARDS THE RATIONAL EMPLOYMENT OF 'THE DEPHLOGISTICATED AIR DESCRIBED BY PRIESTLEY'

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OXYGEN MAKES UP nearly 50% of the mass of this planet. It is the most important single substance in animal biology. It is a powerful therapeutic tool, yet it has been one of the most misused and abused remedies in medicine. Currently its use still rarely conforms to the most elementary rational rules of therapeutics—that is, that a substance is given in a known dosage in a manner which produces a sustained optimal blood level. This lecture deals with the demonstration and the possible remedying of this situation in modern practice.

Historical aspects

One of the most surprising things about oxygen is that it took so long for man to discover it. The circulation of the blood was described in the early 17th century in Harvey's *De Motu Cordis*, and towards the end of that century Boyle, Hooke, Lower, and Mayow established the significance of breathing and some of the clues that would lead to the discovery of oxygen. However, a further century was to elapse because of the phlogiston theory of Stahl. Phlogiston, the fire substance, was the complete antithesis of oxygen. So that when, exactly two centuries ago, Joseph Priestley (1733–1804) carried out experiments on a theme which eventually led him to identify oxygen as a separate entity with, as he put it, 'superior goodness over ordinary air' he termed it 'dephlogisticated air', in full accord with the theories of the time. One of the experiments that he carried out with dephlogisticated air was to burn a candle in it. In one passage of the account of this experiment he predicted not only oxygen therapy, but also oxygen toxicity:

> 'From the greater strength and vivacity of the flame of a candle in this pure air it may be conjectured, that it might be peculiarly salutary to the lungs in certain morbid cases . . . But, perhaps we may also infer from these experiments that though pure dephlogisticated air might be very useful as a medicine, it might not be so proper for us in the usual healthy state of the body for, as a candle burns out much faster in dephlogisticated than in common air so we might, as may be said, live out too fast, and the animal powers be too soon exhausted in this pure kind of air.'[1]

Soon afterwards this new air caught the imagination of John Hunter, whose

Hunterian Lecture delivered on 11th October 1972

(Ann. Roy. Coll. Surg. Engl. 1973, vol. 52)

compass knew no bounds and in whose memory this lecture is given. He commented when writing on resuscitation:

> 'Perhaps the dephlogisticated air described by Priestley may prove more efficacious than common air.'[2]

Priestley stubbornly clung to the phlogiston theory in spite of the cogent evidence put forward by his effervescent French contemporary, Antoine Laurent Lavoisier (1743–1794), who produced the evidence which finally dismissed the phlogiston theory and in 1770 coined the word *oxygine* from the Greek 'acid producer'.

Pneumatic medicine. Oxygen was not the only gas which was discovered at that time, late in the 18th century. These newly manufactured or factitious airs as they were called were eagerly seized upon by those with medical inclinations, for use in the therapy of myriad disease processes. Unfortunately, theories outpaced facts and although the basic physiological role of oxygen was well established, its reputation was tarnished along with the other gases used in the medicine of the time.

The main focus of pneumatic medicine, as it was called, was the short-lived Pneumatic Institute at Clifton, Bristol, the brain-child of the medical philosopher Thomas Beddoes (1760–1808). He elaborated the idea that treatment of disease could be augmented by treatment with factitious airs. The great engineer James Watt (1736–1814) was a willing participant in the establishment of Beddoes' Pneumatic Institute since his son was suffering from consumption, for which orthodox medicine had achieved little. On the opening of the Pneumatic Institute a notice appeared in the *Bristol Gazette* of 21st March 1799, which contained the first of the panaceal claims for treatment with factitious airs (Fig. 1).

Oxygen as a panacea. Humphry Davy (1778–1829) was the superintendent of the Pneumatic Institute, but as a thinker and scientific mind he possessed superior insight. He realized the over-simplification and fallacy of Beddoes' argument, for he later described his work at the Institute as 'the dreams of misemployed genius which the light of experiment and observation has never conducted to truth'[3].

However, the practice of pneumatic medicine and in particular oxygen therapy was taken up by various medical practitioners. Their writings over the next century, tinged with emotion, over-emphasis, and often gross exaggeration, caused a great deal of harm. Their views were disseminated mostly in privately published pamphlets. The first of these was by Daniel Hill, entitled *Practical Observations on the use of Oxygen or Vital Air, in the Cure of Diseases*[4]. Figure 2 shows his second edition of 1820[5], in which he described success in cases of nervous debility, epilepsy, hydrocephalus, and scrophula. He also combined his interest in vegetation as a fellow of the Horticultural Society and described enhanced growth of plants exposed to oxygen!

In 1845, J. E. Riadore published a booklet entitled *On the Remedial Influence of Oxygen or Vital Air . . .*,[6] in which he recommended oxygen for debilitated conditions of the liver and kidneys, asthma, paralysis, and uterine affections.

S. B. Birch wrote several questionable pamphlets in the mid-19th century. In one of these, *A Few Facts Forgotten by the Faculty . . .*,[7] cancer, scrophula, neuralgia, asthma, bronchitis, phthisis, cardiac and hepatic disease, epilepsy, apoplexy, diabetes, paralysis, and indigestion were reportedly all successfully treated by the administration of oxygen. Birch's last unfortunate sully at the reputation of oxygen therapy was in no less a journal than the *Lancet*—'Some

Remarks on the Exhibition of Oxygen as a Therapeutic'[8]—in which he extolled the virtues of oxygenated bread and water.

In 1868 there was an important development. George Barth presented 15 gallons of oxygen compressed into a copper bottle, removing the need for manufacture by the physician at the bedside. Barth was a manufacturing chemist and could at least legitimately advertise[9], although he caused some embarrassment by mentioning doctors by name in his earlier advertising material.

The increasing demand for oxygen led to the necessity for more efficient production. In 1886 Brins Oxygen Co. Ltd., run by the Brin brothers, commenced manufacture at 69 Horseferry Road, not far from Westminster Hospital. Their advertising material published in 1896[10] contained the texts of

NEW MEDICAL INSTITUTION.

THIS Inſtitution is fixed at the upper end of *Dowry-ſquare, Hotwells*, corner houſe. It is intended among other purpoſes for treating diſeaſes, hitherto found incurable, upon a new plan. Among the Subſcribers are almoſt all the Medical Profeſſors at *Edinburgh*, and a large portion of the Phyſicians in England, who have done any thing to improve the practice of their art.

At preſent it is only ready for out patients, and the attendance of perſons in Conſumption, Aſthma, Palſy, Dropſy, obſtinate Venereal Complaints, Scrophula or King's Evil, and other Diſeaſes, which ordinary means have failed to remove, is deſired.

Patients will be treated gratis.

The application of perſons in confirmed Conſumption is principally wiſhed at preſent; and though the diſeaſe has heretofore been deemed hopeleſs, *it is confidently expected that a conſiderable portion of ſuch caſes will be permanently cured.*

It has been perfectly aſcertained by experience, that none of the methods to be purſued are hazardous or painful.

Attendance will be given from Eleven till One o'clock, by THOMAS BEDDOES, or HUMPHRY DAVY.

☞ Subſcriptions for the ſupport of this Inſtitution, received by JOHN SAVERY, Eſq; Narrow Wine-ſtreet; Briſtol.

Fig. 1. Notice in the *Bristol Gazette* of 21st March 1799 on the opening of Beddoes' Pneumatic Institution.

various communications to the leading medical journals. One of the principal discussions that emerged was whether strychnine was necessary or unnecessary as an accompaniment for oxygen. There were advocates not only for airway oxygen—it was applied to the skin and given subcutaneously or intravascularly, via the stomach for resuscitation, via the rectum for cholera or fistula, and also via the urethra, vagina, and os uteri for intractable inflammatory conditions.

Early administration technique. There can be little doubt that in the late 19th century oxygen therapy was at its nadir, not only because of the type of literature which I have just described, but also as a result of the inappropriate and inefficient methods of administration. From the first inhalations of factitious

airs until the advent of anaesthesia in the mid-19th century oxygen was inhaled either directly from the tap on a storage bag or via a tube held in the mouth and then exhaled through the nostrils. Surprisingly, mouthpieces persisted well into the 20th century. Figure 3 shows an inhaler with a mouthpiece similar to that described by Beddoes and Watt but is taken from a Down Bros. catalogue of 1919—over a century later!

PRACTICAL OBSERVATIONS

ON THE USE OF

Oxygen, or Vital Air,

IN THE

CURE OF DISEASES:

TO WHICH ARE ADDED,

A FEW EXPERIMENTS

ON THE

VEGETATION OF PLANTS,

ILLUSTRATED WITH FIVE ENGRAVINGS.

BY DANIEL HILL, M.D. SURGEON,

HONORARY MEMBER OF THE MEDICAL SOCIETY AT GUY'S HOSPITAL, AND FELLOW OF THE HORTICULTURAL SOCIETY.

Sed ne verba dare nos discat quispiam, et assertiones speciosas tantum facere sine fundamento, et non justa de causa innovare: tria confirmanda veniunt: quibus positis, necessario hanc sequi veritatem, et rem palam esse arbitror.—Harvey, Exercitatio Anatomica de Motu Cordis, caput novum.

THE SECOND EDITION, WITH AN APPENDIX.

London:

PRINTED FOR F. C. & J. RIVINGTON, ST. PAUL'S CHURCH-YARD, AND WATERLOO-PLACE, PALL-MALL; T. CADELL, STRAND; J. HATCHARD, PICCADILLY; AND J. CALLOW, PRINCE'S STREET, SOHO.

1820.

Fig. 2. The second edition of Hill's pamphlet (1820[5]).

Oxygen therapy regained some of its lost reputation when it was administered with some success in 1892 by a respected physician, Lauder Brunton[11]. On this occasion the oxygen from a cylinder was blown into the patient's mouth through a tubular glass mouthpiece. However, in a later paper[12] he advocated the routine use of a glass funnel suspended a few inches above the patient's nose and mouth. The use of the glass funnel was another anomaly. Quite when it was first used for oxygen therapy is obscure. However, some early facepieces, like mouthpieces, were made of glass, and it is not difficult to see that the easily available chemical

or domestic type of glass funnel provided a ready-to-hand substitute and thereafter a replacement piece of oxygen therapy equipment. What was not obvious to the administrators was that it was a useless piece of equipment unless closely applied to the face.

In 1912 Leonard Hill[13], of the London Hospital, commented on oxygen therapy by this technique: 'This method is more than inefficient, it is absurd. The oxygen diffuses into the atmosphere.' Further on, he consolidated his point of view with a memorable analogy: 'Ludicrously inefficient as the nozzle and funnel methods are, I have known of a practitioner going a step further in absurdity in allowing the oxygen to escape into the patient's room. A man might as well hope to affect the composition of the sea by emptying his bladder into it.'

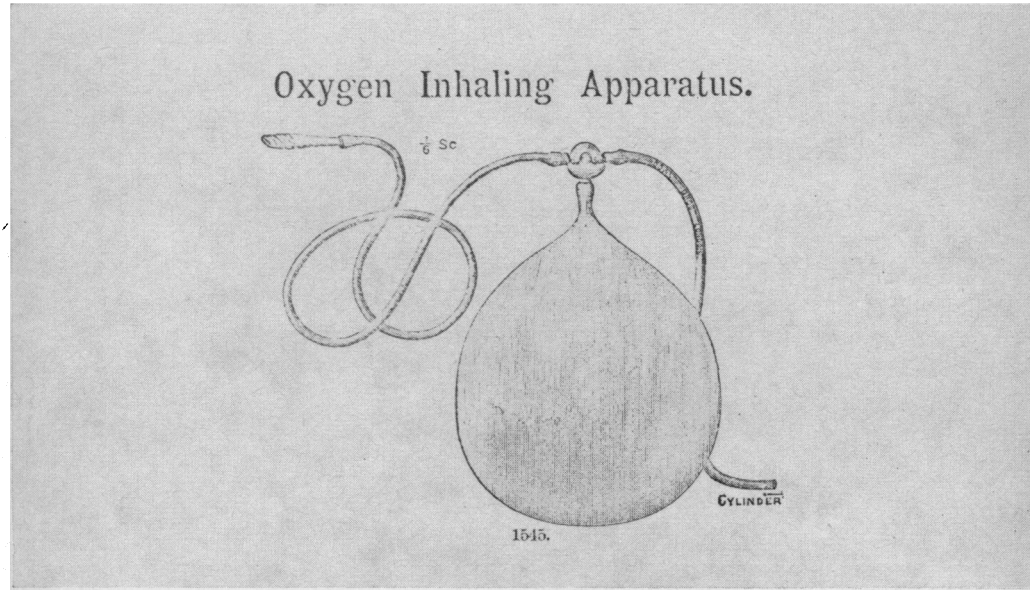

Fig. 3. Oxygen inhaler (Down Bros., 1919).

The advent of modern oxygen therapy. Amongst the gases tried out for therapy was chlorine. In a letter in the *Lancet* by Ellis in 1920[14] successful oxygen therapy was attributed to the chlorine which can contaminate oxygen produced from potassium chlorate and manganese dioxide. Apparently the level of contamination of oxygen by chlorine could be such that it would cause all the brasswork in the room to be tarnished! It is no compliment to mankind that the first demonstrably vital application of oxygen therapy was to be in the treatment of the adverse effects of larger concentrations of chlorine or its congeners when used as weapons of war.

In 1871 F. E. Anstie, physician to Westminster Hospital, had written: "It must at any rate be plain to any candid mind that oxygen is a real though as yet not very well understood therapeutic power. It is the bitterest sarcasm on our respectable and conventional system of therapeutics that nothing like a concerted effort has yet been made by competent and credible men in England to settle what the

true functions of so powerful a therapeutic weapon may be.'[15] In the era before, during, and after the 1914–18 war 'competent and credible men' abounded in a golden era of respiratory physiology. Haldane and the men he inspired, like Priestley and Barcroft, made enormous inroads into unrevealed respiratory physiology and were thus ready and able to treat a generation of war gas victims.

The great advance in conceptual physiology that came out of the work of this group was the recognition of anoxia as a generalized condition which was treatable irrespective of the cause, so that Haldane in 1919[16] was able to discuss anoxaemia under the headings of 'defective saturation' (anoxic anoxia), 'slowing of the circulation' (stagnant anoxia), and 'defective proportion of available haemoglobin' (anaemic anoxia).

Oxygen and carbon dioxide therapy. One aspect of the work of these famous physiologists led to another anomaly in practice—that of combined oxygen and carbon dioxide therapy. This was due to their belief in rapid shallow breathing as a primary pathological entity. Early physiological experiments had shown that carbon dioxide was the main stimulus to breathing[17]. The administration of carbon dioxide would increase the depth of respiration, whereas over-ventilation, which reduces carbon dioxide in the blood, would result in hypopnoea or temporary apnoea. Consequently the frequent finding of hypocarbia due in fact to secondary hyperventilation with anoxaemia led to the use of 3–7% carbon dioxide in oxygen as a therapeutic agent to stimulate deeper ventilation.

Because of these attitudes the demonstration of rebreathing of carbon dioxide with some masks was seen as an advantage rather than a disadvantage. It was not until 1956 that Cotes and Merrick[18] demonstrated the undesirability of devices in which there is rebreathing of alveolar gas.

Intermittent oxygen therapy. Intermittent oxygen therapy has been another great anomaly in the history of oxygen therapy. The first factor concerned in this practice was that when factitious airs, and in particular oxygen, were evolved there was no precedent for continuous administration of any therapeutic agent. Consequently, like contemporary 18th-century medicines oxygen was prescribed in intermittent dosage. The second factor was the belief, already mentioned, in the increased combustion of tissues as a result of an increase in the inspired oxygen concentration. Further factors were the demonstration of toxic effects of oxygen on the central nervous system by Paul Bert in 1878[19] and of pulmonary oxygen toxicity by Lorrain Smith in 1897[20].

Originally it had taken Beddoes six years to arouse interest in oxygen therapy by intermittent dosage. After a century of misguided use 20th-century physicians were diffident in instituting the practice of continuous oxygen therapy although the evidence for its use was available, certainly by the end of the first decade of the present century. For in 1870 Blodgett[21], an American, had described the first use of continuous therapy with oxygen. He published the clinical history of a case of pneumonia in which he was forced by virtue of the patient's severe condition to administer oxygen continuously for a period of 106 hours. In his own words 'the effect of the oxygen was almost as pronounced and evident as is that of a ligature in haemorrhage'. Seventeen years after Blodgett's article an almost identical case history was reported by Myers[22] in the *Lancet* and two years later Vernon[23] showed that breath-holding time could be prolonged significantly by breathing oxygen, thus indicating that breath-holding is dependent upon oxygen stores and that these are fairly modest.

Even the success of continuous oxygen therapy during the First World War and the decade that followed was still not sufficient to break the habit of several generations. On the practice of intermittent oxygen therapy J. S. Haldane is reported to have said: 'Intermittent oxygen therapy is like bringing a drowning man to the surface of the water occasionally'[24] to which Campbell in 1965 still found it necessary to add: 'I think it is like pushing him down between times.'[24]

A more contemporary factor which was thought to be in favour of intermittent oxygen therapy was the effect of oxygen in raising arterial carbon dioxide, particularly in chronic respiratory failure. It was considered that if oxygen was given, for example, for 20 minutes each half-hour there would be an improvement in oxygenation while progressive carbon dioxide retention would be limited. Eventually in 1962 Massaro and his colleagues[25] demonstrated that intermittent oxygen therapy was invariably followed by arterial hypoxaemia to a greater degree than existed before the oxygen was started.

But the practice of intermittent oxygen therapy has continued, for in a survey which I conducted earlier this year 11% of physicians involved in intensive therapy still prescribed it.

Control over the dose of oxygen

The greatest anomaly of oxygen therapy has always been lack of control over dosage. There has been a haphazard development of devices with almost no light being shed on the factors which influence their performance.

There have been many investigations of oxygen masks which have all missed the fundamental point. Even the most superficial consideration of what must happen when oxygen therapy devices are in use should suggest that there can be no consistency in performance. Indeed it would be far more surprising if consistent results were obtained. In spite of this, several generations of investigators have continued to compare the various devices in a hunt for the *indefinable* predictable inspired oxygen concentration.

My own work was commenced in the spring of 1968, at which time I had become aware that the dosage of oxygen given by most devices in a given clinical situation was both an unknown and an unassessable quantity. The difficulty in assessment is that with most devices the inspired mixture is created by the patient–device interrelationship, and is consequently not readily available for analysis. For this reason previous investigations have often been theoretically unsound and consequently inaccurate.

Experimental studies. The method which I have used to explore problems of the performance of oxygen therapy devices utilizes the mathematical theory of the oxygen/carbon dioxide diagram of Rahn and Fenn[26] (Fig. 4). This diagram is a plot of carbon dioxide tension (P_{CO_2}) on the y axis against oxygen tension (P_{O_2}) on the x axis and shows the interrelationships between the two as the gases exchange

either in the blood, on the blood R line, or in the gas of the lungs, on the gas R line. It can be seen that the gas R line joins the inspired point to the ideal alveolar point and is linear, having a slope related to the respiratory quotient—that is, with a slope of roughly 0.8. The message in this gas R line is that any gas coming from the lungs, when analysed for oxygen and carbon dioxide, must lie on this line and that this is always joined to the oxygen axis at the inspired point.

To enlarge further on this, Figures 5*a* and 5*b* show the face of a cathode ray oscilloscope during analysis of tidal gas sucked continuously from between the lips during breathing of air. During inspiration the

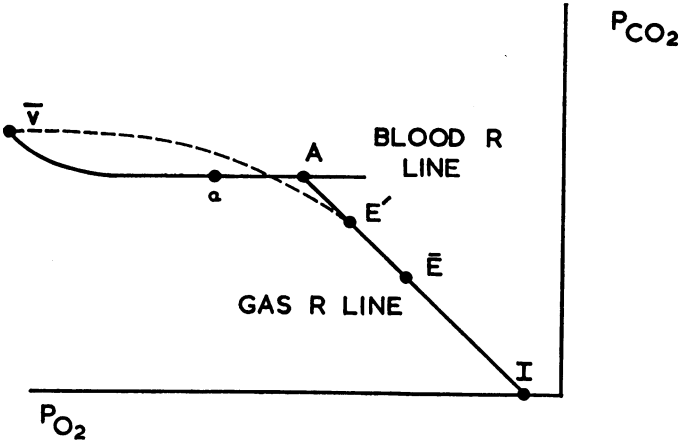

Fig. 4. The O_2/CO_2 diagram of Rahn and Fenn[26]. Under conditions of constant concentration of inspired oxygen all coordinate points of gas coming from the lungs lie on the gas R line. The latter has a slope of approximately 0.8 and is joined to the abscissa at the inspired point I. Reproduced by permission from *Anaesthesia*[27].

carbon dioxide concentration is zero and the oxygen level 21%. During expiration there is a rapid increase in carbon dioxide and a decrease in oxygen to levels of approximately 6% and 15% respectively. And this pattern is repeated, producing uniform waveforms (Fig. 5*a*). When these same data are replayed on the x and y axes of the oscilloscope the gas R line is drawn out with the inspired point fixed on the oxygen axis (Fig. 5*b*). Very few workers have access to this kind of display and I certainly did not in 1968 when my work commenced. However, I used a method based on this by taking samples at random during expiration, analysing them for oxygen and carbon dioxide, and plotting them as points on an O_2/CO_2 diagram. One merely has to take a few samples of gas into a syringe from in front of the lips at any time during expiration and analyse them to produce a series

of points through which a straight line can be extrapolated to the abscissa; 5–7 samples are usually sufficient and the technique is applicable at any concentration.

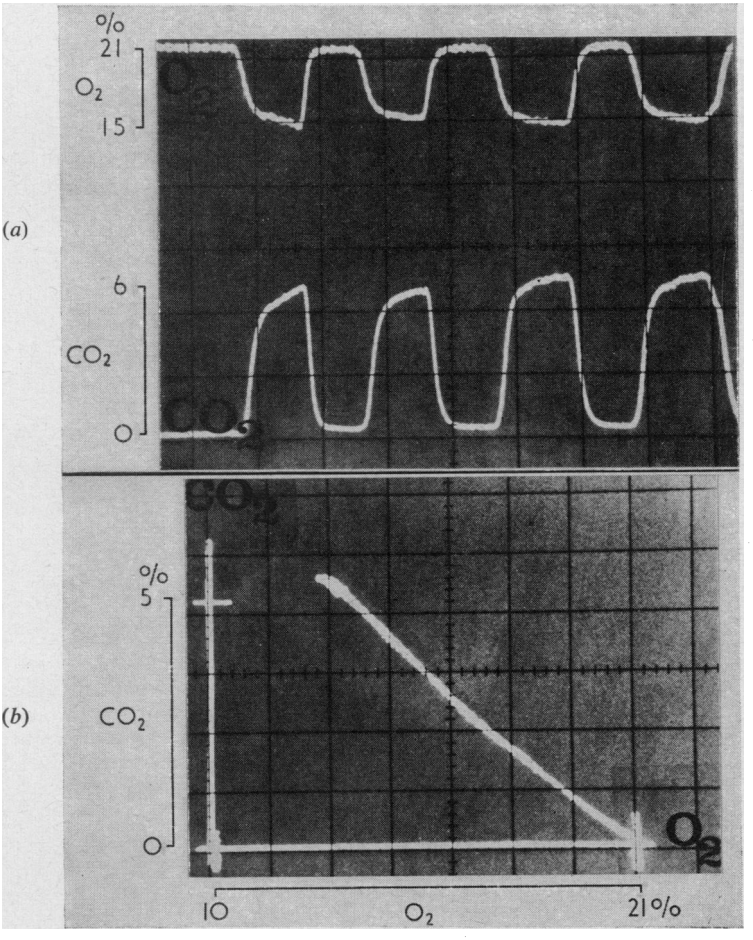

Fig. 5. (*a*) Concentrations at the lips of tidal O_2 (above) and tidal CO_2 (below) during air breathing. (*b*) An x–y plot of the same data—ordinate CO_2, abscissa O_2. The gas R line intersects the abscissa at the inspired (air) point —i.e., 21% O_2.

When this method is applied to oxygen therapy apparatus there are two patterns of results. Either a series of points through which a straight line of slope approximately 0.8 can be drawn, in which case the intersection on the oxygen axis denotes the inspired concentration, or alternatively the points are too scattered. In this event the

TABLE I

BASIC DATA ON FIVE SUBJECTS USED TO COMPARE THE 35% VENTIMASK AND MC MASK

Subject	*Sex*	*Age (yrs)*	*Height (cm)*	*Weight (kg)*	*FVC (l.)*	*FEV_1 (l.)*
1	M	30	196	87.5	8.1	5.25
2	M	32	178	83.5	4.4	3.53
3	M	33	173	76.0	5.2	3.60
4	F	24	165	58.5	3.4	3.00
5	M	39	159	64.0	3.3	2.87

points must come from different R lines which may have the same slope but must have different intercepts, and therefore such results signify variation in performance.

The investigations which I have carried out demonstrate that Ventimasks and anaesthetic circuits can be classified as *fixed-performance systems*, whereas all the other devices are *variable-performance systems*, being subject to patient-to-patient and in most cases breath-to-breath variation[27].

To explore this variation I have performed a detailed study on 5 subjects—4 males and 1 female—of ages varying from 24 to 39 years (Table I). They were deliberately chosen for their height variation from 196 cm (6 ft 5 in) to 159 cm (5 ft 2 in), and their weight range was from 87.5 kg to 58.5 kg. The largest subject was an ex-Olympic oarsman and his vital capacity was 8.1 l., while that of the smallest subject was 3.3 l. The first subject's forced expiratory volume in one second (FEV_1) was larger than everyone else's vital capacity (FVC)! All the subjects breathed from a 35% Ventimask (that is, a fixed-performance system) and I took 6 samples at random during 6 expirations in each subject. When they were plotted in an O_2/CO_2 diagram (Fig. 6, left) with the best straight line drawn through them the intercept suggested

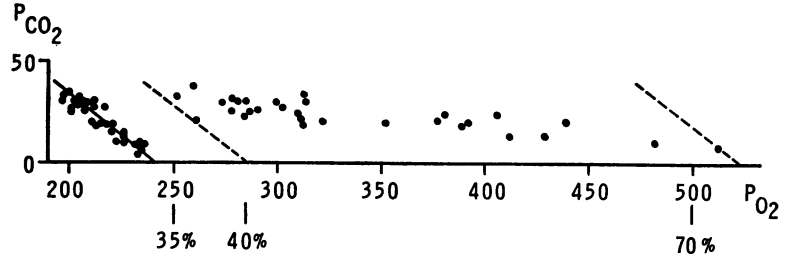

Fig. 6. O_2/CO_2 diagram showing the analysis of separate samples of expiratory gas during the evaluation in 5 subjects of a 35% Ventimask (left-hand side) and an MC mask at 5 l./min. The possible scatter of inspired concentrations with the latter device is indicated by the broken R lines

that this mask was a 34% mask, not a 35% mask, which is within the manufacturers' tolerance.

The same subjects breathed 5 l./min using an MC mask, which is a variable-performance device, and the results (Fig. 6, right) demonstrated an immense spread of points. The R lines drawn at the extremes suggested a scatter of inspired values from 40% to 73%. So there can be little doubt that the one device, the Ventimask, performs constantly irrespective of the characteristics of the person who is using it, whereas the performance of the second, the MC mask, varies from breath to breath and from patient to patient. Table II shows the individual results in the subjects of inspired oxygen fraction, showing the within-subject variation expressed as the range and the between-subject variation expressed as the mid-range, varying from 46 to 62% over the 6 breaths measured in each subject.

TABLE II

INSPIRED OXYGEN CONCENTRATION (F_{IO_2}). THE RANGE REPRESENTS WITHIN-PATIENT (BREATH-TO-BREATH) VARIATION AND THE MID-RANGE REPRESENTS THE BETWEEN-PATIENT VARIATION

Subject	*Range (%)*	*Mid-range (%)*
1	45–62	53
2	41–60	51
3	40–57	48
4	45–48	46
5	50–73	62

Now why does this happen? Consider the gas flow during a single respiratory cycle produced by a pneumotachogram (Fig. 7). As far as oxygen therapy is concerned the important characteristics of this waveform are the peak inspiratory flow rate and the total expiratory time. Inspiratory flow is sinusoidal with a peak value of around 33 l./min; however, it does vary from breath to breath and also the average varies from patient to patient, roughly according to body size. In addition, breathing is irregular in time owing almost entirely to variation in total expiratory time.

If a device is to have constant performance, the gas mixture delivered must match or be greater than the peak inspiratory flow rate. The anaesthetic circuit matches the inspiratory flow rate by collapse of the reservoir bag, while the Ventimask delivers its mixture at a rate always intended to be higher than peak inspiratory flow rate, and therefore its function is independent of patient factors. All other devices deliver fresh oxygen at a rate very much less than inspiratory flow rate so that tidal volume is made up partially of fresh gas flow and partially of air drawn in through the vent, and therefore their performance

will be subject to variation due to breath-to-breath variation in peak inspiratory flow rate. In addition, since these devices mostly have an appreciable capacity, some previous expirate is inspired. With this kind of device, and obviously the MC mask is one of them, the total expiratory time becomes important, for it represents oxygen wash-in time

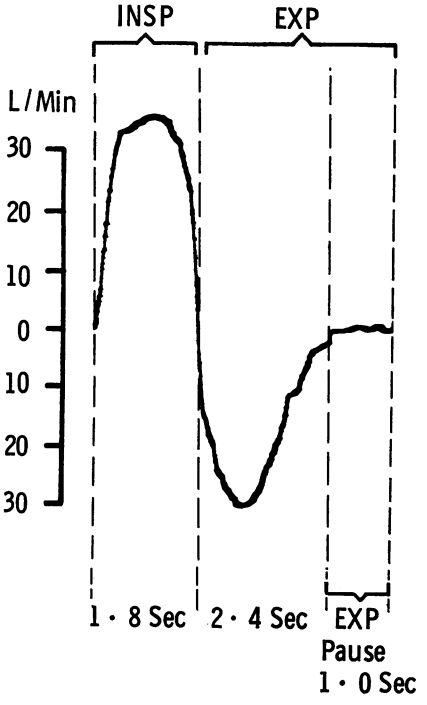

Fig. 7. Gas flow during a single breath, from the pneumotachogram of a resting healthy male subject. The important characteristics from the point of view of oxygen therapy are the peak inspiratory flow rate (which varies from breath to breath and the average varies from subject to subject) and the total expiratory time (which varies from breath to breath during spontaneous breathing). Reproduced by permission from *Scientific Foundations of Anaesthetics*, ed. C. F. Scurr and S. A. Feldman (London, Heinemann, 1970.)

and carbon dioxide wash-out time. Thus any variation in total expiratory time will affect the composition of the next inspiration.

I also measured the inspiratory flow rates and expiratory times of the 5 subjects by recording their inspiratory pneumotachograms while they breathed through a one-way valve. The average peak inspiratory flow rates in the 5 subjects are shown in Table III. They ranged from 24.6 to 40.2 l./min, showing the cause of the between-patient variation. The ranges within the subjects demonstrate the breath-to-breath or

TABLE III

AVERAGE AND RANGE OF PEAK INSPIRATORY FLOW RATES IN THE FIVE SUBJECTS STUDIED

Subject	*Mean peak inspiratory flow rate (±SD) (l./min)*	*Range (l./min)*
1	40.2±1.4	33.0–47.0
2	26.7±5.3	19.5–46.8
3	36.8±2.9	31.2–44.4
4	28.9±2.0	21.3–30.7
5	24.6±2.0	21.8–30.0

within-subject variation. Similarly, the contribution to the variation made by variations in the expiratory times, which have relatively bigger standard deviations and a bigger range on a percentage basis, can be seen in Table IV. Thus we can explain the way in which variable-performance devices are dependent on patient factors. *If you were conducting a trial of treatment and you gave all these subjects 5 l./min from an MC mask thinking they were getting the same dose, this would just not be so.*

In all these experiments the actual values found when the percentage varied from breath to breath and subject to subject are totally irrelevant. What is important is the fact that they vary. Previous workers have striven to describe an actual value which could be expected for a given flow rate with a given mask and have not been explicit in pointing out the factor of variation.

What can one do, therefore, in order to produce devices in which the inspired oxygen concentration can be chosen by the administrator? If one excludes the vent to air, one can use an anaesthetic circuit and have a reservoir bag to match inspiratory flow rate and then give known mixtures of oxygen and air, or nitrogen, to obtain a prescribable dose. However, it would be unrealistic to expect ill patients to cope with such a device as its correct function would depend upon a tight fit to the face and the exclusion of leaks.

The only device which would work irrespective of a tight fit to the face would be a high-flow device—that is, an extension of the Ventimask

TABLE IV

MEAN AND RANGE OF EXPIRATORY TIMES IN THE FIVE SUBJECTS STUDIED

Subject	*Mean expiratory time (±SD) (seconds)*	*Range (seconds)*
1	4.2±0.45	3.2–5.1
2	3.4±0.77	2.4–6.5
3	4.6±0 39	3.5–5.3
4	2.0±0.23	1.6–2.4
5	3.5±0.27	2.9–4.1

series. I have already pointed out that these devices deliver the mixture at flows above peak inspiratory flow rate. In these masks a venturi entrains a fixed proportion of air—the so-called high air flow with

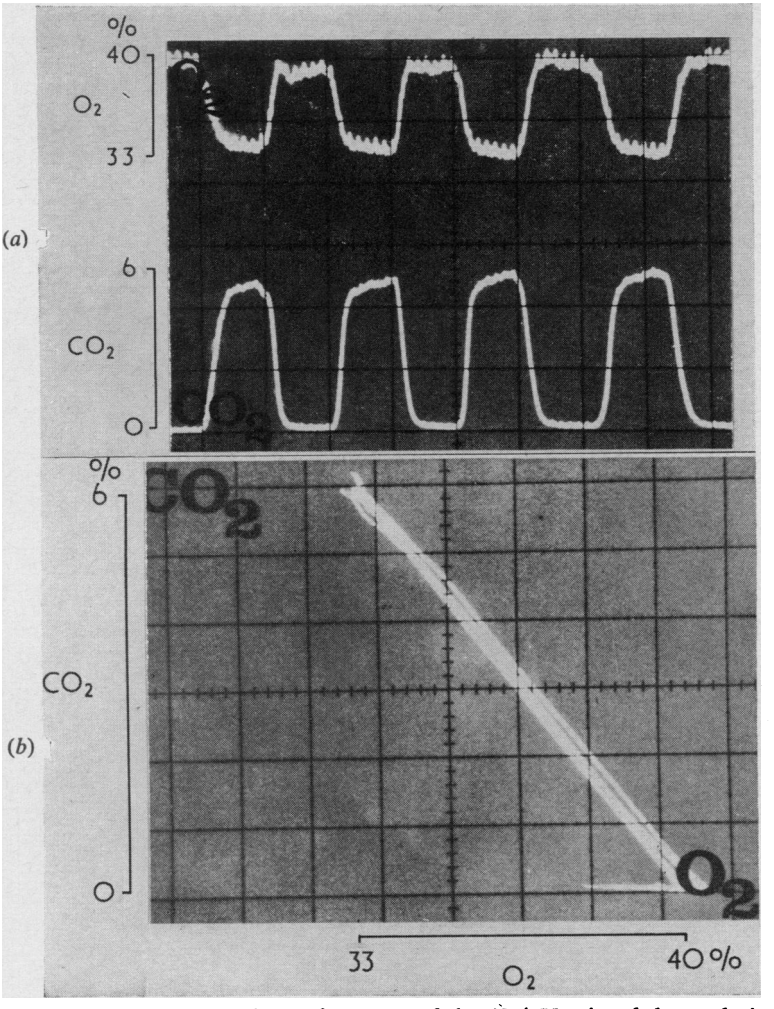

Fig. 8. Assessment of the performance of the 40% Ventimask by analysis of O_2 and CO_2 at the lips with rapid-response analysers. (*a*) Concentrations against time. (*b*) O_2/CO_2 diagram. The uniform O_2 waveforms of (*a*) and the linear R line of (*b*) show that this is a constant-performance device.

oxygen enrichment, or HAFOE, principle. By the application of a simple mixing equation one can calculate the flows or volumes of air and oxygen which have to be mixed in order to produce known concentrations and design a mask accordingly.

Evaluation of devices by continuous analysis of O_2 and CO_2. Figures 5*a* and *b* showed some waveforms produced by analysis of O_2 and CO_2 concentration at the lips with rapid-response analysers. Those data came from some very recent experiments which permit more effective demonstration of the ways in which devices operate.

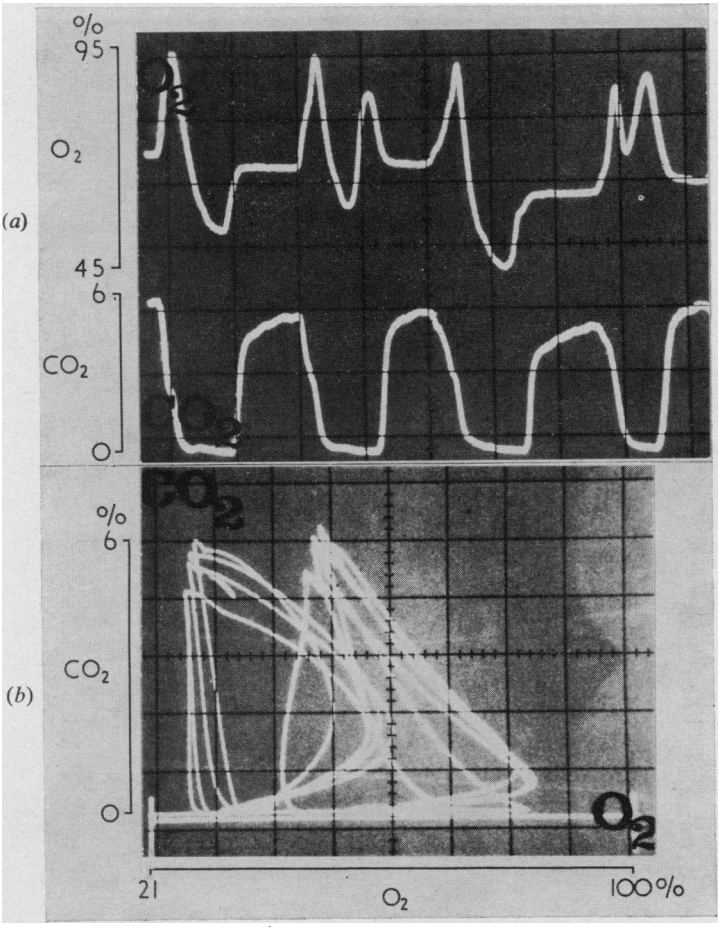

Fig. 9 (*a*). Assessment of the performance of the MC mask (10 l./min flow) by analysis of O_2 and CO_2 at the lips with rapid-response analysers. The irregular O_2 waveforms show a variation during inspiration from 95–45% O_2. The end-tidal plateaux show a variation of 10% in O_2 concentration. (*b*) O_2/CO_2 diagram during assessment of the MC mask at flows of both 10 and 5 l./min. The inspiratory portion of the ratio shows a Z-shaped pattern as the oxygen concentration first rises, falls, and then rises again as the inspiratory flow rate varies. The expiratory R lines are separated. Thus the mask is a variable-performance device.

During constant performance, such as air breathing, the two waveforms of oxygen and carbon dioxide are symmetrical waveforms of approximately square shape which, when replotted in the x–y mode, show a straight line, the gas R line. Figures 8*a* and 8*b* show the 40% Ventimask under test and demonstrate precisely the features specified above. When using devices other than Ventimasks one is potentially in an unstable stage lying between two R lines, one joined to the oxygen axis at air (21%) and the other to the oxygen axis at 100%, and one does not know exactly where one is between this range.

Figure 9*a* shows rapid analysis of O_2 concentration at the top and CO_2 concentration at the bottom, taken at the lips during breathing with an MC mask at 10 l./min. There are 4 inspirations with 4 fairly typical CO_2 waveforms, but notice how each of the O_2 waveforms rises at the commencement of inspiration towards 100%, but does not quite reach it, and falls within the same inspiration towards 21% as the inspired flow rate exceeds that of the fresh oxygen inflow. But end-tidal levels are reached during expiration, and over the 5 expirations in this illustration there is an end-tidal variation in oxygen concentration of 10%. In addition, the peak swings in oxygen during inspiration vary between 95 and 45%, the higher value being at the beginning of inspiration. This suggests that better ventilated alveoli may well be exposed, under these circumstances, to toxic levels of oxygen. When the same data are replotted on the O_2/CO_2 diagram (Fig. 9*b*, right hand side) the inspiratory portion of the ratio shows a Z-shaped pattern due to the changes in oxygen concentration described above, whereas the expiratory portion shows the more typical R-line slope, but the R lines are separated. Figure 9*b* also shows the MC mask at 5 l./min on the O_2/CO_2 diagram. Once more the same features apply, with the Z-shaped inspiratory portion and separated R lines during expiration, demonstrating breath-to-breath variation.

A new Ventimask prototype

The obvious method for achieving the goal of freedom of choice of dose is to apply the HAFOE principle and to extend the series of Ventimasks. The current prototype has a rotating disc with holes of various sizes which can vary the entrainment ratio at the choice of the administrator to give 50, 60, or 70% oxygen. This has been tested both by random sampling and by the rapid analysis technique. Figure 10*a* shows the assessment of the first prototype in this format by rapid gas analysis and demonstrates the symmetrical waveforms of a constant-performance device. The tracings represent a test of a mask intended to give a nominal 70, 60, and 50%. In fact it was giving 78, 65, and 53%, but nevertheless its performance was constant. These defects have been remedied in later prototypes. The x–y replot of these data (Fig.

10*b*) shows clearly that the device is a constant-performance one, there being a fixed inspiratory point and a fixed end-tidal point on the R lines. Although phasing difficulties with the two analysers resulted in

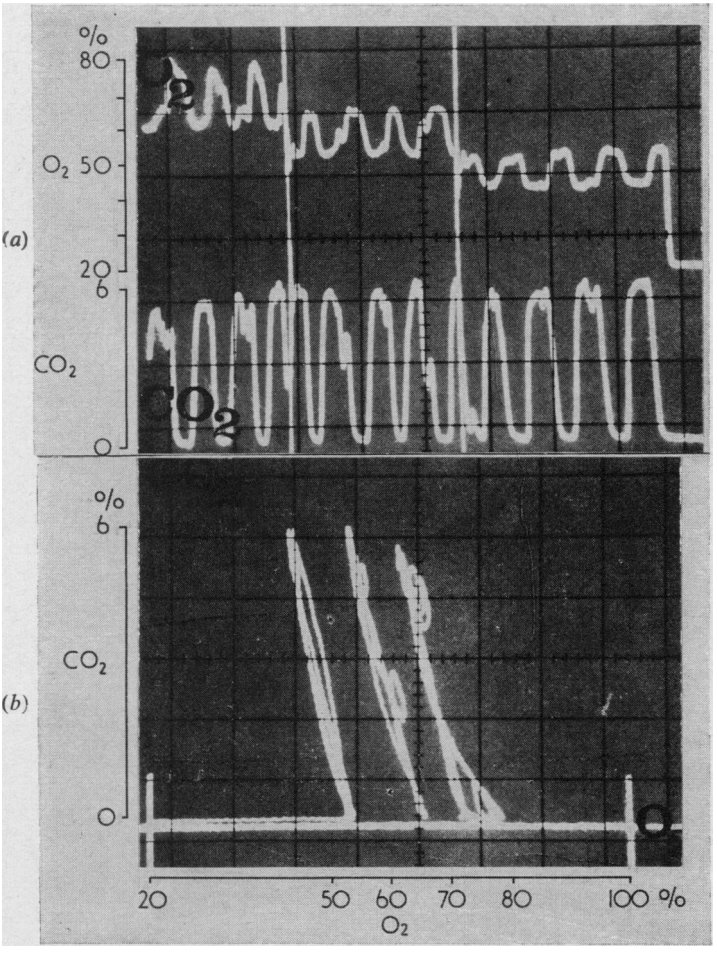

Fig. 10. Assessment of the performance of a prototype Ventimask giving nominal 70, 60, and 50% O_2. The uniform waveforms (*a*) and linear R lines (*b*), denote a constant-performance device, though the actual inspired concentrations are 78, 65 and 53%.

some distortion, the pattern is quite clearly totally different from that produced by variable performance devices.

Prototype devices have already been of assistance to me in the intensive-care situation, but the question one might ask is: 'Is clinical opinion yet ready to shake off the shackles of several generations and use this

TABLE V

RESULTS OF QUESTIONNAIRE: THE FIRST CHOICE OF OXYGEN THERAPY DEVICE IN VARIOUS CATEGORIES OF DISEASED PATIENTS (240 RESPONSES).

Device	*Responses*
Ventimask	62
Nasal catheter	11
Nasal 'prongs'	5
Edinburgh mask	21
MC mask	96
Harris mask	23
BLB mask	3
Oxyaire mask	1
Polymask	8
Pneumask	3
Oxygen tent	0
Puritan system	7

type of device to enhance clinical management?' To elucidate this point I carried out a survey of a large number of clinicians. One of the questions which I asked was: 'What devices do you use as the first choice of oxygen therapy apparatus in various categories of diseased patients?' Table V summarizes the results and it is evident that the majority used fixed-performance predictable-dose devices (the Ventimask) or variable-performance small-dead-space devices (MC, Edinburgh, and Harris), which represents a considerable advance over the past few years.

A further question I asked was: 'What is the maximum percentage of oxygen which you are prepared to give to relieve arterial hypoxaemia in spontaneously breathing patients suffering from a variety of conditions?' I suggested no percentages and the results are summarized in Table VI. What emerges is that responders were prepared to answer this question by choosing a dose. Ventimasks giving 24, 28, and 35%

TABLE VI

RESULTS OF QUESTIONNAIRE: THE MAXIMUM PERCENTAGE OF OXYGEN WHICH RESPONDERS WERE PREPARED TO GIVE TO RELIEVE ARTERIAL HYPOXAEMIA IN SPONTANEOUSLY BREATHING PATIENTS (216 RESPONSES)

Oxygen Percentage	*Responses*
24	1
28	25
30	6
35	12
40	22
50	16
60	29
70	7
80	7
90	1
100	90

were available and, since my work began, a 40% Ventimask has been produced, but it is plain that in the region above that people cannot be satisfied; at the moment they cannot choose and administer a dose.

In response to the direct question 79% of responders stated that they would use the proposed new device either often or always.

Discussion

The largest number of patients who receive oxygen therapy from variable-performance devices are those who have just undergone surgery. This field of application is very necessary to combat the postoperative hypoxaemia which is the obligatory sequel to anaesthesia and surgery. The studies which I have performed indicate that the dose is not predictable. Too little will not combat the hypoxaemia, whereas too much introduces the twin risks of either pulmonary oxygen toxicity or depressed respiration with carbon dioxide narcosis. The latter is especially possible when patients have residual narcotic agents in their systems.

The administration of oxygen to a patient must be regarded as a therapeutic trial. The value of such a trial is infinitely greater if the inspired oxygen concentration is always known. Under such circumstances repeated assessment of patient response to a given oxygen concentration, whether clinical or by direct blood measurement, is of both diagnostic and prognostic significance.

Across the board in therapeutics there is no precedent for the dosage of a drug to be an unknown quantity. With a vital substance such as oxygen, dosage should surely be accurate whether at low or high concentrations. The burden of proof lies more with those who claim that control of dosage is unnecessary rather than with those who wish to introduce accuracy in dosage.

This approach which I am suggesting should improve the quality of patient management. By reviewing the history of oxygen therapy and in my own experimental work, I have demonstrated that the use of oxygen in medicine has always been attended by anomalies of practice of which the remaining one is the inability to choose a dose in the higher range owing to inconsistency of performance of devices. After almost 200 years John Hunter's singularly rational comment has not yet fully been allowed to bear fruit. Perhaps we can now realize his prediction and move towards the rational employment of 'the dephlogisticated air described by Priestley'.

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