

OUTPATIENT ANAESTHESIA
WITH PARTICULAR REFERENCE TO
NITROUS OXIDE

by

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CORRIGENDA

Corrigenda. Volume One.

- Page 21. Para. 1. Line 2. The dates 1771 and 1772 should be in the reverse order.
- Page 37. Para. 1. Line 24. "come" should be "some"
- Page 52. Para. 1. Line 18. "adament" should be "adamant"
- Page 108. Para. 3. Line 3. "arterial pressure" should be "partial pressure".
- Page 377. After "Sharpey-Schafer..... 30, 450. (3)" insert "(see also reference Vol II, page 748)"

Corrigenda. Volume Two.

- Page 421. Para. 4. Line 2. "related....with" should be "related.... to".
- Page 539. Para. 1. Line 15. At end of paragraph the following sentence should be inserted "Furthermore Severinghaus¹ figures did not include the volume of nitrous oxide accommodated in the lungs".
- Page 568. Para. 3. The paragraph "Sampling at.....80ml/min A.T.P." should be deleted.
- Page 635. Para. 1. Line 3. "micture" should be "mixture".

ABSTRACT

Outpatient dental anaesthesia was studied in August, 1961, to ascertain the techniques employed at a Teaching Hospital, observe the physiological response of patients and explore potential hazards (Volume Two, Part IV). Gas mixtures administered, pressures within the nose-piece, systolic blood pressure and brachial pulse were recorded. Analysis of results was restricted by the number of variables, but they suggest that hypoxia is undesirable, and they invite investigation into the recovery period and effects of surgical stimulation.

Volume One describes preparatory studies. The literature is reviewed, preliminary clinical observations reported, problems posed and the overall plan of investigation stated (Part I). Assessment of resistance to gas flow through apparatus is related to its clinical application; delays in passage of gas mixtures through breathing systems are analysed theoretically and experimentally; and the performance of the Walton Five dental anaesthetic machine used for the studies is assessed (Part II). Apparatus employed for the clinical investigation was proved while studying the effects of expiratory resistance, oxygen and hypoxia on volunteers. Results suggest that hypoxia alters the response to pressure breathing. Speed of induction of anaesthesia is also related to the gas mixtures administered (Part III).

Examination of alternative techniques involved the pharmacokinetics of inhalation anaesthetics, which is related here to outpatient anaesthesia. Two studies of nitrous oxide uptake produced erroneous results, but they defined the problems associated with the use of pneumotachography. Experiments using spirometry and bag-in-box systems demonstrated the uptake, distribution and elimination of

nitrous oxide (Volume Two, Part V). Appendices include observations on a condenser-heat-exchanger, the lack of nitrous oxide uptake by the nose and naso-pharynx, the unsuitability of ballistocardiography for measurement of cardiac output, the jerkin plethysmograph, and recovery from outpatient anaesthesia.

Volume Three contains reprints detailing the history of nitrous oxide and oxygen anaesthesia.

ACKNOWLEDGEMENTS

Acknowledgements are made on the title page of each Chapter and Appendix.

Implied criticism of early teaching expresses reaction to the state of outpatient anaesthesia at the time and not complaint against my teachers. I owe them gratitude.

My first anaesthetic appointment was under Dr. V. J. Keating, at the University College Hospital of the West Indies when it was in its infancy. For a while I was his only apprentice and assistant. His example encouraged keeping accurate records and an interest in research, and it was while under his tutelage that I first considered seriously the implications of outpatient anaesthesia.

I value also the year then spent in Canada, at the University Hospital, Saskatoon, with Professor G. M. Wyant, Dr. A. B. Dobkin and Dr. C. Kilduff. Although few outpatient anaesthetics were administered there, the training was relevant and the importance of oxygen stressed.

Dr. R. F. W. Shackleton, as Director of the Anaesthetic Department of the Southampton Hospital Group, provided opportunity for plenty of clinical experience in a congenial environment. Study time was available, much of which I devoted to a study of outpatient anaesthesia. Dr. Shackleton encouraged its presentation to a Regional Anaesthetic Society Meeting, which was attended by the late Professor R. F. Woolmer, and it was this that led to my greater involvement in research. He also encouraged its publication.

The first typescript submitted to the British Journal of

Anaesthesia was returned by Professor T. C. Gray, then editor, with numerous critical comments. Although at first wounding to pride, this personal attention was greatly appreciated. Respect for the British Journal of Anaesthesia was increased on learning subsequently that it was editorial policy never to return a manuscript without full explanation, particularly when dealing with inexperienced authors. Token of this respect is the fact that the published papers which have been modified for this thesis were all submitted to the British Journal of Anaesthesia, and I welcome the opportunity for acknowledging the very helpful way in which they were considered by Dr. J. E. Riding, the present editor. Our correspondence would fill another volume.

Professor Woolmer arranged for my initiation into research at Vickers Research Ltd., where I spent nearly a year in the Department of Human Engineering, and was instructed in the use of the Respiratory Analyser. The sudden change from a clinical appointment to an industrial research establishment was not easy, but I soon came under the spell of friendliness and enthusiasm of Dr. K. G. Williams and Mr. (now Dr.) Peter Scott, who included me in their widely ranging discussions which were invariably stimulating. The practical experience gained under their supervision has proved invaluable.

The three year period spent in the Research Department of Anaesthetics, the Royal College of Surgeons, under Professor R. F. Woolmer, was made possible by a Wellcome Research Fellowship which was granted initially for one year and was twice renewed. I am grateful to the Wellcome Trust for this, and for purchasing a Respiratory Analyser.

Professor Woolmer encouraged and provided every facility for much of the research reported in this thesis, and other members of the department helped in many ways. Specific contributions of Dr. R. A. Butler, Dr. D. W. Hill, Dr. M. Bookallil, Mr. J. C. Hook, Mr. S. Mable, Mr. S. Askill, Miss D. C. Casselle and Mr. A. W. Muir are acknowledged under appropriate chapter headings. Many less tangible contributions were made in casual conversation and I would like to add the names of Dr. J. Bowes and Dr. J. Freeman.

Dr. (now Professor) J. F. Nunn deserves special mention. He made no specific contribution to any of my research projects at the Royal College of Surgeons, except as a volunteer, but he was undoubtedly the most ubiquitous stimulant in the Department, and his comments were often thought provoking. By inviting a contribution to an educational number of the British Journal of Anaesthesia which he edited, he compelled me to crystallise my ideas about the pharmacokinetics of outpatient inhalation anaesthesia. Later, while at the University of Leeds, it was through Professor Nunn that I was invited to contribute to a Symposium at the Second European Congress of Anaesthesiology, and this motivated the experiments described in Chapter 21. He has also encouraged continuation of research into the history of nitrous oxide and oxygen anaesthesia.

It was through Professor Woolmer that I was introduced to Dr. R. Blair Gould and Mr. J. N. W. McCaigie and their colleagues at the Royal Dental Hospital of London. I received full and friendly co-operation from all concerned, but I am especially indebted to the anaesthetic staff for their ungrudging permission to investigate their anaesthetics.

All photography connected with projects carried out while at

the Royal College of Surgeons was done by Mr. C. H. Redman and his staff. No matter how great the pressure under which the Photographic Unit was working, requests were always received in good humour and met on time. Mr. Redman very kindly undertook responsibility for reproduction of all the figures in this thesis, except for a few which belong to a later period. Mr. A. L. Pegg, of the Department of Medical Photography, Leeds University, no less co-operative, is responsible for the reproduction of figure 2.3, and figures 9.1 to 9.12 and 21.2 to 21.11. Mr. H. G. Lumby and Miss R. Bailey, of the Department of Medical Illustration, Leeds University, very kindly prepared the final drawings for the figures used in Chapter 21.

Completion of the work outstanding when my Wellcome Research Fellowship expired, was made possible by a six month Geigy Research Fellowship. This was arranged through Professor J. P. Payne.

I owe both thanks and apologies to Miss E. M. Bowditch who typed the first fourteen chapters of what was to have been an introductory historical volume. These were later re-written and published in the form of the ten articles bound in Volume Three.

Credit for the final appearance of this thesis goes to Miss Ann Wright who typed it all. Errors were inevitable, but I was responsible for most of them. Their correction involved additional labour, and in many instances complete pages were re-typed. I am most grateful.

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CHAPTER 1

HISTORY OF NITROUS OXIDE AND OXYGEN ANAESTHESIA

This chapter presents in outline the contents of a series of articles on the history of nitrous oxide and oxygen anaesthesia which have been published in the British Journal of Anaesthesia, together with a few "second thoughts", a little additional information, and an extension of the history towards the present time under the sub-headings:

The development of the use of Hewitt's "Mixture" (of gas and oxygen).

The development of nasal administration of nitrous oxide.

Developments in America.

Nitrous oxide anaesthesia between World Wars.

Reprints of the articles are bound with this thesis and references contained in them are not repeated at the end of this volume. Detailed acknowledgements are made at the end of each article. The greater part of the historical research was carried out between leaving the Royal College of Surgeons at the end of June, 1964, and joining the University of Leeds in the beginning of December of the same year.

Nitrous oxide and oxygen were isolated by Joseph Priestly in 1771 and 1772 respectively. He considered nitrous oxide to be irrespirable. His researches on 'factitious airs' stimulated an interest in the possibilities of pneumatic medicine, and a particular enthusiast was Thomas Beddoes who, with financial support from friends, set up a Pneumatic Institute in Clifton, Bristol. Its first superintendent was Humphry Davy who started work there towards the end of 1798, shortly before his twenty-first birthday. The apparatus used for preparing, purifying, storing and experimenting with the "airs" was designed and provided by James Watt.

Davy made a special study of nitrous oxide. Although Mitchell had previously asserted that "nitrous oxide was capable of producing the most terrible effects when respired by animals in the minutest quantities or even when applied to the skin or a muscle fibre", Davy demonstrated that the gas could be respired without disastrous consequences. Within little more than a year he had carried out a systematic investigation of its chemical and physical properties, of the best means of preparing and purifying it, and of its effects on many forms of plant and animal life. He published his researches in 1800, and bearing in mind his age and experience, his facilities, the time taken, and the actual content, one cannot fail to be deeply impressed. His "Researches" contain much of interest to anaesthetists, including his emphasis on the need for the gas to be pure, his observations on its effects on animals when administered alone and with oxygen, its effects on human volunteers, and his measurements of nitrous oxide uptake and of lung volumes, but the most quoted passage is: "As nitrous oxide in its extensive operation appears capable of destroying physical pain, it may probably be used

with advantage during surgical operations....." (Smith, 1965, Part I).

Davy did not pursue his idea of using nitrous oxide during surgical operations. He became deeply involved in other matters. Many years later, however, when writing Salmonia in 1827-8 (Davy, 1840 p. 74), he brought out comments on nitrous oxide, insensibility and pain, in an imaginary conversation between "Haleius", "Ornither", Poietes" and "Physicus" in which they discussed whether fishing was cruel:

"PHYS. - I think as I did before I was an angler, as to the merciless character of field-sports; but I doubt if this part of the process of the fly-fisher ought so strongly to alarm your feelings. As far as analogies from warm-blooded animals can apply to the case, the death that follows obstructed respiration, is quick, and preceded by insensibility. There are many instances of persons who have recovered from the apparent death produced by drowning, and had no recollection of any violence or intense agony; indeed, the alarm or passion of fear, generally absorbs all the sensibility, and the physical suffering is lost in mental agitation. I can answer from my own experience, that there is no pain which precedes the insensibility occasioned by breathing gases unfitted for supporting life, but oftener a pleasurable feeling, as in the case of the respiration of nitrous oxide. And in the suffocation produced by the gradual abstraction of air in a close room, where charcoal is burning, we have the record of the son of the celebrated chemist, that the sensation which precedes the deep sleep that ends in death, is agreeable. There is far more pain in recovering from the insensibility produced by the abstraction of air, than in under-going it, as I can answer from my own feelings; and it is, I believe, quite true, what has been asserted, that the pain of being born, which is

acquiring the power of respiration, is greater than that of dying, which is losing the power.

"ORN. - I have heard that persons, who have been recovered from the insensibility produced by hanging, have never any recollection of the sufferings which preceded it; and as the blood is immediately determined to the head in this operation, probably apoplectic insensibility is almost instantaneous.

"HAL. - The laws of nature are all directed by Divine Wisdom for the purpose of preserving life, and increasing happiness. Pain seems in all cases to precede the mutilation or destruction of those organs which are essential to vitality, and for the end of preserving them; but the mere process of dying, seems to be the falling into a deep slumber; and in animals who have no fear of death dependent upon imagination, it can hardly be accompanied by very intense suffering....."

Even if the full potential of the analgesic property of nitrous oxide was at first missed, its inebriating property caught the public imagination and the inhalation of nitrous oxide became a favourite pastime (Smith, 1965, Part II). It was, indeed, as a result of interest in nitrous oxide being kept alive in this way that its analgesic property was later rediscovered and applied. That nitrous oxide could relieve pain was in fact mentioned on at least three occasions during this period: by Stodart (1802); Barton (1808) (Smith, 1965, Part II); and by the anonymous author of Dr. Syntax in Paris, in 1820. This fascinating doggerel, among other things, describes the use of nitrous oxide to relieve pain following a dental extraction (Smith, 1965, Part III).

It was also during this period that Henry Hill Hickman suggested the possibility of carrying out surgical operations after

inducing a state of suspended animation in the patient. At first he advocated achieving this by the administration of carbon dioxide, but he may later have tried other gases. There is no definite evidence that he used nitrous oxide. Having carried out some animal experiments, Hickman drew the attention of T. A. Knight, F.R.S. to the idea, first in a letter written in February, 1824, and then in the form of a printed pamphlet dated August of the same year (it may not have been circulated until 1825 or 1826). A point about the title page of this pamphlet, which hitherto had been overlooked, is that the printed words "AND READ BEFORE IT BY SIR HUMPHRY DAVY" were deleted by strokes of a pen. This was noticed after coming across a criticism of the pamphlet in the correspondence section of the Lancet. This had also been overlooked, and furthermore, it led to the discovery that the greater part of Hickman's pamphlet had been reproduced in the Shrewsbury Chronicle. Hickman failed to attract interest either in this country or in France where he appealed to Charles X in 1828. He died two years later (Smith, 1966, Part IV).

The above quoted passage from Salmonia makes all the more interesting reading in relation to Hickman's presumed hopes of attracting the attention of Davy, through T. A. Knight. Apart from Davy and Knight both being Fellows of the Royal Society, Davy also devoted part of Salmonia to Downton, where Knight lived:

"HAL. - I do not think, as the day advances, there will be any deficiency of light; and I shall not be sorry for this, as it will enable you to see the grounds of Downton, and the distances in the landscape, to more advantage; nor will light interfere much with our sport in this valley, where, as you see, there is no want of shade.

"POIET. - This spot is really very fine. The fall of water,

the picturesque mill, the abrupt cliff, and the bank, covered with noble oaks, above the river, compose a scene such as I have rarely beheld in this island.

"HAL. - We will wander a little longer through the walks. There you will enter a subterraneous passage in the rock beyond the mossy grotto. Behold, the castle, or mansion house, clothed in beautiful vegetables, of which the red creeper is most distinct, rises above on the hill! After we have finished our walk and our fishing, I will, if you please, take you to the house, and introduce you to its worthy master, whom to know is to love, to whom all good anglers should be grateful, and who has a strong claim to a more extensive gratitude - that of his country and of society - by his scientific researches on vegetable nature, which are not merely curious, but useful, and which have already led to great improvements in our fruits and plants, and generally extended the popularity of horticulture.

"PHYS. - We shall be much obliged to you for the favour - provided always, you know it will not be an intrusion.

"HAL. - Trust this to me.....

Corroboratory evidence that the friendship between Davy and Knight was more than merely casual is contained in the unpublished reminiscences of Mrs Stackhouse Acton, who was T. A. Knight's daughter (Knight, (Frances), Mrs Stackhouse Acton. - The late Mr. E. L. Morley kindly drew my attention to this document):

"My Father had occasional visits from the scientific men he met in London and I think it must have been in the Autumn of 1806 that we were told that the young philosopher, Mr. Davy, who had distinguished himself by some discoveries in chemistry,..... the eloquence of whose lectures had made all the fine people of London

run after him, was coming to Elton where we then lived and we looked forward to his arrival with considerable awe, but to our surprise came a shy young man who blushed and held his head down when he was spoken to and was very soon running races with us on the lawn, and from that time till his marriage in 1812 he always spent a week at Easter and another in August with my Father for grayling fishing either at Elton or at Downton where we removed in 1808. He was said to have been spoiled by the way he was courted by great people but to us he was always unaffected and affectionate and there was a combination of poetry with science in his conversation that was particularly attractive and which I have never met in any other person. One of the chapters in his "Salmonia" describes a day at Downton.....

"My Father had visits from his scientific and horticultural friends and in the Autumn of 1811 a visit from Sir Humphry Davy caused some amusement. To his surprise my Father heard that D. and party had established themselves at the little Inn at Leintwardine instead of coming to the Castle as usual and a messenger was at once despatched to learn the cause of so unusual a proceeding. The next morning Sir H. appeared in person and after some hesitation said that "a lady was of the party." It soon appeared that the lady was Mrs A. Preece, a blue-stocking widow, to whose literary soirées Sir H. had taken my Father in the preceding Spring. An invitation was then sent to the whole party; Mr. Warburton and Mr. Solly forming the quartette. Mrs P. explained that she was on the way to visit Mr. Clifford in Herefordshire and that she had been induced to linger a few days on her road by the beauty of the country. She was showy in person and conversation, handsomely dressed and highly rouged. Her admiration for Sir H.'s talents was very evident

and no other conclusion could be come to but that she intended to bestow herself and her fortune on him and we suspected that the latter was the most attractive to him. I was at that time engaged to be married and as our old friend he expressed his wishes for my happiness. I asked him if he had no secret to confide in me, to which his only answer was a laugh and I believe at the time he felt he had only to make the offer to be accepted, but that he was not quite determined on the step. They were married in the following Spring and it is generally known that the marriage was not a happy one; he was often abroad and his visits to Downton were not so frequent as they had formerly been; but when his last illness came at Geneva she hastened to him and his brother Dr. Davy told us that she made him an excellent nurse and he gave her credit for many good qualities which her inordinate vanity prevented the world giving her credit for.

"It was on one of Sir H.'s previous visits that he and my Father tried some experiments by passing rays of light through glass of different colours on a piece of white leather which had been washed over with citrate of silver. The object, I believe, was to ascertain whether the amount of heat was affected by the coloured medium but it has since struck me as being an imperfect commencement of photography."

The significance of the above quotations from Salmonia in relation to Hickman's pamphlet is open to argument. My own interpretation of this evidence is that it lessens the chances of Davy having actually seen the pamphlet.

A few points made in the article about Hickman which has been published (Smith, 1966, Part IV) require further comment. It has been established that the portrait of Hickman shown in figure 1

is not a reproduction of the original oil painting, but of a copy painted by an unknown artist. The original painting has now been traced to a descendant living in Australia. Figure 2 which shows Hickman experimenting with animals is a reproduction of a painting which was commissioned by C. J. S. Thompson in 1912. (The attempts to relate this painting with Fouchespool were out of place). It has always been stated that although Hickman received at least part of his medical training in Edinburgh, he was not a matriculand of the University. This must now be corrected. He was a matriculand of the University and evidence exists to indicate two of the courses which he attended. The error apparently arose because in the alphabetical list of names Hickman was placed before Hickes, presumably because the latter was regarded as a form of Hicks.

It was a young dentist in America, Horace Wells, who rediscovered the analgesic property of nitrous oxide in 1844. At that time advances were being made in the preparation of false teeth, so the idea of applying his discovery for the painless extraction of teeth came naturally to him. He had attended a public lecture on nitrous oxide given by Gardner Quincy Colton, and he noticed that one of the volunteers - Samuel Cooley - who had rebreathed the gas from a bag, injured his leg against the furniture apparently without experiencing pain. The significance of this was immediately apparent to Wells who, on the following day, persuaded Colton to administer the gas to him immediately before a colleague, Dr. Riggs, extracted one of his teeth. The experiment was successful. Wells repeated it with equal success on a few patients, but it failed when he attempted to give a public demonstration at the Massachusetts General Hospital, - as explained by Hewitt (1897): "...the chief

cause of the discredit into which the gas fell was the want of knowledge which necessarily prevailed as to the principles which should be followed in its administration". He returned home bitterly disappointed, and nitrous oxide was soon eclipsed following Morton's successful demonstration of ether anaesthesia in the same hospital the following year, after which Simpson introduced chloroform (Smith, 1966, Part V).

Gardner Quincy Colton re-introduced nitrous oxide for dental anaesthesia in 1862, and this soon spread throughout America (Smith, 1966, Part V). He was not, however, quite the first to use nitrous oxide for dental extraction after Wells abandoned the idea. Some time between 1856 and 1858, in Burton-upon-Trent, England, a patient by the name of Turton, at his own suggestion, and with the assistance of a friend called Hallam, had two teeth extracted while he was under the influence of nitrous oxide, by William Lloyd Poundall (Smith, 1966, Part VI).

In London, in 1864, Samuel Lee Rymer published the results of his attempts to emulate Colton. He was frankly perplexed by Colton's success and he did not persevere with his trials (Smith, 1966, Part V). Meanwhile, in 1867, Colton visited Paris and demonstrated his apparatus (made by Sprague) and methods to T. W. Evans, an American dentist who had a high class practice there. Evans was quick in the uptake, adopted Colton's ideas, and the following year, with a great show of enthusiasm and generosity, spent a week in London giving his own demonstrations. These had a mixed reception at first, but his visit coincided with a period of growing alarm at the number of deaths that had occurred under chloroform anaesthesia, and nitrous oxide anaesthesia had come to stay. There was, however, a difference between the nitrous oxide

anaesthetics given then and those previously given by Wells. Non-rebreathing valves now came into use, and many observers were at first somewhat alarmed at the amount of cyanosis, to quote Kidd (1868): "The sudden startling cyanosis, the horrible struggle and gasp for life, as the black blood fills the arteries in about three minutes under "laughing gas", as I have observed it in some fifty cases of dentistry with Dr. Colton.....have not impressed me favourably". Colton (1868) had maintained: "But let a bag containing eight gallons of gas be used, and anaesthesia is reached before the oxygen is absorbed, and no such ill effects attend the operation". The saving grace was that patients were anaesthetised to unconsciousness, and then teeth were extracted during the short recovery period. Many now familiar ideas were introduced in that first year of nitrous oxide anaesthesia in this country. Cattlin introduced his reservoir bag; Coleman tried out soda lime absorption in order to conserve nitrous oxide; Clover adapted his nose-piece (which he had previously used for chloroform anaesthesia) for nitrous oxide; Clover and Fox tried using mixtures of nitrous oxide and air. (Smith, 1966, Part VII).

Apart from the development of apparatus for making, purifying and storing the gas (Smith, 1967, Part X), and the use of nitrous oxide as an induction agent before ether, no great advances were made during the following twenty years, indeed, towards the end of this period there were signs of disquietude at the lack of research and progress (Smith, 1966, Part VIII).

Various workers had tried using oxygen with nitrous oxide (Hermann, 1867; Andrews, 1868; Lilly, 1868; Coleman, 1872), but success was limited by the dilution of nitrous oxide with nitrogen as it was then manufactured, and also by the lack of suitable apparatus for readily controlling the proportion of oxygen and nitrous

oxide delivered. Then in 1878 Paul Bert captured attention by demonstrating the possibility of using hyperbaric mixtures of nitrous oxide and oxygen in animals. In the following year the plan was used successfully for anaesthetising human patients and following this hyperbaric nitrous oxide and oxygen anaesthesia came into use in a number of centres. In Geneva, Guillermin even used it routinely for dental anaesthesia. The method, however, was complicated and cumbersome and it did not survive the test of time. (None-the-less, Dale and Hill (1921) later tried to revive interest in anaesthesia under pressure, and further experiments were also carried out by Ambard and de Martel (Brille, 1936), and by Tindal in 1941). Paul Bert then directed his attention to inducing anaesthesia with 100 per cent nitrous oxide at atmospheric pressure and maintaining anaesthesia with mixtures of nitrous oxide and oxygen. This idea was taken up first by Hillischer in Vienna, and then by Hewitt in this country. Hewitt, after much experimentation, designed the first practicable nitrous oxide and oxygen mixing chamber, although by our latest standards, the control of the mixture was poor, and his anaesthetics would be regarded as hypoxic. Oxygen was used, but often not more than 7-10 per cent. It must be remembered, however, that the anaesthetics were still brief when nitrous oxide was used, and surgery was carried out during the recovery period. (Smith, 1966, Part IX).

The development of the use of Hewitt's "Mixture" (of gas and oxygen)

Hewitt's development of techniques using "the mixture" seems to have arisen as much from attempts to increase the depth and the economy of the anaesthesia obtained with nitrous oxide as with its safety. In 1885 he published a paper on "A new method of administering and economising nitrous oxide", in which he advocated

first getting rid of the air in the lungs, by using non-return valves on a face-piece of his own design, (during which half the contents of a 2 gallon bag were emptied), and then by pushing a knob, throwing the valves out of action so that the patient rebreathed the remaining contents of the bag. He usually tested for leaks before commencing the administration and waited for slight twitching of the muscles before removing the mask.

In the following year he reviewed the then classical methods of nitrous oxide anaesthesia and reported on a comparison of seven techniques in his own hands. At that time, on the use of oxygen, all he wrote was: "I think I need do no more than allude to the mode of giving nitrous oxide and oxygen together under a greater pressure than that of the atmosphere. This plan, which is advocated by M. Paul Bert, is carried out by ingenious and somewhat complicated apparatus, the most important of which consists of an airtight chamber in which the operation is performed. The outlay necessary for the administration of nitrous oxide by this method would, I think, mitigate against the reception of such a plan into general use."

The techniques which he compared were: 1) rebreathing into a 2 gallon bag; 2) the same, but using a carbon dioxide absorber; (Using these first two methods the patients were not asked to exhale forcibly before the first inspiration); 3) the technique he described in 1885; 4) the same, but using a carbon dioxide absorber; 5) the same as 3 except that a $3\frac{1}{2}$ gallon bag was used and non-rebreathing was continued for an average of $11\frac{1}{2}$ breaths instead of an average of $6\frac{1}{2}$ breaths; 6) non-rebreathing from a gasometer until the onset of anaesthesia, and then rebreathing $1.1\frac{1}{4}$ gallons of gas; 7) the ordinary method, i. e. non-rebreathing until anaesthesia was "complete". He concluded: "I can confidently assert that the period of anaesthesia

in method 6 is, as a rule, longer than that of any other method in general use". In his discussion he made it quite clear that "the period during which anaesthesia persists depends, as a rule, upon the amount of gas which can be thrown into the circulation", and that his aim was to "endeavour to get a large volume of gas absorbed". He continued: "If, after allowing the patient to breathe pure gas until anaesthesia commences, we present to the lungs and so to the blood and cerebral centres an atmosphere of nitrous oxide which is not quite so concentrated - in other words, one which contains a little oxygen - the respiratory centre will continue to discharge rhythmical impulses, and so respiration will be allowed to proceed longer than it would proceed were fresh gas to be continuously inhaled. In this way the whole blood becomes saturated - not a portion of it - and the anaesthesia is prolonged". This evaluation of the place of oxygen makes strange reading now, and his final sentence foreshadowed the now discredited method of "secondary saturation" of McKesson (1920). He started his experiments using oxygen later that year.

In his "preliminary notice" (Hewitt, 1889; Smith, 1966, Part IX) "On the anaesthesia produced by the administration of mixtures of nitrous oxide and oxygen", he presented the disadvantage of the asphyxial properties of nitrous oxide as being that they necessitated the withdrawal of the anaesthetic and the admission of air to the lungs. He did not appear to be over-concerned with safety, for example he wrote: "It is true that experience has taught us that the phenomena mentioned are practically unattended by any risk to the patient; yet they have their objectionable aspect.....", and he said "I have elsewhere brought forward evidence to show that the longer the patient can be made to inhale nitrous oxide, within certain limits, the longer will be the resulting anaesthesia; and it seems to me that the

fact may be taken to explain the longer available anaesthesia which undoubtedly occurs when using nitrous oxide and oxygen".

By 1892, when Hewitt gave a more detailed presentation of the method and of apparatus for administering mixtures of gas and oxygen, it was obvious that he appreciated the added safety; for example, he said: "Of the cases in which I have myself administered oxygen with nitrous oxide, I have never seen the slightest approach to any dangerous condition..... I have given the mixture to a patient with advanced morbis cordis, and to one or two with pulmonary affections of a severe nature,"--and, surprisingly: "I once anaesthetised a patient who, about a quarter of an hour previously, had fainted two or three times during the attempted extraction of a tooth without an anaesthetic. When I gave her the mixture her pulse was very small and feeble, and her face quite blanched. She had no stimulant in the meantime; and was placed vertically in the chair. I gave somewhat more oxygen than normal". On the whole, however, he was cautious about pointing out the potential dangers of hypoxia and the added safety in avoiding it. This may have been because he was not too impressed by these aspects himself, (after all it is unlikely that his own training would have encouraged any other attitude), or it may have been out of deference to the general feeling prevailing at the time, of which he gave a clear indication: "Nitrous oxide has proved such an excellent anaesthetic in dental surgery that it seems almost ungracious to draw attention to the few and comparatively unimportant disadvantages which are connected with its employment. Its great safety, its rapidity of action, and its reasonable freedom from after effects, all combine to render it superior to other anaesthetics for brief operations. But like every other therapeutic agent it has its drawbacks; and it is with the object of lessening or

removing these that the admixture of oxygen with nitrous oxide has been suggested..... I am aware that this Society has lately had before it a very able and thoughtful paper from Dr. Dudley Buxton, in which he has attempted to show that nitrous oxide administered in a proper manner produces no asphyxial phenomena - that the latter only supervene when the agent is unduly pressed. I will not therefore re-open any discussion on this point. All I state is this, that the three phenomena referred to (stertor, jactitation and lividity) - which are, to a greater and lesser degree, essential to success in ordinary nitrous oxide administration in dental practice - do not appear when oxygen is used with nitrous oxide".

Eleven years after beginning his studies on the use of oxygen, Hewitt (1897) decided to "place in the hands of the medical and dental professions (a) small treatise dealing more particularly with the practical aspects of the subject" and he published "The Administration of Nitrous Oxide and Oxygen for Dental Operations". In the preface he wrote, quite uncompromisingly: "Safe and thoroughly efficient anaesthesia for dental operations is of such importance that it behoves every dental practitioner to carefully consider whether he should not abandon the prevalent but comparatively crude and unscientific method of producing insensibility from nitrous oxide, and avail himself of the new system". Practical advice about the use of his apparatus indicates his appreciation of its limitations, and some of the difficulties in the manufacture of such devices; "All the valves are made of thin sheet india-rubber, and it is important that they should be in good order. Should they become inelastic from age, or should they in any way fail to act, as they are intended to act, with perfect accuracy, the apparatus will not produce good results. For example, an apparatus may let through much larger proportions of oxygen than usual if the nitrous oxide valve should happen to adhere along part of

its circumference, to the rim upon which it rests...." He went on to say: ".....trifling defects in the apparatus are liable to interfere with results. The connections must be tested, the bags inspected frequently; the stop cock taken to pieces occasionally - in fact, the anaesthetist must take a personal interest in his apparatus if he wishes to succeed with it".

Two years later Hewitt (1899) reported the investigation upon which much of his practical advice had been based. Using a gasometer of 20 gallons capacity, he used various known mixtures of nitrous oxide and air or oxygen in anaesthetising 231 patients. With the aid of assistants, of whom one was Bellamy Gardner, he recorded each anaesthetic in detail, including notes on: 1) anoxaemic convulsions; 2) duskiness, lividity and cyanosis; 3) stertor; 4) retching movements; 5) phonation; 6) excitement and reflex movements; 7) after effects; 8) laboured or 'catching' respiration; 9) unpleasant dreams; and 10) duration of anaesthesia after inhalation. He allocated "bad marks" to each of these side effects according to their importance and severity, for example, 20, 35 and 50 were allocated to slight, moderate and extreme anoxaemic convulsions; 10, 20 and 30 to change of colour; and 5, 15 and 40 to degrees of stertor. Anaesthetics lasting less than 20 seconds were allocated 20 marks, 25 to 29 seconds 10 marks, and more than 30 seconds, no marks. In this way he was able to arrive at a figure for the "badness" of a given administration, which took into account all the above factors. A metronome was used for timing, its bell being adjusted to sound once every three seconds, and "metronome bells" were numbered down the left hand margins of the record sheets so that notes could be timed accurately. He found that anoxaemic convulsions did not occur if he used more than 6 per cent oxygen or 25 per cent air. He saw little or no alteration in colour if

he used more than 9 per cent oxygen. Stertor was avoided by using more than 13 per cent oxygen. Reflex movements increased as the concentration of oxygen was increased above 7 per cent. Duration of anaesthesia was greatest when about 7 per cent oxygen was used, but the fewest "bad marks" were obtained with a concentration of 9 per cent oxygen, although he found "There is no one mixture of nitrous oxide with air or oxygen which will successfully anaesthetise every patient". He noted that "The most marked cyanosis is met with when very small percentages of air (3 to 6 per cent) or oxygen (under 3 per cent) are administered with nitrous oxide. With pure nitrous oxide cyanosis may not have time, as it were, to become pronounced, for the administration may be cut short by deep stertor". He concluded that "In order to obtain the best form of anaesthesia, oxygen should be administered with nitrous oxide by means of a regulating apparatus, the percentage of the former gas being progressively increased from 2 per cent or 3 per cent at the commencement of the administration to 7, 8, 9 or 10 per cent according to the circumstances of the case. The longer the administration lasts, the greater may be the percentages of oxygen administered". In discussion Dr. John S. Haldane, "after complimenting the author" said: "the paper raised the question, what was it that produced anaesthesia in nitrous oxide administration? Was it the want of oxygen or was it some definite specific action of the nitrous oxide gas? He thought that the paper proved that the anaesthesia was due to some specific action of the gas, since there was no lack of oxygen".

The slow acceptance of the virtues of using Hewitt's "mixture" is evident from a series of 6657 anaesthetics administered at the London Hospital during the year 1897 (Hewitt, 1898). Of these 1362 were 'straight' nitrous oxide anaesthetics, 282 used nitrous oxide

as the induction agent before ether, and 240 were nitrous oxide and oxygen anaesthetics. In the same paper Hewitt described preliminary trials with the use of nitrous oxide and oxygen for surgical operations. The apparatus he used was similar to that devised for dental anaesthesia "except that the channels for the oxygen were double the size.....and that the bags are about three times as large". While acknowledging that: "It is quite possible, as our knowledge and experience increase, that further developments may render the use of nitrous oxide and oxygen more satisfactory for long operations than it is at present", and that "The two great recommendations of this plan of anaesthetizing are that it is the safest at present known and that by its employment the often distressing after-effects of anaesthesia may usually be avoided", he reported that: "I have used it in several surgical cases, but I cannot say that I have been satisfied with the results in many of them".

Bellamy Gardner (1899) reported more fully on the use of nitrous oxide and oxygen for surgical cases, but also with guarded enthusiasm. After initial trials he concluded "that 10 per cent of oxygen, the largest amount yielded by Dr. Hewitt's apparatus, might be enough in dental cases and other short inhalations, but possibly a percentage of oxygen more nearly approaching that present in atmospheric air.....would be required, after all the residual oxygen present in the patients system at the moment of the first breath of the mixture, had been expired.... To obviate, as I thought, all symptoms of asphyxia in these anaesthesias with nitrous oxide gas, a percentage of 15 to 20 of oxygen should be available after the first few minutes of inhalation, and I therefore had the last three apertures in Dr. Hewitt's regulating dial enlarged in diameter, so as to admit the necessary amount to the mixing chamber". He also found that

"Retching movements and sickness cannot be controlled by more gas and oxygen, as with other anaesthetics, this is a great drawback, and negatives the value of the mixture in boys and girls, about ten to fifteen years of age, who seem prone to sickness.... Profuse sweating is very common,.... Florid, alcoholic, and muscular men are not such good subjects as the more ordinary type, nor can it be recommended for small children". With regard to administering the mixture he made the particular point that "To obtain anything approaching accuracy in the percentage proportions of the mixture, the double gas bag of Dr. Hewitt's apparatus must hang free of the couch....." In conclusion he said ".....from my experience of a thorough trial of the mixture in surgery, I must say that, though we have not discovered in this method an inhalation which can in any general sense supplant the use of ether or chloroform, we probably have one which has distinct advantages over gas or gas and ether for operations of minor and of very moderate severity". In the discussion that followed, Dr. Dudley Buxton commented that: "He had employed gas and oxygen for a good many years, both for surgical and dental work. He and Mr. Gardner agreed in regard to it in many points, though perhaps Mr. Gardner was more sanguine about the method than he was..... It had been demonstrated by not only Mr. Gardner, but by others, that the anaesthetic was a very valuable mixture in its own place. The only danger was that it should be elevated as he feared it was, not by professional men, but by the public, into a position of absolute safety, absolute pleasantness, in fact into the position of an anaesthetic panacea..... he thought they would agree with Dr. Silk and Mr. Crouch in their wise remark that it was better to mark time for the present, and see how this matter was going to turn out".

In the same year Paterson (1899) also pleaded for a more extended use of nitrous oxide anaesthesia in general surgery, and "To prevent misunderstanding" he explained that "when I refer to the use of gas or nitrous oxide anaesthesia, I imply that the gas is given with suitable proportions of either air or oxygen". On seven occasions he had administered gas and oxygen for more than an hour.

The development of nasal administration of nitrous oxide.

At the end of the last century there was a revival of interest in prolonging unconsciousness during operations in the mouth when Coleman (1898), Coxon (1898), Hilliard (1898, 1902) and McCardie (1899) presented papers on the subject. Alfred Coleman had by then retired so he relied upon the assistance of Dr. Hewitt and Mr. Paterson in trying out his apparatus. This was a development of apparatus originally designed for the administration of chloroform through the nose. In his own words, (at a meeting of the Society of Anaesthetists), "It consists of a nose-piece made to loosely cover the nose and fit accurately to its base, and which is connected with a very flat tube also adapted to fit accurately over the forehead. To the latter is attached a piece of stout rubber tubing having at its further extremity a very lightly constructed two-way stop-cock which is connected with the ordinary gas-bag, but between the two is placed a valve which opens towards the nose. The gas-bag is connected by a long tube to the gas-bottle. When using the apparatus it is well to instruct the patient to breathe in at the nose and out at the mouth for a few times, and then to adapt the nose-piece, the same form of breathing being continued. An air-padded face-piece, rather larger than is ordinarily employed, and having only the outlet valve, is

placed over the nose-piece and mouth and the gas turned on. When the patient is fully narcotised the face-piece is removed and the operation commenced, whilst sufficient gas is admitted into the bag to slightly distend it beyond its normal capacity". Paterson had tried this out on fifteen patients, the average duration of anaesthesia being about $2\frac{1}{2}$ minutes and the longest anaesthetic 5 minutes.

Coxon (1898), at the same meeting, favoured playing a jet of gas into the mouth, using a curved tube which could also be employed as a tongue depressor. He found that the patient's mouth got very cold, so passed the gas through a copper coil immersed in hot water. Paterson (1898) had tried instead conveying nitrous oxide through a catheter inserted into the nose, but "He found hospital patients were very liable to bleed at the nose through the catheter being passed". Since then he had been lent Mr. Coleman's apparatus and "All he could say was that from his short experience with it he could not commend it too highly in dental work.....he thought that some modifications might be made with advantage". McCardie, in the following year, reported favourably on his own experience of Coxon's method of oral administration, to which he added the use of a nasal clamp. He noted that there was occasionally a feeling of faintness afterwards. Willett commented in the discussion that "it seemed to him that the gas and oxygen introduced by Dr. Hewitt was so much superior to ordinary gas for dental cases that this new method of Mr. McCardie's¹ was not so important as it would have been if they had not had Dr. Hewitt's method". Hilliard (1898) also presented a short paper on the use of a nasopharyngeal tube for the administration of nitrous oxide, which he elaborated in 1902, but after that the idea seemed to peter out.

In passing, another method of prolonging nitrous oxide and oxygen anaesthesia may be mentioned, although its professed purpose

was to make administration more comfortable for the patient, who was enabled to breathe the gas at atmospheric pressure; and to maintain free access of air. Flux (1899) introduced open inhalers which could be applied to the face so that, with the face, the inhaler formed an open vessel into which nitrous oxide could be 'poured' as required. He had used this method in 350 cases and for administrations lasting as long as 12 minutes.

Paterson (1899) took the next step in designing: "a metal cover made to fit the nose accurately, with the aid of a rubber pad..... Two small metal tubes are let into the nose-piece, and to these are attached two rubber tubes which lead to an ordinary gas bag, a two way stop-cock intervening". After the patient had taken a few breaths of nitrous oxide, a celluloid cover, fitted with an expiratory valve, was placed over the mouth. This was removed after about 30 seconds, and, in his own words "The patient is now taking in gas through the nose, and a limited amount of air through the mouth, and there is no difficulty in maintaining anaesthesia, indeed the stop-cock has often to be turned off occasionally in order to allow the patient to obtain more air than is admitted by the mouth". Nine minutes and fifty five seconds was the duration of the longest anaesthetic that he had given by this means. The only disadvantage that he reported was that he was unable to assist the operation as in giving the gas in the ordinary way.

Kirkpatrick (1902), however, found difficulty in getting patients to inspire by the nose and expire by the mouth and even using the mouth cover he experienced great difficulty in using Paterson's method. His solution was to fit an expiratory valve to the nose-piece so that the patient breathed entirely through the nose, keeping the mouth closed during the induction of anaesthesia. A Mason's gag was then

used for opening the mouth (he checked the apposition of teeth beforehand, and if necessary inserted a small prop, just sufficient to keep the teeth apart). He also introduced a sponge into the back of the mouth so as to "occlude, or at all events limit, the air way from it". By fitting a moveable cap over the expiratory valve he closed the valve when he wanted to increase the pressure in the gas bag and so "raise the gas pressure in the nasopharynx to such an extent that the soft palate was pushed forward against the tongue, so closing the mouth way from behind....".

Throughout all these developments no-one appears to have tried administering nitrous oxide and oxygen by the nasal route. One reason for this was probably that the administrators thought that the patients were getting enough air through the mouth and through leaks around the nose-piece. Another reason, explained by Bellamy Gardner (1907), was that it was not possible to use slight "plus pressure" on the bags of Hewitt's apparatus without altering the composition of the mixture delivered. Of this Hewitt was well aware (Smith, 1966, Part IX), and in an attempt to get over this difficulty, in the later models of his apparatus (Hewitt, 1897) he arranged for the two bags to share a common septum in the hope of keeping the two gases at the same pressure. Dr. A. G. Levy (cited Gardner, 1907) went one better than this by placing the oxygen bag inside the nitrous oxide bag, so that provided the inner bag was not over distended, the two gases were at approximately the same pressure. This development enabled Bellamy Gardner to introduce the technique of nasal administration, of nitrous oxide and oxygen mixtures by combining the apparatuses of Hewitt and Paterson, incorporating the bag system of Levy (but enlarging the oxygen bag), and adding his own "reversible valve chimney" which permitted either rebreathing or non-rebreathing of gas and

oxygen. His technique was to prop open the mouth, using a Hewitt's prop between the molar teeth, and administer 6 per cent oxygen with nitrous oxide through the nose; the patient was then allowed to rebreathe, a little nitrous oxide being run in to replace that taken up; then the oxygen concentration was increased to 10 per cent after one minute and 15 per cent after a minute and a half. "Plus pressure" was used if the patient began to breathe through the mouth.

Frank Coleman (1908) (Alfred Coleman's son) introduced a sliding clamp to hold the twin tubes together, behind the patients head (he had not begun to use oxygen). Trewby (1909) added a mouth-cover with expiratory valve to which nitrous oxide was automatically supplied when it was swung into place over the mouth, and cut off when it was swung away. Coleman (1910) then observed that "no one form of inhaler is capable of satisfying the demands of every anaesthetist", and he presented an apparatus which "allows the induction of anaesthesia by the two chief methods at present employed". This also included a kind of spring cage for compressing the bag. This was followed by a "naso-oral inhaler" with separate but communicating mouth and nose-pieces, which has not survived (Warner, 1911). This was really a development of Coleman's (1898) original design. There was, in fact, no real change in the design of apparatus for nasal administration until the invention of sophisticated anaesthetic machines and Goldman's (1936) introduction of a single wide-bore tube for connection to the nose-piece, in place of Paterson's twin tubes.

Developments in America

In 1909, Teter wrote "Thirteen thousand successful administrations of nitrous oxide and oxygen by one anaesthetist covering a period of

nine years for practically every kind of operation to its completion, under varying degrees of hazard, and varying in time from a few minutes to three hours, furnishes sufficient data, it seems to me, to establish to some degree, at least, the efficiency of nitrous oxide with oxygen as an anaesthetic". He went on to acknowledge that Hewitt had done more to bring this anaesthetic before the profession than any one man, and that his book was the best on the subject that had ever been published, but, he continued "He, however, has not had the experience with this particular anaesthetic that some men in America have". He claimed to have used nitrous oxide with oxygen "many times as an anaesthetic throughout the following operations: laporotomies, consisting of hysterectomy, salpingectomy, oophorectomy, appendicectomy, cholecystectomy, choledochotomy, gastrectomy, gastroduodenostomy, uretrosigmoidostomy. Other operations, such as abdominal Caesarian Section, prostatectomy, removal of large tumours and inflammatory adhesions, radical cure of hernia, varicocele, hydrocele and orchidectomy; amputations of breasts, amputations of extremities, and a large number of thoracentesis..... In brain surgery nitrous oxide has been especially advised against, owing largely to the asphyxiation that is concomitant with the administration of nitrous oxide with air..... Nitrous oxide with varying proportions of oxygen, however, if skilfully given, is a different proposition. My experience in this line of work has been good, for I have not had a single case in which difficulties arose". These claims contrast strikingly with the more cautious statements made in the United Kingdom. Teter, however, did acknowledge that he had learned that it was not always best to continue with nitrous oxide and oxygen under all circumstances "for it may be next to impossible to retain the desired depth of narcosis in certain cases".

Since 1906, he had auscultated the chest continuously during anaesthesia. In order to overcome the rigidity which he found in about 10 per cent of cases in major surgery, he used injections of morphine sulphate 7.5-15 mgm and Atropine 0.4-0.6 mgm half an hour before the operation, but he warned against respiratory depression.

Teter also laid down specifications for the apparatus required and he designed his own. These included spare cylinders for rapid change over as each cylinder emptied; means of warming the gas; and large unobstructed channels from bag to inhaler, the gases being under a slight pressure. He thought that "A certain amount of cyanosis is not objectionable" and that "The most noticeable effect from extreme cyanosis is a severe headache, which will not subside in some cases for two to three hours". This cyanosis was of significance in relation to the contamination of nitrous oxide which occurred at Lakeside Hospital, Cleveland, where Teter worked (Smith, 1967, Part X).

As a result of the interest shown in Teter's (1909) article on nitrous oxide and oxygen, he felt it advisable, three years later, to follow with another (Teter, 1912) "to make clear the requirements and limitations of this combination, in order to maintain its present popularity as approaching the principles of an ideal anaesthetic, and to avoid the sacrifice of life which may result in consequence of ignorance concerning the action of these peculiar gases". He repeated the advisability of using premedication. He made it clear that anything from 80 to 95 per cent nitrous oxide, might be necessary, the average patient requiring 88 per cent, (although later he stated that the average amount of oxygen used was $16\frac{2}{3}$ per cent). He tried "to secure definite known percentages of nitrous oxide and

oxygen put up in high-pressure cylinders. This was found to be impracticable for the reason that the percentages changed, as shown by daily tests". He pointed out: "Many accidents have been caused by the failure of the patients to receive the amount of oxygen indicated on the apparatus. It is impossible to control the percentages of the gases by having the controlling valves between the gas bags and the inhaler, on account of the impossibility of maintaining definite pressures in the bags. The only positive way is to have the gases at known pressures and the controlling valves between the gas bags and the gas supply". He also favoured rebreathing nitrous oxide (See Gatch, 1910, below). He considered gas and oxygen to be contra-indicated for children under 5 years of age, and in old people, and he did not consider it ideal for major surgery on patients possessing strong, vigorous constitutions or extremely nervous temperaments, or in those addicted to drugs or the excessive use of tobacco.

Gatch (1910) gave the "results of a trial of nitrous-oxid-oxygen anaesthesia in the service of Professor Halsted at the John Hopkins Hospital". His object, at the outset "was to develop a method of administering these gases so simple, cheap and effective as to make possible their more general use". It seemed to him "that the solution, in so far as cost and convenience are concerned, must be in using them over instead of wasting them after one inhalation". His results led him "to believe that within certain limits the method is not only harmless but beneficial". His apparatus did not allow accurate control of the composition of gas mixtures. A "valve box" on the face-piece provided for 1) non-rebreathing room air 2) non-rebreathing gas "(with oxygen if desired)" 3) rebreathing into a bag of 6-8 litre capacity through a tube of 1 inch diameter and $2\frac{1}{2}$ feet

long (capacity about 350 ml). Each of two nitrous oxide cylinders and one oxygen cylinder was connected, through its own narrow bore tubing, to an L-shaped tube between the bag and the 1 inch dia. connecting tubing. An ether vaporizer was provided within the mask. The procedure was for the patient to non-rebreathe gas until he was slightly cyanotic. He then rebreathed into the bag and "At this moment a small puff of oxygen is admitted to the bag, just enough to restore the natural colour of the face. The patient now rebreathes a mixture of nitrous oxide and oxygen until the valve is moved back to its mid (non-rebreathing) position. He then exhales each breath into the air until the bag is empty. The anaesthetizer then fills it with a fresh mixture of gases, which the patient again rebreathes. No attempt is made to measure the exact percentage of oxygen given. This we regard as unnecessary". The patient rebreathed each bag-full sixteen times. Gatch had used the method on about 700 patients for almost every abdominal and peripheral operation except craniotomy and operations on the female pelvic organs. The alleged advantages appeared to be mainly theoretical and based upon his own interpretations of what was then known as the physiology of respiration and of "shock".

By the following year (Gatch, 1911) he had used this method for 2,500 gas-oxygen and gas-oxygen-ether anaesthesias. There were three deaths during or immediately after operations and one never regained consciousness and died eight hours afterwards. (In the United Kingdom, Guy and Ross (1912), followed Gatch's example, except that in their apparatus they provided for the injection of oxygen in increments by squeezing a rubber bulb, fitted with one-way valves, which was connected to the oxygen supply and had a 2 oz capacity.)

McKesson (1911) then brought out apparatus with a view to obtaining an easier and more accurate administration of nitrous oxide

and oxygen. This incorporated a rebreathing bag, but check valves prevented expired gases from entering the two supply bags which, through valves, supplied a mixing chamber. The mixing chamber control had 20 graduations. The gases were warmed by an electric lamp. The rebreathing bag was also adjustable and calibrated for volume so that the amount of rebreathing could be controlled ("Fractional Rebreathing"). This could presumably have been adjusted so that only dead space gas was rebreathed, in which case it would have functioned in a manner similar to the "Magill" breathing system (Kain and Nunn, 1967).

Peairs, R. P. (1910) also devised apparatus with which nitrous oxide could be given pure or with oxygen in any proportion from 1 per cent to 15 per cent, but he did not give details of his mixing chamber. He wrote "At the present time nitrous oxid and oxygen is the best anaesthetic for short operations.....but it is to its use in major surgery that I wish to draw attention. During the past two years I have administered the gas in a number of major surgical operations. My first experience was with a fixed mixture containing 2 per cent oxygen. This was satisfactory in some cases; in others it was not because the amount of oxygen could not be varied". The concentration of oxygen administered to patients subsequently using his apparatus, was not stated. The longest administration was one hour and fifty-four minutes.

Mandell (1911) preferred the "Davis" apparatus, it "seemed less complicated than the Teter and was preferred to the "Gatch", only because the "Davis" has two bags, one for gas and one for oxygen, enabling the operator to stop gas instantly and give pure oxygen".

Early in 1912, Allen (1912) sounded a warning, drawing attention to the fact that the majority of the vast series of nitrous oxide and oxygen anaesthetics being reported were in fact for dentistry or minor surgical procedures - and not for major surgery. Quoting Crile, he provided the following table of 17,716 administrations by Teter of gas and oxygen without a death:

12,886	lasted less than 5 minutes.
865	" 15 to 30 " "
346	" 30 to 60 " "
228	" 1 to 2 hours
22	" 2 to 3 "
2	" 3 to 4 "

He went on to say that anaesthetic deaths occurring during the use of nitrous oxide and oxygen in major surgery were not uncommon.

Skeel (1913), who also came from Cleveland, presented 1120 anaesthetics of which 731 were for laparotomies with a view to discussing the selection of anaesthesia. He confessed that one of his motives was "a subconscious desire to stamp as altogether wrong the idea that there exists at the present time a universally safe anaesthetic or one which under any and all circumstances meets every indication". He said that "Nitrous oxide and oxygen were selected for a great variety of reasons first and foremost among which was the fact that a skilled and experienced nitrous oxide anaesthetist was always available. In the absence of such an expert, nitrous oxide would have had a very limited field of application". In this well balanced but forthright paper, Skiel made plain the world of difference that lay between the use of nitrous oxide for dental operations and its use for major surgery, and he emphasised the potential danger of asphyxia. With frankness he asserted that

"Exploitation by those personally interested is, I am sorry to say, another very potent reason for the popular belief in the safety of nitrous oxide. For this the exuberance and enthusiasm of some very prominent members of the profession are directly to blame, and I believe that could they have foreseen the results of their utterances they would have been more circumspect in what they said and wrote. Working under the most favourable circumstances with expert anaesthetists they have not hesitated to proclaim the entire safety of nitrous oxide with the result that large numbers of medical men and dentists have equipped themselves with the necessary apparatus and after observing a half dozen administrations, have rushed home to announce the possibility of anaesthesia without danger, discomfort during its use or uncomfortable after-effects.....".

In the discussion that followed, McKesson agreed that "There is more in the anaesthetist than there is in the drug used". Humiston, also of Cleveland, confirmed "In the hospital with which I am connected there have been cases recently of death following nitrous oxide and oxygen anaesthesia. These deaths have not been published. One was a simple case of appendicitis, with a short operation. The patient expired at the close of the operation from nitrous oxide and oxygen given by a man who has had considerable experience". Bainbridge, in support, said that "Many who attended (the discussion of anaesthesia by the sections on Pharmacology and Physiology of the American Medical Association) and who listened attentively were appalled at the number of casualties presented by the honest statement of facts concerning the administration of nitrous oxide and the various inhalation anaesthetics".

Meanwhile Boothby and Cotton (Boothby, 1912; Cotton and Boothby, 1912) had made worth while advances in the design of

of apparatus. In order to facilitate control of the flow of nitrous oxide and oxygen they used reducing valves to bring their pressures down from 700 p.s.i. and 2000 p.s.i. respectively, to 20 p.s.i. (They cast special yokes for taking the cylinders so that they could be changed easily. Cut-out valves were incorporated. The nitrous oxide reducing valve was surrounded by an electric heating coil to prevent freezing). Knowledge of the amount of each gas being used was "obtained by passing the gases through water into a mixing chamber; the rate of the bubbling of the gas through the water gives a very accurate index of the percentages of the two gases as administered to the patient. In addition, this procedure adds a desirable degree of moisture to the gases". An ether vaporiser was included and the gases were warmed. The action of the inspiratory valve could be controlled to allow some rebreathing. An electric motor and air pump were added so that the apparatus could be used for intra-tracheal insufflation. This system was fitted with a safety valve. In their description of the clinical use of this apparatus they were adamant that "To be safe, effective and suitable for major surgical work a nitrous oxide-oxygen anaesthesia must be so conducted that the patient is never in the least degree cyanotic; on the contrary the patient must always be pink..... In those cases that cannot be sufficiently relaxed for the purpose in hand by the use of nitrous oxide with a sufficient proportion of oxygen to prevent cyanosis, the anaesthesia should be deepened by the addition of as much ether vapour as may be needed....."

The subsequent development of anaesthetic machines in America has been outlined by Miller (1941) and Jackson (1955). By 1915 they had standardised into the two main types: intermittent flow and steady flow. The use of the Rotameter for the latter type has been

described by Foregger (1946 and 1952) and by Mörch (1952).

Some of the stimulus to nitrous oxide and oxygen anaesthesia of those days came from Crile's interest in it in relation to his ideas on "anoci-association" (Crile, 1911). The details that he gave in his paper of 1911 however, referred more to nitrous oxide than to nitrous oxide and oxygen, although his anaesthetists were apparently using the latter. But he did give a few clues on their success. Apart from saying that "the anaesthetist must be an individual of the keenest perception of the precise condition of the patient at every moment, i.e., the anaesthetist must be a most delicate human recording apparatus", he mentioned that "The muscular rigidity may be overcome by switching on the ether in a Teter apparatus until relaxation is secured, after which nitrous oxide alone continues the relaxation". He also raised "a very important surgical point that relates to nitrous oxide anaesthesia - that is, rough surgery excites a greater involuntary reactive opposition of the patient to the surgeon than ether does..... Those who wish to do rough surgery will scarcely find nitrous oxide suitable for the purpose. The use of premedicant drugs was mentioned by Teter (1909), but Crile added: "Combined with this method of anaesthesia there has also been developed a gentle technique and a more careful management of patients from the time of their entrance to the hospital until their discharge". And further, after commenting that "every surgeon can recall instances in which the combination of light anaesthesia and perhaps vigorous surgical procedure have elicited an unmistakeable, perhaps even vigorous attempt at escape from the table", he described how: "If one combines a complete local anaesthesia with a general anaesthesia and avoids fear, then it matters not how poor the risk, nor how extensive the operation..... No one

who has witnessed the astonishing immunity that is conferred upon the patient by this method could doubt the correctness of the promises".

Despite the claims of Teter, the apparatus and admonitions of Cotton and Boothby, and the approach and high example set by Crile, one cannot be too surprised at Baldwin publishing a paper in 1916 with the dramatic title "Nitrous oxide-oxygen, the most dangerous anaesthetic" (Smith, 1967, Part X): although one may feel disappointment that McKesson (1920) should have introduced his "technic of secondary saturation" four years later - in his own words: "In a primary saturation only the actively circulating blood is saturated before oxygen must be administered. There remains in the muscles, and in all other tissues, considerable volumes of nitrogen and oxygen, which in the early minutes of narcosis enters the blood stream and dilutes the nitrous oxid which prevents a deeper anesthesia. In order to displace more of the non-anaesthetic gases in the body with nitrous oxid, the technic to be described as secondary saturation has been devised..... The extraction specialists of years ago and today produced primary saturation and approached secondary saturation in many of their obstreperous patients before beginning to extract teeth. Had they required the relaxation needed in abdominal surgery and possessed the means for using oxygen which we now have, the technic for secondary saturation no doubt would have been developed by them, because they were not afraid of cyanosis, which is the stumbling block in the minds of ether or chloroform-trained anaesthetists".

Nitrous oxide anaesthesia between the World Wars

When nitrous oxide anaesthesia was first introduced it was used

primarily for dental anaesthesia. Its use for minor surgery soon followed and there were a few reports of its use for operations such as amputations and mastectomies. Then during the early years of this century it began to be used more and more for major surgery. It was supplemented when necessary, usually with ether. With many of the large series of cases of nitrous oxide anaesthesia reported before the First World War it was not always clear what proportion of them referred to outpatient anaesthesia and what proportion to inpatient anaesthesia, but many of the problems were common to both, at least in kind, if not in degree.

The basic methods of outpatient anaesthesia changed little in the inter-war years. The anaesthetic machines used became, on the whole, more functional and accurate. New inhalation agents came to be used to supplement nitrous oxide and oxygen anaesthesia, and towards the end of the period intravenous induction agents were used. The introduction of endotracheal anaesthesia for plastic surgery (Rowbotham and Magill, 1921; Magill, 1928) during this period may also be mentioned, as this is occasionally used in outpatient anaesthesia. Some of the techniques before the First World War survived well into the post-Second World War era.

The best known anaesthetic machine in this country today is the so-called Boyle machine. This bears little relation to the "Nitrous Oxide-Oxygen-Ether Outfit" shown by Capt. H. E. E. Boyle, R.A.M.C. (T) at the Royal Society of Medicine in 1917 (Boyle, 1917a, 1919). Boyle's first machine was in fact lent to him by Gwathmey (Boyle, 1917b, 1917c). The "outfit" came in three sizes, and had two cylinders of nitrous oxide and two of oxygen. Each cylinder was provided with a fine adjustment valve and tap, and this was regarded as one of the main features of the machine. It was provided with a watersight feed

and an ether bottle, together with rebreathing bag, face-piece and "ordinary three way valves". There was also a spirit lamp for warming the reducing valves of the nitrous oxide cylinders. An analysis of the developments in anaesthetic machines since that time could form a major study of its own.

In 1921, following a visit to Canada and America, Boyle gave a first hand report of McKesson practising his own method: "He anaesthetised a young woman who was to have her knee opened. She had no preparation at all. McKesson began to get her under, and I noticed that her face was getting a curious gray colour, and that her breathing was becoming shallower, with a little prolonged expiration. Suddenly I heard a noise in the machine, and I realised Dr. McKesson was giving oxygen under considerable pressure, so much so, that the patient's cheeks were blown out beneath the facepiece. Gradually she regained her colour, and he said 'That is primary saturation'. As soon as she became pink, he proceeded to saturate her a second time, and the same process was gone through. I must admit that the anaesthetic was very fine afterwards; he obtained good relaxation with it. I doubt whether we have a machine in this country which would be capable of giving oxygen under the pressure he delivered it. I asked him subsequently whether this was a method one could teach students. He was perfectly candid about it; he said 'No, it is a method for the expert, and for the expert only'. He added, 'You can do it perfectly well if you want to; I have done it for twelve years, and I believe in it'". McKesson (1926) described the method again on a visit to this country.

From a talk given by McCardie (1923), at the Royal Society of Medicine, it was apparent that even five years after the First World War the merits of the use of oxygen were far from generally recognised. McCardie used gas alone, at which Boyle expressed surprise in the

discussion. Bellamy Gardner also expressed surprise that the benefits of nitrous oxide and oxygen were not more generally recognised for dental anaesthesia. Hughes, however, agreed that for most routine cases gas and air gave excellent results, especially by the nasal method. McCardie, in reply, said that he believed it was better for students to be taught to administer nitrous oxide alone because the signs of anaesthesia were so definite; it was used in practice by both doctor and dentist, and the necessary apparatus was simple. By properly regulated admission of air nearly as good a result could be attained as by the addition of oxygen.

At the next discussion on dental anaesthesia at the Royal Society of Medicine (Gardner and Spain, 1927) both the main speakers advocated the use of gas and oxygen for the majority of cases, and there was no serious argument from the floor. The use of ethyl chloride appeared to be gaining popularity at that time and Magill said that more stress might have been laid on the value of endotracheal anaesthesia in long and difficult dental operations. Then in a further discussion in 1944, the use of cyclopropane (Pinson, 1944; Gillies, 1944), thiopentone (Roberts, 1944), nitrous oxide and oxygen anaesthesia (Marston, 1944) and trichlorethylene (Galley, 1944) were described. Public discussion of 'straight gas' or 'gas and air' appeared to have disappeared, but Marston (1944) described the initial administration of pure nitrous oxide until the onset of slight cyanosis, twitchings of the palpebral muscles, absence of the conjunctival reflex and automatic respiration. Marston then suggested: "In the average case, if the gases are being delivered at a pressure between 5 and 10 mm Hg, then 5% O_2 , gradually increased to 7% and then, if necessary, to 10%, will suffice".

We will probably never know how many patients died needlessly

from anoxia in the years immediately before the First World War. In the light of published papers we should not be surprised that Courville (1939) was able to report in some detail on a series of deaths during anaesthesia, due to anoxia, in the inter-war years. Few of his cases, however, can be placed under the heading of 'outpatient' anaesthesia. Usually we can survive brief anoxic assaults, but we may never know at what cost in intellectual capacity.

CHAPTER 2

PRELIMINARY TEACHING, EXPERIENCE

AND OBSERVATIONS:

THE EMERGENCE OF SPECIFIC PROBLEMS

The clinical measurements reported in this chapter were made while an anaesthetic registrar at the Southampton Hospital Group. They would not have been possible without the patient co-operation of Sister D. S. Wilkes and her staff, and of the succession of casualty officers in the Casualty Department of the Royal South Hants Hospital, from 1957 to 1959.

With the encouragement and the permission of Dr. R. P. W. Shackleton, much of this material was presented in a paper read before the South West Metropolitan and Wessex Regional Society of Anaesthetists, on 30th May, 1959, and later published (Smith, W.D.A. (1960). Nitrous oxide anaesthesia for ambulatory patients. *Brit.J.Anaesth.*, 32, 600).

Other observations were made while a resident anaesthetist at the University Hospital, Saskatoon; an anaesthetic registrar, and earlier a rotating house officer, at the University College Hospital of the West Indies, Jamaica; a house physician at the King Edward VII Memorial Hospital, Ealing; and while a clinical medical student.

I am also grateful to Dr. H. A. Burgess for anaesthetising me for a dental extraction, using nitrous oxide and oxygen; and to him and Mr. Robert Montgomery for subsequently allowing me to observe the administration of dental anaesthetics in a private dental surgery.

"Learning from history is never simply a one-way process. To learn about the present in the light of the past also means to learn about the past in the light of the present. The function of history is to promote a profounder understanding of both past and present through the interrelation between them."

(Carr, 1961)

Recently Bourne (1964) commented that "The very first administration of nitrous oxide in this country was given nearly a hundred years ago. And really, throughout all the years that have passed since then, the method, in essence, has changed very little. In fact, in almost every respect, the dental anaesthesia we have inherited is Victorian; at least it was so up to 1960, when I closed my investigation and went to print with the results." There need be no surprise, therefore, if in the opening section of this chapter I may appear to have re-lived some of the history of nitrous oxide and oxygen anaesthesia.

Early training and experience

As a medical student I was instructed by a consultant anaesthetist in the administration of "gas and air" for dental extractions. In the Casualty Department instruction in the use of "gas and oxygen" was given by the casualty house surgeon. Anaesthesia was induced using 100 per cent nitrous oxide, from a Boyle anaesthetic machine, and when the patient appeared to have lost consciousness, oxygen was added. The gas flow rates used were chosen empirically. We recorded in a book whether the patient had vomited, and frequently he had.

One of the duties that went with my first appointment as a house physician was to administer anaesthetics in the Casualty Department and to stand in for the resident anaesthetist on one afternoon per week and every other week-end. My predecessor passed on a few tips

about the administration of anaesthesia in the Casualty Department, which included the possibilities of using more oxygen than I had thought customary during the maintenance of anaesthesia, and of using supplementary agents. The recommended flow rates of nitrous oxide and oxygen were not obviously related to physiological considerations, apart from a warning to avoid too much cyanosis. By trial and error I discovered that occasionally, during some of the longer surgical procedures carried out in the Casualty Department, it was possible to admit quite surprising proportions of oxygen without the patient regaining consciousness.

My second appointment, as a rotating house officer in the University College Hospital of the West Indies, started with a period in the Anaesthetic Department. At first I continued the usual practice of inducing anaesthesia in the Outpatient Department by administering 100 per cent nitrous oxide until the onset of "regular respiration", and then using a mixture of nitrous oxide and oxygen, the emphasis being more upon the maintenance of anaesthesia using nitrous oxide than upon the maintenance of adequate oxygenation. As experience was gained, however, this basic technique was modified. Cyanosis was found to be difficult to assess through pigmented skin. Furthermore, many Jamaicans were so anaemic that concentrations of reduced haemoglobin sufficient to exhibit cyanosis were barely possible without dangerous hypoxia. My growing doubts were brought into sharp focus by the unconscious humour of a negro patient to whom I had been asked to "give a whiff" because he was not tolerating some minor procedure which was being attempted without general anaesthesia. During the administration of 100 per cent nitrous oxide the patient sang beneath the mask a currently popular song; "Pretend you're happy when you're blue." From that time I never deliberately administered 100 per cent nitrous oxide for more than six breaths,

and then I continued anaesthesia using flows of 2 litres per minute of oxygen and not more than 10 litres per minute of nitrous oxide (i. e. not less than 16.5 per cent oxygen). If anaesthesia was still inadequate, trichloroethylene was used as a supplement.

As an anaesthetic registrar in the same hospital, I later considered seriously the possibility of hypoxia precipitating a sickle cell crisis. A tuberculous patient whom I had anaesthetised for a spinal fusion relapsed into coma after regaining consciousness. The cause of the coma remained unknown until he died on the second post-operative day. At post mortem he was found to have had an acute sickle cell crisis with the involvement of the cerebral vessels. Knowing that sickling could be detected in vitro by subjecting red blood cells to lowered oxygen tensions, I suggested that the crisis might have been precipitated by an acute period of hypoxia which could have occurred during a difficult endotracheal intubation. I could think of no other way in which the anaesthetic might have contributed to the crisis, although thinking back to the case after a lapse of thirteen years, it is quite possible that blood replacement was inadequate. Hypoxia during induction of anaesthesia was accepted as the probable explanation (Golding, 1956), although at that time - 1954 - there seemed to be some doubt as to whether the precipitation of a sickle cell crisis by an acute period of hypoxia had been reported in vivo, and there may have been other equally potent contributory factors. The possibility of this hazard has since been confirmed and stressed (Shapiro and Poe, 1955; Browne, 1965).

While I was at the University Hospital, Saskatoon, instruction placed much emphasis upon the avoidance of hypoxia, but anaesthetics were only rarely administered to outpatients. It was during this period that Bedford (1955) reported that in a group of 1193 patients over the

age of 50 years who had had surgical operations, 120 showed some degree of mental deterioration, while 29 had become demented. Discussing hypoxia as a possible cause, he mentioned the occasional catastrophic effects of anoxia during nitrous oxide anaesthesia, which had been emphasised by Courville (1955) and by Bourne (1952): (Courville (1955) did not quote case histories, but most of the 26 cases previously reported by him (Courville, 1939) were inpatients. Some of them were in poor general condition before anaesthesia. When nitrous oxide was used, McKesson's (1926) particularly hypoxic technique of "secondary saturation" was probably employed. Four of the deaths were associated with dental extractions, but in these cases anaesthesia lasted 10, 30, 40 and 45 minutes respectively). Bourne (1952) stressed the inevitable hypoxia associated with brief nitrous oxide anaesthetics and he quoted Macintosh (see Macintosh, 1949) as having knowledge of five deaths, within as many months, due to the effects of such hypoxia on the myocardium. Previously Bourne (1936) had shown that hypoxia could produce reversible yet undesirable damage, such as that suggested by the impairment of hepatic function produced by nitrous oxide anaesthesia with cyanosis.

In the following year, Tom (1956), with the object of avoiding the hazards of hypoxia, applied what Klock (1951, 1955) had earlier described as "amnalgesia" to anaesthesia for dental extractions. He advocated starting the induction of anaesthesia by administering a few breaths of 100 per cent nitrous oxide, and then continuing with 15 per cent oxygen. He claimed that the state of "amnalgesia" was produced after about 40 breaths, and that it was often preceded by a hesitation in breathing which could be corrected by verbal encouragement to "keep blowing" (this is unlikely - see below, and the respiratory patterns, shown in chapter 20, of subjects who were not

encouraged to keep blowing, but yet resumed respiration after a period of hesitation). Breathing then became free and regular, the patient being sufficiently anaesthetised after a few more breaths. Dental extraction was accompanied by some movement and phonation. This technique was similar to that described above and used by myself for anaesthesia in the Casualty Department, except that Tom did not describe the use of supplementary agents such as Trichloroethylene. Correspondents (Atkins, 1956; Young, 1956) were also quick to point out that Tom's technique was not new. In practice the technique may have permitted more hypoxia than might be expected during the maintenance of anaesthesia using 15 per cent oxygen, because the calibration of dental anaesthetic machines can be grossly inaccurate (Goldman, 1958; Bourne, 1960). (Many years before Guedel (1922) concluded, on theoretical grounds, that it was preferable to take time over the induction of nitrous oxide anaesthesia and to maintain oxygenation. He appeared, however, to favour the administration of 90 per cent nitrous oxide and 10 per cent oxygen throughout.)

I resumed contact with outpatient anaesthesia upon return to the United Kingdom towards the end of 1956, at first while holding a number of locum anaesthetic registrar appointments, and then, from 1957 to 1959, as an anaesthetic registrar in the Southampton Hospital Group. Two particularly relevant publications appeared in this period. Bourne (1957) placed great stress upon the hazard of fainting in the dental chair, and Mostert (1958) suggested the preliminary administration of 100 per cent oxygen for two minutes in order to replace 98 per cent of the nitrogen in the lungs by oxygen. Following this pre-oxygenation, he recommended the administration of 100 per cent nitrous oxide for one minute at a flow greater than the patient's assumed minute volume.

This, he maintained, provided adequate anaesthesia within the next half minute. Breath holding was said to be rare. For 15 to 30 seconds, while the surgeon started the operation, he administered 10 to 15 per cent oxygen, and he added supplementary agents if the operation lasted for more than 2 to 3 minutes. (Neff et al (1950) had previously suggested facilitating the induction of anaesthesia by pre-oxygenation. The advantage was said to be due to the elimination of nitrogen, yet they held the inspired concentration of oxygen near 20 per cent when adding nitrous oxide).

Within this period I also gained insight into nitrous oxide and oxygen anaesthesia as a patient. The anaesthetic was for a dental extraction. The anaesthetist was a general practitioner who used the technique described by Tom (1956). The only unpleasantness was the resistance to expiration arising in the relief valve which was experienced at the start of the induction. This soon became tolerable. From the start of the administration I counted each breath to myself. The first subjective change was noted at the sixth or seventh breath. At the twelfth breath the general practitioner was heard to say "He seems to be taking it all right" (there was some surprise shown when I reported this later). At the thirteenth breath there was cerebation to the extent of realising that thirteen was supposed to be an unlucky number, of calculating that twice thirteen was twenty six, and of wondering whether breaths would be counted up to that figure. Afterwards there was no memory of having counted beyond thirteen.

Upon recovery there was at first an awareness of an indistinct figure who clarified into the general practitioner, and soon afterwards I was feeling fully awake, standing up and asking how long it had taken. It was alleged that I had stared menacingly at the general practitioner and demanded "Who are you?", but I had no memory of this. It was

also alleged that before asking how long it had taken, I had let out an expletive. This I could not remember with certainty, although it "rang true".

This insight into the experience of being anaesthetised with nitrous oxide and oxygen was of undoubted value when later I anaesthetised outpatients. It also brought out the vagueness of the boundaries between consciousness, forgetfulness and unconsciousness. Under these circumstances it is not easy to distinguish with any certainty between anaesthesia and amnesia. It also drew attention to the resistance to respiration which can be imposed during anaesthesia.

Although I was unaware of it at the time, a similar experience had been reported by Macintosh (1932) twenty-five years before. He was anaesthetised with nitrous oxide by a friend who counted aloud and at irregular intervals asked "Can you hear me now?", to which he replied by moving his right hand. The last number he remembered was thirteen, yet he still responded up to the time when his friend counted twenty-one. On another occasion, at his own request, nitrous oxide with 10 per cent oxygen were administered under considerable pressure. He found the suffocating feeling most disagreeable and he was convinced that collapse and sickness result more from gas given under pressure than from the patient being denied oxygen.

Theoretical considerations

Against this background, it seemed that there was some doubt about how outpatient anaesthetics should be administered. The empirical techniques normally used had gained favour because of their expediency and their apparant safety; but were they so safe?

Hypoxia is an obvious potential hazard of the classical methods

of administering nitrous oxide and oxygen anaesthesia. Although the partial pressure of oxygen in the alveoli is of greater significance than its partial pressure in the gases inspired, hypoxia occurring during nitrous oxide anaesthesia may be put into perspective by relating given mixtures of nitrous oxide and oxygen inhaled at sea level, to the altitudes at which atmospheric air would contain the same partial pressures of oxygen. For example, the mixture of 2 litres of oxygen with 10 litres of nitrous oxide per minute, described above for the maintenance of anaesthesia, provides an inspired oxygen concentration of 16.7 per cent. The partial pressure of this corresponds with that in air at 6,000 feet.

The relationships between anaesthetic mixtures at sea level, partial pressures of oxygen and altitudes are indicated in figure 2.1. This has been derived from tables (Dittmer and Grebe, 1958). In a mixture of 10 litres of nitrous oxide with 1 litre of oxygen (or 9 per cent oxygen), the partial pressure of oxygen at sea level is the same as that in air at an altitude of 22,500 feet. At this height above sea level even the fittest of acclimatized mountaineers become dyspnoeic upon the slightest exertion. A patient inspiring such a mixture during anaesthesia would also be subjected to the flow resistance of an anaesthetic breathing system, in particular to the resistance of the expiratory valve. To what height would it be reasonable suddenly to project a patient with whom one has made only the briefest acquaintance, within whom may lurk unsuspected disease, and whose physiological powers of adaptation may be limited? (Example. Recently I was asked to anaesthetise an outpatient for a minor orthopaedic procedure. He was a fit looking white male aged 38 years who was employed as a security officer in "Securicor". His orthopaedic condition was interfering

with his job which entailed much walking, but he would undoubtedly have passed the screening test, used in one hospital (Chapter 13) of having to walk up to the third floor. His notes revealed, however, that he had had a coronary occlusion three years previously, and had experienced occasional angina since then. He told me that this had been precipitated by the anxiety associated with a visit to the Dental Hospital. He had been sent home for a few hours because it was not immediately convenient to carry out a surgical procedure on his jaw under local anaesthesia. It was during the anxious waiting period that he experienced pain in his chest, the cause of which was diagnosed by electrocardiography).

Apart from the knowledge of the composition of gases inhaled by the patient, the only specific clinical guide to alveolar oxygen tension in a normal patient is peripheral cyanosis. If it is accepted that cyanosis is indicative of excessive hypoxia, then there is no clinical warning of its approach during a nitrous oxide induction. (The unreliability of cyanosis as a guide to arterial oxygen tension is well known. It may vary according to local peripheral circulation, haemoglobin level, individual acuity of blue vision (Comroe et al, 1962); according to the immediate lighting conditions (Kelman and Nunn, 1966); and according to the lighting conditions to which the observer may recently have become adapted).

Since measurement of breath-by-breath alveolar composition is not practicable during anaesthesia in outpatient departments, an attempt was made to calculate approximate values that might be expected during the induction of anaesthesia, by each of two techniques, in an hypothetical patient (Figure 2.2). Allowance was made for the dilution of 3000 ml of functional residual air with an alveolar tidal volume of 300 ml at a respiratory rate of 15 per

minute; for the solution and transport away from the alveoli during each respiratory cycle of 20 ml of oxygen plus the volume of nitrous oxide calculated to be soluble in one-fifteenth of a cardiac output of 5000 ml per minute, at the calculated prevailing partial pressure (blood/gas partition coefficient was taken as 0.47); and for the replacement of these dissolved gases by carbon dioxide and dead space gas from the previous expiration. (It is upon this replacement of nitrous oxide taken up from the alveoli by a mixture in which nitrous oxide is diluted by oxygen, that the "Concentration Effect" of Eger (1963, a, b & c) depends. This is discussed further in chapter 16). The figures chosen and calculated may have a very doubtful relationship with the true state of affairs existing in any given patient (the patterns of respiration and the changes in cardiac output etc. would also be different in the two cases), but they should give some idea of the relative orders and patterns of change in alveolar composition when the techniques of Tom (1956) and Mostert (1958) are used. These calculations suggest that there is a greater margin of safety after preoxygenation. When induction of anaesthesia is started using six breaths of 100 per cent nitrous oxide without preoxygenation, hypoxia may contribute to loss of consciousness, especially in those patients with whom contact is lost rapidly.

Hypoxia, by itself, can undoubtedly produce unconsciousness (see chapters 3 and 11), but it is not clear how much hypoxia may accelerate the onset of unconsciousness produced by the administration of 100 per cent nitrous oxide. Bennet and Seevers (1937) found that reducing the inhaled oxygen concentration to 9 per cent made little difference to the threshold to painful stimuli during the administration of 30 per cent nitrous oxide. Following

experiments lasting 15 minutes, however, their subjects complained of marked fatigue which lasted for an hour or more and, in some instances, headache of even longer duration. When the inhaled oxygen concentration was reduced to 6 per cent (with 30 per cent nitrous oxide), unconsciousness was produced within 5 minutes in 6 out of 13 experiments. When 6 per cent oxygen was administered with 94 per cent nitrogen, amnesia was produced in 16 of 19 trials in 7 subjects, although in each instance the subject responded correctly to commands throughout the experiments (preliminary experiments designed to compare different methods of inducing nitrous oxide anaesthesia are described in chapter 12). In clinical practice the justification of even short periods of deliberate hypoxia is open to question.

Methods of clinical investigation

A Boyle anaesthetic machine was used for administering anaesthetics in the Casualty Department of the Royal South Hants Hospital. Oxygen, nitrous oxide and cyclopropane were available for use in a Magill semi-closed breathing system. Latterly the standard vaporizer bottle for trichloroethylene was replaced by a bottle calibrated by I.C.I. for halothane administration. For dental anaesthesia an old Walton intermittent flow machine was used. A thick-walled reservoir bag was included in the breathing system.

A hard-backed note book, ruled in 1/4 inch squares, was adapted for keeping records of anaesthetics administered in the Casualty Department. Details of the patients were kept on the left-hand pages, and a time scale was marked off from above downwards in the margins of the right-hand pages (two squares per minute). A stop watch was started as the patient took the first breath of nitrous oxide and comments were recorded in the note book

against the appropriate times (Figure 2.3).

In an attempt to determine when consciousness was lost, and the degree of amnesia, patients were told that each breath they took during the induction of anaesthesia would be counted aloud and they were requested to nod slightly in response. Upon recovery, enquiry was made as to the last count heard.

A non-linear pressure-recording device was constructed for keeping a continuous record of respiration during anaesthesia (Figures 2.3 and 2.4). It was connected to the Magill anaesthetic breathing system between the reservoir bag and the corrugated tubing. The pressure sensor was a thin rubber (surgical glove) tambour which was stretched across the lower half of a shallow circular tin (type-writer ribbon tin). The centre of this rubber diaphragm was linked to the balance wheel of a watch, to which was secured the "recording pen". The "pen" was an hypodermic needle through which a length of thread was passed, a short "tail" being allowed to protrude from the needle, while excess thread was contained within the hub. The hub was bent upwards and filled with proofing ink (Figure 2.4). Movements of the protruding "tail" (transmitted from the tambour as a result of pressure changes in the anaesthetic breathing system) produced an ink record on adding machine paper which was drawn beneath the pen by means of a clockwork mechanism (originally designed as part of a time-bomb). The clockwork mechanism contained electrical contacts which 'made' once per minute. They were used to actuate a one-minute time marker through a solenoid to which was secured a second "hypodermic recording pen" (top trace of figure 2.4). A third "hypodermic recording pen", secured to another solenoid, was used as an event marker (bottom trace). Anaesthetic charts prepared from these

records are shown in figures 2.5, 2.6 and 2.7. Tracings of two of the records are shown at the top of figures 2.5 and 2.7.

Clinical observations were supplemented by further data abstracted from the official record of anaesthetics administered in the Casualty Department.

During 1960 some dental anaesthetics administered in a private surgery by Dr. H. A. Burgess were observed. The above recording apparatus was not used, but details recorded in a note book were supplemented by using a tape recorder. The noise of the escape of gases from the relief valve during expiration was usually recorded, in addition to the comments by the anaesthetist, the dentist and the patient.

An attempted modification of Mostert's technique

Considering the many differences between patients, the set time of one minute for the administration of 100 per cent nitrous oxide, following preoxygenation, advocated by Mostert (1958), seemed too rigid. An alternative suggested itself in the administration of 100 per cent nitrous oxide for as long as the patient would respond, by nodding, to the anaesthetist counting aloud each breath. This was tried only once.

The patient was a tall active female of 67 years, requiring reduction of a Colles fracture. She nodded in response to the counting aloud of 25 breaths during the induction of anaesthesia, but at this stage cyanosis was evident. It was realised afterwards that these 25 breaths had taken about two minutes, although the nitrous oxide may have been diluted by air (Figure 2.7). Gas flows were then altered to 6 litres of nitrous oxide and 2 litres of oxygen per minute. There was a short period of apnoea, but cyanosis soon disappeared as respiration resumed. Respiration

then became obstructed and an airway was inserted. The conditions for operation were excellent. The management of anaesthesia could have been much safer.

The latent period between the inhalation and the action of an anaesthetic agent

One obvious factor overlooked in the above reasoning was the delay between the inhalation of a gas, its transport in solution and its effective action upon the central nervous system. To investigate this, 15 patients, of average age 38 years, were asked to signal, by raising the hand, the very first onset of subjective change after inhaling a single deep breath of nitrous oxide. The delays ranged from 15 to 55 seconds and averaged 32 seconds. These figures may be compared with the figure of 35 seconds given by Wylie (1953) as the time taken for 75 per cent nitrous oxide with oxygen to become fully effective when used in midwifery; and with the 10 to 12 seconds given by Guedel (1953) as the time of passage of blood from the lungs to the brain. I experienced a delay of 20 seconds between taking a single breath of nitrous oxide and becoming aware of any subjective effects. This was consistent with the half-dozen breaths actually counted before appreciating any change during a nitrous oxide induction for a dental extraction. No subjective effects followed a single deep breath of 100 per cent nitrogen.

Loss of consciousness, amnesia and analgesia

The results obtained using the technique of breath counting during the induction of anaesthesia, as described above, are displayed in figure 2.8. Each horizontal stick represents an anaesthetic. Its total length indicates the number of nods observed by the anaesthetist, and the black portion indicates the number of nods remembered by the patient. There was much variation. On

average just over half the nods were remembered. Counts were not always definite. Some patients stopped nodding early but resumed on command. Nodding sometimes became unrelated to counting. Some patients began shaking their heads instead of nodding and occasionally nodding became so exaggerated as to require restraint. (In a few instances patients raised their shoulders as well as their heads. If the shoulders were then held down, these patients tended to raise their legs instead). The last number remembered was not always definite, a lower figure often being given soon after return of consciousness than could be given later. That patients were in fact responding to the spoken voice and not nodding automatically with respiration was sometimes checked by asking them to shake the head instead of nod. Compliance with this request was variable and non-compliance was of uncertain significance, as shown by the following example. An engineer of 44 years nodded 25 times. The later nods looked automatic. He did not comply with the request to shake his head. Other observers considered that he responded satisfactorily to only 21 or 22 counts. In fact he not only remembered counts up to the 25th, thereby demonstrating negligible amnesia, but he also remembered being asked to shake his head. He could not explain why he had not done so.

Any hesitation in breathing that occurred was always noted after the last nod. It seems unlikely that exhortations to "keep blowing" would have made any difference. (See Tom's technique described above).

If this experiment were to be repeated using the lower partial pressures of nitrous oxide commonly administered during abdominal and thoracic surgery, it might be found that we are more often "amnalgetists" than anaesthetists. Indeed, Gray (1954) and Rosen (1959)

have made relevant observations. Gray described a level of narcosis at which subjects obey commands yet afterwards assert that they have been unconscious. Using a pressure analgesiometer, to which the subjects responded by raising an arm, he found that onset of analgesia was close in time to loss of consciousness. According to analyses carried out on arterial blood drawn at this time, the partial pressure of nitrous oxide was then about 320 mm Hg. Rosen (1959), on the other hand was able to establish contact, in some instances, with patients stabilized on nitrous oxide and oxygen mixtures containing up to 73 per cent nitrous oxide, but almost half the patients with whom good contact was made had total amnesia. Further cases of awareness during surgery were reviewed and reported by Hutchinson (1961).

From observation of patients in the Casualty Department who had preoperative pain, I had suspected the late onset of analgesia referred to by Gray. Relief from pain during induction of anaesthesia was denied by headshaking even when attempts were made to ameliorate the pain by suggestion. Although Chapman, Arrowood and Beecher (1943) concluded that 20 per cent nitrous oxide with oxygen had an analgesic potency equivalent to morphine 16 mg against pain produced by radiant heat and ischaemia, this effect took 10 minutes to reach maximum. "Gas" and hypoxia, however, are still combined in midwifery in the use of self administered gas and air (at least this was the case until very recently). Pain and analgesia need to be defined in every context in which these words are used.

The use of supplementary agents

The indications for the use of particular gas mixtures and supplementary anaesthetic agents vary with the anaesthetist. An examination of the casualty operations register at the Royal South

Hants Hospital was made in order to ascertain how frequently nitrous oxide and oxygen mixtures were in fact administered with and without supplementary agents. Over a 17-month period 45 per cent of 1259 nitrous oxide anaesthetics were administered without the use of supplementary agents (Figure 2.9). A more detailed analysis was made of a series of 131 personally administered anaesthetics, 48 per cent of which were not supplemented (Figure 2.10).

Anaesthetics were given 1.8 times as often for bone and joint surgery (B/J = 84) as for scissions and sutures (S/S = 47), but supplementation was required 1.6 times as frequently for scissions and sutures ($32/47 = 68$ per cent) as for bone and joint surgery ($36/84 = 43$ per cent). This was presumably related to the intensity, quality and duration of the surgical stimuli, and perhaps also to ease of restraint. The greatest incidence of bone and joint surgery was in the early and later years of life. The early years involved males more than females and the later years females more than males. Those patients who were over the age of 50 years were more easily anaesthetised by nitrous oxide and oxygen alone than those below this age. The incidence of scissions and sutures declined steadily with increasing age.

Walsh (1958) described the use of halothane as a supplement to nitrous oxide anaesthesia for dental extractions. Subsequently he introduced it to the Casualty Department of the Royal South Hants Hospital. Previously trichloroethylene had been the most favoured supplementary agent.

A technique which I tried was to induce anaesthesia using 3 litres of nitrous oxide and 2 litres of oxygen per minute with a nominal concentration of 0.15 to 0.3 per cent halothane. The administration of halothane was then stopped, maintained or increased according

to the reaction of the patient to surgical stimulation. The cost of using halothane in the Casualty Department in this manner was about two shillings per anaesthetic. Impressions from brief experience with this technique suggest that induction of anaesthesia is not unpleasant and takes about 5 minutes. Loss of consciousness appears to be rapid after allowing for the delay between first inhalation and effective action. Restraint may be needed in the early stages but relaxation soon follows. There may be some movement upon surgical stimulation. Return to consciousness is a little slower than after nitrous oxide and oxygen anaesthesia. The time at which recovery is complete is difficult to assess but it appears to be much later. The ears remain flushed and nystagmus may be observed even after the patient has risen from the table and professed to be fully recovered.

The following case report provides a warning about the use of the above technique for patients in the dental chair. A tall, fit, tough welder, in his early twenties, attended for dental extraction with a note to the effect that it was not possible to anaesthetise him with nitrous oxide. The above technique using halothane was tried, employing an uncalibrated vaporizer. The anaesthetic appeared to be entirely satisfactory. The patient recovered consciousness quickly, smiled and expressed surprise and pleasure at the ease with which the operation had been carried out. Shortly afterwards he slumped in the chair and lost consciousness. He was pink. His superficial temporal pulse was still palpable but rather slow and of low tension. He was placed horizontal, whereupon he repeated the performance of waking up, smiling, talking, sitting up and slumping. After being kept horizontal for a period there was no further trouble. Although the vaporizer used was uncalibrated, the patient's quick

recovery suggested that an excessive concentration of halothane had not been administered. Even if the patient had received a high concentration of halothane, this would have been for a very short time and the total dose taken up would soon have been distributed throughout his body at a very low partial pressure. Either the patient was particularly susceptible to halothane, or there was at least some other contributory cause for the episode of postural hypotension.

Supplementary observations in a private dental surgery

Most of the patients observed subsequently in a private surgery were children. The majority received oxygen throughout anaesthesia, all of them inhaling 20 per cent oxygen within 35 seconds from the start of the induction of anaesthesia.

The advantage of administering anaesthesia in quiet surroundings was obvious.

Too few anaesthetics were observed to justify detailed analysis. One patient, however, may be worth mentioning. He was a boy, aged 9 years, who tended to feel nauseated in the dental chair even without anaesthesia. He was anaesthetised for 2 minutes and 40 seconds, using nitrous oxide and oxygen, and three teeth were extracted. He recovered quickly and appeared alert, but half a minute later he became somewhat languid and confused. After a further minute and a half he looked fully awake and alert, but became languid, unsteady on his feet and 'not quite himself' when he got out of the chair half a minute later.

Problems emerging

These preliminary observations left no doubt that there were objections to the classical methods of administering nitrous oxide to outpatients. Hypoxia was inevitable, potentially hazardous and

sometimes disastrous.

The modifications in technique suggested by Tom (1956) and Mostert (1958) had not been fully assessed. The efficacy of these techniques in preventing hypoxia under clinical conditions was unproved, indeed, these techniques could not be used properly without accurately calibrated anaesthetic machines. It seemed probable that they were still associated with some hypoxia, and this immediately raised the question as to how much risk was associated with how much hypoxia. Even if the risks of these techniques proved to be negligible, it appeared that they could be used successfully with only about 50 per cent of outpatients, unless supplementary agents were added.

The avoidance of hypoxia and the use of supplementary agents, however, did not give complete protection against hypotension occurring in a sitting patient, and the causes and mechanism of this occasional complication required elucidation. Possibilities that arose were that supplementary agents themselves might cause the hypotension, and that high pressures in the breathing system, due to high supply flow rates and obstructing relief valves, might contribute.

The use of full oxygenation, even with supplementary anaesthetic agents, tended to prolong anaesthesia and total recovery time, and assessment of full recovery was another factor which appeared to require further investigation.

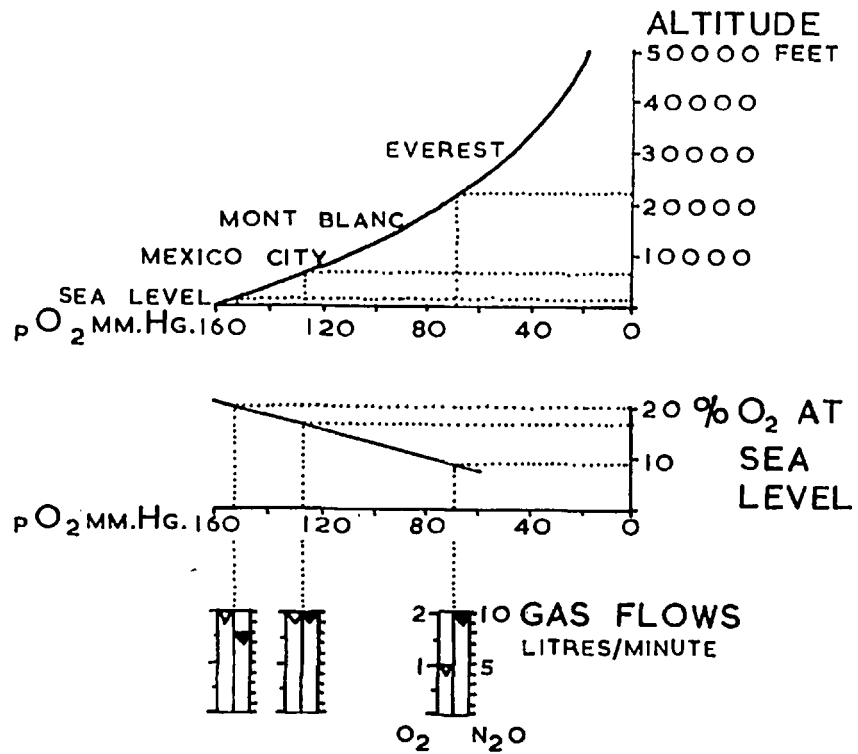
In short, consideration of the most satisfactory means of giving a safe and effective outpatient anaesthetic brings one face to face with many of the really basic concepts of anaesthesia.

FIGURE 2.1

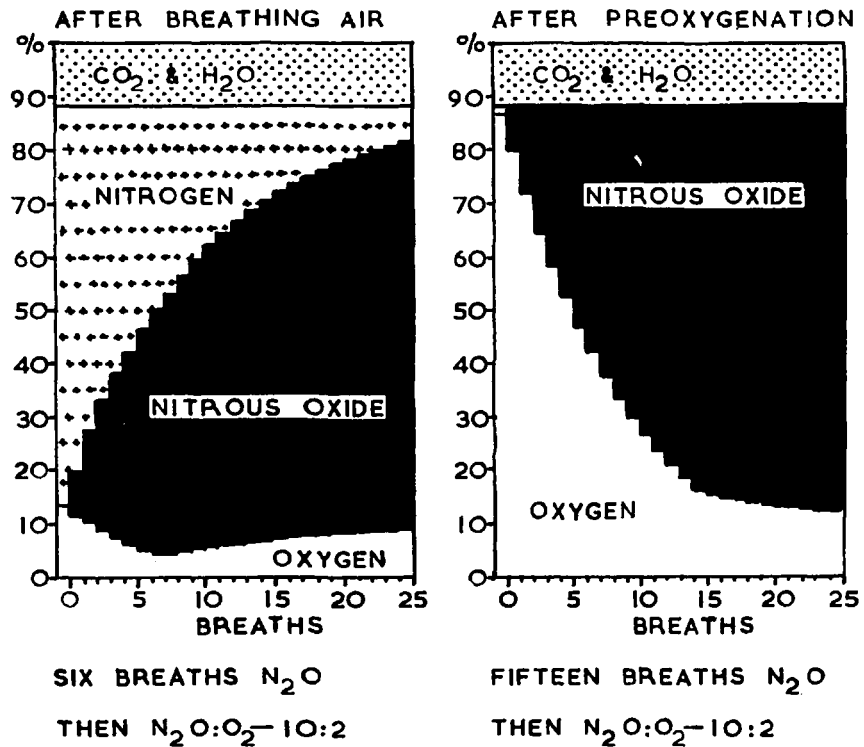
Altitudes at which the partial pressure of inspired oxygen would be the same as that in given mixtures of nitrous oxide and oxygen at sea level. Gas flow rates corresponding with typical gas mixtures are indicated.

FIGURE 2.2

A theoretical comparison of two techniques of inducing nitrous oxide anaesthesia, by calculation of breath-by-breath concentrations of alveolar gases in a given hypothetical patient.



NITROUS OXIDE INDUCTION ALVEOLAR GAS CONCENTRATIONS



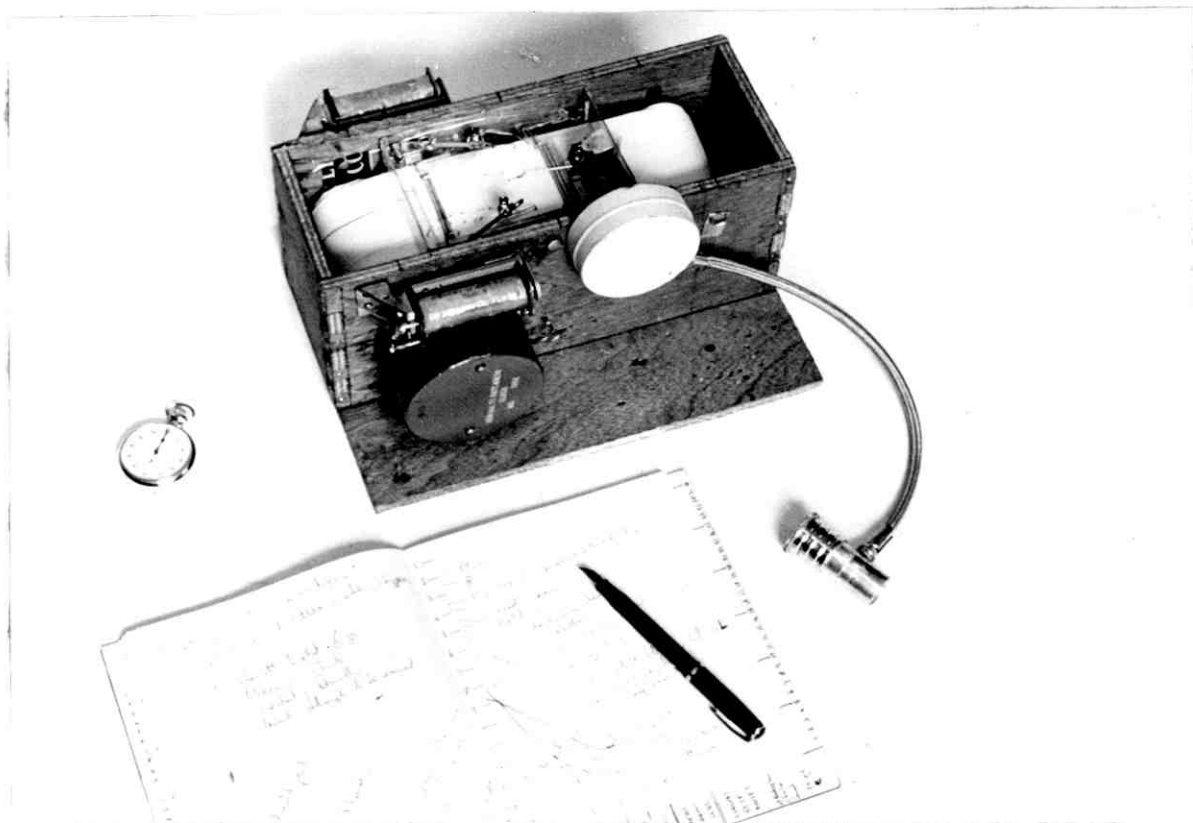


FIGURE 2.3

The note book and apparatus used for recording anaesthetics administered in the Casualty Department of the Royal South Hants Hospital. A full description is given in the text and a diagram of the apparatus is given in figure 2.4.

FIGURE 2.4

Diagram of apparatus, shown in figure 2.3, used for recording respiration during anaesthesia.

- Upper trace - one minute time signal.
- Middle trace - pressure fluctuations (static pressure calibration is shown above and to left, dynamic 'overshoot' is unknown).
- Lower trace - 'event' record.

FIGURE 2.5

Specimen record (above) obtained using the apparatus shown in figures 2.3 and 2.4, and a chart of the anaesthetic as derived from the record and from the notes made at the time. Note the event marks which facilitated the precise timing of the notes in relation to the record.

Some preoxygenation was always used with this apparatus, in order to ensure a proper seal between mask and face before the start of anaesthesia.

100 per cent nitrous oxide was administered for 8 breaths, then 16.5 per cent oxygen for nearly three minutes, and finally 20 per cent oxygen for just over one minute.

Note the extreme tachypnoea during surgical stimulation. Restraint was necessary. No supplementary anaesthetic agents were used. Nausea was transient.

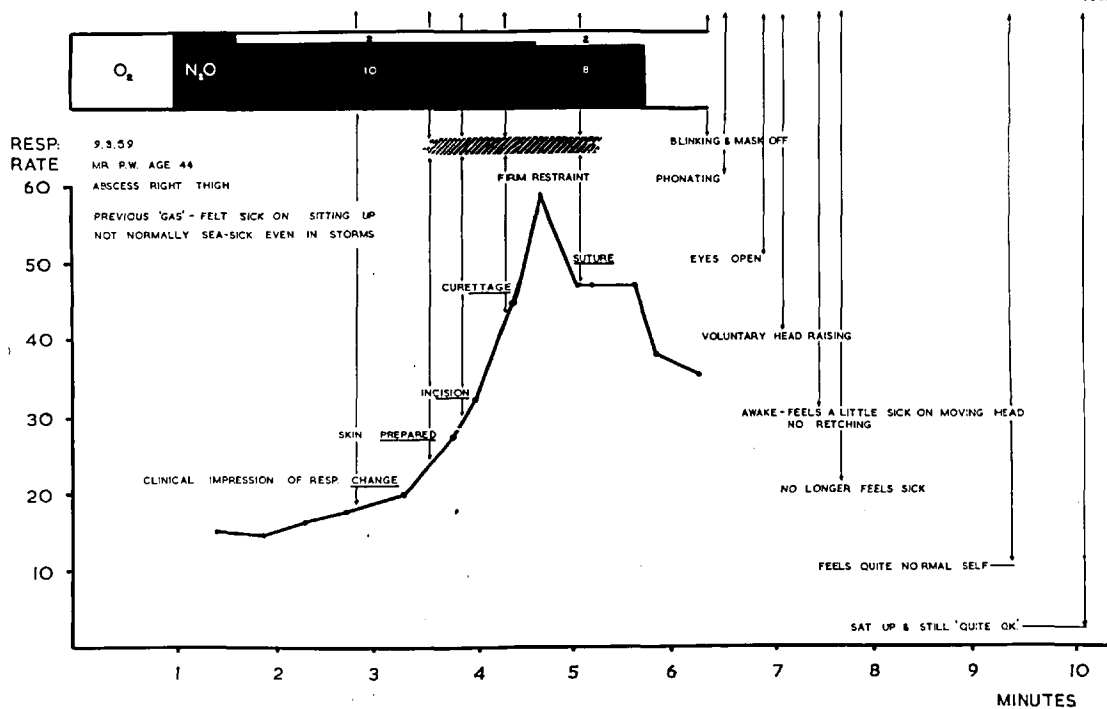
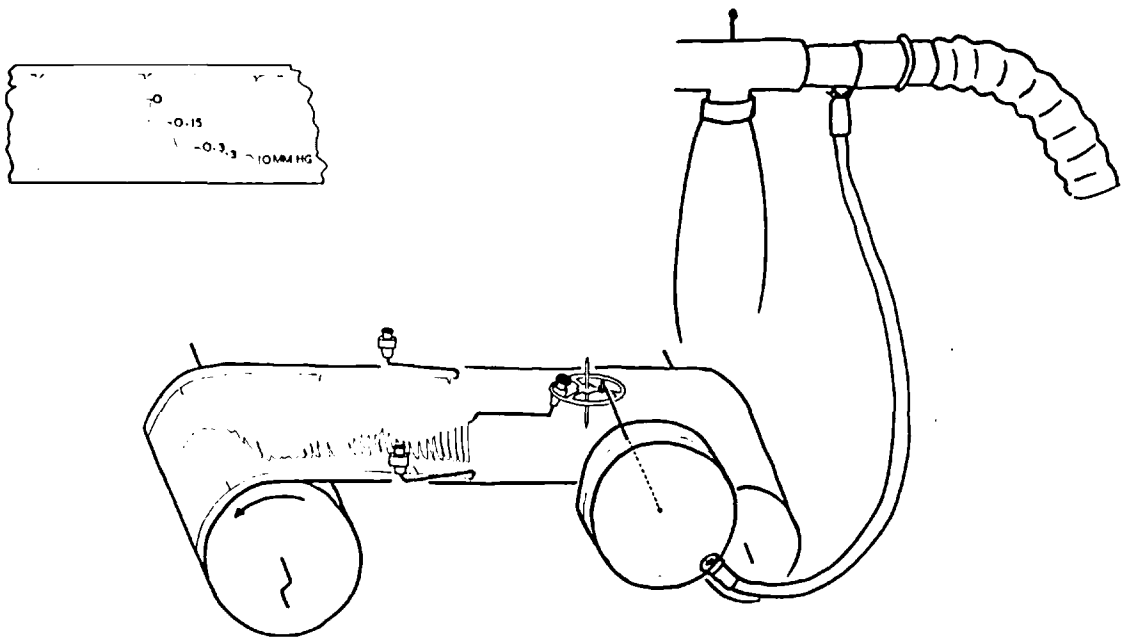


FIGURE 2.6

It is not clear from this anaesthetic chart alone whether the absence of recorded pressure changes during the sixth minute was due to apnoea or to respiratory obstruction (see also figure 13.2.). The subsequent phonation on expiration suggests that the breath may have been held with the glottis closed. The tachypnoea during surgical stimulation was not as pronounced as immediately after the a ventilatory period.

FIGURE 2.7

Following pre-oxygenation for 2 minutes, 100 per cent nitrous oxide was delivered until the patient stopped responding to numbers spoken in time with her expirations. This was not until 100 per cent nitrous oxide had been administered for two minutes, by which time cyanosis was evident. Despite the cyanosis there was little ventilatory response to hypoxia.

Note the period of apnoea when oxygen was first admitted. This would have occurred within the lung-brain circulation time, so a causal relationship cannot be assumed.

Surgical stimulation appeared to produce deeper rather than more rapid respiration.

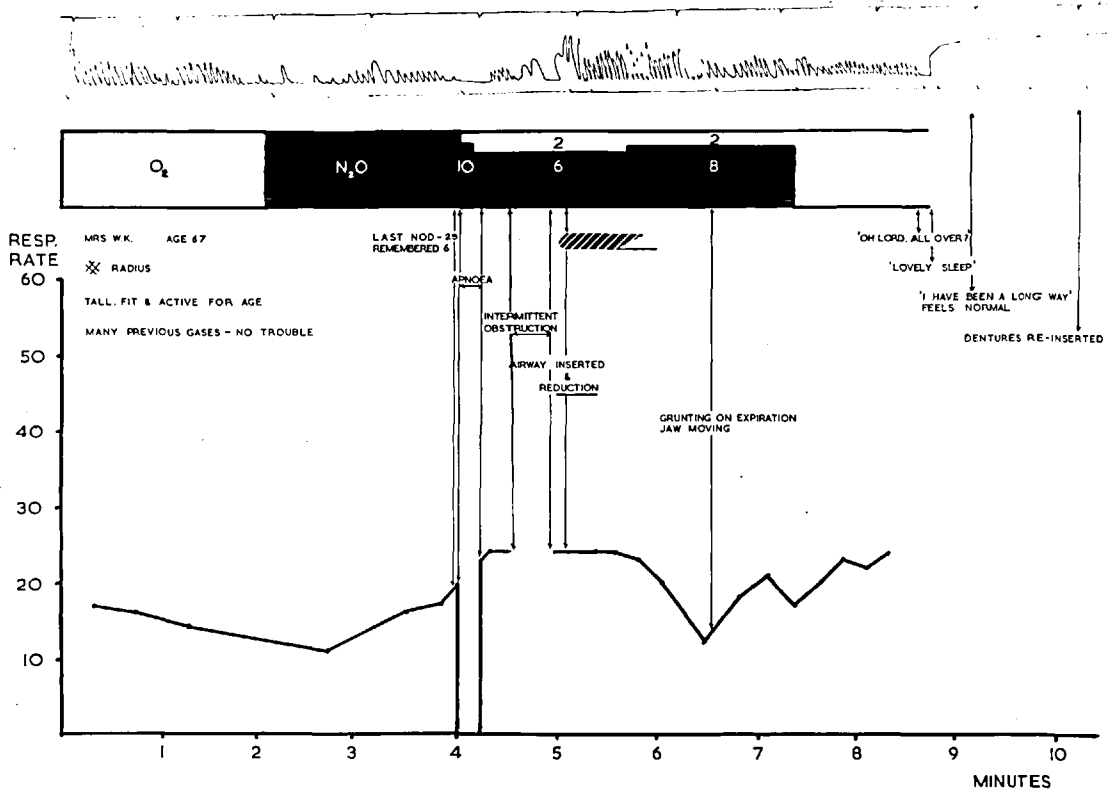
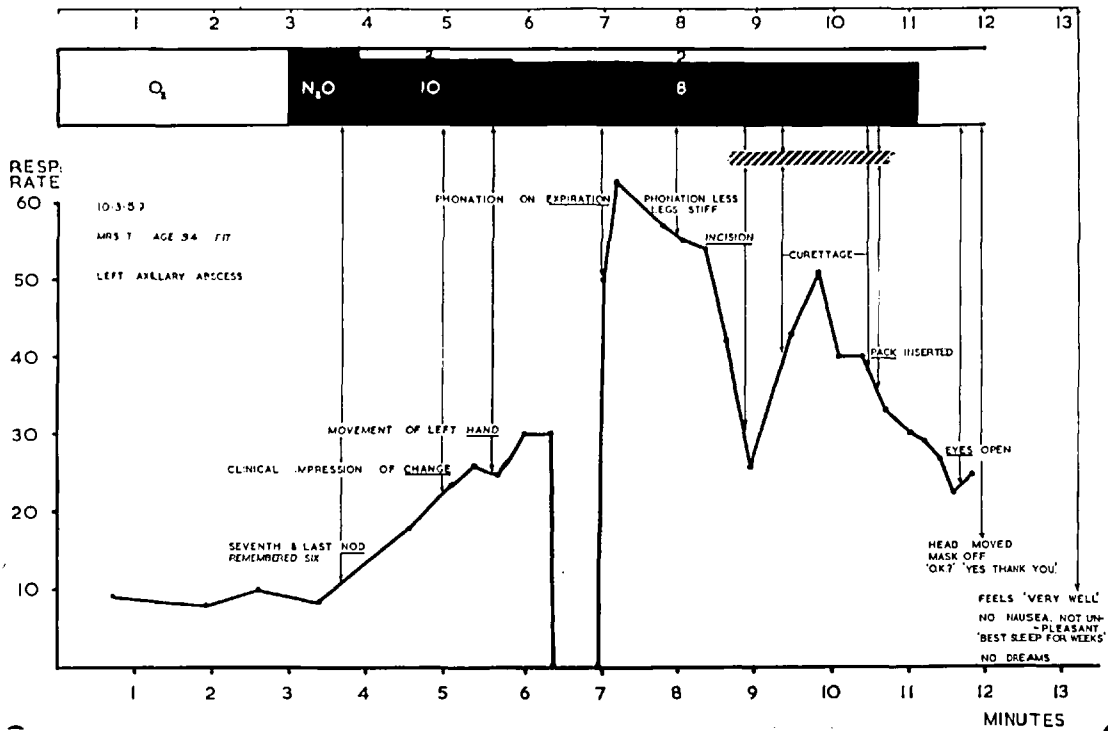


FIGURE 2.8

Each horizontal 'stick' represents a single anaesthetic. The 'sticks' are arranged, above downwards, in order of the number of respirations observed between the start of the induction of anaesthesia and apparent loss of consciousness.

The anaesthetist counted aloud at each expiration, and the patient responded by nodding the head. The total length of each stick indicates the number of nods observed. The black portion indicates the number of nods (counts) remembered by the patient.

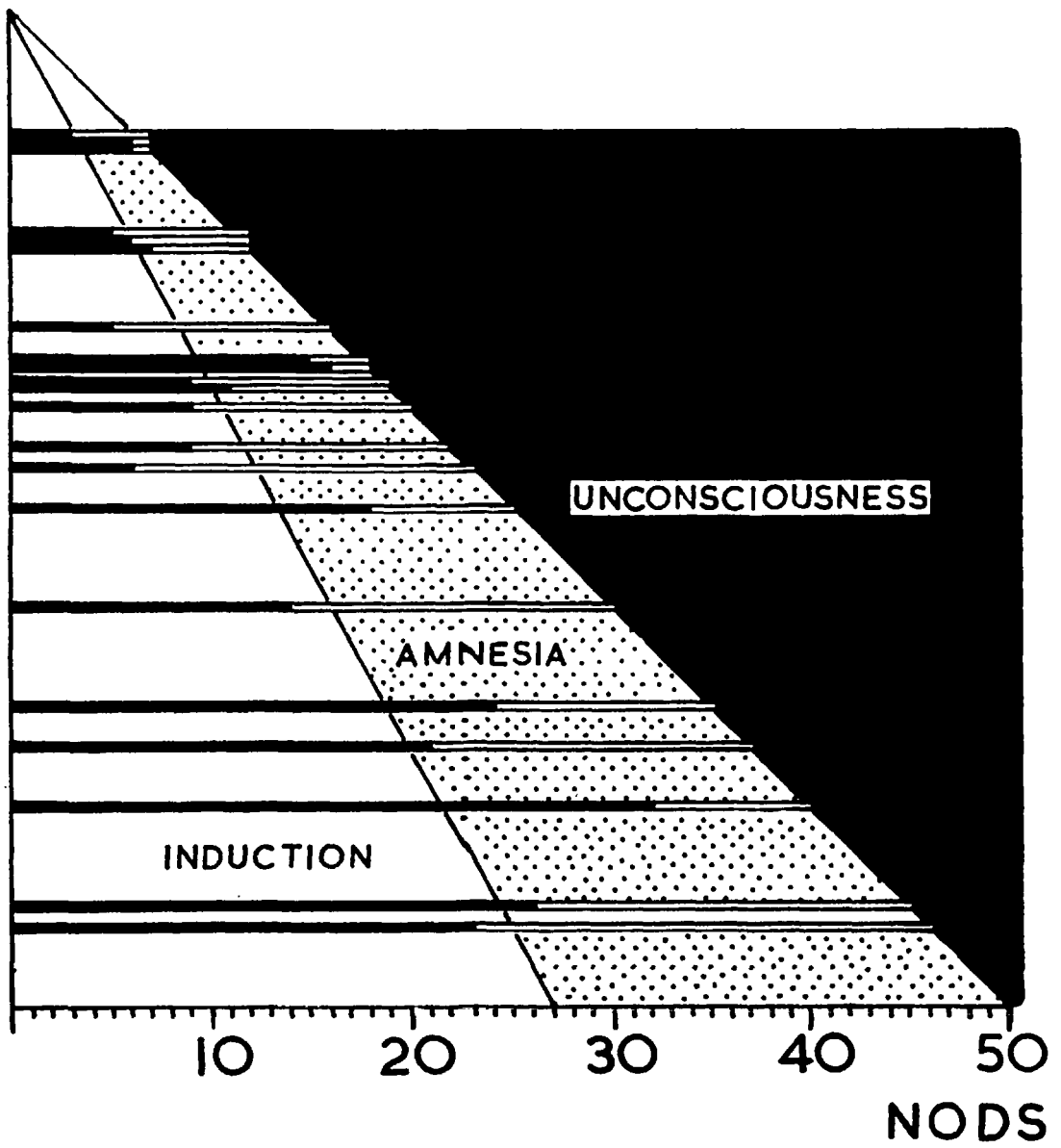
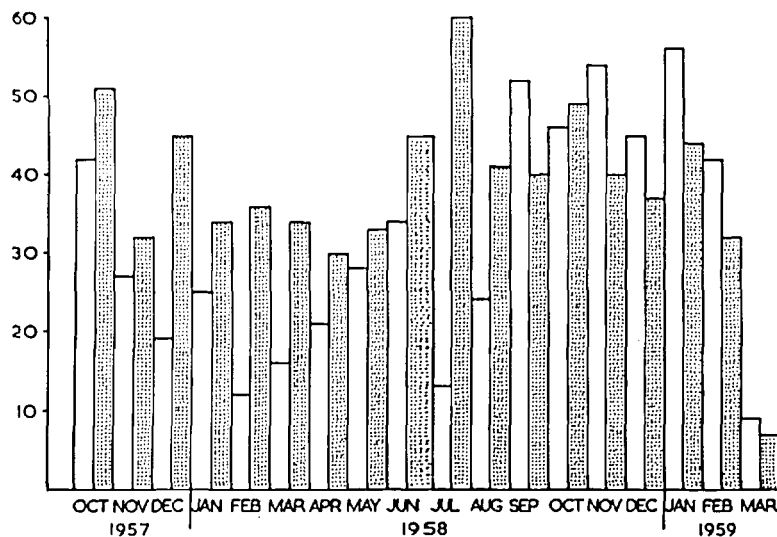
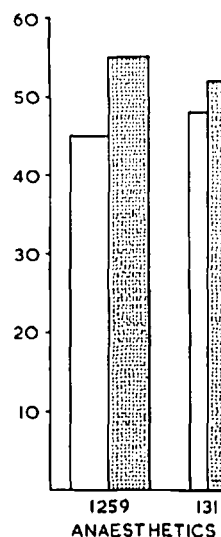


FIGURE 2.9

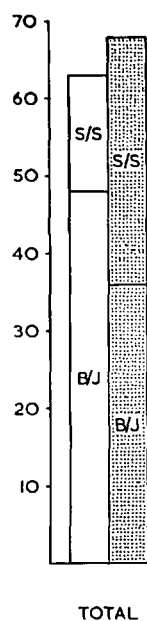
Month-by-month analysis of 1259 anaesthetics administered in the Casualty Department of the Royal South Hants Hospital. These included 131 personally administered anaesthetics. Stippling indicates supplementation of nitrous oxide and oxygen anaesthesia using some other inhalation anaesthetic.

FIGURE 2.10

Analysis of 131 personally administered anaesthetics which are included in Figure 2.9. Stippling indicates supplementation of nitrous oxide and oxygen anaesthesia.

NUMBER OF
ANAESTHETICSPER CENT OF
ANAESTHETICS

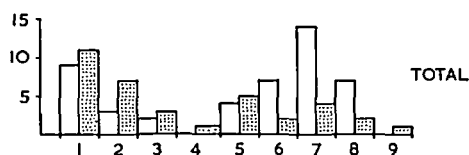
ANAESTHETICS



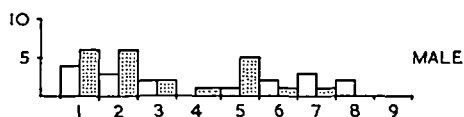
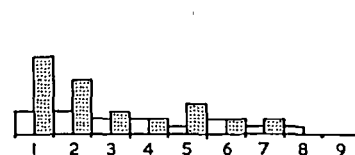
TYPE OF OPERATION

BONE/JOINT

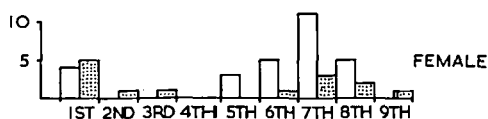
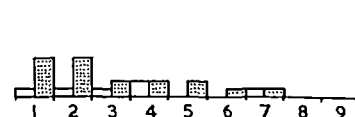
SCISSION/SUTURE



TOTAL



MALE



FEMALE

AGE IN DECADES

CHAPTER 3

SOME POSSIBLE HAZARDS DURING
OUTPATIENT ANAESTHESIA AND RELATED PHENOMENA

The greater part of the section of this chapter on the effects of external resistance to respiration was included in Vickers Research Limited Report No. 21, and with the Directors' permission, was subsequently published (Smith, W.D.A. (1961). The effects of external resistance to respiration. Part I: General review. *Brit.J.Anaesth.*, 33, 549).

Much of the sections dealing with hypoxia and hypotension was written while holding a Wellcome Research Fellowship in the Research Department of Anaesthetics, the Royal College of Surgeons of England, and has been published (Smith, W.D.A. (1963). The effects of expiratory resistance, oxygen and hypoxia in relation to dental anaesthesia. Part I: Introduction. *Brit.J.Anaesth.*, 35, 28).

It is obvious from chapters 1 and 2 that hypoxia is a serious potential hazard of outpatient anaesthesia in which nitrous oxide is used as the main anaesthetic, and that the most dreaded complication is irreversible cerebral damage (Barach and Rovenstine, 1945). The consequence of this may be death (Courville, 1939), demonstrably impaired intellectual or neurological function (Batten and Courville, 1940; Bedford, 1955), and probably less dramatic changes which are not detectable by casual observation. Before discussing possible contributory causes and the physiological events which may be associated with this catastrophe, however, it may help to get a measure of the size of the problem, and to examine a few individual case histories.

Mortality

Mortality figures are often quoted to indicate the safety or the risk of anaesthesia. They are not available for outpatient anaesthesia as a whole, but figures for the mortality of dental anaesthesia are published from time to time. In an editorial in the British Medical Journal of 1954 it was stated that "the Registrar General's Reports show that in England and Wales an average of some 60 deaths a year have been reported for the last twenty years due to nitrous oxide alone...". Goldman (1958) deduced that over the four years from 1952 to 1955, out of 6,682,750 anaesthetics given to ambulant patients in the Health Service there were 56 deaths of which 20 had received an intravenous anaesthetic. In 1960 he gave a more detailed analysis for the years 1952 to 1958, during which seven year period there were 100 deaths. A further improvement was reported in an Editorial in the British Dental Journal in 1963. According to this the average number of deaths per year over the five year period 1952

to 1956 was 17, and over the following five year period 1957 to 1961 it was 9.4. In 1962, four patients, two of whom were over 70 years of age, died out of 2,007,647 who had dental anaesthetics within the National Health Service for dental ~~extractions~~. The recent Report of a Joint Sub-Committee on Dental Anaesthesia quotes a total of 25 deaths in the five year period 1962 to 1965, an average of five per year (Ministry of Health, 1967).

This trend is heartening, but a death is a death and its occurrence should also be reported in detail. One would like to know more about the people who died - whether they were apparently fit, active and productive before they succumbed to what was presumably expected to be no more than a minor procedure lasting a minute or so. One would like to know precisely how they were anaesthetised; how they reacted to each stage of the anaesthetic and to surgical stimulation; at what point it was noticed that anything was wrong, and what was done about it; how, when and why they died, and what resuscitative measures were tried.

The overall figures of mortality would also have more meaning if they could be presented side by side with the corresponding figures for the mortality of dental extraction under local anaesthesia.

As suggested in a letter by Mandell (1963), the improvement may well have been due to the introduction of safer adjuvants and the greater use of intravenous induction, both resulting in a reduction in the risk of restricting oxygen in the anaesthetic mixture.

Published on the opposite page of the same journal, however, was another letter describing a cardiac arrest in a frightened, tense, eight year old girl who was anaesthetised with nitrous oxide, oxygen and halothane for the extraction of two deciduous teeth. On recovery from anaesthesia there was a sudden onset of pallor and wide pupillary

dilatation; and radial pulse, apex beat and bleeding were absent. It took oxygenation and two periods of external cardiac massage to resuscitate her. Consciousness then returned within ten minutes and she was rational within twenty-five minutes (Jarvis, 1963).

This suggests that the reduction in mortality over recent years could also have been due to a greater alertness to the possibility of hypotension in the sitting patient, and to a greater awareness of appropriate resuscitative measures. A few years previously, under similar circumstances, that child would very likely have died. Although Tanner (1892) wrote: "Death has invariably resulted from one of two causes, either asphyxia or syncope....in nearly every case the patient was left sitting in the chair while attempts at restoration were made. Now it cannot be denied that syncope is much more likely to occur in the upright than the recumbent position...." the credit for the greater alertness in recent years to the possibility of hypotension occurring during anaesthesia in the dental chair should go to Bourne (1957, 1960).

Case Histories

Reports of deaths under nitrous oxide in this country go back at least to 1873 (British Journal of Dental Science), but in most of them the details given have been unsatisfactory, except that it was usually evident that there had been hypoxia, often in a sitting patient. Luke (1915) presented a report of 'collapse' after one hour of nitrous oxide and oxygen anaesthesia for radical mastectomy being treated by requesting the surgeon to stop the dissection, and by administering oxygen and ether. Disaster was averted.

Bourne (1960) cited six cases of immediate death in the dental chair, which are summarised below, using his case numbers:

8. A boy of 2 became pale and stopped breathing after the rapid

extraction of two incisor teeth.

9. A man of 22 had fourteen teeth extracted, after which he was given oxygen because he was cyanosed, and at that moment he became deathly pale and stopped breathing.

10. A woman of 52 was to have had ten teeth extracted, but after the extraction of two, respiration suddenly ceased and she became cyanosed.

11. A woman of 32 had fifteen teeth extracted in five or six minutes, during which her breathing and colour were noted to be normal. At the end she was given oxygen, whereupon she suddenly turned pale and stopped breathing.

12. A healthy miner, aged 46, was given gas for the extraction of twenty-five teeth, after coming off night shift. Oxygen was given at the end. He opened his eyes and looked at the receptionist; his eyes rolled upwards and closed, his face became grey, and his breathing became very shallow.

13. A boy of 7 had three teeth extracted quickly under gas. As he was recovering he cried out. He was taken from the chair to the recovery room where he was found to be collapsed.

Nitrous oxide without supplementary anaesthetic agents was used with all the above cases. In all except one there seemed to have been something particularly fatal about the end of anaesthesia. In three of the patients, collapse coincided with the administration of oxygen, and one of these was certainly cyanosed. The combination of starvation and fatigue may be presumed in one patient, and he may also have lost an appreciable amount of blood during the extraction of twenty-five teeth.

Similar features presented in three cases of delayed death cited by Bourne (1960). He also gave details of seven cases of delayed recovery. With three of these there were insufficient data for comment.

In one, collapse occurred after the extraction of three teeth. In another, collapse was noticed after the extraction of a single tooth, although it may have occurred earlier. In a third there was gross hypoxia, and another went grey before extraction started.

In a more recent case of immediate death (Kyle, 1960), "a male aged 22, healthy and of average build, who was to have a routine extraction of three teeth. Induction under N_2O by McKesson machine was not too smooth, the patient becoming violent. Trilene was added to the mixture but without much progress being made, the patient remaining unmanageable. The anaesthetic was terminated and no extraction was performed. Within ten seconds of removing the nose-piece, extreme pallor became evident, followed by a "gasping" type respiration. No carotid pulse could be felt and cardiac arrest was presumed. Resuscitation by means of inflation of the lungs with O_2 and intracardiac adrenaline was unsuccessful. Post-mortem showed nothing abnormal of note".

A letter from Boyle (1925) describing two patients who collapsed but survived is probably worth quoting in full: "I should be very much obliged if one or more of your readers would give me the real explanation of why one occasionally meets with cases of sudden collapse after the administration of Gas, or Gas and Oxygen for Dental extractions. I have had two such cases during the last year, and they have given rise to a good deal of anxiety, and, to be perfectly candid, I am at a loss to understand the reason why they did collapse.

"The first case was a man of about forty-five, about 6ft. 2in. in height, spare of build and looking septic. He was anaesthetised with Gas and Oxygen with Hewitt's machine, and the anaesthesia continued with Gas by an ordinary nose-piece. The anaesthesia was

perfectly normal; he came round and was rinsing his mouth with water, when he exclaimed, "Oh! I do feel rotten!" Almost before I could get to him he had fainted. His pupils were widely dilated, he was pale and cold. I thought for a moment that he was dead, but I rapidly depressed his head between his knees and in a few moments he became conscious again and sweated profusely. His pulse was very feeble, but after the administration of a little brandy he recovered somewhat. He was not, however, fit to leave the dentist's room for nearly an hour. He volunteered the statement that he had never fainted before.

"The other case was a man of similar build and of extremely nervous disposition. Here the anaesthetic was a very short and simple affair, and about five minutes afterwards the patient said he was feeling very ill. He then fainted, but, in contra-distinction to the other case, his pupils remained contracted all the time. His own doctor was present, and he administered, firstly strychnine, and then later caffeine, and as neither of these injections seemed to have much effect, we then gave him a little brandy by the mouth, and as he was a life-long teetotaler this seemed to have a good result. In this case it was about ten minutes before the patient told us that he could see! Here again it was a full hour before he was fit enough to be sent home with his doctor.

"The question I should like to ask is: "Why do these cases occur, and what is the cause of it?" I shall be very grateful to any of your readers who can give me a really clear and satisfactory explanation.

"I am led to write this letter, because a week or so ago I saw in the lay Press that a man had died after the extraction of teeth with Gas. He had collapsed and died. That was the brief statement, but

it leaves us no wiser.

"In an experience of nearly twenty-five years I have only had these two cases that I now report, and I cannot but think that it would be of advantage to all of us if we could get views and experience of some of the other anaesthetists on this topic".

Except for Buxton (1897), in relation to one particular case, so far as I know, no one else has made a particular point of collapse occurring after the extraction of teeth with gas, although this does appear to be a feature which is common to many of the cases. It happened in the patient referred to in chapter 2, whom I anaesthetised with nitrous oxide, oxygen and halothane, without cyanosis, and so far as I could tell with the anaesthetic machine used, without any hypoxia. The 9 year old boy observed subsequently in a private dental surgery became languid and unsteady about half a minute after regaining consciousness, although he did not collapse. This does suggest that whatever may be the cause of collapse, and there may be a number of different causes, there is often a time lag between the cause arising during anaesthesia, and the effect; or ~~that~~ the cause may be related in some way to stopping the administration of anaesthesia.

Hypoxia

Irreversible cerebral damage may result from severe or from prolonged anoxia, which, by classical description may be anoxic, anaemic, stagnant, or any combination of these (it should not be necessary to consider histotoxic hypoxia in the present context). It is important, therefore, to consider the possible causes of hypoxia, and its effects, in the context of outpatient anaesthesia.

Some degree of anoxic anoxia is inevitable if the gases administered to a patient during anaesthesia are deficient in oxygen. It may also result from respiratory obstruction or from central

respiratory depression. All three of these causes may arise together during outpatient anaesthesia, particularly during dental anaesthesia, with which a rapid induction of anaesthesia using 100 per cent nitrous oxide and the minimal use of supplementary agents is often encouraged by the tradition of "rapid turnover" of patients. The effects of hypoxia can be accelerated by a high oxygen consumption which may be associated with apprehension or with recent exercise. They may also be exaggerated by pre-existing pulmonary or cardiovascular disease.

The significance of anaemia should be considered when a patient is assessed for anaesthesia. If higher oxides of nitrogen should happen to adulterate the nitrous oxide administered to a patient, haemoglobin may be converted to methaemoglobin during anaesthesia, and this condition may be mistaken for cyanosis. Hypotension may also be associated with contamination with higher oxides of nitrogen (Toothill, 1967; Greenbaum et al., 1967; Smith, 1967, Part X).

Stagnant anoxia is most likely to be associated with an episode of hypotension, and so far as the brain is concerned, this is most likely to be significant in an upright or sitting patient (Bourne, 1960). The circumstance in which an anaesthetised outpatient is most likely to be sitting up is during dental anaesthesia.

Arterial blood pressure during dental anaesthesia.

Arterial blood pressure is a factor which the dental anaesthetist may find difficult to assess and over which he has little direct control (except by tilting the dental chair into the horizontal position in the event of a fall of blood pressure).

Guy, Goodall and Reid (1910) compared the effects of different anaesthetic agents upon systolic blood pressure, using a Riva-Rocci sphygmomanometer. Foot bellows were used for inflating the cuff.

They reported neither the surgical operations performed nor the posture of the patients, so it is not known how many of the nitrous oxide anaesthetics were for dental operations, although Guy was Dean of the Edinburgh Dental Hospital. So far as nitrous oxide was concerned they compared the effects of its administration through valves (i.e. non-rebreathing), with a rebreathing technique using a two-gallon bag. They reported: "with both methods there is a considerable rise in blood pressure, but that the rise is greater when valves are employed. The rise of pressure is associated with constriction of the arterioles and is asphyxial in origin. The cases anaesthetised with valves in action all became cyanosed". They then made a series of observations of: "Nitrous oxide (rebreathing) preceded by oxygen.....with the view (1) of ascertaining whether the symptoms of asphyxia were to be accounted for by deprivation of oxygen, or by accumulation of CO₂, and (2) of finding an easy method whereby a satisfactory anaesthesia could be obtained quite free from the asphyxial element..... A one-gallon bag was filled with oxygen. This was inhaled by the patient, who exhaled through valves, so his lungs were washed out with oxygen. As soon as the bag became empty a bag containing two gallons of nitrous oxide was substituted, and the patient then inhaled gas, and at the same time rebreathed his expired air, which, to begin with, contained an unusually high percentage of oxygen.

"The effect on the systolic pressure was remarkable. The maximum rise in any case was only 15 per cent, and this increase was only once noted. The average maximum increase was only 3 per cent".

Goldman, Cornwell and Lethbridge (1958) maintained that the usual tendency is for the blood pressure to rise during dental anaesthesia, although it was admitted that it might fall slightly at the

end of anaesthesia, upon the introduction of oxygen, and occasionally during induction. Bourne (1957, 1960), on the other hand, emphasised the dangers of fainting in the sitting position, especially when this coincides with anoxic anoxia.

The incidence and the causes of hypotension during dental anaesthesia are not clear. Many of the possible causes have been reviewed by Bourne (1960). Emotional factors may be concerned when hypotension occurs before or during the early stages of anaesthesia (Sharpey-Schafer, 1958), but this explanation is less convincing when hypotension occurs towards the end of, or following anaesthesia, which frequently seems to be the case.

Many factors may contribute towards changes in blood pressure during outpatient anaesthesia, and the sudden reversal of an environmental change may be of as much importance as its initial introduction. Some of the more obvious considerations are: the pharmacological properties of the anaesthetic agents; movement and struggling; surgical stimuli; hypoxia, pre-oxygenation and re-oxygenation; the application and the removal of raised airway pressures due to the use of high flow rates and of apparatus with high flow resistance; the nature of the surgical procedures and the duration of anaesthesia. Factors less easy to define are those concerning the individual patient. Apart from race, sex, age, physique, disease, alcohol or drug tolerance, and individual patterns of emotional, autonomic and vasomotor control, the intensity and duration of pre-operative pain, the recent quota of sleep, the time of the last meal, previous exercise and activity, and the heat and humidity of the day may all play a part.

The effects of hypoxia

Johnson (1891) "obtained from the Scotch and Irish Oxygen Company of Glasgow a cylinder containing 100 cubic feet of compressed

nitrogen, in which the proportion of oxygen present was only 0.5 per cent by volume, with 0.3 per cent of CO_2 . As a preliminary trial, Mr. F. W. Braine was good enough to administer the gas in five instances to members of the staff of King's College, who volunteered to submit to the experiments. The result was in each case the production of complete anaesthesia and of general phenomena precisely similar to those observed from the inhalation of nitrous oxide. Encouraged by these results, Mr. Braine felt justified in administering the gas to patients at the Dental Hospital for anaesthetic purposes. Nine patients took the gas. In every case the result was the production of complete anaesthesia, with general phenomena precisely similar to those observed during nitrous oxide inhalation. The pulse was first full and throbbing, then feeble. In the advanced stage the respiration was deep and rapid, and there was lividity of the surface; the pupils were dilated, and there was more or less jactitation of the limbs. The only difference, in the opinion of those present, being that the anaesthesia was less rapidly produced, and somewhat less durable, than that from nitrous oxide, though in each case the tooth was extracted without pain", (Smith, 1966, Part IX).

Schneider (1918) subjected seventy fit male volunteers to progressively decreasing inspired oxygen concentrations during rebreathing experiments lasting up to half an hour, and found that the occasional subject suddenly breathed less and then fainted. Some subjects responded to the increasing hypoxia with an initial acceleration of the pulse rate but then, after maintaining a constant rate for a while, the heart suddenly slowed and this was a sure indication that the limit of endurance had been reached. The change in systolic pressure in response to hypoxia was variable. In what Schneider described as the "optimal" type of response, the systolic blood pressure remained

unchanged until the inspired oxygen concentration had fallen to between 14 and 9 per cent; the blood pressure then rose gradually. Some subjects inhaled mixtures containing as little as 6.6 per cent oxygen before the systolic blood pressure rose. In other cases the systolic blood pressure rose by 40 to 60 mm Hg. A few subjects showed a fall in systolic blood pressure at about the time that the pulse rate began to rise and these were less tolerant of low inspired oxygen concentrations. Many subjects showed a sharp and sudden fall in systolic pressure at low inspired oxygen concentrations and this, if allowed to continue, led to fainting. Normal blood pressures were usually recovered on return to air, although after fainting full return to normal might take up to one or two hours.

It is worth noting that if a man were even slightly below the best physical condition, his tolerance of hypoxia was reduced. A cold, indigestion, late hours or worry might reduce his resistance to hypoxia temporarily by the altitude equivalent of many thousands of feet. More serious indisposition affected him to a corresponding extent. Caution should be exercised, however, in interpreting these results in relation to the hypoxia which may occur during brief nitrous oxide anaesthesia. The two sets of conditions are not the same. In Schneider's experiments hypoxia was introduced gradually and was progressive and prolonged. During outpatient anaesthesia the introduction of hypoxia is usually sudden and often profound, but it should not be prolonged and it is usually progressively reduced. Keys, Stapp and Violante (1943), however, reported fainting in ten subjects between 2.8 and 15 minutes after starting to breathe 10 per cent oxygen. The possibility that hypoxia may be one of the causes of hypotension in the dental chair deserves serious consideration. It was expected by Sharpey-Schafer (1958) but not proved.

Ward and Wright (1929) observed the effects of nitrous oxide anaesthesia on the electrocardiogram, in recumbent healthy young adults who volunteered for the purpose. In most of the experiments "pure nitrous oxide was given in the usual dental fashion". They found marked tachycardia. In one case the pulse rate increased from 90 to 124 per minute, the T-wave was abolished and the R-wave was reduced. The administration was stopped after 53 seconds. When the experiment was repeated using nitrous oxide with adequate oxygen for 4 minutes and 15 seconds, the pulse rate did not rise above 73 per minute, and the ventricular complex was not markedly different from that in the control E.C.G. They commented: "even in our healthy subjects recovery (of the E.C.G.) was sometimes not complete after several minutes. It is possible that in patients with heart disease the immediate changes might be of a more serious nature, and it is conceivable, too, that they might be of a more lasting character".

Jacoby et al (1955) recorded electrocardiographic changes during endotracheal intubation and correlated these with blood oxygen saturation. They found that intubation produced arrhythmias in 9 per cent of well oxygenated patients, and in 36 per cent of the most hypoxic patients (oxygen saturation 50-60 per cent). Alterations of the pulse rate occurred in 47 per cent of the former and in 91 per cent of the latter. They concluded that cardiac responses to vagal stimulation are more frequent and more serious when hypoxia is present.

Hypoxia, circulating blood volume and fainting

Anderson and his colleagues (1946) investigated the circulatory changes during fainting induced by oxygen lack. Inspired oxygen concentrations between 6 and 10 per cent were used and faints were induced in three out of thirteen subjects by this means. The charts of their results indicate that fainting did not occur until after about 5

minutes from the start of hypoxia but these subjects lay on a couch with their backs supported at about 45 degrees. Their legs were not dependent. One volunteer subsequently fainted much sooner when tourniquets were used to dam back blood in his legs. His pulse rate fell to 58 per minute and his blood pressure to 80/65 mm Hg. He was breathing 8.4 per cent oxygen. Inhalation of this hypoxic mixture was continued, yet within two to three minutes his blood pressure began to rise again. Five other subjects recovered from fainting under similar circumstances. This suggests the possibility of a patient both fainting and recovering from the faint while still anaesthetised in the dental chair. Thirteen subjects are also not very many. If a larger series had been investigated it is quite possible that some would have fainted sooner. The initial hypoxia was also less severe than can occur during the induction of anaesthesia using 100 per cent nitrous oxide.

The use of venous tourniquets to dam back blood in the legs was equivalent to bleeding the volunteers, and that fainting could occur during bleeding was evident from experience with blood donors, although emotional factors could also be involved. Greenbury (1942) found an incidence of 4.9 per cent in 5,897 donors, Poles and Boycott (1942) found an incidence of 2.8 per cent in 100,000 donors. In both series fainting was found to be commoner in the young. The latter workers also commented: "The most dangerous type of faint is that which occurs $\frac{1}{2}$ -6 hours after bleeding when the donor is back at his work or out in the street. A number of these donors have been found to have a transient orthostatic hypotension after being bled, and when this can be detected the subsequent faint can probably be prevented by giving the donor additional rest". In view of Schneider's (1918) finding that complete recovery may take up to two hours after a faint due to hypoxia, it would probably be wise to bear this in mind when

faced with the possibility of fainting from any cause. A case that may be relevant is that of an adult female who had teeth extracted under nitrous oxide anaesthesia, during which there was convulsive movement. She recovered and later walked 400 yards to the station. In the train she was "siezed with faintness, pallor and active convulsion". She was put to bed unconscious. On the next day she was still insensible, with pupils widely dilated, pulse irregular and weak, breathing feeble and she "was sometimes convulsed". Recovery took several weeks (Lancet, 1893).

Posthaemorrhagic fainting was investigated further by Barcroft, Edholm, McMichael and Sharpey-Shafer (1944), who found that during bleeding the heart rate increased while cardiac output and right auricular pressure fell (in a typical case the heart rate rose from 72 to 102 per minute while the cardiac output fell from about 8 to 4 litres per minute and the right auricular pressure from about 12 to 7 cm saline). The blood pressure was largely maintained. A few minutes after withdrawing about one litre of blood, the blood pressure fell suddenly and the pulse slowed (from about 120 to 40 mm Hg and from 102 to 62 per minute respectively in the above typical case), but the cardiac output and the right auricular pressure rose slightly. There was, therefore, a sudden fall in total peripheral resistance. Five out of six subjects showed an increase in forearm blood flow, and as the skin was blanched it was assumed that the vasodilatation had occurred mainly in muscle. (The findings of this study are consistent with an observation made by Hunter (1793): "I bled a lady, whose blood at first was of a dark colour; but she fainted, and while she continued in the fit the colour of the blood that came from the vein was a fine scarlet".).

In six subjects they were able to block the forearm vasodilatation

reaction during fainting by using procaine to block the nervous pathways, and so they concluded that the muscle vasodilatation during fainting was mediated by vasomotor nerves. From calculations of the total peripheral resistance they concluded that muscle vasodilatation was sufficient to explain the changes occurring during a faint, and that splanchnic and skin vasoconstriction persisted. They concluded, therefore, that the controlling mechanism was not the same as during the hypotension and bradycardia that is associated with stimulation of the carotid sinus (the similarity had been suggested by Lewis in 1932), because the latter was associated with splanchnic vasodilatation. Their suggestion as to the mechanism was; "If the faint is a reflex it follows an unrecognised pathway. One possibility is that a low pressure in the right auricle may be the trigger mechanism on the afferent side". Since then it has been suggested that the reflex is fired by large pressure transients which develop when the ventricles are contracting on a virtually empty chamber during systole. The incidence of fainting with blood loss appears to be about 10 per cent when 500 ml is lost, and about 60 per cent when 1000 ml is lost (Sharpey-Shafer, 1958).

The effects of re-oxygenation following hypoxia

Schneider (1918), commenting upon the significance of hypoxia in relation to aircraft accidents, observed: "In another class of accidents, or near accidents, the pilot's failure occurs near the end of a rapid descent. Often he has no recollection of how the crash occurred; he had lost consciousness, was asleep. This is highly significant; for this is a state which is induced by ample supply of oxygen, or fresh air, at full pressure, after a period of deprivation. This interval of unconsciousness, or collapse, is often met with by students of low oxygen problems. It occurs in a wide variety of

conditions, in miners escaping from 'after damp', city firemen coming out of smoke, and low oxygen experiments in the laboratory".

This effect has since been called the "oxygen paradox". Latham (1951) has reviewed the relevant literature and investigated it further. He demonstrated the paradox reaction in thirteen out of fifty-two subjects. It began between the 9th and 12th seconds after starting to breathe oxygen following a period of hypoxia (4-5 minutes at a simulated altitude of 20,000 feet). The initial effect was a disturbance of the central nervous system as shown by an increase in writing test errors. A secondary rise in the number of test errors written coincided with cardiovascular changes which were most pronounced after about 30 seconds of oxygen breathing. There was sometimes a sharp fall in systolic pressure within the first 2 to 4 seconds which Latham explained by an increase in the capacity of the pulmonary capillary bed causing a momentary reduction in cardiac filling. A greater fall in blood pressure was recorded after about 30 seconds and this coincided with an increase in forearm blood flow. The forearm blood flow usually began to increase at about the 9th or 10th second, reached a maximum at about 35 seconds, and had returned to normal within 60 seconds. There was no significant change in forearm blood flow during the preliminary period of hypoxia. Latham suggested that a constitutional element is important in deciding whether or not the nervous manifestations of the paradoxical reaction are further complicated by circulatory collapse.

The sudden administration of oxygen may also increase an already present tendency to cerebral vasoconstriction resulting from a reduction in arterial pressure of carbon dioxide produced by hyperventilation associated with the period of hypoxia.

It may be relevant to repeat here that Goldman, Cornwell and

Lethbridge (1958) sometimes found a slight fall in blood pressure at the end of anaesthesia and upon the introduction of oxygen. The oxygen paradox might conceivably contribute to the high incidence of collapse at the end of anaesthesia, as mentioned above. In three of the cases quoted from Bourne (1960) collapse coincided with the administration of oxygen, and one of these was certainly cyanosed.

"Fainting" and surgical operations

It has been alleged that in Baron Larrey's Hospital in Paris, it was the usual custom, in the days before chloroform, to lay a patient upon his back, and then lift him up very suddenly to the standing posture whenever it was wished to induce fainting for the purpose of relaxing muscles in cases of dislocation (Brunton, 1873). This story is consistent with the report that Baron Larrey defended Hickman's ideas on the possibility of operating on patients when they were in suspended animation (Smith, 1966, Part IV).

Imlach (1848), talking about the use of chloroform in dental surgery ("300 times, and without one single accident or drawback of any kind".) made the following comparison with the days before anaesthesia: "I have not had a single person faint in my house after any operation performed under its influence, whilst before, I often had them lying on my sofa in this state, or in a state approaching it. Beside all this, the patients used to come into the dentist's room with their faces pale, their lips quivering, their mouths parched, and every symptom of terror depicted on their countenances. Now, on the other hand, they seem to think it a good joke to have a tooth taken out; and many a tooth I have taken out because the patient could get it done without pain". From that account it is not clear whether the patients used to faint because of the pain they suffered or because of their fear of pain.

An earlier account by Abernethy leaves little doubt that patients did faint from fear of a surgical operation. In this instance, after preliminary exercises in resuscitation, the operation was carried out during a period of hypotension: "Mr. Abernethy, in a lecture on amputation of the leg, introduced the case of a female (whose leg was amputated by the late Mr. Pott in Bartholomew's Hospital), for the purpose of showing the influence of fear, etc. The patient, when the surgeon was about to commence the operation, fainted, and the operator in consequence put down the knife, and assisted in resuscitating her. As soon as she became sensible, she enquired if the operation was finished, and on being told that it was not, she expressed great regret. The tourniquet being again applied, and the surgeon in an attitude for operating, the patient again swooned; and the surgeon not thinking it right to perform the amputation during a fainting fit, the knife was again laid aside till she had recovered. When she became sensible, she enquired if her "leg was off", and on being told that it was not, she said, "Oh dear, I wish you had performed the operation when I was in the fit. All being again arranged for the operation, the patient again fainted, and the surgeon finding her pulse good lost no time in removing the limb. As soon as the operation was completely finished, she recovered, and the first question was, as before, "Is my leg off?". The surgeon replying in the affirmative, she looked at the stump, and exclaimed, "Thank God, it is off" (The Monthly Gazette of Health, 1826). Even in this case, however, one could argue that the tourniquet contributed to the faint. I have not succeeded in finding out in what position Mr. Pott placed his patients before amputating a leg.

One cannot dissociate pain from emotion, so one hesitates to say categorically that a given case of fainting was triggered off by

pain rather than by fear, but reliable observers have implied that this can be so. Astley Cooper (cited Brunton, 1873) for example wrote: "A person has a bougie passed into his urethra for the first time; the urethra is irritated by it; he says, "I feel faint", becomes sick, looks pale, and, without care he drops at your feet. His pulse has nearly ceased, and his body is covered with a cold perspiration. You place him on a sofa with his head a little lower than his body, and as soon as blood freely enters the brain all his functions are restored". He also described two amputations of the thigh to support his contention that the stimulus of mechanical injury to bone was particularly potent: "One case was for severe traumatic injury, the other for chronic disease of the knee joint, which had greatly weakened the patient. In both cases the pain and loss of blood during the operation was only a little greater than usual, yet, in both, immediately after the bone had been sawn through the face became pale, the eyes staring, the pupils dilated, a peculiar rigidity of the body occurred, and death immediately took place".

Travers (1827) also commented, in the days before anaesthesia: "Syncope following a slight injury is very common and very unimportant; syncope following a severe injury, not attended by haemorrhage is rare, and in the highest degree dangerous. In the first case the shock is partial, slight and evanescent; in the latter it is extended, deep and permanent". To illustrate the effects of slight injuries he wrote: "Such is the effect of the transient bodily pain experienced in the extraction of a tooth, or the extirpation of a wart or a corn, as in some persons to produce syncope, retching or convulsions". He went on to say "The influence of pain on the stomach to excite nausea and vomiting, and on the kidneys to suspend the secretion of urine, is well known. Surgeons have frequent opportunities of witnessing the first

of these effects succeeding to injuries and operation". To illustrate the more dangerous syncopes he quoted John Hunter: "I have seen a man die almost immediately upon the loss of a testicle. I have seen convulsions immediately attend the operation for the hydrocele, so that I have almost despaired of recovery..... The loss of a limb above the knee is more than many can bear, the cutting for the stone where it breaks, and may be an hour in extracting, is also more than many can bear".

Death following dental extraction without anaesthesia has also been reported, for example: "It is not uncommon to find indications of faintness where extraction of teeth is performed without an anaesthetic, and instances are occasionally recorded of fatal syncope. Such a case formed the occasion of a coroner's inquest at Brierely Hill on 16th ult. The patient, a woman, died a few minutes after the extraction of a molar by a registered dentist". (British Journal of Dental Science, 1896).

Early writings about nitrous oxide anaesthesia display a concern about fainting which was attributed variously to fear, "pain", "shock", fatigue, and fasting. As these comments and case histories concern outpatient anaesthesia in particular, quotations are given from several of them.

Thomas (1870) wrote: "There are many persons who will swoon in ordinary conversation if the subject of surgical operations be broached. It is in this class of patients who constitute the majority of those who are affected or manifest unpleasant symptoms at the time of or subsequent to operations". (The underlining is mine). Thomas had met about 25 to 30 such patients out of 3478 whom he had anaesthetised with nitrous oxide. Coleman (1881) wrote: "Independently of danger, nitrous oxide may be attended with disagreeable after

conditions; of these we may have vomiting, and vomiting combined with syncope, more commonly, as we have observed, in hot weather.... A prolonged sleepy condition, much as if the patient had taken a powerful narcotic, is occasionally manifested; in our opinion it is best to let the patient sleep this off, under guarded observation". The first death under nitrous oxide in Canada was reported from Montreal as follows: "A man aged twenty four went to the office of a dentist, to have a tooth extracted, and requested to have some nitrous oxide administered. After assuring himself that the patient was not suffering from heart or lung disease, the dentist administered the gas. No sooner had the tooth been extracted than the patient gave a gasp and fell over in the chair. He was placed upon the floor and artificial respiration was performed, but without restoring animation. The patient was not under the influence of liquor and five hours had elapsed since last taking food (breakfast)..... The verdict of the jury was that the man died from syncope, caused by the administration of nitrous oxide, and they exonerated the dentist from blame." (British Journal of Dental Science, 1890).

Underwood (1893) maintained that "Fainting occurs in a few cases, and is then not unfrequently due to the excessive zeal of the medical man, which leads him to order a long fast before hand". More recently, in relation to the fainting of blood donors, this impression of the contribution of hunger, and of fatigue, has been confirmed (Greebury, 1942; Poles and Boycott, 1942; Seldin, Lundy and Adams, 1946).

Breakall (1895) took the view that: "there is a danger of giving too little gas, which is an error more easily perpetrated than that of overdosing. One might say "Well, in the event of not giving sufficient gas, one is on the safe side". But is this so? Think of the shock caused by extracting a tooth when there is just sufficient consciousness

to feel and magnify the pain, and not sufficient to understand the why and the wherefore of such pain, for we must remember that one effect of the gas is to exaggerate the special senses just before unconsciousness takes place". See also Hilliard (1899).

From America, Hare (1897) reported a death under nitrous oxide of a man between fifty and sixty years of age who "visited a dentist who makes a speciality of administering nitrous oxide gas, to have a couple of teeth extracted. He had taken gas on previous occasions without trouble. On this occasion he took the ordinary quantity, his teeth were extracted and he rapidly returned to consciousness. He left the chair and walked to a wash stand to rinse his mouth. He then complained of numbness in his right hand which extended up his arm and to his right leg and side. He was put on a sofa where he became unconscious. In a few minutes he became completely insensible. He died twelve hours after taking the anaesthetic. The rise in arterial pressure produced by the gas, may cause rupture of a blood vessel in those having a tendency to apoplexy".

Buxton (1897) when commenting upon the death of a nurse under nitrous oxide gas and ether, reasoned as follows: "the patient was healthy, not unacquainted with the mysteries of anaesthesia, and not spoken of as either being nervous about, or in dread of the operation. She was however, fasting. The operation took place at 3 p.m. or after; the stomach was quite empty..... Nurse Gath had suffered a very prolonged fast. She was seated in a chair. The anaesthetic given was nitrous oxide gas followed by an extremely small quantity of ether.....there seems no doubt Nurse Gath died from cardiac syncope. This was not due to ether. Was it the result of nitrous oxide administration? The collapse took place after the facepiece was removed, and after three teeth had been extracted. It appears then

that either some circumstances existed which prevented the gas escaping from the lungs (see Chapter 21), or the operation played a part at least as important in bringing about death as did the anaesthetic. No mention is made of any spasm or anatomical condition such as would interfere with expiration..... What have we to learn? Surely, first, that neither nitrous oxide gas or ether are discredited by this sad occurrence. 2. That prolonged fasts are at least as dangerous as distended stomachs. 3. That it is not only the inhalation which constitutes the danger of any operation, but the collateral circumstances, the actual surgical procedure, (and here the experience and care of the operator become an important factor), the many possible accidents connected with the procedure. In no case must the possibility of simple or shock syncope occurring be forgotten. As to the best measures for resuscitation, views differ; the writer attaches more importance to forced respiration and total or semi-inversion in cases of threatened cardiac failure. Laborde's rhythmic traction upon the tongue, and Mass' rapid palpation of the heart, are also measures of established value".

Morrison (1873) had earlier brought out some of the significant points: "It has been ascertained that 40 per cent of all the accidents from anaesthetics are cases of syncope.....in a severe Dental operation, we have a formidable combination of the causes of syncope. The terror of the operation; the shock to the nervous system; the loss of blood; the erect posture; the depressing effects of the anaesthetic; and often unobserved organic lesions, are the most prominent of these causes, and they are sufficiently alarming to make the stoutest heart shudder for the safety of his patients and for his own reputation, if he is not ignorant of the dangers around him". He went on to quote Dr. Kidd of Dublin; "About 90 per cent of the cases are in trivial, small

operations in persons in perfect health, viz. Dentist's cases, operations of convenience". (See also British Journal of Dental Science, 1889 and 1897).

In more recent times Lewis (1932) made a detailed study of fainting, and on its relation to pain he wrote: "Of syncope, occurring as it is well known it may in response to pain, I speak a little more diffidently, but I have strong reason to suspect that syncope during the painful phase of coronary thrombosis, during the manipulation of diseased joints, in gall-stone colic, and in renal colic, is of the kind discussed; but in the case of most of these, sufficient observations have not been made as yet positively to identify the form of syncope; they should be made, and that is chiefly why I am instancing them". Since then, however, he has written: "While painful sensations derived from the human skin are associated with brisk movements, with rise of pulse rate, and with a sense of invigoration, those derived from deeper structures are often associated with quiescence, with slowing of the pulse, a fall in blood pressure, sweating, and nausea. The last phenomenon, nausea, is responsible for the common designation "sickening", which is applied to pain derived from the deeper structures but never to cutaneous pain. This syndrome, or vasovagal response, to deep pain occurs frequently when joints are painfully stimulated; it has also been witnessed in painful stimulation of muscle, deep fascia, and periosteum and in puncturing arteries (see below). It occurs in association with all the chief severe visceral pains - such as angina, gallstone, renal, and bowel colic - and in blows on the testicle and bladder pain. It never occurs, apparently, with cutaneous pain".

Rushmer (1944) confirmed "the production of syncope in man from relatively painless arterial punctures". This occurred in 15 out of 45 individuals in the sitting posture. The skin over the brachial artery was anaesthetised using 2 per cent procaine chloride. The

subcutaneous tissue was infiltrated and care was taken to infiltrate well about the artery. A short beveled, 19 gauge needle was then introduced into the lumen of the artery. In some of his cases, at least, it would seem that fainting was unlikely to have been due to psychic factors; but whatever the relevant stimuli may have been, this report, taken with the personal observations of Lewis (1942), does mean that great caution is needed in interpreting the results of any study of sitting dental patients in whom arterial puncture has been performed. (See Bourne, 1957).

It may be objected that fainting does not occur during anaesthesia. De Wardener and associates (1953) found that controlled haemorrhage sufficient to trigger the fainting reflex in a high proportion of conscious subjects did not produce fainting in any of fourteen patients under light cyclopropane or light ether anaesthesia during operations on varicose veins. They suggested that the fainting reaction could be prevented by anaesthesia. If this be true, then it might possibly provide an explanation for some of those cases in which fainting, whatever its cause, appears to have been postponed until the end of anaesthesia.

On the other hand it should be remembered that it takes an appreciable time to obtain the full effect of nitrous oxide, and that early loss of consciousness during a nitrous oxide induction may be produced by hypoxia as well as by the anaesthetic properties of nitrous oxide. It is possible that there may be no protection against fainting under these circumstances. In this connection Sharpey-Shafer (1958) commented: "There is one example where fainting occurs with an anaesthetic: the dental gas".

Furthermore, hypotension with bradycardia, whatever its mechanism, can occur during nitrous oxide, oxygen and relaxant anaesthesia. Eather, Peterson and Dripps (1949), for example,

presented a continuous record of blood pressure under anaesthesia showing a fall from 122/66 to 85/57 mm Hg. during traction on the transverse colon. The blood pressure returned to its previous value on releasing the traction. Prime and Gray (1952) reported an example of hypotension in a man of 38 years towards the end of a partial gastrectomy under thiopentone, nitrous oxide and relaxant anaesthesia. The anaesthetist lightened the level of anaesthesia by decreasing the percentage of nitrous oxide administered. Soon afterwards, the patient, who had been quiet up to that time, was seen to be moving his fingers, and the blood pressure and the pulse rate fell while the forearm blood flow increased. This phenomenon has since been examined in more detail by Folkow et al (1961).

The carotid sinus

Burstein (1949) suggested that application of digital pressure in the carotid sinus area when supporting the jaw might result in bradycardia and hypotension. External pressure on the carotid sinus would be particularly easy to produce during dental extraction. The review of Weiss and Baker (1933), however, suggests that although this could happen with hypertensive patients, it would be most unlikely in normal patients. In 30 per cent of subjects with a normal cardiovascular system they found no response to mechanical stimulation of the carotid sinus, and in the remaining 70 per cent this manoeuvre produced a fall in the blood pressure of less than 10 mm Hg, and very little slowing of the heart rate. They reported in detail on 15 affected patients of whom 13 complained of spontaneous dizziness or fainting. 11 patients were over 50 years of age and usually the carotid sinus appeared to be involved in generalised arterial disease. These findings were later confirmed by a further review of 32 additional cases. (Ferris, Capps and Weiss, 1935).

The effects of external resistance to respiration

Conscious man usually breathes from and into the atmosphere with only the limitations of his own respiratory system to impede him. Anaesthetised man, breathing spontaneously, however, usually breathes through apparatus which offers additional resistance to gas flow. This resistance is usually incidental and it may be harmful.

A syncopal reaction has been reported in a young conscious male subject while breathing against a pressure of 20 cm H₂O (14.7 mm Hg), without hypoxia and while wearing a compensating vest - although the duration of the pressure breathing was not stated (Barach et al, 1947). Pressures of this magnitude may be approached for short periods during dental anaesthesia when the pressure in the mask is deliberately increased, with the intention either of deepening anaesthesia or of preventing dilution with air (Rolleston and Moncrieff, 1938; Minnitt and Gillies, 1945; Clement, 1951). It is possible that even lower mask pressures might have similar effects when combined with hypoxia, or with any of the other possible contributory causes of hypotension during anaesthesia.

Assessment of this possibility requires consideration of the pressure changes which occur during respiration, and of the effects of abnormal pressures in conscious and anaesthetised subjects. The following review may leave the boundaries of outpatient anaesthesia, but in so doing it draws attention to factors which could none-the-less be relevant.

The pressure changes occurring during respiration

During normal inspiration a subatmospheric alveolar pressure is necessary for the generation of inspiratory airflow. The pressure gradient across the respiratory tract, between the mouth and the alveoli, is related to the minute ventilation, to the inspiratory flow

pattern and to the resistance offered to airflow by the respiratory tract.

For the generation of expiratory airflow the alveolar pressure must be correspondingly raised above atmospheric pressure.

If apparatus offering resistance to airflow is interposed between the upper respiratory tract and the atmosphere, then the total resistance to airflow will be increased. If the same minute ventilation and the same respiratory flow pattern are to be maintained, then the inspiratory and expiratory pressure gradients between the alveoli and the atmosphere must be increased by the amounts needed to overcome the resistance of the apparatus. The alveolar pressure changes will be correspondingly increased.

The reduction in alveolar pressure required to bring about an inspiratory inflow of air is generated by the muscles of respiration. These exert an outward pull upon the walls of the thorax. The thorax expands and the outward pulling forces are transmitted from the thoracic walls to the alveoli via all the intervening structures. During expiration the respiratory muscles relax. The inward pull of the elastic structures now predominates. The alveoli are compressed and the alveolar pressure rises.

The active muscular effort of inspiration is usually performed more quickly than the passive expiratory recoil and the peak inspiratory flows are greater than the peak expiratory flows. When breathing through an external resistance, therefore, the peak pressure gradients across it will be greater during inspiration than during expiration and the alveolar pressure swings will be increased correspondingly. Although Cain and Otis (1949) found that the normal respiratory pattern was not maintained when conscious subjects breathed through an external resistance, the peak inspiratory flows remained greater than

the peak expiratory flows. The above argument, therefore, still applies.

If the volume of air expired through the external resistance equals the volume of air inspired through it, then the mean pressure change at the mouth over a complete respiratory cycle will depend upon whether the airflow through the external resistance is laminar or turbulent.

During laminar airflow through the external resistance the pressure drop across it will be proportional to the airflow through it. It follows that the mean pressure at the mouth over a complete respiratory cycle will be atmospheric. The external resistance, therefore, should not cause any change in the mean alveolar pressure, despite the greater increase in the peak inspiratory pressures than in the peak expiratory pressures.

If the airflow through the external resistance is turbulent, then the pressure gradient across it will not be proportional to the flow through it. As the flow increases the pressure gradient will increase more than would be expected during laminar flow, and this effect increases with increasing flows. Under the circumstances of turbulent flow the pressure gradient across the external resistance will be relatively greater during inspiration than during expiration as compared with the corresponding pressure changes occurring during laminar flow. The overall resistance to the inspiration of the tidal volume of air will therefore be greater than the resistance to its expiration. The mean pressure at the mouth over a complete respiratory cycle and the corresponding mean alveolar pressure will therefore be subatmospheric (see Mushin, 1955).

The resistance to respiratory airflow offered by an anaesthetic breathing system varies with the phase of respiration. Let a Magill semiclosed system be taken as an example (Mapleson system A.

(Mapleson, 1954b), Rotameters, reservoir bag, corrugated tubing, expiratory valve and mask connected in series). During inspiration the subject breathes through the resistance of the complete circuit up to the reservoir bag. Some of the energy required to overcome this resistance to inspiratory flow will have been imparted to the gas supply, according to the supply flow rate, and some will be provided by the energy stored in the distended reservoir bag. During expiration, after the expiratory valve has opened, the subject will breathe through the resistance of the circuit up to the expiratory valve and not through that part of the circuit between the expiratory valve and the reservoir bag. The mouth pressure during expiration will be governed by the pressure required to overcome the resistance of the circuit between the mouth and the expiratory valve, by the pressure exerted by the opposing gas supply, by the pressure required to open the expiratory valve and by the resistance opposing flow through it. In practice the characteristics of the expiratory valve become of major importance and a rise in mean alveolar pressure may be expected.

When using conventional dental anaesthetic breathing systems without a reservoir bag in the circuit, the flow of the nitrous oxide and oxygen mixture is usually adjusted to be within the range of normal inspiratory peak flows. The energy imparted to the supplied gases will therefore overcome resistance to inspiratory gas flow. Whenever this energy is greater than that required to overcome the external resistance to inspiratory flow the surplus will contribute to a rise in pressure at the mouth and therefore in the alveoli. This will apply throughout expiration and during a part of inspiration according to the pressure-supply-flowrate characteristics of the anaesthetic machine (see Chapters 7, 8 and 9).

The muscular and elastic forces which generate the changes in

alveolar pressure required for respiratory airflow are transmitted to all structures within the thorax, although there will be local variations due to the physical properties of individual tissues. The oesophagus, the heart, the blood and lymph vessels and sensory nerve endings in the thorax are all involved in pressure changes corresponding to those occurring in the alveoli. If local variations are ignored, the absolute value of the pressure applied to the structures lying between the alveoli and the chest walls may be considered to be equal to the alveolar pressure less that due to the inward elastic pull of the lungs. The latter will depend upon the degree of pulmonary distension. If the alveolar pressure swings are increased in order to overcome external resistance to airflow, then all intra-thoracic structures will be involved in correspondingly increased pressure swings. It follows that external resistances to airflow, according to their magnitude, direction and duration, may be expected to affect circulatory as well as respiratory function. Such effects may be modified by compensating reflexes.

The effects of abnormal airway pressures upon conscious fit, young, male adults.

Most of the experimental work concerned with the effects of abnormal airway pressures, upon conscious subjects, during spontaneous respiration, has been performed upon fit, young, male adults. The purpose of this work was to assess the possibility of applying positive airway pressures to aircrews flying at high altitudes in order to raise the partial pressure of inspired oxygen. The pressures used were higher than those that should be applied to anaesthetised patients, but the possibility of similar effects being produced in unfit anaesthetised patients at considerably lower pressures should be considered.

That changes in airway pressure do cause corresponding changes

in the pressure applied to the heart and the aorta was confirmed by Dern and Fenn (1947). They found that in subjects who are lying down the arterial pressure followed approximately the intrapleural pressure. The arterial pressure usually reached equilibrium within a minute of increased or decreased airway pressure. When positive airway pressures were applied to sitting subjects, however, the systolic blood pressure was found to rise more than when they were supine. With some subjects there was a fall in pulse rate. Barach and his colleagues (1946) reported corresponding changes in venous pressure. Using cardiac catheterization they demonstrated that the rise in peripheral venous pressure was equal to the rise in central venous pressure as measured in the right auricle during positive pressure breathing.

The above changes in systolic and venous blood pressure occurring in supine subjects during pressure breathing could be explained by mechanical transmission of pressure from the respiratory tract to the heart and the great vessels. Using lower limb plethysmography, however, Fenn and his co-workers (1947) demonstrated a reflex vasoconstriction during pressure breathing against 15 to 30 cm H₂O. The vasoconstriction was found to outlast the pressure breathing by 20 to 30 seconds. Further evidence of such reflex vasoconstriction was found by Fenn and Chadwick (1947), using finger plethysmography. The finger volume pulse was found to decrease for a few seconds immediately after the start of positive pressure breathing but rose to a level near normal on continued exposure to positive airway pressure. Upon return to normal breathing pressures the volume pulse rose above the original value for a short time and then subsided gradually. Individuals varied considerably in the degree and the time relations of their responses. Some individuals gave different results upon different

occasions. Confirmation of these results was given by de Lalla (1948) who demonstrated a drop in finger skin temperature during positive pressure breathing against 20 cm H₂O.

Fenn and his co-workers (1947), using a teeterboard, concluded that 500 ml of blood were displaced from the lungs of a supine subject while breathing against a pressure of 30 cm H₂O. Using a lower limb plethysmograph they also demonstrated an increase in lower limb volume at the onset of pressure breathing. The blood displaced from the chest during pressure breathing was replaced by air. In addition the chest expanded and Barach and his colleagues (1946) reported a 1000-ml change in "chest position" in subjects breathing against a pressure of 20 cm H₂O. They found a coincident increase in ventilation and in tidal volume of the order of 25 per cent.

An important longer term circulatory disturbance occurring during pressure breathing is a loss of circulating blood volume. Barach and his colleagues (1946) found a haemoconcentration and changes in blood oxygen capacity and in plasma protein concentration consistent with a loss of 300 ml from the circulating blood volume while breathing against a pressure of 20 cm H₂O for periods of up to 1 hour. One subject had a syncopal reaction during this series of experiments, even when wearing a pressure compensating vest. Barach and others (1947) recorded a loss of 4 per cent of the circulating blood volume after breathing against a pressure of 30 mm Hg (41 cm H₂O) for 30 minutes. This they attributed to capillary filtration caused by the elevated venous pressure. They concluded that most healthy young men can tolerate breathing against a continuous pressure of 20 cm H₂O, but that at higher pressures the incidence of collapse rises readily.

Discussing the significance of the loss of blood volume into the

limbs during pressure breathing, Henry (1951) mentioned two contributory factors, venous pooling and the filtration of fluid into the tissue spaces. Whereas venous pooling due to venous distension occurs rapidly, within seconds, filtration of fluid into the tissue spaces is more insidious. Both may be increased by a warm environment. Henry found that an upright seated man breathing against 60 mm Hg (82 cm H₂O) might pool approximately 150 ml extra blood volume when cool, and nearly 500 ml when hot. He estimated a loss of 2.9 per cent of the blood volume into the tissues when breathing against a pressure of 30 mm Hg (41 cm H₂O) for 20 minutes at 50°F. The comparable loss at 120°F was 5.1 per cent.

Recently Ernsting (1966) has re-affirmed that raising the intra-pulmonary pressure reduces the effective blood volume; that collapse occurs when the reduction exceeds 700 to 800 ml; and that collapse under these circumstances has all the features of vasovagal syncope and may be precipitated during pressure breathing by hypoxia, hypocapnia, discomfort and pain.

The effects of abnormal airway pressures during general anaesthesia.

In the context of anaesthetic practice the effects of increased airway pressure upon the circulation have been considered mainly in terms of the consequent rise in peripheral venous pressure, and the reduction of venous return to the heart. The possibility that reduced alveolar pressures occurring during respiratory obstruction might contribute to the production of pulmonary oedema has also been considered (Mushin, 1955). The effects of short-term airflow resistances upon ventilation during anaesthesia in supine subjects have been reported by Nunn and Ezi-Ashi (1961).

The most serious consequences of raised peripheral venous pressure probably occur in relation to head injuries and neurosurgery.

When the skull is intact a rise in venous pressure causes an increase in intracranial pressure. (Changes in intracranial pressure may be relevant to the headaches which sometimes occur following outpatient anaesthesia). When the skull is open it causes an increase in volume of the intracranial contents and an increase in venous oozing. It was in order to minimize venous congestion during neurosurgery that Ayre (1937a) introduced the T-piece technique. This, because it has no valves, offers a relatively low resistance to respiration. He also suggested that the technique might be used with advantage for operations upon the head and neck which can be hampered by venous oozing, and in particular during operations for the repair of hare-lip and cleft palate (Ayre, 1937b).

Little experimental work appears to have been reported upon the effects of intermittent positive expiratory pressures such as may occur during inhalational anaesthesia with spontaneous respiration.

During intermittent positive pressure respiration a major concern has been to assess the extent to which a raised mean intrathoracic pressure may impede the return of venous blood to the heart. The problems involved have been reviewed by Watrous et al (1950) and by Nunn (1957). Beecher, Bennett and Bassett (1943) observed that some patients would not tolerate even a moderate increase in airway pressure, while others showed signs of deteriorating circulation when an elevated airway pressure was maintained. On subjecting anaesthetised dogs to an airway pressure of 10 cm H₂O above atmospheric pressure they found a marked rise in venous pressure and a slight fall in blood pressure, blood flow and respiratory rate. If the blood volume of the dogs was first reduced by haemorrhage, then there was a pronounced fall in cardiac output which was attributed to a reduction in venous return to the heart. Knoefel and others (1945) found that the cardiac

output was reduced by 40 per cent after subjecting anaesthetised dogs to a raised airway pressure of 7 mm Hg (9.5 cm H₂O) for 3 hours, but there was little change in cardiac output over the first hour.

Cournand and his colleagues (1948) applied various patterns of positive airway pressure to human subjects during intermittent positive pressure respiration and concluded that cardiac output was decreased more or less in proportion to the increase in mean airway pressure. Maloney and others (1953) found no significant change during intermittent positive pressure respiration when applied to fit patients but in patients with circulatory inadequacy they found a serious fall in cardiac output and in blood pressure. This could be prevented by using a subatmospheric pressure of 10 cm H₂O during expiration. Enderby (1958) has drawn attention to the marked reduction in venous return caused by raised airway pressures following the administration of ganglion blocking drugs. Used with great care, moderation and skill, he has suggested that the use of positive pressure respiration under such circumstances might be of value in maintaining a steady controlled hypotension.

In clinical anaesthetic practice, with spontaneous respiration, relatively high expiratory pressures may be expected during dental anaesthesia using nitrous oxide and oxygen, since high supply flowrates and expiratory valves offering high resistance are frequently used. Furthermore, the respiratory depression usually associated with deeper anaesthesia should not occur. It might be relevant, therefore, to consider the blood pressure variations recorded during nitrous oxide and oxygen anaesthesia in the dental chair, even though the corresponding airway pressures and details of the gas flows supplied are not available.

Goldman, Cornwell and Lethbridge (1958) found that unsupplemented nitrous oxide and oxygen anaesthesia in the dental chair was associated

with a rise in blood pressure in 94 out of a series of 100 unselected patients. A rise in blood pressure of up to 10 mm Hg was recorded in 17 patients; of between 10 and 20 mm Hg in 29 patients; of between 20 and 30 mm Hg in 23 patients; and of between 30 and 40 mm Hg in 12 patients. The greatest rise recorded was 90 mm Hg which occurred in 2 patients. At the end of the period of anaesthesia the blood pressure fell, usually 5 to 10 mm Hg below the pre-operative level. Nine cases showed an initial fall of blood pressure but not to a level lower than occurred during the postanaesthetic period. Twenty-one patients showed an initial rise of blood pressure followed by a fall on the introduction of oxygen, but not to a level lower than that recorded during the postanaesthetic period.

Walsh (1958), while using halothane as a supplement to nitrous oxide and oxygen anaesthesia in the dental chair, noted that this drug had little effect in modifying the rise in blood pressure recorded by Goldman, Cornwell and Lethbridge.

This rise in blood pressure occurring during nitrous oxide oxygen anaesthesia in the dental chair may be related partly to the pressures at which the gases are respired. A rise in blood pressure equal to the rise in intrathoracic pressure should be expected. The observations of Dern and Fenn (1947), quoted above, suggest that higher pressures may be expected in sitting patients. The postanaesthetic fall in blood pressure reported by Goldman, Cornwell and Lethbridge (1958) is consistent with, although not necessarily related to, the rise in finger blood flow reported by Fenn and Chadwick (1947) as occurring immediately after pressure breathing. These changes, however, as mentioned above, may be related mainly to hypoxia, and perhaps also to surgical stimulation.

CHAPTER 4

THE CHARACTERISTICS OF ANAESTHETIC APPARATUS

The greater part of the section of this chapter on the flow resistance characteristics of anaesthetic breathing systems was included in Vickers Research Limited Report No. 21, which, with the Directors' permission, was subsequently published (Smith, W.D.A. (1961). The effects of external resistance to respiration. Part II: resistance to respiration due to anaesthetic apparatus. Brit.J.Anaesth. 33, 610).

It is convenient to consider anaesthetic apparatus under two main headings: anaesthetic machines and anaesthetic breathing systems. The function of an anaesthetic machine is to supply an anaesthetic mixture, of controlled composition, to a breathing system. The function of an anaesthetic breathing system is to facilitate the administration of the anaesthetic mixture to a patient. It should not be forgotten, however, that an anaesthetic machine, the breathing system which it supplies, and the patient to whom the anaesthetic is administered, may influence each other's behaviour according to their own particular characteristics.

In the context of the preceding chapters, two characteristics of anaesthetic apparatus are of special interest: the accuracy with which it can control the composition of an anaesthetic mixture, and its influence on the conditions of flow and pressure under which the anaesthetic mixture is administered to a patient.

Continuous flow anaesthetic machines

The commonest type of continuous flow anaesthetic machine used in this country is the 'Boyle' machine. Mixtures of oxygen and nitrous oxide (and/or cyclopropane) can be obtained from this machine by appropriate manipulation of needle valves controlling the flow of the gases through Rotameters. Properly calibrated and mounted, these are capable of providing an accuracy of ± 2 per cent (Macintosh, Mushin and Epstein, 1958). Using this apparatus, therefore, it should be possible to obtain a concentration of oxygen between 19.4 and 20.6 per cent by setting the bobbins of the oxygen and the nitrous oxide Rotameters to read 2 and 8 litres per minute respectively. For clinical purposes this accuracy is quite acceptable. Pressure fluctuations in the breathing system are usually small compared with the pressure gradient across the needle valves and

the Rotameters, so they have little effect on the gas flows delivered.

Few of these machines are designed to supply total gas mixture flow rates of more than 12 to 15 litres per minute. This is less than the peak inspiratory flow rate of most anaesthetised patients, so it is necessary to use a Boyle anaesthetic machine with a breathing system in which a reservoir bag is incorporated. On the other hand, 12 to 15 litres per minute is greater than the minute volume of the average anaesthetised patient. Even flow rates as high as this, however, may not be adequate in the face of pronounced hyperventilation (e.g. in response to the administration of an hypoxic anaesthetic mixture, or to surgical stimulation under very light anaesthesia). It may also be an advantage to supply higher flow rates if there is a major leak between the patient and the breathing system, such as may occur when a patient breathes partly through the mouth while the anaesthetic is being administered through a nose-piece. This is why continuous flow anaesthetic machines tend to be unpopular for dental anaesthesia.

If a Boyle anaesthetic machine is used for delivering a supplementary volatile anaesthetic, the accuracy with which this agent may be controlled depends upon the particular vaporizer employed.

Intermittent flow (Demand) anaesthetic machines

Intermittent flow anaesthetic machines are designed to provide independent control of the relative flows of nitrous oxide and oxygen (by means of a mixture control), and of the total flow of the mixture of nitrous oxide and oxygen (by means of a "pressure" control). There is also a deliberate interaction between the pressure in the breathing system and the behaviour of the anaesthetic machine. According to the setting of the "pressure" control, flow is first

reduced and then stopped altogether as the pressure in the breathing system rises. In this way the supply of the anaesthetic mixture is reduced or stopped during expiration, and it is at a maximum during inspiration. Flow rates up to 100 to 150 litres per minute can be supplied, provided that the flow resistance of the breathing system is low. Under these circumstances it becomes possible to consider dispensing with the reservoir bag. This general type of machine tends to be used for dental anaesthesia and for obstetrical analgesia.

As these anaesthetic machines do not provide for independent measurement and control of individual gas flows, the anaesthetist has no ready means of knowing the accuracy of the calibration of the mixture control, except by watching the reactions of the patients, and this is not acceptable as the sole means (see preceding chapters and chapter 9). It is important, therefore, that the calibration of these machines should be stable and accurate with prolonged use and under all conditions of use. Regrettably this is not always the case, and in many of the older machines, the pressure developed in the breathing system influences the proportions of oxygen and nitrous oxide delivered for a given setting of the mixture control (Goldman, 1958; Hunter and Fraser, 1959; Bourne, 1960; Nainby-Luxmore, 1967). An indication of the number of old machines in use in 1963 may be gathered from the following record of the various types of dental anaesthetic machine then on the files of the British Oxygen Company as in use. (Sales representatives used to keep a record of the dental anaesthetic machines they found deployed. The data on the Walton series of machines, manufactured by the British Oxygen Company, is likely to be the most accurate. I am greatly indebted to Mr. D. C. Smith of the British Oxygen Company for

this information, and for permission to quote it).

WALTON ONE	417	
WALTON TWO	2184	
WALTON THREE	1140	
WALTON FOUR	349	
	4090	
WALTON FIVE	556	
McKESSON	1907	(both old and new types)
JECTAFLOW	276	
OTHERS	534	

A Walton Five anaesthetic machine, methods of testing it, and its performance, are discussed in chapter 8. The Cyprane A.E. Dental Anaesthetic Machine probably has comparable performance (Hunter and Fraser, 1959).

The performance of these machines when set to supply anaesthetic mixtures at low flow rates, however, does not appear to have been fully explored. Since the work described in this thesis was started, there appears to have been an increasing tendency to avoid hypoxia when administering dental anaesthesia, and to supplement nitrous oxide and oxygen anaesthesia with halothane and/or intravenous agents. Hyperventilation, therefore, is less likely to be encountered. Young and Whitwam (1964) have also published a method of administering dental anaesthetics using a reservoir bag and a non-rebreathing system connected to a Walton Five anaesthetic machine. This could encourage the use of low supply flow rates, especially when anaesthetising children. The performance data on the Walton Five Machine, as supplied by the manufacturers, suggests that the concentration of oxygen

delivered does tend to fall off, for a given setting of the mixture control, when flow rates of less than 20 litres per minute are delivered.

Flow resistance characteristics of anaesthetic breathing systems

The elements used to make up a breathing system may include conducting tubing, reservoir bag, relief valve, and a mask or an endotracheal tube and its connections. The flow resistance characteristics of this apparatus must be understood before the influence of breathing systems upon anaesthetic machines and upon patients can be discussed.

Resistance to airflow through anaesthetic apparatus, is usually measured in terms of the pressure gradient occurring across it during the maintenance of a known airflow through it. Nearly all the measurements reported in the literature have been made under steady flow conditions (Macon and Bruner, 1950; Gaensler, Maloney and Bjork, 1952; Crkin, Siegel and Rovenstine, 1954, 1957; Mushin and Mapleson, 1954; Bullough, 1955; Galloon, 1957; Macintosh, Mushin and Epstein, 1958; Chandler, 1958).

The experimental method described by Gaensler, Maloney and Bjork (1952) has been adopted by subsequent workers. They arranged for a steady airflow to be supplied to the item under investigation through a large container, the other end of the item being open to atmosphere. The pressure gradient between the container and the atmosphere, that is, across the anaesthetic item, was measured while a steady known flow was passed through it. An advantage of this method, as observed by Macintosh, Mushin and Epstein (1958), is that since the linear velocity of the air passing through such a container is small, the pressure changes due to kinetic energy effects are negligible. On the other hand, the large dead space

involved prohibits the use of this method for making measurements during actual respiration.

Orkin, Siegel and Rovenstine (1954, 1957) concluded that the overall resistance of combinations of anaesthetic equipment equalled the sum of the resistances of their individual components. This has not been a universal finding. Bullough (1955) for example, found that the resistance of a Cobb endotracheal connector was reduced by connecting an endotracheal tube to it. Macintosh, Mushin and Epstein (1958) noted that the overall resistance of an endotracheal tube combined with a connector was usually less than the sum of the individual resistances.

Macintosh, Mushin and Epstein (1958) drew attention to the inadequacy of measurements made under steady flow conditions as an indication of the resistance to the intermittent flows that occur during respiration. Cooper (1961) also affirmed that the present methods of testing breathing apparatus were unsatisfactory. Little work, however, appears to have been done on the measurement of the resistance to airflow through anaesthetic apparatus under varying flow conditions. Hunt (1955) compared the resistances of disc valves and of canisters under steady flow and under varying flow conditions. He found close agreement between the measurements of resistance made under the two sets of conditions. The variable flow was generated using a variable stroke plunger in a cylinder and a specially cut cam. The variations in flow so produced were not as rapid as the rate of change of flow that may occur during normal respiration. The flows were calculated from the speed of the driving motor and the instantaneous position of the piston. A capacitance pressure transducer was used for pressure measurements under varying flow conditions.

What was required was a method of measuring the flow-pressure characteristics of apparatus under circumstances comparable with those of its actual use. The description of such a method, and its application, is given in chapter 7.

While breathing into an anaesthetic breathing system gas has to be moved against resistance. Considering the system from the point of view of its possible effect upon the patient, it might seem logical to explore the possibility of assessing the system in terms of the cost to the patient of moving a given volume of gas through the system, under respiratory flow conditions. This was not attempted, but Cooper (1961) adopted this approach for the assessment of respiratory apparatus. For conscious miners, rescue workers etc. he recommended that the total rate of respiratory work done on a breathing apparatus, expressed as $\text{kg} \cdot \text{m} / \text{min}.$, should be not greater than one quarter of the minute volume in $\text{l} / \text{min}.$ and preferably not greater than one half of this standard; and that expiratory work should comprise not more than 50 per cent of the total.

CHAPTER 5

PLAN OF AN INVESTIGATION OF OUTPATIENT
ANAESTHESIA, WITH PARTICULAR REFERENCE TO
ANAESTHESIA IN THE DENTAL CHAIR

The plan of investigation outlined in this chapter began to take shape while I was an Anaesthetic Registrar in the Southampton Hospital Group, in 1959. It arose from the clinical studies described in Chapter 2. The plan was developed, and some of the early work was carried out, while I was holding a Research Appointment at the Vickers Group Research Establishment in 1959-60 (Chapter 7). The overall plan was completed during late 1960 and early 1961, while holding a Wellcome Research Fellowship at the Research Department of Anaesthetics, the Royal College of Surgeons of England.

In the light of personal experience and published data it seemed that there was a strong case for further research into outpatient anaesthesia. So far as considerations of safety were concerned, two aspects of the problem were obviously inseparable: the measurement of the anaesthetic techniques actually used, and the measurement of relevant physiological changes in the patients.

Although from time to time anaesthetists have described their favourite techniques, and their disciples have claimed to have used them, precise knowledge of the procedures, the time sequences and the circumstances of given routine administrations have usually been lacking. It seemed important, therefore, to make an attempt to define the precise technique employed with every anaesthetic investigated.

Anaesthetic techniques vary with the beliefs, the experience and the ability of individual anaesthetists. In some centres each anaesthetist is a law unto himself. In others, the techniques used by different anaesthetists tend to follow a common pattern. Before seeking clinical facilities for research into outpatient anaesthesia, therefore, a decision had to be made as to the type of anaesthetic technique which it was desirable to investigate. I decided that, in the first instance, it would be preferable to carry out a pilot study of a reasonably broad spectrum of anaesthetic techniques, so I sought a centre where there was no dominant opinion in favour of any particular technique. I hoped that, in the light of the experience gained with the pilot study, it might then be possible to persuade different anaesthetists at the same centre to use different techniques, so that these might be compared. This part of the overall plan, however, did not materialise.

My interest was in outpatient anaesthesia in general, but there were two good reasons for choosing to investigate dental anaesthesia in particular. In the first place, although it may be questionable whether

the majority of the general anaesthetics administered for dental surgery are absolutely necessary, by far the greatest number of outpatient anaesthetics are administered for this purpose. Secondly, the potential hazards of anaesthetics administered to upright patients for oral surgery are, on the whole, greater than those administered to supine patients for surgical operations which do not encroach upon the upper respiratory tract.

These considerations led to facilities being sought at the Royal Dental Hospital of London, and they were most generously granted. Added advantages of carrying out the study at a reputable Teaching Hospital were that the techniques studied were likely to be closely related to those used by past students, and therefore in fairly extensive use; and that there was a sufficient attendance of patients to make a study of a reasonable number of anaesthetics a practical proposition.

Despite the potential risks of dental anaesthesia, the chances of meeting serious anaesthetic difficulties in a single manageable series of well conducted administrations would appear to be small. Seldin (1947), for example, reported that one surgeon, who practised "secondary saturation" (McKesson, 1920), met one case of delayed recovery following anaesthesia, per 3,000 anaesthetics. Bourne (1957, 1960) concluded that there were about 500 cases per year in the United Kingdom of delayed recovery of half an hour or more following dental anaesthesia. If the total number of dental anaesthetics administered per annum at that time be taken as about 2,000,000, then one such case of delayed recovery might be expected for every 4,000 dental anaesthetics. McConnel (1958) suggested that an experienced dental anaesthetist might see the results of oxygen lack, with grave threat to life, about once in 2,000 cases. Even this incidence of serious hypoxic phenomena makes the investigation of it under clinical conditions a formidable task. If

morbidity since that time has followed the same trend as mortality (Chapter 3), a much lower incidence may now be anticipated.

For these reasons, it was desirable to include as many patients in the pilot study as possible. The number actually included was governed by the fact that the most favourable time for carrying out the investigation was the month of August, when students did not attend the "gas room".

The above figures confirm that for every patient who has died as a result of the performance of a dental operation under general anaesthesia as an outpatient, a number came alarmingly near to death or permanent cerebral damage. Likewise one might expect that for every patient who has been near to death, a number have probably given some indication of an approach to danger. Jactitation is an obvious example, but one would expect other clues, and it was partly with this possibility in mind that the clinical investigation was launched. There seemed to be a fair chance that useful information might be gained even from a pilot study.

In order to include as many patients in the study as possible, it was essential that the apparatus used should work well under the somewhat hectic circumstances of outpatient dental anaesthesia, and that the methods of measurement should interfere as little as possible with normal routine.

As a means of obtaining background physiological data relevant to the circumstances of dental anaesthesia; and of developing and perfecting the apparatus, adapting it for its intended employment under clinical circumstances, and of gaining expertise in its operation; preliminary studies to be carried out on volunteers in the laboratory were also planned.

No inhalation dental anaesthetic can be defined without knowledge

of the concentrations of nitrous oxide, supplementary agents and oxygen administered from moment to moment. Continuous analysis of the inhalation anaesthetic mixtures administered would have been the most desirable means of obtaining this information, but this was impracticable at the time. The alternative was to use an anaesthetic machine of known and stable calibration. A Walton Five anaesthetic machine was accordingly obtained on loan from the British Oxygen Company in order that it might be used throughout the preliminary study on volunteers and the clinical study at the Royal Dental Hospital of London - after its performance had been assessed under realistic test conditions. Test conditions had to be defined, and it was found that there was a paucity of quantitative information on respiration during dental anaesthesia, so it became a secondary purpose of the clinical study to make good this deficiency.

Related to the performance of a dental anaesthetic machine are the pressure fluctuations to which it is subjected. These depend upon the respiratory pattern of the patient and upon the pressure-flowrate characteristics of the breathing system used. In addition to the effects of patient and breathing system upon the performance of the anaesthetic machine, the breathing system may, at least temporarily, deliver a different gas mixture to the patient from that delivered by the anaesthetic machine. An understanding of the performance of anaesthetic breathing systems, therefore, was required in order to define realistic conditions for testing dental anaesthetic machines, and in order to interpret the results of the clinical study. Appropriate studies were planned (Chapters 7 and 9).

There are difficulties in making measurements during routine dental anaesthesia. The apparatus used with patients must be capable of rapid application, adjustment and removal, and it must inconvenience

neither the patients nor the hospital staff. These considerations limit the methods of investigation available.

Ideally, the crucial measurement during dental anaesthesia would be cerebral oxygenation, which would be indicated by the oxygen tension in venous blood draining the brain. The next best would be the oxygen tension in arterial blood together with cerebral blood flow. Direct measurements of these are obviously out of the question. Continuous measurement of arterial blood pressure, to which cerebral blood flow is related, was used by Bourne (1957, 1960), but this does not meet the above requirements for routine conditions, and arterial puncture in conscious sitting patients may itself precipitate fainting (Chapter 3). It was decided to accept the very indirect measurements of systolic blood pressure, pulse rate, and the oxygen concentration delivered by the anaesthetic machine (determined from its previous calibration), as practicable, even if very inferior alternatives. Suitable means for making and recording these measurements had to be developed and tried out during the studies on volunteers.

Of the various factors relevant to the safety of dental anaesthesia, which are reasonable to investigate in conscious sitting volunteers, are the effects of low and high inspired oxygen concentrations and/or the effects of a raised pressure in the breathing system during expiration, upon systolic blood pressure, pulse rate and respiration. A study of these factors in volunteers was planned. For this purpose the Walton Five anaesthetic machine was recalibrated for mixtures of oxygen and nitrogen, and apparatus had to be developed for controlling the pressure in the breathing system regardless of the subject's breathing pattern. Pressure in the breathing system was recorded continuously by electromanometry during both the study of conscious volunteers and during the clinical investigation.

The overall plan leading up to the clinical investigation is summarised by the Contents of this volume, under the headings of Parts II and III. Part IV covers the clinical study and this is in Volume 2.

The first requirement of the plan was a study of anaesthetic apparatus (Part II) which was necessary before the final object of a clinical investigation could be achieved. An investigation of the pressure-flowrate characteristics of anaesthetic apparatus is described in Chapter 7, and this is followed by an assessment of the performance of a Walton Five anaesthetic machine in Chapter 8. The effect of breathing systems in modifying the anaesthetic mixtures delivered to a patient is dealt with in Chapter 9.

The second requirement before achieving the final clinical objective was a study on volunteers (Part III). The apparatus developed for measuring and recording indirect systolic blood pressure and pulse rate; the apparatus developed for controlling the pressure applied to volunteers; and the plan of the study on conscious volunteers, are described in Chapter 10. The results are given in Chapter 11. An additional study of the effects of different mixtures of nitrous oxide and oxygen, and of pressure within the breathing system, upon speed of induction of anaesthesia, was added later and this is covered in Chapter 12.

The plan was to be completed by a clinical study of routine dental anaesthesia (Part IV). The methods used are described in Chapter 13, and the patients' reactions in Chapter 14. Data on conditions of respiration during anaesthesia are reported in Chapter 15.

Plans were prepared later for a comparison of different anaesthetic techniques - along the above general lines - together with further assessments of anaesthetic apparatus, further studies on volunteers,

and follow-up studies on patients, but it did not become possible to put these into effect. A few observations on a small pilot study of recovery from outpatient anaesthesia for orthopaedic procedures, however, are offered in Appendix E.

As mentioned at the end of Chapter 2, consideration of the most satisfactory means of giving a safe and effective outpatient anaesthetic brings one face to face with many of the really basic concepts of anaesthesia. My reasons for subsequently directing attention to pharmacokinetic aspects of the subject (Part V of this thesis) were also based upon clinical considerations, and they are explained in Chapter 16.

PART II: STUDIES OF ANAESTHETIC APPARATUS

CHAPTER 6

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CHAPTER 6

METHODS OF MEASUREMENT OF PRESSURE
AND GAS FLOW RATE

The author was first introduced to the Respiratory Analyser by Dr. K. G. Williams and Dr. Peter Scott at Vickers Research Limited, Sunningdale, in 1960. This apparatus was subsequently purchased by The Wellcome Trust for the Research Department of Anaesthetics, The Royal College of Surgeons of England, where he continued to use it.

The Parkinson and Cowan C.D.1. dry gas meter was checked at Watson House by Mr. C. P. Henshilwood and Mr. Sharman.

Experiments described in chapters 7, 8 and 9 entailed the measurement of steady and fluctuating pressures and flow rates in anaesthetic apparatus. The methods used are described in this chapter.

Additional problems associated with the measurement of flow rate during respiration - due to changes in temperature and humidity between inspiration and expiration, and due to changes in the composition of gases respired during the induction of anaesthesia - are considered in chapters 17 and 19 and in appendix A.

MEASUREMENTS DURING CONDITIONS OF STEADY FLOW

Pressure

Pressures relative to atmospheric pressure, and pressure gradients across items of apparatus, were measured by means of an inclined manometer for values of 2 cm H₂O or less, and by means of a U-tube water manometer for greater values.

Flow rates of air

Rotameters of appropriate range, calibrated for air at 760 mm Hg and 16°C, were used for measuring air flow rates.

Flow rates of gas mixtures other than air

A Rotameter calibrated for air flow over the range 14 to 150 l/min was recalibrated for mixtures of nitrous oxide and oxygen, and nitrogen and oxygen, containing 0, 20, 50 and 100 per cent oxygen.

Known gas mixtures were obtained from a calibrated Walton Five anaesthetic machine (see chapter 8), and passed through the Rotameter in series with a Parkinson and Cowan C.D.1. dry gas meter. (The calibration of the dry gas meter at different flow rates had been checked previously at the Gas Council's Watson House meter laboratory, and it was subsequently adjusted and rechecked

by the makers.) For each gas mixture flows were adjusted to give readings on the Rotameter scale of 30, 50 and 100 l/min. Meanwhile, using a stopwatch, the time for a given volume of gas mixture to pass through the gas meter was noted. The true flow rate was then calculated, and the correction factor to be applied to the Rotameter reading for each of the gas mixtures at each of the flow rates used was determined. For a given gas mixture there was little difference between the correction factors derived for each flow rate. The mean of these was therefore taken as the correction factor for that gas mixture. The experimentally determined correction factors are shown in figure 6.1. They were related to the density of the gas mixtures used.

Flow rates during "free flow"

The pressure drop across the bobbin of the Rotameter provided an impediment to flow from the Walton Five anaesthetic machine. When testing this machine under conditions of "free flow", therefore, a low flow-resistance flow transducer (pneumotachograph) was used for measuring flow rate. It is described below.

MEASUREMENTS DURING CONDITIONS OF VARYING FLOW

The Vickers Research Limited Respiratory Analyser and associated transducers

For measurements under conditions of actual or simulated respiratory flow, Vickers Research Limited pressure and flow transducers were used in conjunction with a Respiratory Analyser (Scott and Williams, 1960; Williams, 1960). The ranges of the capacitance type pressure transducers were ± 25 cm H₂O, ± 7.5 cm H₂O and ± 0.5 cm H₂O. The latter was used with the flow transducer having linear pressure-flow characteristics up to flow rates of 200 l/min of air.

The Vickers Research Limited flow transducer (pneumotachograph head) consists of a series of near parallel plates, 2.2 cm wide and 5.1 cm long, contained within a closely fitting hollow body which is open at both ends. Near each end is a pressure tapping. Each pressure tapping communicates with a circumferential groove on the inner aspect of the hollow body. The grooves are 31 mm apart. They serve to average any small differences in pressure around the circumference of the assembly of plates, in the plane of the pressure tapping. The pressure gradient along the length of the plates between the two pressure tapping points may be measured using an appropriate pressure transducer. The pressure gradient for the transducer used was 0.5 cm H₂O for a flow of air of 200 l/min.

The characteristics of the Vickers Research Limited flow transducer are not altered by the condensation of water from expired air because the plates of the flow-resistance element are made of hydrophobic material and they are well spaced. Electrical heating of the transducer is unnecessary.

The capacitance pressure transducers for measurement of pressure, and, in conjunction with the flow transducer, for the measurement of flow rate, are connected to the "pressure" and "flow" input sockets on the Respiratory Analyser respectively. The output channels may be switched to give signals proportional to the pressures and the flows being measured. An electronic integrator can also be switched into circuit for integration of "flowrate" voltages with respect to time, to produce output signals proportional to volume. (Output signals proportional to work and rate of work are also available but they were not used in these experiments).

Calibration

The pressure transducers were calibrated against the manometers.

The flow transducer was calibrated against the Rotameter using airflow generated by a pump, or mixtures from the Walton Five anaesthetic machine, as appropriate. The experimentally determined correction factors are shown in figure 6.2. They were related to the viscosities of the gas mixtures used.

The flow transducer was calibrated using room air and dry gas mixtures at room temperature. No corrections were made for humidity and temperature when the flow transducer was used while a subject breathed through anaesthetic apparatus in some of the experiments described in chapter 7. These experiments, however, did not call for precise measurements.

Frequency response of the pressure transducers

A pistophone was not available for checking the frequency response of the pressure transducers. There is reason to believe, however, that the frequency response of the ± 0.5 cm H₂O transducer was barely adequate for the measurement of changes in flow rate during respiration. This transducer has a silvered 'Melinex' diaphragm which has not the stiffness of the metal diaphragms of the ± 7.5 cm H₂O and ± 25 cm H₂O transducers. Figure 7.10, for example, suggests that the ± 0.5 cm H₂O transducer lagged behind the pressure drop across the flow transducer during early inspiration and expiration, when the rate of change of flow rate is greatest. There appeared to be no lag during the later parts of inspiration and expiration.

Further confirmation was obtained by making a direct comparison between the ± 0.5 cm H₂O transducer and the ± 7.5 cm H₂O transducer. They were both connected to the same flow transducer. The two output signals from the Respiratory Analyser were connected to the X and Y plates of a cathode ray oscilloscope respectively. The amplitudes of the final signals from the two channels were adjusted to be the same. During slow quiet respiration a straight line at 45° to the axes was obtained. With rapidly changing flow rates during rapid respiration, however, open figures were obtained on the oscilloscope.

When comparing pressure-flow characteristics measured during respiration with those measured during conditions of steady flow, peak values were used.

FIGURE 6.1

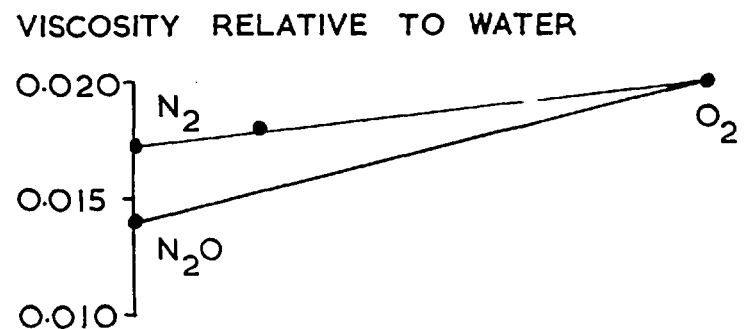
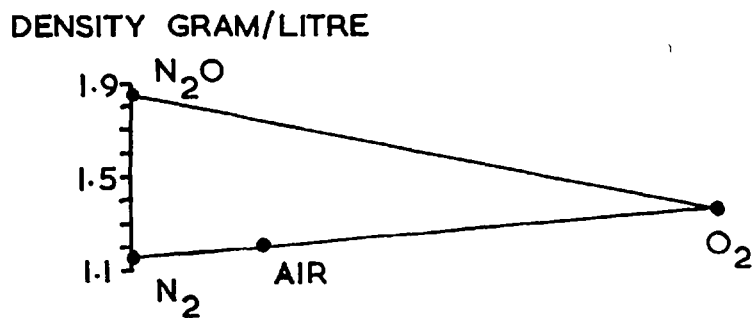
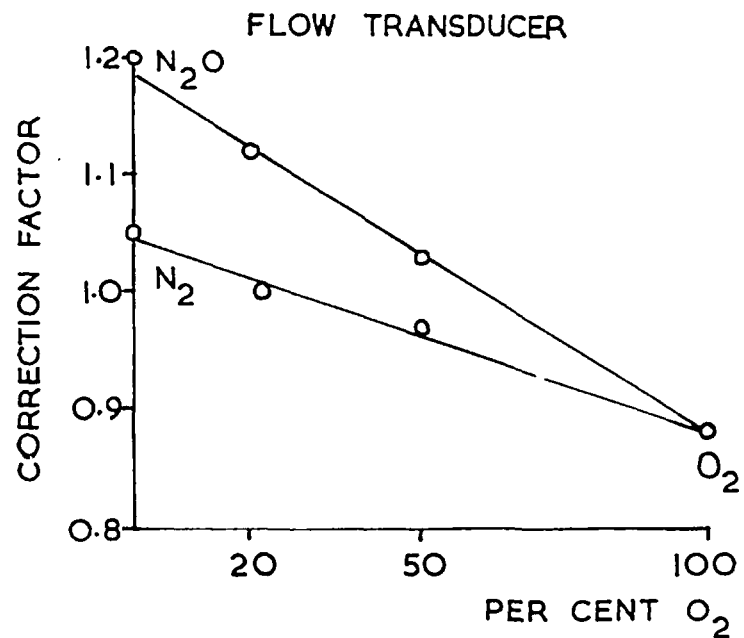
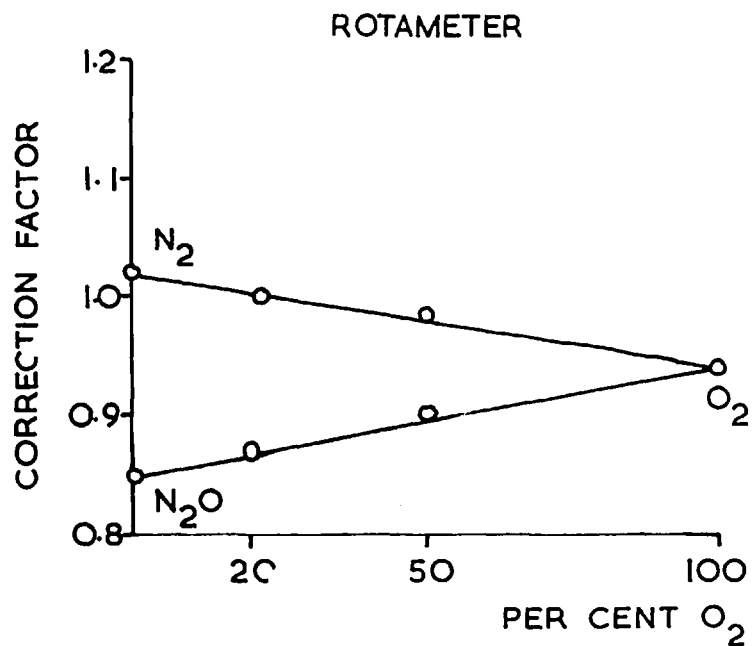
The experimentally determined correction factors for the 14-150 l./min Rotameter calibrated for air, when used with mixtures of nitrous oxide and oxygen, and of nitrogen and oxygen.

The densities of these gas mixtures are indicated for comparison.

FIGURE 6.2

The experimentally determined correction factors for the Vickers Research Limited flow transducers calibrated for air, when used with mixtures of nitrous oxide and oxygen, and of nitrogen and oxygen.

The viscosities of these gas mixtures are indicated for comparison.



CHAPTER 7

PRESSURE/FLOW CHARACTERISTICS OF
ITEMS OF ANAESTHETIC BREATHING APPARATUS

This work was carried out during a nine-month research appointment held at the Vickers Group Research Establishment in 1959-60. Dr. K. G. Williams and Dr. P. Scott gave helpful advice and encouragement. It was first written up as Vickers Research Limited Report No. 21. Later, with the Directors' permission, it was published. (Smith, W. D. A. (1961). The effects of external resistance to respiration. Part II: resistance to respiration due to anaesthetic apparatus. *Brit. J. Anaesth.* 33, 610.)

The purpose of this investigation was to measure and compare the resistance to steady gas flows, and to the varying gas flows occurring during normal respiration, of some commonly used anaesthetic apparatus. A preliminary study of the pressure-flow characteristics of semiclosed anaesthetic breathing systems has also been made. The items of equipment investigated were: a Magill attachment consisting of a reservoir bag, a corrugated rubber tube with its end fitting and a Heidbrink expiratory valve; an endotracheal catheter mount; a No. 4 Cobb suction union; a No. 9 curved Magill endotracheal connector*; a No. 10 endotracheal tube ** and a Coxeter expiratory valve. These items were considered individually, connected together and assembled to form the equivalent of semiclosed anaesthetic systems.

The effect of each arrangement upon the respiratory pattern of a conscious seated subject was recorded. These records were not analyzed in detail but the peak flow rates should give an indication of the gas flows that anaesthetic apparatus should be capable of accepting without undue impediment.

The pressure required to fill the reservoir bag used in this investigation was measured under both static conditions and under dynamic conditions equivalent to those under which it would be used in clinical practice.

The same subject was used throughout the investigation as a source of variable respiratory flow. The airflow resistance of his

* 8 mm I.D. at entrance to endotracheal tube.

** 9.5 mm I.D.

nose and nasopharynx was determined in order to put the measured resistances of the anaesthetic equipment into perspective

METHODS

The method of Gaensler, Maloney and Bjork (1952) (see chapter 4) was not used because the deadspace in the large container would have been excessive for the respiratory flow experiments. A method equally suitable for measurements under both respiratory flow and steady flow conditions was needed.

A symmetrical arrangement was tried. Tubes of equal length were fitted snugly over each end of the anaesthetic item. A simple pressure tapping was made in each tube. For steady flow measurements known airflows were passed into the open end of one tube and the corresponding pressure differences between the pressure tappings were measured using the appropriate manometer. For measurements under respiratory flow conditions the subject breathed through the flow transducer into the open end of the same tube, the appropriate pressure transducers being used in conjunction with the Respiratory Analyser for flow and pressure measurements. Using this method it was found that consistent results could be obtained during a given experiment. Examples are shown in figure 7.1. Even under steady flow conditions, however, the results were not repeated quantitatively from day to day. They were found to be dependent upon the precise way in which the experiment was set up, particularly with regard to the pressure tappings. The method was abandoned.

It was decided to make all pressure measurements relative to atmosphere and to make them always from the same pressure tapping. One of the carefully designed pressure tapping points

incorporated in the flow transducer was used for the purpose. Anaesthetic items were arranged only as they might be connected in actual use. The flow transducer was connected to the anaesthetic item, or system, at the end which would normally be in direct communication with the patient's airway. For making the connection between the flow transducer and the endotracheal tube a special connector was drawn from glass tubing, one end having the same internal diameter as the entrance to the flow transducer and the other end being made just large enough to accommodate the end of the endotracheal tube (an alternative to the special glass connector, in the form of a simulated trachea, might have been preferable, but this was not tried).

For measurements under steady flow conditions air was blown into and sucked out of the flow transducer via a Rotameter. The pressure tapping on the flow transducer nearest to the anaesthetic apparatus was connected to a manometer for measurement of the pressure gradients across the apparatus corresponding to the known flows passing through it. The second flow transducer pressure tapping was occluded to prevent air leakage.

For measurements under respiratory flow conditions a conscious seated subject breathed into the open end of the flow transducer using either a mouthpiece consisting of a short wide bore tube, his nose being clipped, or a standard anaesthetic face-piece. Pressure and flow were recorded continuously. The same pressure tapping was used for pressure measurements under respiratory flow conditions as was used during the steady flow experiments. The tubing used to connect the pressure tapping points to the pressure transducers was kept as short as possible and each tube was cut to the same length. During the course of

each series of measurements the dynamic measuring equipment was calibrated for flow rate in both directions and for pressures above and below atmospheric pressure.

RESULTS

The pressure-flow characteristics of tubular items under steady flow conditions

Using the above arrangement the characteristics of the flow transducer plus the glass connector were determined. Steady flows in both directions, in increments of 10 l./min up to 100 l./min., were passed through the system while corresponding pressures with respect to atmosphere were measured. The end of the endotracheal tube was then inserted into the open end of the glass connector and the pressure measurements were repeated, using the same flows as before. These measurements were repeated as the Magill endotracheal connector, the rubber tubing of the catheter mount, the metal fitting of the catheter mount and the Heidbrink valve were each in turn added to the system. Finally a further series of measurements were made using the Cobb suction union in the system instead of the Magill endotracheal connector.

This arrangement has the advantage of measuring all resistances from the standpoint of a subject breathing through the apparatus, and resistance and streamlining effects at the junctions between the items of anaesthetic equipment are automatically included in the measurements. The results are shown in figures 7.2 and 7.3.

By taking the differences between successive pressure readings at a given flow rate, the contribution of each item to the resistance of the system may be derived. These values indicate

the resistance offered by each item only in the context of the particular arrangement described, which is also the arrangement in which it would be employed in clinical practice. The derived characteristics are shown in figure 7.4. The values plotted were obtained from experiments carried out on two entirely separate occasions between which all the apparatus had been dismantled. They indicate how constant are the results of repeated experiments carried out by this method.

The pressure-flow characteristics of the corrugated tube and reservoir bag fitting were then determined with the reservoir bag tap open. The same general method as above was used except that the tubing was connected directly to the flow transducer, the glass connector being omitted. At a flow rate of 100 l./min the pressure between the ends of the tube lying straight upon a bench was 0.6 cm H₂O. Connection of the reservoir bag and end fittings increased this to 1 cm H₂O. At 45 l./min the resistance of the corrugated tube, reservoir bag and end fittings was only 0.25 cm H₂O. These pressures are very small in relation to the pressures, developed at comparable flow rates, across items of anaesthetic equipment to which the tubing is usually connected.

The pressure-flow characteristics of tubular items under respiratory flow conditions

The same assembly and arrangements of anaesthetic equipment were re-examined under respiratory flow conditions. The seated subject relaxed as much as possible and breathed quietly through the open end of the flow transducer. When respiration had become stable, continuous recordings were made of pressure and flow while breathing through each arrangement of the equipment. Recording was then continued while the subject varied the

amplitude of his respiration. The measurements of pressure and flow under steady flow conditions were repeated before disturbing the assembly and these measurements were used for comparison with those obtained under respiratory flow conditions.

Any phase difference between the recorded peak flows and the corresponding peak pressures was negligible. For each arrangement of the equipment peak flows were plotted against the simultaneously recorded peak pressures together with the values for flow and pressure obtained under steady flow conditions. For all practical purposes the characteristics determined under the two sets of conditions were identical. Three examples are given. Figure 7.5 shows the characteristics of the end of the flow transducer plus the glass connector plus the endotracheal tube. Figures 7.6 and 7.8 show the characteristics of the complete assembly using the Magill endotracheal connector and the Cobb suction union respectively. The range of values recorded during quiet stable respiration is indicated. Typical respiratory flow and pressure patterns are shown in figure 7.7.

Although the pressure and flow peaks appear to occur simultaneously and to be consistent with the pressure-flow characteristics determined under steady flow conditions, it does not necessarily follow that the same correlation applies throughout the respiratory cycle. Two records of simultaneous pressure and flow, each of a complete respiratory cycle, were examined in detail. Both records were made while the subject was breathing through the assembly described above, one including the Magill endotracheal connector and the other the Cobb suction union. Simultaneous pressures and flows occurring at a number of instants during each cycle were measured. They are shown plotted in

figure 7.10. The previously determined pressure-flow characteristics, as indicated in figures 7.6 and 7.8, are shown as broken lines. It can be seen that during the first part of each half-cycle, while pressure and flow are increasing rapidly, the measured pressure rises more rapidly relative to the simultaneously measured flow than would be expected from the results of the previous experiments. During the second part of each half-cycle, while pressure and flow are waning more gradually, the pressure-flow characteristics follow almost exactly those previously determined.

A less laborious method of demonstrating the instantaneous variations of pressure-flow relationships throughout a respiratory cycle is to feed the output voltages from the Respiratory Analyser, which are proportional to the flows and pressures being measured, to the X and Y terminals of the oscilloscope. If the same pressure-flow characteristic curve applies throughout the respiratory cycle, then this curve will be described on the cathode ray tube as a single curved line. If the pressure-flow characteristics vary during the respiratory cycle, then "loop" patterns will be formed. Examples of such loops are shown in figure 7.9. They may be compared with the loops in figure 7.10.

The deviations from the steady flow characteristics occur in the direction that might be expected. Since a pressure drop must occur between the ends of the system before air can flow through it, a relatively greater pressure might be expected during the initial rapid acceleration of the airflow. There appears to be time for conditions to stabilize during the peak period. The subsequent flow deceleration is less rapid.

The deviations are small during slow quiet respiration of

the subject used in these experiments. With more rapid respiration the deviations are increased. It is probable that the discrepancy is due to the method of measurement which was used as described in chapter 6.

The pressure-flow characteristics of expiratory valves

For the measurement of the characteristics of expiratory valves under steady flow conditions the method used was similar to that described by Mushin and Mapleson (1954). A cork occluded one end of the expiratory valve mount. Air was blown into the other end at known flows via a Rotameter and the flow transducer. The pressures developed in the system at the known flows were measured.

For measurements under respiratory flow conditions a 1-inch diameter Y-piece was added to the system. The stem of the Y was connected to the flow transducer. A very light non-return valve was connected to one limb of the Y and the expiratory valve was connected to the other limb. The subject breathed into the flow transducer. The non-return valve opened on inspiration. It closed on expiration so that air could be expired only through the expiratory valve.

The Heidbrink valve was opened fully and its pressure-flow characteristics were measured under both steady and respiratory flow conditions. Peak flow and pressure values were taken for the latter and care was taken not to disturb the valve setting between readings. The valve was then closed by half a turn at a time and measurements were repeated at each new valve setting. Two and a third turns were required to close the valve completely. The results are shown in figure 7.11.

The control setting on the Coxeter valve is graduated from

0 to 8. The characteristics of this valve, under both sets of conditions, were measured with the valve fully open and when the control was set to positions 1, 2 and 3 only. The results are shown in figure 7.12.

By allowing the pressure within these valves to build up very slowly it can be shown that there is variation in the opening pressure for a given setting. Sometimes the Heidbrink valve appeared to open in two distinct steps. Such effects are due to friction. But despite such variations, the agreement between the characteristics determined under the two sets of conditions is close. Any differences between the characteristics found under steady flow and respiratory flow conditions are unlikely to be of practical importance in the context of their present use. This is in agreement with the conclusions of Hunt (1955).

The pressure-volume characteristics of a reservoir bag.

One end of the reservoir bag fitting was occluded by a cork. The reservoir bag was emptied by external compression and the tap was closed. A calibrated, manually operated piston pump was connected to the other end of the reservoir bag fitting. The tap was opened, a known volume of air was injected into the bag, and the tap was closed again. The pump was removed and in its place a cork was inserted. This cork was pierced by a pressure tapping which was connected to an inclined manometer. The tap was opened and the pressure within the system was measured. This procedure was repeated using various known volumes of air. The plotted characteristics are shown in figure 7.13. They are similar to those shown by Mapleson (1954a).

The pressure required to fill the bag under dynamic conditions was then measured. A semi-closed breathing system

was used. The arrangement was similar to the standard Magill circuit except that the usual Heidbrink expiratory valve was replaced by a light non-return valve. The subject breathed quietly into the facepiece while the system was supplied with air at 15 l./min. The non-return valve was then loaded with just sufficient weight of plasticine for the opening pressure to be enough to allow the reservoir bag to fill comfortably during each expiration. A length of 3-mm-diameter p.v.c. tubing was inserted into the reservoir bag and connected to the ± 0.5 cm H_2O pressure transducer for these measurements. The pressure within the reservoir bag was measured continuously. No peak pressure greater than 0.25 cm H_2O was recorded.

The resistance to flow through a nose and nasopharynx

The subject breathed through the nose into a facepiece. Airflow through the facepiece was measured using the flow transducer. An open glass tube, bent to a convenient angle, was held in the closed mouth of the subject, as far back into the mouth as he could tolerate. The other end of the tube passed through an airtight seal in the facepiece. Differential pressure between the glass tube and the facepiece was recorded continuously and simultaneously with airflow. This pressure was taken as representative of the pressure drop across the nose and nasopharynx. The subject varied the amplitude of his breathing. Peak values are plotted in figure 7.14. The experiment was repeated while each nostril was occluded in turn. The resistance through the left nostril was much greater than that through the right. The resistance through the right nostril was close to that through the whole nose. There was little change in the resistance after the instillation of 0.25 per cent phenylephrine nasal drops.

Consistent results were not obtained until it was realised that there was a tendency for the facepiece to compress the nose, thereby causing a significant increase in the resistance to airflow. It was necessary to distort the shape of the facepiece. The effects of compressing the soft parts of the nose should evidently receive careful consideration in facepiece design.

A preliminary study of anaesthetic breathing systems

A preliminary study has been made of anaesthetic breathing systems. The results have not been fully evaluated, nor has it been decided which are the best parameters to record and describe when assessing the flow mechanics of such systems. Some of the methods available are indicated.

It has been assumed that a complete anaesthetic breathing system can only be assessed properly under dynamic working conditions, although it is not denied that important points may be deduced from the steady flow characteristics of the component items. The dynamic flow and pressure measurements were made between the mouth of the subject and the breathing system being studied.

A Magill attachment was supplied with air at 15 l./min. The reservoir bag was included in the circuit. The subject breathed either into the facepiece or into the endotracheal tube. The latter was connected using both the Magill endotracheal connector and the Cobb suction union in turn. Various settings of the Heidbrink expiratory valve were tried.

To reproduce conditions comparable with those occurring in dental anaesthesia the Magill attachment was supplied with air at 50 l./min. The subject breathed through the facepiece only. The system was tried both with and without the reservoir bag and with

various settings of both the Heidbrink and Coxeter expiratory valves.

A cock placed in series with the air supply from the air pump was adjusted to give the above flow rates. A Rotameter was used for their measurement. It was noted that while using this arrangement the supply flow rate sometimes fell by about 5 l./min during expiration.

Figure 7.15 shows examples of pressure and flow patterns obtained when using the Magill semi-closed systems. It can be seen that the inclusion of the reservoir bag causes a phase shift between the peak pressure and the peak flow changes as measured at the mouth. During expiration the subject meets with relatively little resistance until the reservoir bag has been filled. High flows are possible during this initial expiratory period. The flow rate then drops while the pressure rises until the expiratory valve opens, when there may be a second expiratory peak flow.

The pressure and flow patterns vary both with the subject's respiratory pattern when breathing into the system and with the precise arrangement of the apparatus. It is evident that under these circumstances it is of relatively little value to relate peak flows with the out-of-phase peak pressures. With careful interpretation the patterns of the flow changes considered together with the corresponding patterns of pressure change are more informative.

The flow-pressure loop obtained over a single respiratory cycle, as described above, probably gives an even more revealing picture of the events happening within that cycle. Some examples, with key diagrams, are shown in figures 7.16, 7.17 and 7.18. The shapes during inspiration and during the early part of expiration depend upon the airflow resistance of the equipment and upon the supply flow rate. The greater part of the flow-pressure

loop pattern formed during expiration is governed by the characteristics of the expiratory valve, and the supply flow rate. If the reservoir bag empties, or if the inspiratory flow exceeds the supply flow rate when the reservoir bag is not used, then a sharp negative pressure change may be seen at the peak of inspiration.

DISCUSSION

Some of the fundamental considerations in the design and selection of anaesthetic equipment have been stressed by those workers cited in chapter 6 who have made valuable contributions towards the measurement of airflow resistance. It is surprising how much of this good advice appears to have been ignored. The Cobb suction union provides an example. Many of the above workers have commented adversely upon this particular item or upon similar right-angled connectors. Criticism of it is either made or implied in modern textbooks of anaesthesia. Yet this item is still used. It is still sufficiently popular for it to be manufactured and displayed for sale. No special apparatus is needed in order to demonstrate its resistance to airflow. All that is necessary is to breathe through it. Not only can the resistance then be experienced but the turbulence can be heard. The blurring during the peak inspiratory period of the flow-pressure loop shown in figure 7.18.B is due to turbulence caused by the Cobb connector, despite damping in the endotracheal tube connected between it and the flow transducer.

Mushin and Mapleson (1954) observed that the opening pressure of the expiratory valve used in the Magill semiclosed system needs to be sufficient only to fill the reservoir bag. It was evident from their results, as it is from the present investigation,

that the minimum opening pressure when using the Heidbrink valve fully open is far in excess of that needed. Yet this is one of the more commonly used valves in inhalational anaesthesia, and there is still a demand for the sale of the Coxeter valve within which high pressures may be generated easily. As long as anaesthetists demand such equipment it is not surprising that manufacturers should supply it. There would appear to be room for a greater appreciation, on both sides, of the magnitude of the abnormal pressure changes that may occur using current anaesthetic apparatus and of the possible clinical effects of such changes.

The flow mechanics of the ideal breathing system for inhalational anaesthesia should be such that there is no more pressure change at the mouth or nose than occurs in normal respiration. It should be self-compensating for its own airflow resistance. Such a machine may not be practicable for everyday use but the ideal might be approached more nearly than is usual at the present time.

The experience gained in the present investigation indicates that any statement of the airflow resistance of an item of anaesthetic equipment should be accompanied by a statement as to precisely how it was measured. Even then care is needed in interpretation. A standard endotracheal catheter mount may be taken as an example. Upon naked eye examination it can be seen that the lumen of the catheter mount used in this investigation is smaller than it need be, and that the internal diameter changes suddenly. The sharp ledge produced by this sudden change in diameter might be expected to disturb airflow through the catheter mount. These points receive confirmation in figure 7.1. Under the circumstances of that experiment it was found that its airflow resistance was

slightly greater than that of the Magill endotracheal connector. Furthermore, its airflow resistance could be reduced by "streamlining" the internal ledge with plasticine. But when its airflow resistance was measured in the context of its normal use, as indicated in figures 7.2, 7.3 and 7.4, it was shown to have a "negative" resistance due to a streamlining effect which depended upon the endotracheal connector on to which it was fitted. This does not necessarily invalidate the first conclusions. Had the other items in the system been different and had they offered less resistance, then the resistance of the catheter mount might have been found to be "positive" rather than "negative".

The comparison of the measurements of airflow resistance under steady flow conditions with those made under the dynamic conditions of respiration using peak values suggests that, for all present practical purposes, either may be used for the assessment of the airflow resistance of anaesthetic equipment. When making such measurements, however, the measuring system must be defined. In terms of the initial cost of test equipment it would be cheaper to use basic Rotameter flowmeters and appropriate manometers for steady flow measurements. In terms of the subsequent time spent and the simplicity of actually making measurements it would be quicker and easier, and therefore cheaper, to use a flow and pressure transducer system, such as that described above, in conjunction with a suitable generator of variable airflow. The basic Rotameter and manometer equipment would still be required for calibration purposes. The flow-pressure characteristics of any item or assembly of equipment could be obtained from a single cycle of the variable flow generator, using the X and Y terminals of an oscilloscope or an

X-Y recorder.

Throughout this investigation flows were measured at the subject's mouth. When investigating anaesthetic breathing systems, however, invaluable information might be obtained by placing the flow transducer in alternative positions. For example, it would be of interest to measure the flows at the gas supply side of the expiratory valve in the Magill semiclosed system, particularly during expiration. It would be interesting to compare such measurements with the amount of carbon dioxide accumulation in the circuit under the same conditions. It would also be of interest to measure these parameters in the expiratory limb of a circle system while using moderate or high supply flows and keeping the expiratory valve open.

In considering the measurements which have been made of the airflow resistance through complete systems incorporating an endotracheal tube, it should be realised that the airflow resistance of that part of the subject's respiratory tract within which the endotracheal tube would lie should be subtracted from the overall resistance values obtained for the complete system. No attempt has been made to measure the airway resistance of the subject of this experiment between the mouth and the upper part of the trachea. The airflow resistance of his nose and nasopharynx, as obtained using peak values, was about 30 per cent greater than that of the endotracheal tube, but the resistance to flow through the left nostril was high.

FIGURE 7.1

Pressure/flowrate characteristics, for air, of items of anaesthetic equipment measured individually.

FIGURE 7.2

Pressure/flowrate characteristics, for air, of anaesthetic equipment, measured as each individual item was added to form an assembly incorporating a Magill endotracheal connector.

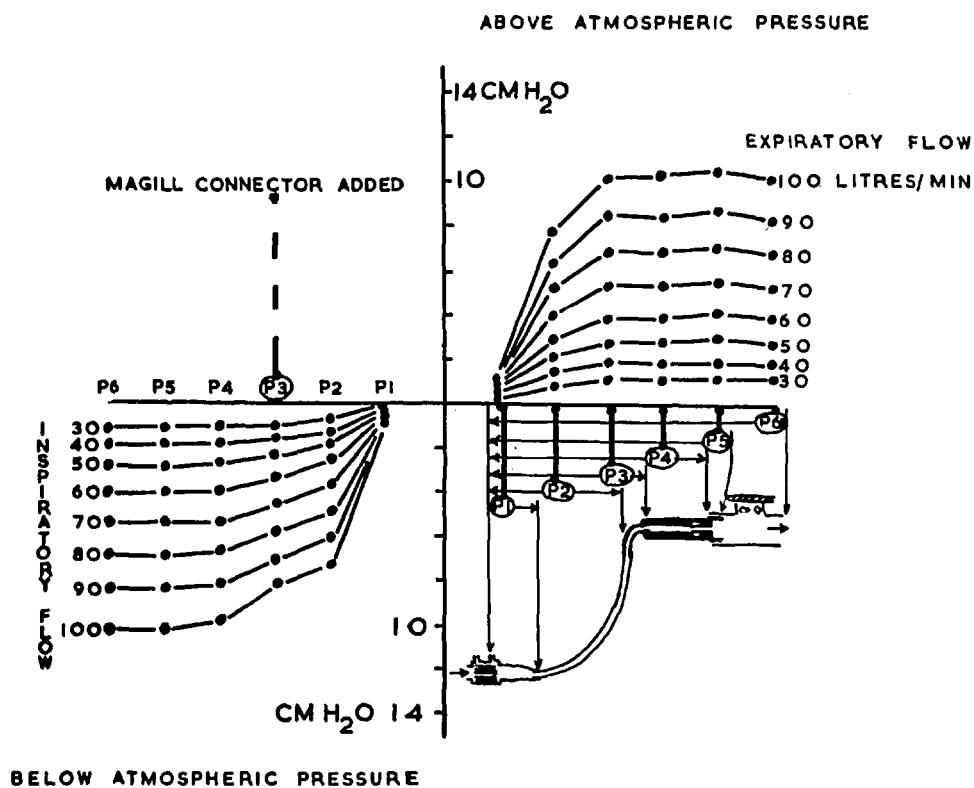
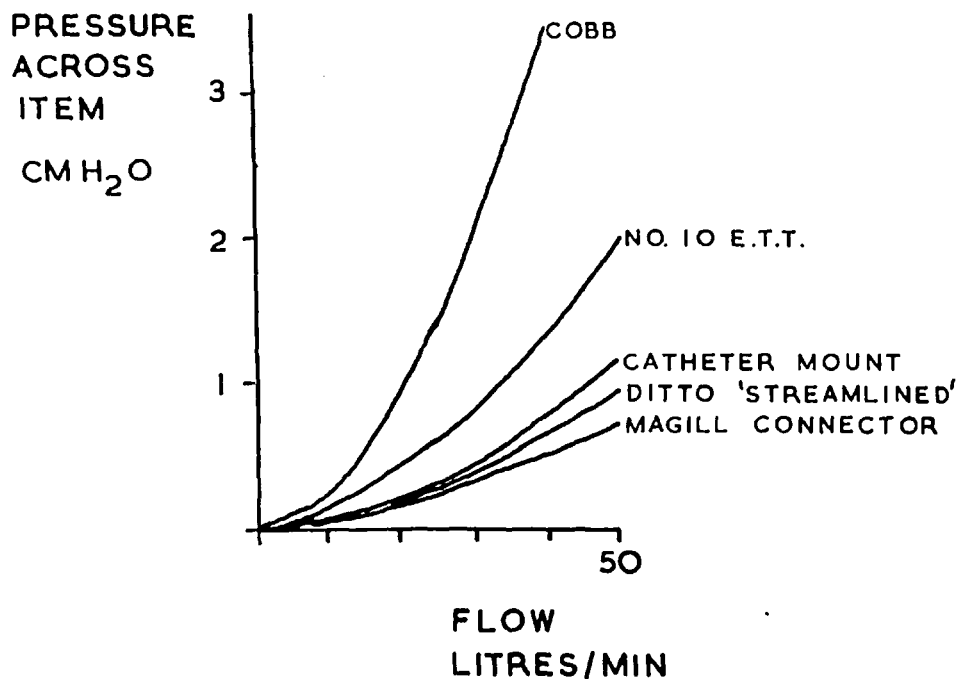


FIGURE 7.3

Pressure/flowrate characteristics, for air, of anaesthetic equipment, measured as each individual item was added to form an assembly incorporating a Cobb Suction Union in place of the Magill endotracheal connector.

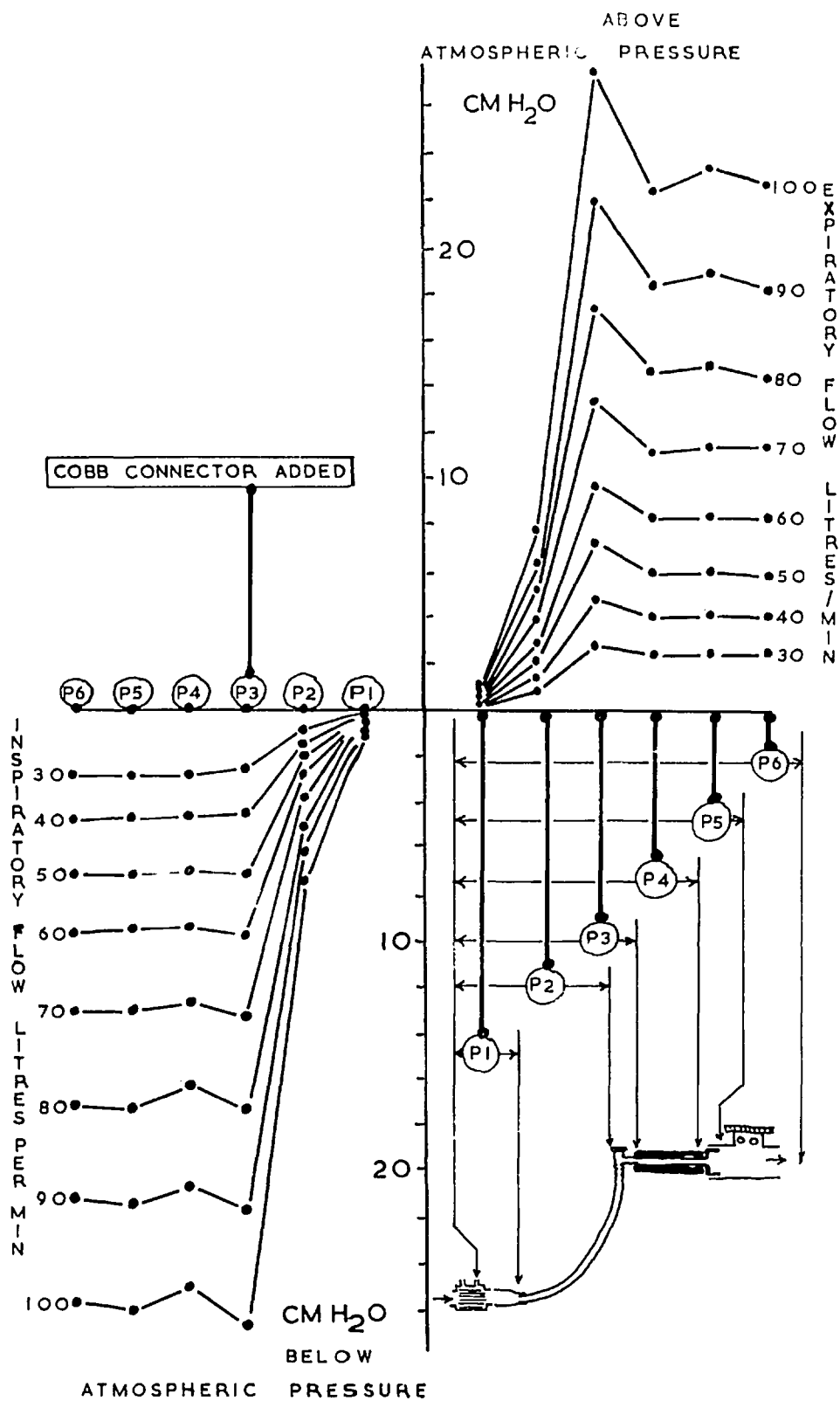


FIGURE 7.4

The effective pressure /flowrate characteristics, for air, of individual items of anaesthetic equipment when assembled as for normal use; derived from values given in figures 7.2 and 7.3 by subtraction of successive pressure readings at given flow rates (E.T.T. = endotracheal tube).

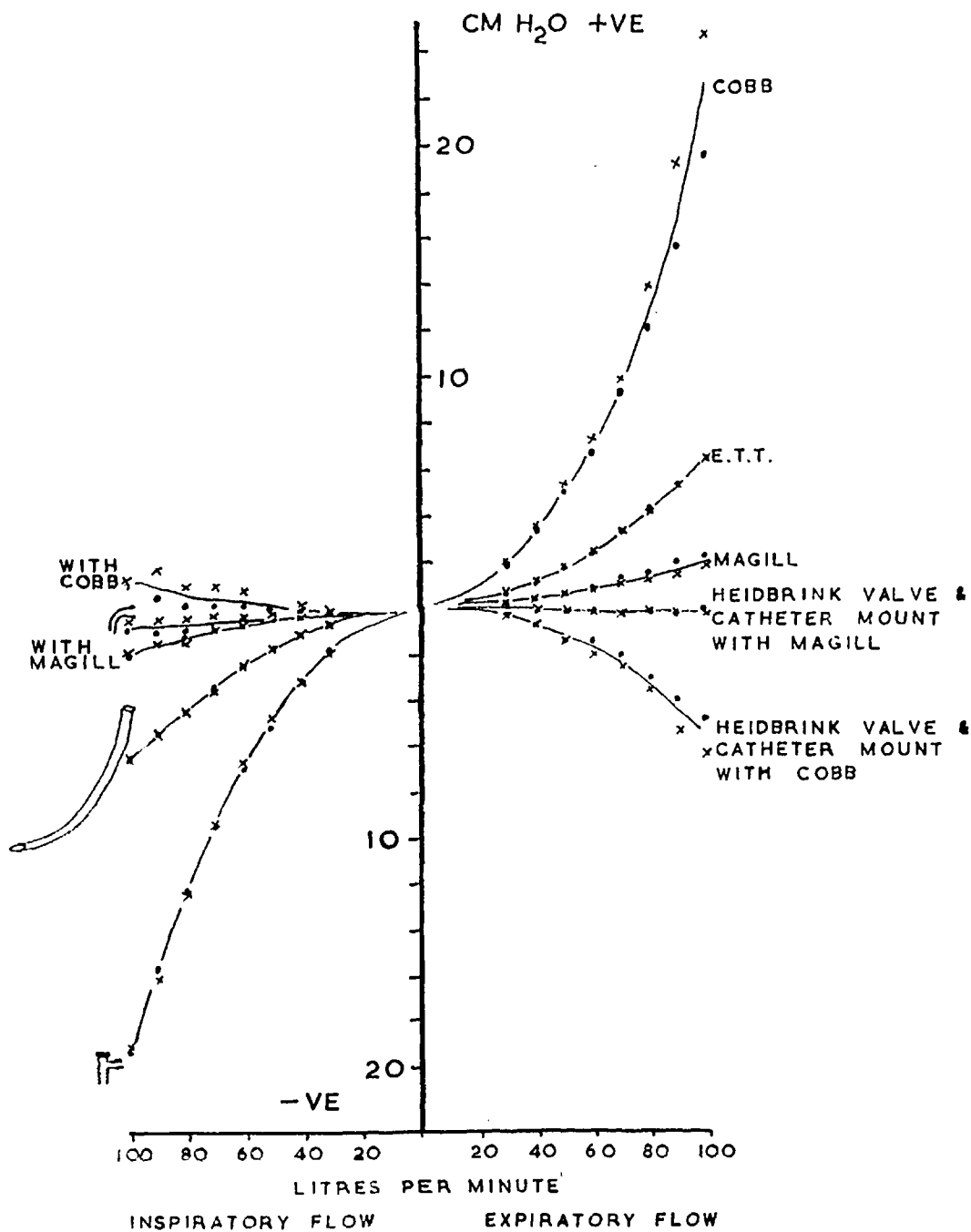


FIGURE 7.5

The pressure/flowrate characteristics of the flow transducer and glass connector and endotracheal tube, measured during peak respiratory flow (x x x x), compared with those measured under conditions of steady flow (• • • •). (Dotted lines indicate quiet respiration)

FIGURE 7.6

As figure 7.5, but for the complete assembly of anaesthetic equipment incorporating the Magill connector. (Dotted lines indicate quiet respiration)

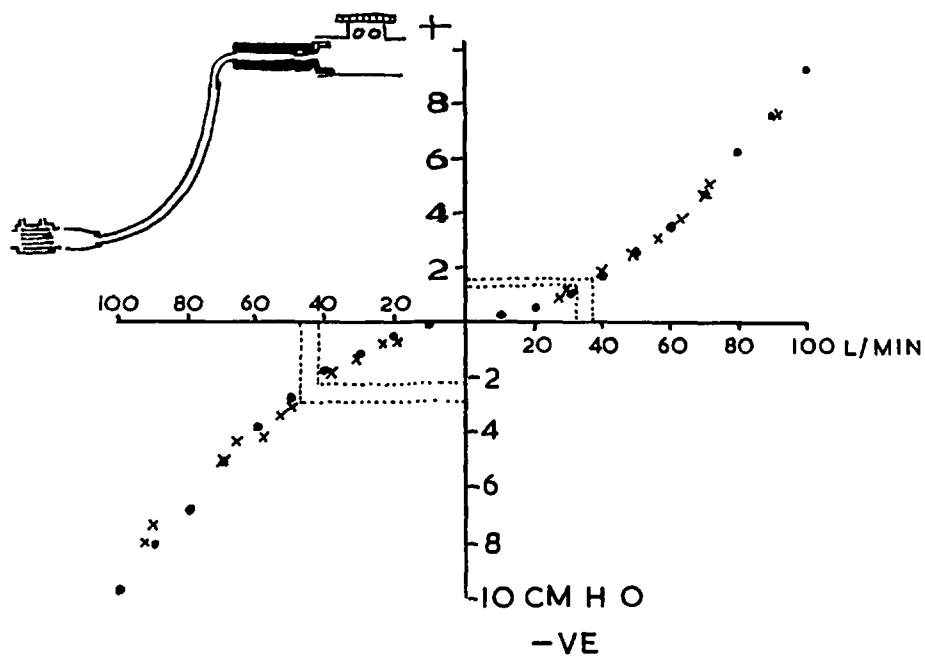
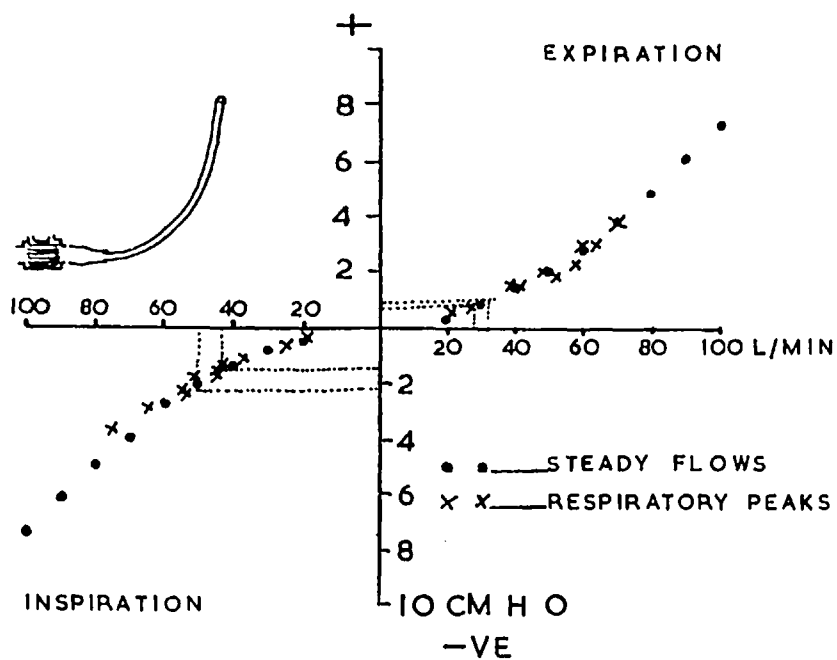


FIGURE 7.7

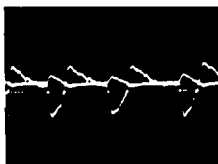
Records of the changes in pressure and flow rate obtained while breathing through different assemblies of apparatus, the calibrations being the same in each case. Records on the left were obtained during stable respiration. Note the slower respiratory rate while breathing through the assembly offering the greatest flow resistance (bottom record).

FIGURE 7.8

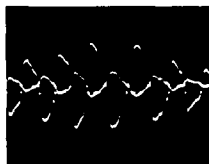
As figure 7.6, but using the Cobb suction union in place of the Magill endotracheal connector.

(Dotted lines indicate quiet respiration)

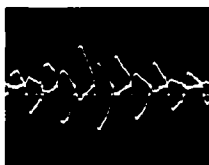
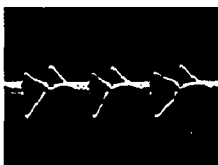
STABLE RESPIRATION



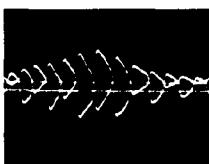
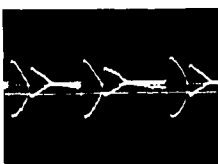
VARYING RESPIRATION



BREATHING THROUGH FLOW TRANSDUCER & ENDOTRACHEAL TUBE



BREATHING THROUGH ASSEMBLY USING MAGILL CONNECTOR



BREATHING THROUGH ASSEMBLY USING COBB SUCTION UNION

(NB. BASE LINES ARE DISPLACED)

EXAMPLES OF PRESSURE AND FLOW PATTERNS OBTAINED DURING QUIET STABLE AND DURING VARYING RESPIRATION

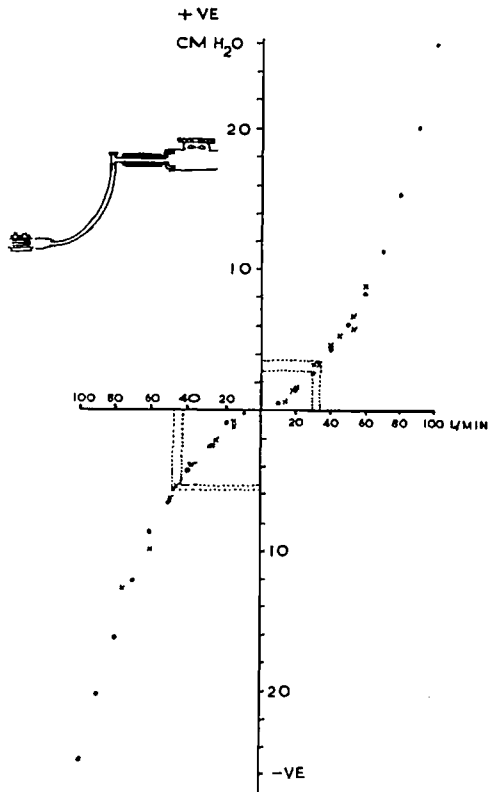
UPPER TRACE PRESSURE δ -VE δ +VE
LOWER TRACE FLOW δ INSP δ EXP.

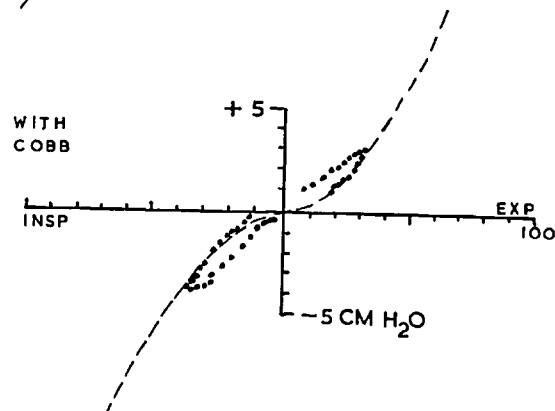
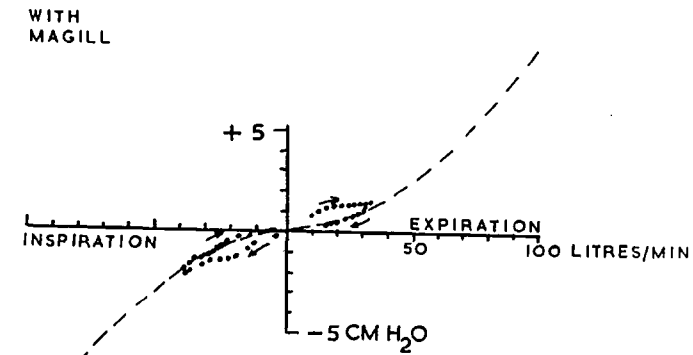
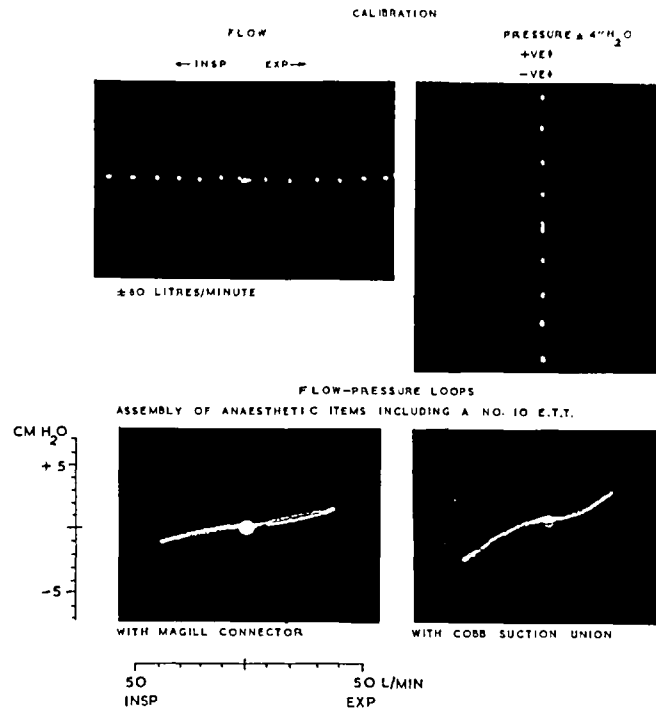
FIGURE 7.9

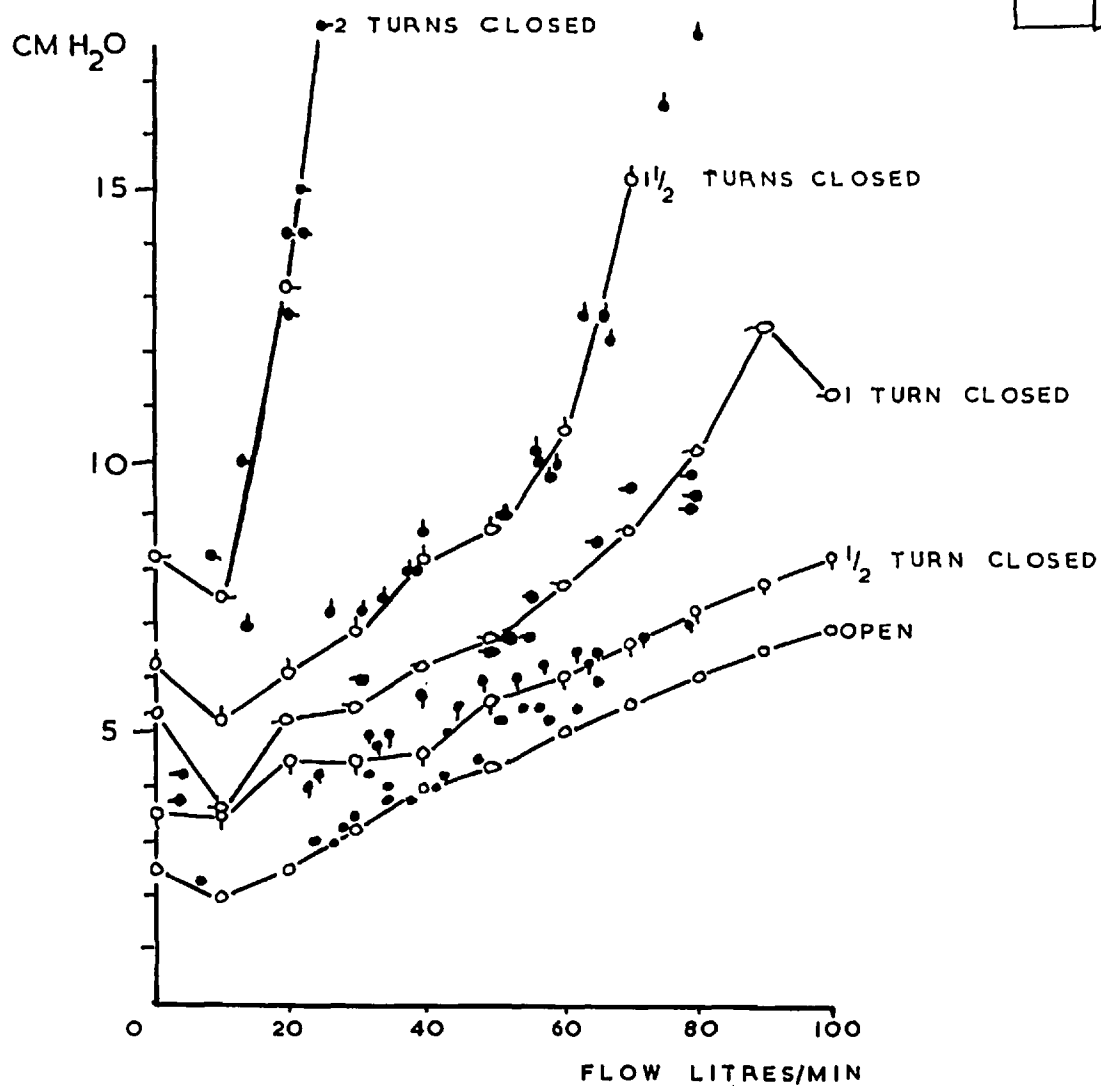
Above: Calibration exposures. The output from the Respiratory Analyser corresponding with flowrate was fed to the X-plates of a cathode ray oscilloscope (left), and the output corresponding with pressure to the Y-plates (right).

Below: Flow-pressure "loops" obtained during single respiratory cycles while breathing through assemblies incorporating a Magill endotracheal connector (left), and a Cobb suction union (right).

FIGURE 7.10

The pressure/flowrate characteristics of assemblies incorporating a Magill endotracheal connector (above) and a Cobb Suction Union (below), as measured during a single respiratory cycle (....), and compared with those measured under conditions of steady flow (----).

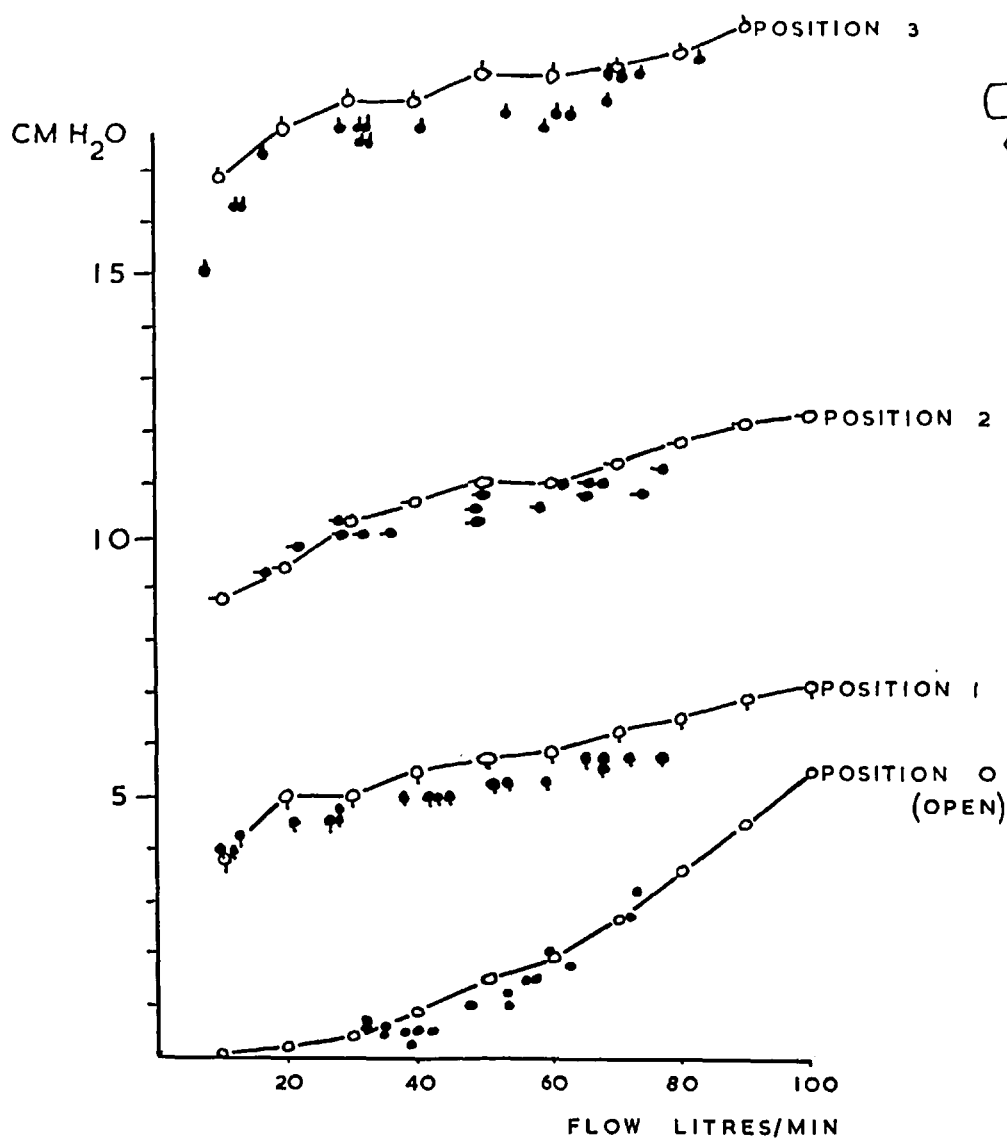




PRESSURE-FLOW CHARACTERISTICS OF AN HEIDBRINK
EXPIRATORY VALVE

○ ○ ○ STEADY FLOW CONDITIONS
● ● ● RESPIRATORY FLOW CONDITIONS

FIGURE 7.11



PRESSURE-FLOW CHARACTERISTICS OF A COXETER
EXPIRATORY VALVE

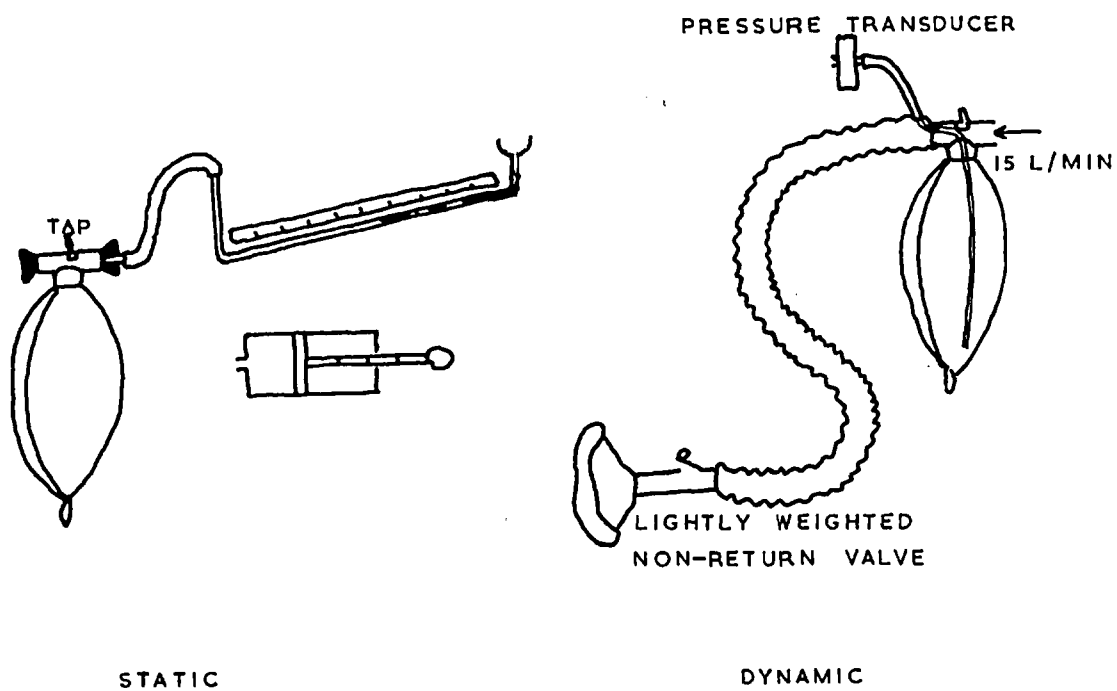
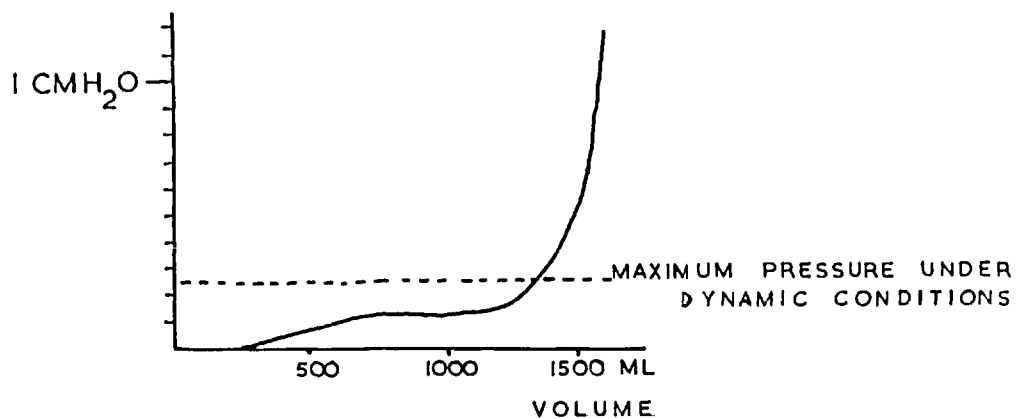
○ ○ STEADY FLOW CONDITIONS
● ● RESPIRATORY FLOW CONDITIONS

FIGURE 7.12

FIGURE 7.13

Above: The pressure-volume characteristics (compliance) of a reservoir bag under static (continuous line) and under dynamic (broken line) conditions.

Below: Methods of determining the pressure-volume characteristics of a reservoir bag under static (left) and under dynamic (right) conditions.

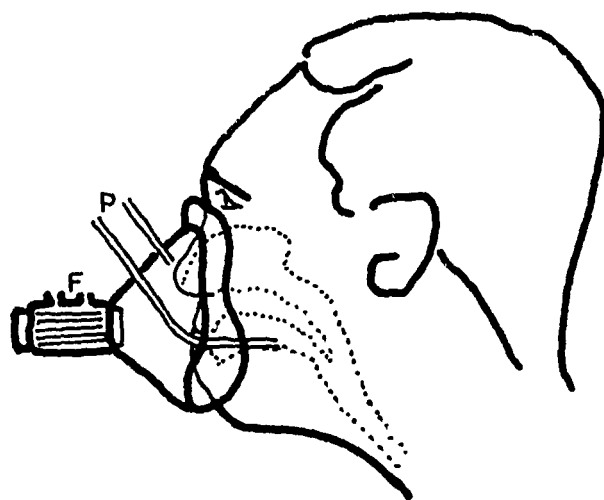
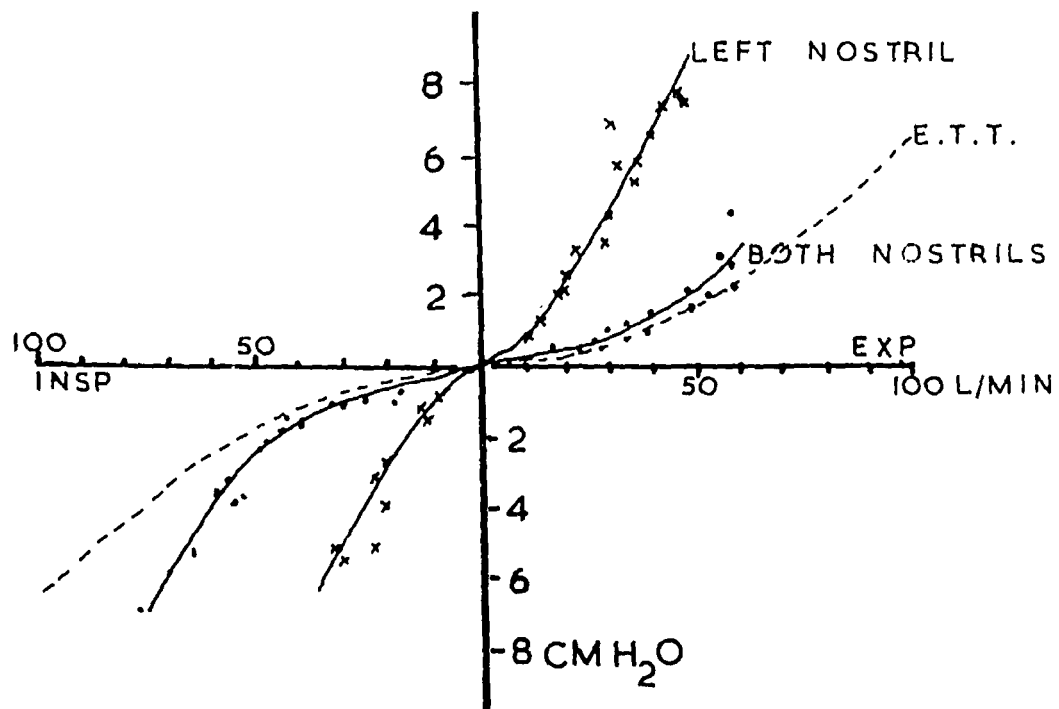


PRESSURE—VOLUME CHARACTERISTICS OF A RESERVOIR BAG

FIGURE 7.14

Above: The pressure/flowrate characteristics of a nose and nasopharynx, compared with those of a No. 10 (9.5 mm I.D.) endotracheal tube. (Peak values for pressure and flowrate have been plotted).

Below: The method of measuring the pressure/flowrate characteristics of nose and nasopharynx. The differential pressure between the face mask and the glass tube held in the closed mouth was measured continuously and simultaneously with airflow.

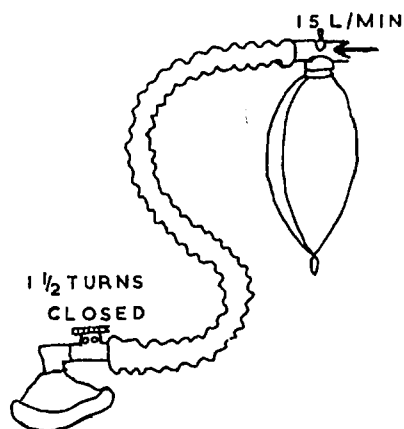
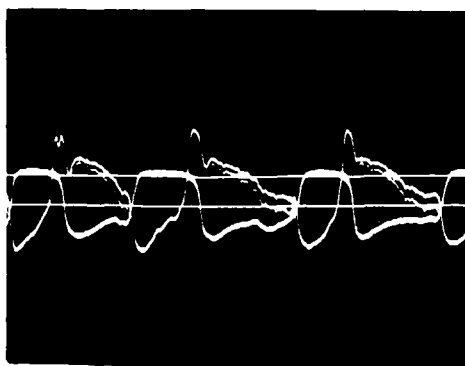
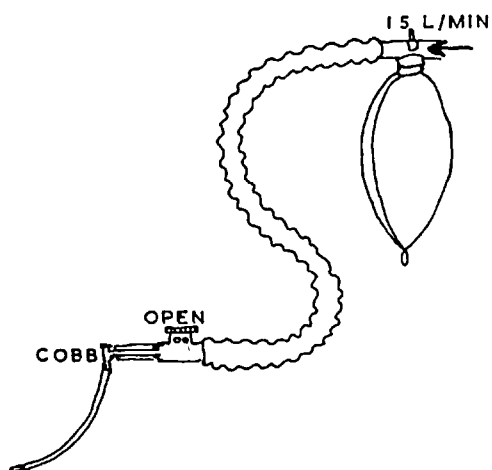
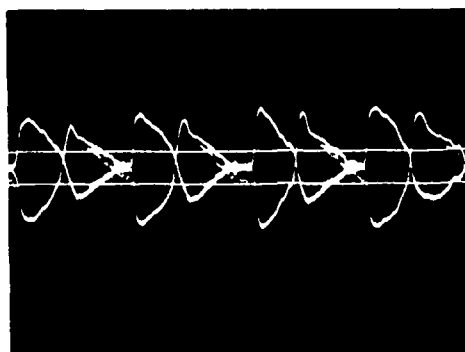
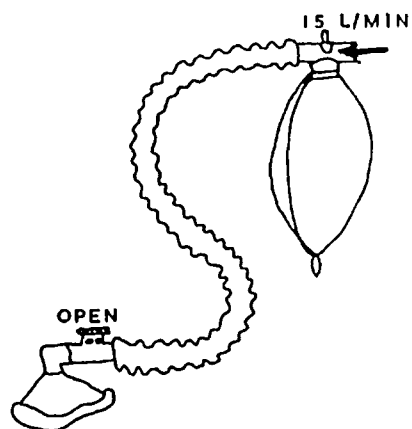
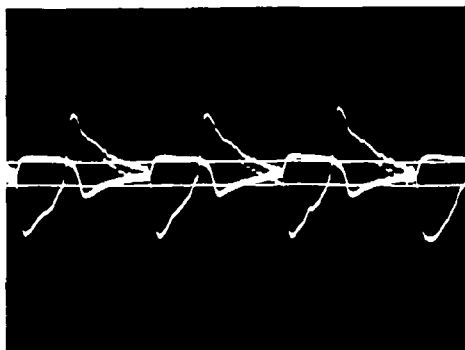


AIRFLOW RESISTANCE OF A NOSE

FIGURE 7.15

Records of the changes in pressure and flowrate, measured between the subject and the breathing system, while breathing quietly into the anaesthetic breathing systems indicated. In each case the thicker of the two traces is the record of pressure.

Note the difference in times of occurrence of peak pressure and peak flowrate, which results from inclusion of the reservoir bag.



PRESSURE AND FLOW PATTERNS OBTAINED WHILE BREATHING QUIETLY
INTO A MAGILL SEMI-CLOSED ANAESTHETIC BREATHING SYSTEM

UPPER TRACE PRESSURE $\uparrow$ -VE $\downarrow$ +VE
LOWER TRACE FLOW $\downarrow$ INSP $\uparrow$ EXP

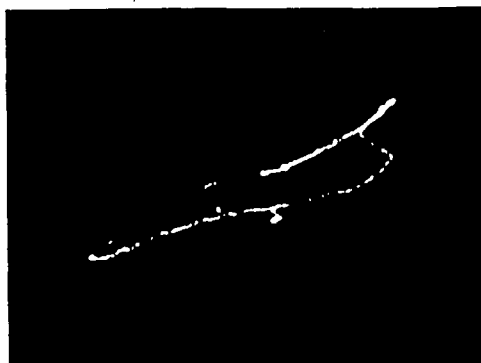
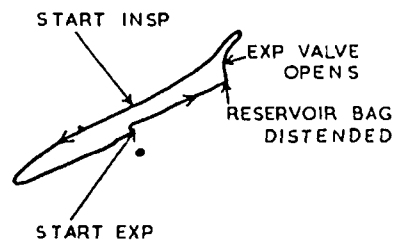
FIGURE 7.16

Flow-pressure loops obtained on a cathode ray oscilloscope (see figure 7.9) while breathing into a "Magill" "semi-closed" system (see figure 7.15), using the items indicated.

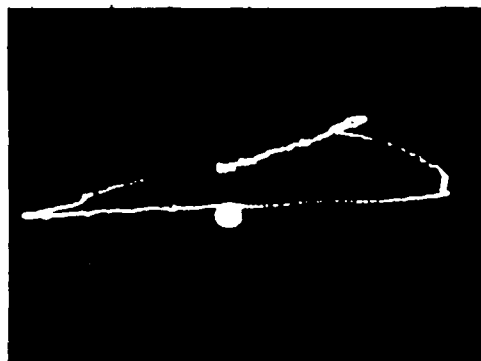
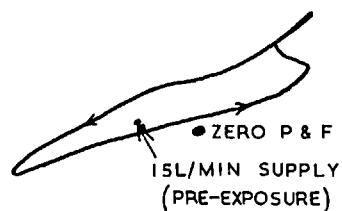
On the original records the calibration was the same during these experiments as during those illustrated in figure 7.9, but the record shown in figure 7.9 has been reduced. A 15 l./min calibration exposure can be seen on the middle record of this figure.



MAGILL SYSTEM. 15L/MIN SUPPLY
E.T.T. & COBB. HEIDBRINK VALVE OPEN



AS ABOVE EXCEPT MAGILL CONNECTOR
IN PLACE OF COBB



AS ABOVE EXCEPT E.T.T. & CONNECTOR
REPLACED BY MASK



NOTE CHANGE OF SLOPE & SHAPE WITH
CHANGE OF AIRFLOW RESISTANCE

PRESSURE - FLOW LOOPS

CALIBRATION AS IN FIGURE 7.9

FIGURE 7.17

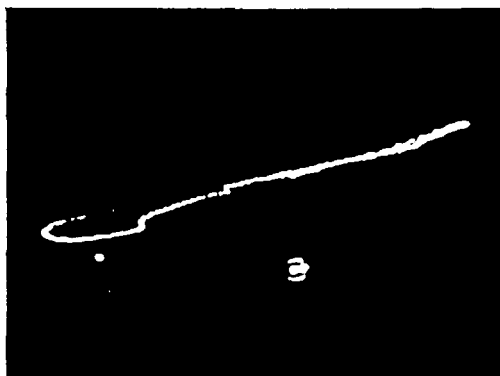
Flow-pressure loops

A 50 l./min calibration exposure can be seen to left on each record. Lower right-hand spot indicates zero pressure and flow.

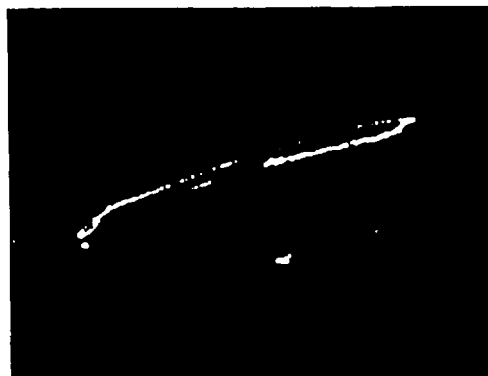
Upper Left: Some pressure remained in the reservoir bag even during peak inspiration.

Upper Right: There was a sharp fall of the pressure towards atmospheric pressure as the inspiratory flow-rate approached the supply flowrate of 50 l./min, when there was no reservoir bag. If the subject had attempted to inspire at more than 50 l./min the pressure would have become sub-atmospheric.

Below: The reservoir bag remained distended and there was a significant pressure in the system even during peak inspiration.

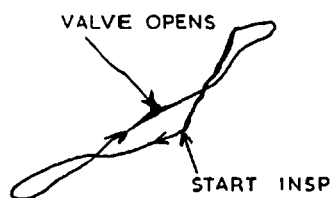


USING RESERVOIR BAG



WITHOUT RESERVOIR BAG (NOTE PEAK INSP)

MAGILL SYSTEM USING MASK. HEIDBRINK VALVE OPEN. 50 L/MIN SUPPLY

AS ABOVE USING RESERVOIR BAG AND THE
HEIDBRINK VALVE $1\frac{1}{2}$ TURNS CLOSED

•
ZERO PRESSURE & FLOW

50 L/MIN 0

FIGURE 7.18

Flow-pressure loops as in figures 7.9, 7.16 and 7.17.

Large white spot indicates zero pressure and flow.

Upper Records: 15 l./min supply. Reservoir bag included in the system. Heidbrink valve $1\frac{1}{2}$ turns closed. No. 10 (9.5 mm I. D.) endotracheal tube connected.

Left: Magill connector. Right: Cobb suction union.

Note the sub-atmospheric pressure while inspiring against the resistance of the Cobb suction union.

Lower 4 Records: 50 l./min supply using a Coxeter valve and a Face Mask.

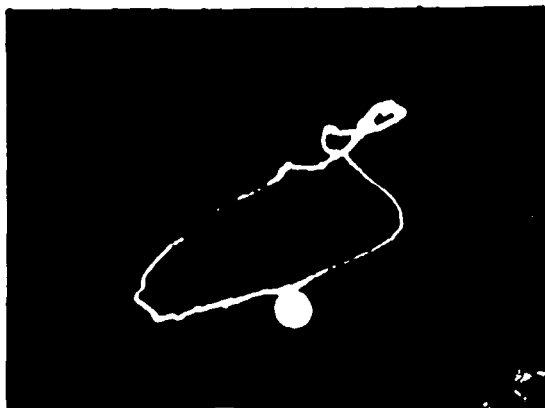
Middle Left: Reservoir bag excluded (note end inspiration and compare with figure 7.17 and adjacent figure).

Coxeter valve in position 1.

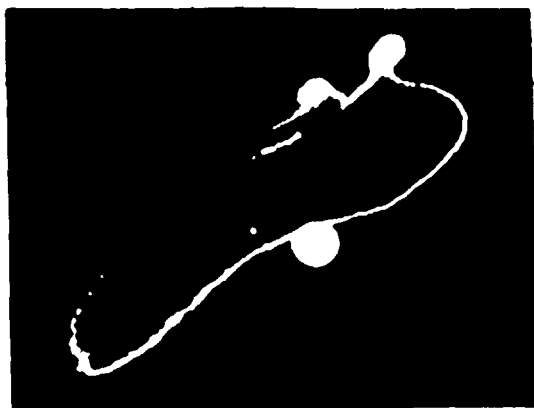
Middle Right: Reservoir bag included (compare adjacent figure). Coxeter valve in position 1.

Lower Left: Reservoir bag excluded. Coxeter valve in position 2. (i.e. greater resistance. Note higher pressure in system throughout the cycle. This occurs even during peak inspiration if the peak inspiratory flow rate is less than the supply flow rate).

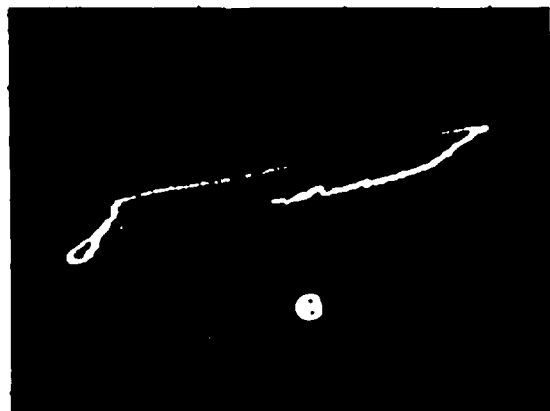
Lower Right: Reservoir bag included. Coxeter valve in position 2.



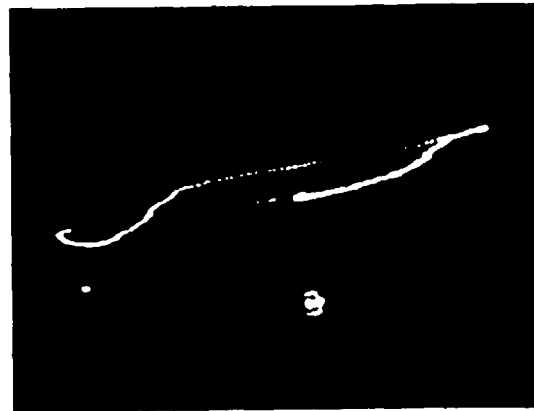
A



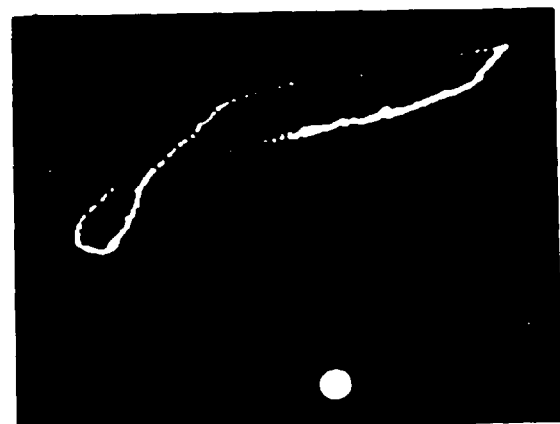
B



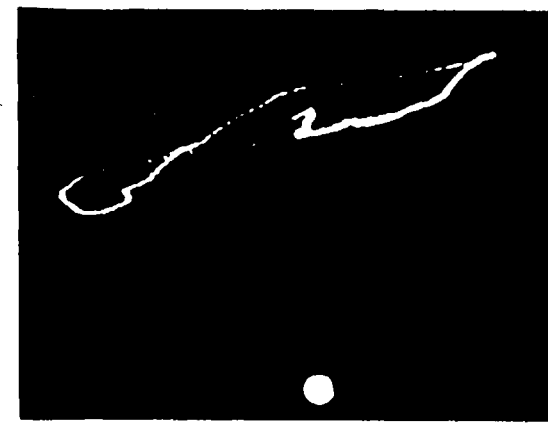
C



D



E



F

Fig. 7.18

CHAPTER 8

ASSESSMENT OF THE
WALTON FIVE ANAESTHETIC MACHINE

The work described in this chapter was carried out while holding a Wellcome Research Fellowship in the Research Department of Anaesthetics, Royal College of Surgeons of England. It has been published (Smith, W.D. A. (1961). The performance of a Walton Five anaesthetic machine. *Brit. J. Anaesth.*, 33, 440).

The Walton Five anaesthetic machine was supplied, on indefinite loan, by the British Oxygen Co. Ltd.

The Lloyd-Haldane and the Scholander gas analyses were carried out by Miss D. C. Casselle.

The Walton Five dental anaesthetic machine is designed to deliver known mixtures of oxygen and nitrous oxide. It has three controls: a mixture control, a pressure control, and an emergency oxygen control. The lever of the mixture control rotates around a scale calibrated in oxygen percentage. The markings are in 1 per cent divisions between 0 and 15 per cent, and at 20, 50 and 100 per cent. The pressure control is calibrated in mm Hg up to 20 mm. The pressure indicated at a given setting of the pressure control does not refer to the pressure at which the gas mixture is delivered. It refers to the pressure developed when the outlet of the machine is occluded. The emergency oxygen control is a sprung button.

Two safety devices are designed to prevent catastrophe in the event of failure of the oxygen supply. An automatic cut-off valve prevents the administration of nitrous oxide in the absence of an available oxygen supply; and an inspiratory valve opens at a subatmospheric pressure, thus permitting the inspiration of air and preventing asphyxia in the absence of a gas supply. Failure of the nitrous oxide supply also results in the oxygen supply being cut off but under these circumstances oxygen may still be administered by depressing the emergency oxygen button.

The particular Walton Five anaesthetic machine used in these studies was tested in the laboratory. The factors which were varied were the setting of the mixture control, the setting of the pressure control, the use of the emergency oxygen control, the "expiratory" resistance and the flow pattern. Both steady flows and simulated respiratory flow patterns were used. Measurements were made of the oxygen content of the gas mixture delivered and of pressures and flows.

METHODS

The measurement of oxygen concentration

A Beckman D.2 paramagnetic oxygen analyser was used for measuring the oxygen content of the gas mixtures. Its calibration was checked against Lloyd-Haldane and Scholander apparatuses, using various mixtures of oxygen and nitrogen. The gas mixtures delivered by the anaesthetic machine were sampled continuously by means of a small diaphragm pump, the analysed sample being returned to the circuit under investigation. A given gas mixture was sampled for 2 minutes before a reading was taken. It was confirmed that any local pressure changes due to the sampling pump were not sufficient to affect the readings given by the oxygen analyser.

The arrangement used for the measurement of the oxygen percentage in the delivered gas mixtures under steady flow conditions is shown in figure 8.1. Nitrous oxide and oxygen mixtures were delivered to a Heidbrink expiratory valve via corrugated tubing and they were sampled just proximal to the valve. The distal opening of the valve mount was occluded. Measurements of the oxygen content were made when the mixture control was set to 5, 10, 15, 20 and 50 per cent oxygen, while the pressure control was set to 5, 7.5, 10, 15 and 20 mm Hg, and while the expiratory valve was fully open and $\frac{1}{2}$ turn, 1 turn and $1\frac{1}{2}$ turns closed. The oxygen content of the gas mixture delivered was also determined while the emergency oxygen control was depressed, the mixture and the pressure controls being placed at different settings.

A versatile piston-type variable flow generator was used to represent a patient breathing into the system (Hill, Hook and Bell, 1961).

The arrangement used for making measurements under simulated respiratory flow conditions is shown in figure 8.2. The generated flow waveform is indicated. The gas mixtures were delivered to a Heidbrink expiratory valve via a reservoir bag and corrugated rubber tubing. The expiratory valve was enclosed in order that the "expired" gas might be collected in a Douglas bag for subsequent analysis. A narrow-bore sampling tube was inserted between the tap and the Douglas bag. The distal end of the Heidbrink valve was connected to one limb of a wide-bore Y-piece. The other limb of the Y-piece was connected to the variable flow generator and the stem of the Y-piece was used for continuous sampling of "respired" gas mixtures.

Under simulated respiratory flow conditions measurements of oxygen percentage were made when the mixture control was set to deliver 10 and 20 per cent oxygen only. The pressure control settings used were 5 and 10 mm Hg. The expiratory valve was used fully open and $\frac{1}{2}$ turn, 1 turn and $1\frac{1}{2}$ turns closed. Table 8.1 indicates the approximate tidal and minute volumes, the "respiratory" rates and the corresponding subsequently determined peak "inspiratory" and "expiratory" flow rates used. One measurement was made while the pressure control was set at 3 mm Hg.

At the start of each experimental run the Douglas bag was emptied and the tap was closed, so that the expiratory valve vented to air. After half a minute the tap was opened and the Douglas bag was filled with "expired" gas. The bag was again emptied and then finally filled with "expired" gas for subsequent analysis. Meanwhile the gas mixture was sampled continuously at the Y-piece and analysed by the Beckman analyser. At the end of the run the oxygen content of the gas mixture in the Douglas bag was determined.

There was little difference between the two sets of readings taken during and at the end of each experimental run.

The measurement of flow and pressure

A Rotameter, calibrated for air over the range 14 to 150 l./min, and flow transducers made by Vickers Research Limited were used for flow measurements. The latter were used in conjunction with the Vickers Research Limited Respiratory Analyser and associated capacitance type ± 7 mm H₂O pressure transducer (Williams, 1960; Scott & Williams, 1960). An oscilloscope and a camera were used for recording.

A water manometer and the Respiratory Analyser in conjunction with its associated ± 30 cm H₂O pressure transducer were used for pressure measurements.

The calibration and use of the Vickers Research Limited, Respiratory Analyser and associated transducers are described in chapter 6.

Using the water manometer, the calibration of the pressure control of the anaesthetic machine was checked. With the outlet occluded, the pressure at the delivery tube was first measured while the pressure control was placed at different settings. Free flow was then permitted while the position of the pressure and the mixture controls were varied. The pressure developed when these free flows were totally obstructed was measured. An initial high pressure reading was obtained before the pressure settled to a value comparable with that indicated by the pressure control setting. The contribution of the inertia of the water in the manometer to this initial reading was uncertain. Further measurements were therefore made, using the pressure transducer.

Neither continuous free flow nor complete obstruction is usual in normal use. The machine has to deliver gases against fluctuating flow resistances, the actual flow and pressure patterns being governed by the characteristics of the anaesthetic machine, the characteristics of the expiratory valve at the particular setting at which it is used and the respiratory pattern of the patient. The pressures generated against the resistance of the expiratory valve under steady flow and under simulated respiratory flow conditions were therefore determined. For the former an arrangement similar to that shown in figure 8.1 was used, except that the water manometer was connected to a pressure tapping in place of the sampling tubes. Pressures were measured while the pressure control was set at 5, 10, 15 and 20 mm Hg, while the position of the mixture control was varied between the 0 and 100 per cent positions, and while the expiratory valve was open and $\frac{1}{2}$ turn, 1 turn and $1\frac{1}{2}$ turns closed. The method used for measuring the pressure swings occurring during simulated respiratory flow conditions is described below.

The measurement of pressure-flow characteristics

The flow resistance characteristics of the particular Heidbrink valve used in this investigation were determined, both to air and to a mixture of 20 per cent oxygen with nitrous oxide. The Rotameter and the water manometer were used and the method was essentially that described by Mushin and Mapleson (1954). The flow resistance characteristics of the twin tubing supplying a nasal inhaler, and of the combination of the twin supply tubing and the expiratory valve incorporated with the nasal inhaler, were also measured.

For the determination of the pressure-flow characteristics of the anaesthetic machine under steady flow conditions, the 0 to

200 l./min flow transducer was used for flow measurement during free unobstructed flow. The Rotameter was used for measuring steady flows against resistance. The water manometer was used for pressure measurements. The experimental arrangement used is shown in figure 8.3. Throughout this experiment the mixture control was set to deliver 20 per cent oxygen with nitrous oxide. First, allowing free unobstructed flow, the flow rates were measured when the pressure control was set to 5, 10, 15 and 20 mm Hg. Then the occluded expiratory valve was connected to the outlet from the Rotameter. The flows achieved and the corresponding pressures generated were measured while the pressure control was again set to 5, 10, 15 and 20 mm Hg. The expiratory valve was used in the same open and partially closed positions as in the previous experiments. Finally, the pressures developed when the outlet was completely obstructed were confirmed for each setting of the pressure control.

Using the respiratory flow simulator the pressure-flow characteristics of the machine were then determined under tidal flow conditions. Transducers were used for both the pressure and the flow measurements. The experimental layout is indicated in figure 8.4. Measurements were made both with and without the reservoir bag in the circuit. The combinations of tidal volume and rate used were 500 ml at a rate of 13 per minute, 1,000 ml at a rate of 13 per minute, and 500 ml at a rate of 24 per minute.

The measurement of volume and "back-flow"

It was found that under conditions of simulated respiration, a slight reverse flow, back into the anaesthetic machine, could occur when the pressure within the system was raised during

"expiration". In order to measure this, the flow transducer was connected in the supply line, as indicated in figure 8.5. The "flow" signals were integrated with respect to time to obtain an output signal proportional to volume, which was recorded by an Ediswan pen recorder in place of the oscilloscope and camera. The mixture control was set to deliver 20 per cent oxygen. The pressure control was set at 5 and 10 mm Hg only, since "rebreathing" was not observed when higher supply pressures were tried. The same expiratory valve settings and variations of tidal volume and of rate were used as in the previous experiment. Measurements were made both with and without the reservoir bag in the circuit. These were repeated after replacing the corrugated tubing by an equal length of non-expansile tubing.

RESULTS

The characteristics of the expiratory valve

Since the characteristics of the particular expiratory valve used in this investigation are relevant to all the tests carried out, they are mentioned first. The pressure-flow curves obtained for this valve are shown in figure 8.6. The resistance of the valve in the open position is fairly representative for this type of valve. The resistance of the valve when partially closed, however, is high. The machine was therefore tested under correspondingly extreme conditions. The resistance of the valve to the nitrous oxide and oxygen mixture was greater than that to air, except at low flows.

The calibration of the mixture control

The percentage of oxygen delivered was always found to be the same for a given set of test conditions. The full spread of

the measurements is shown in figure 8.7. The broken line indicates the ideal calibration. The readings of 19.5 and 19 per cent were obtained while the mixture control was at the 20 per cent setting, while the pressure control was set to 5 and 7.5 mm Hg, and while the Heidbrink valve was 1 turn and $1\frac{1}{2}$ turns closed respectively. The solitary measurement of 9.5 per cent oxygen was obtained while the mixture control was placed at 10 per cent setting, while the pressure control was set at 3 mm Hg and while the respiratory flow simulator was adjusted to give a tidal volume of 300 ml at a rate of 18 per minute. All other oxygen percentage measurements within the range of normal use either coincided with or were slightly greater than the percentage indicated by the mixture control.

Whereas under steady flow conditions an increase in the resistance to flow, produced by screwing down the expiratory valve, was found to depress slightly the percentage of oxygen delivered, under simulated respiratory flow conditions an increase in the resistance to flow tended to cause a slight rise in the percentage of oxygen. Under both steady flow and tidal flow conditions an increase in the setting of the pressure control tended to cause an increase in the percentage of oxygen delivered.

The effect of depressing the emergency oxygen control upon the percentage of oxygen delivered is shown in figure 8.8. It can be seen that, subject to the setting of the mixture control, the higher the setting of the pressure control the less the effectiveness of the emergency oxygen control. With the pressure control set at 5 mm Hg, the percentage of oxygen delivered while the oxygen button was depressed was always greater than 75 per cent, regardless of the position of the mixture control. The

Heidbrink valve was in the open position throughout this experiment.

The calibration of the pressure control

With the mixture control set at 20 per cent oxygen, the pressures developed at different settings of the pressure control under the test conditions already described are shown in figure 8.9. When the outlet was kept occluded no pressure was measurable until the control was advanced up to nearly 2 mm Hg. The pressure fluctuated 1 cm H₂O above and below the mean value at a rate which increased from 4 to 24 cycles per minute as the setting of the pressure control was increased. This oscillation was reduced when free flow was permitted before occluding the outlet. The magnitude of the initial steep pressure rise, already referred to, increased with the setting of the pressure control and with the percentage of oxygen. If the pressure control was set to any mark above 5 mm Hg (6.8 cm H₂O) while the mixture control was set at 100 per cent oxygen, the pressure rose initially to 41 cm H₂O (30 mm Hg); with the mixture control at other settings the initial peak pressure was also related to the speed of occlusion.

The effect of the setting of the mixture control upon pressure

Although the setting of the mixture control had negligible effect upon the pressures developed during no-flow conditions, this was not found to be the case during steady flow conditions. Figure 8.10 reveals that for a given flow resistance and a given setting of the pressure control, the pressure within the anaesthetic circuit was increased as the percentage of oxygen was increased.

Depression of the oxygen button during steady conditions

When the emergency oxygen control was depressed while the outlet was occluded, the pressure settled between 40 and 41 cm H₂O (30 mm Hg), regardless of the setting of the mixture control. Trying different settings of the mixture control during steady flow conditions, however, a variable pressure increase was found when the oxygen button was depressed. This is shown in figure 8.13, and it is also referred to below under the heading of "pressure-supply-flowrate characteristics".

The pressures occurring during tidal flow

Figure 8.11 shows the pressure swings that were observed during simulated respiratory flow, while the pressure control was set at 5 mm Hg and at 15 mm Hg, while the Heidbrink valve was open, and while the tidal volume, the "respiratory" rate and the mixture control setting were varied. The probable explanation of the discrepancies between figures 8.10 and 8.11 is that the valve settings were not identical, the two experiments having been performed on different occasions. There was a tendency for the pressure to rise as the oxygen percentage was increased, except that there was sometimes a fall of pressure upon reaching the 100 per cent oxygen position of the mixture control. In all cases there was an increase of pressure, of up to 2 cm H₂O, upon depressing the emergency oxygen button. As might be expected, both the mean pressures and the pressure swings varied with the tidal volumes and with rate.

Figure 8.12 shows the effect of closing the expiratory valve and of increasing the setting of the pressure control while other factors are kept constant (mixture control at 20 per cent oxygen; tidal volume of 750 ml; rate of 13 per minute). An

increase of either causes an increase both in the mean pressure and in the pressure swing.

The pressure-supply-flowrate characteristics

The flows supplied by the Walton Five anaesthetic machine when the flow resistance and the pressure control setting were varied under steady flow conditions, and while the mixture control was set to 20 per cent oxygen, are shown in figure 8.13. The solid lines indicate the flows delivered against different resistances while the pressure control was set to 5, 10, 15 and 20 mm Hg. The flow resistance characteristics of the Heidbrink valve are shown in broken lines. This diagram may be used for relating the pressure-supply-flowrate characteristics of the anaesthetic machine with the flow resistance characteristics of associated equipment, and both, with reservations indicated below, may be related to any defined peak respiratory flow rates. The effect of depressing the emergency oxygen control under each set of conditions is also shown. This caused an increase in both pressure and flow. The oxygen percentage delivered during depression of the emergency oxygen control was measured in order that the appropriate corrections might be made to the Rotameter readings.

The pressure-flow characteristics during tidal flow

Using the experimental arrangement shown in figure 8.4, the peak flows delivered by the machine, during conditions of simulated respiration, were derived by measuring the flow through the flow transducer and allowing for the peak flow rates generated by the respiratory flow simulator (see table 8.1). It was then possible to compare the pressure-supply-flowrate characteristics of the Walton Five under conditions of peak flow

during simulated respiration, with those under conditions of steady flow. Such a comparison is shown in figure 8.14. The pressures recorded during "expiration" tended to be higher than would have been expected from the steady flow characteristics. This may be related to the initially high pressures recorded upon obstructing the outlet under steady flow conditions (see "The calibration of the pressure control" above). The pressure-flow characteristics (20 per cent oxygen with nitrous oxide) of the twin supply tubing used with a nasal inhaler and of the nasal inhaler's expiratory valve (not the valve used for testing the machine) are also shown.

Including the reservoir bag in the circuit, or excluding it, made very little difference to the peak "inspiratory" and "expiratory" flows and pressures measured. (A length of corrugated tubing was used in these experiments as indicated in figure 8.4, and not the narrow bore twin supply tubes). The greatest change observed was a reduction in the "inspiratory" pressure when the reservoir bag was excluded while the pressure control was set to 5 mm Hg. On one occasion the pressure became slightly subatmospheric under these circumstances. At greater supply pressures the differences between peak values recorded with and without the reservoir bag in circuit were barely measurable. Examination of the records, however, did reveal that nearly all minor pressure fluctuations were smoothed out when the reservoir bag was used.

Back-flow

The unexpected results of this experiment are displayed in figure 8.15. With the pressure control set at 10 mm Hg, reverse flow occurred only when the expiratory valve was very

nearly closed, and then it was negligible. Only the results obtained while the pressure control was set to 5 mm Hg have therefore been given. There was not a great deal of difference between the reverse flows recorded under the four sets of conditions - corrugated tubing with and without the reservoir bag, and non-expansile tubing with and without the reservoir bag. Using the corrugated tubing, the reverse flow was only slightly greater when the reservoir bag was in the circuit than when it was not. A larger difference was expected. It was suggested that much of the reverse flow might have been taken up in expanding the corrugated tubing. Using non-expansile tubing, however, the reverse flow was often greater than when corrugated tubing was used, and sometimes it was greater when the reservoir bag was excluded from the circuit than when it was included. This effect has not been fully investigated, but careful scrutiny of the records revealed that when the reverse flow was greatest in the presence of the reservoir bag, it occurred during the early part of "expiration" only. This was expected. When the reverse flow was greatest in the absence of the reservoir, however, it was prolonged throughout the greater part of "expiration". This suggests that the reverse flow occurs as the result of an intermittent leak within the anaesthetic machine.

Other observations

No deliberate tests were carried out to determine the precise performance of the safety devices, but at one time or another they were brought into action during this investigation and found to be working satisfactorily. The safety valve opened at -4 cm H₂O.

It was observed that when the pressure control was in the "off" position a very slight flow of oxygen still occurred. This

was revealed by a small but measurable increase in pressure which eventually built up when the outlet was left occluded while the pressure control was in the "off" position. When the outlet was not occluded there was an increase in the oxygen concentration of the gas in the corrugated tube, to well above 20 per cent, when the pressure control was left in the "off" position.

DISCUSSION

The purpose of this investigation was to determine the performance of a particular Walton Five dental anaesthetic machine as a preliminary to using it for a specific experimental project. The steady flow tests were carried out because they were relatively simple. The simulated respiratory flow pattern tests were carried out because the assessment of any machine should include tests carried out under controlled circumstances comparable with those under which it would be used - unless it can be shown that simpler tests are adequate. In the absence of data on the respiratory patterns which actually occur during dental anaesthesia, the choice of the "respiratory" variables was arbitrary. (Subsequent measurements of peak inspiratory flowrate made during routine dental anaesthesia indicated that under conditions of oxygen restriction, or of surgical stimulation under light anaesthesia, flow rates greater than 65 l./min can occur. See PART IV). Although the original intention was not to cast judgment upon the machine, a few comments will be offered.

The performance of this machine does live up to the claims published in the manufacturer's leaflet.

The usual, and probably the most serious, criticism of dental anaesthetic machines concerns the inaccuracy of the calibration of their mixture controls. There is no doubt about

the calibration of the mixture control of this machine, even under extreme testing conditions, being a very considerable improvement over the calibration of many machines in current use, such as those tested by Goldman (1958), by Hunter and Fraser (1959) and by Bourne (1960). The calibration may give all the accuracy that clinical circumstances require but to acknowledge this would imply that the required accuracy has been defined. Pask (1960) has drawn attention to the precipitous arterial oxygen deprivation that may be expected when the inspired oxygen concentration falls to about 7 per cent. A case might therefore be made for a very high order of accuracy of the calibration of the mixture control in the 5 to 10 per cent oxygen region - if it is considered that there are occasions when it is justifiable to administer mixtures containing such low concentrations of oxygen, and that anaesthetic machines should be designed to cater for this.

The effects and the possible dangers of raised airway pressures during dental anaesthesia in sitting patients do not appear to have received much consideration. Since they may be of some importance, attention has been paid to the pressures which may be generated by the Walton Five anaesthetic machine. The findings are reported but opinion as to their significance is reserved.

From the observations made upon the extent and circumstances of back-flow during "expiration", it is evident that any opinions expressed with regard to the effects of using, or of not using, a reservoir bag in conjunction with a dental anaesthetic machine should be viewed with caution.

The economics of using the Walton Five should also be

considered. It can be seen from figures 8.13 and 8.14 that high flows, with correspondingly high gas consumption, are easily obtainable. Flows used in practice depend upon the patient's respiratory pattern, upon the apparatus used in conjunction with the anaesthetic machine, and upon the anaesthetist. If narrow-bore twin supply tubing is used to connect the anaesthetic machine to the nasal inhaler, then, if inspiration against resistance is to be avoided, the supply flow rate should be sufficient to meet the peak inspiratory demand of the patient. If the wide-bore tubing of negligible resistance is used without a reservoir bag, then the supply flow rate should still be sufficient to meet the peak inspiratory demand. In the first case, however, the pressure control will have to be turned up higher than in the second. If the wide-bore tubing is used with the reservoir bag in circuit, and if unobstructed nasal breathing is fully established, then the supply flow rate need not be appreciably greater than the patient's minute volume. In practice, however, fine control of flow rate by manipulation of the pressure control at the lower end of the scale is not easy. (The calibration of the mixture control at such low flows was not checked.) If there is an air leak between the mouth and the pharynx during nasal breathing, then the pressure control should be turned up sufficiently to overcome the resistance of the nose and nasopharynx at the peak inspiratory flow rate. It will be appreciated that the more the pressure control is turned up the greater will be the gas wastage and the airway pressure during expiration. It is suggested that the use of wide-bore tubing is indicated and that easy control of low flow rates, without sacrifice of the accuracy of the mixture control calibration, would be advantageous.

TABLE 8.1

Simulated Respiratory Variables

Tidal volume ml	Rate per min.	Minute volume l./min	Peak "inspiration" l./min	Peak "expiration" l./min
500	13	6.5	33	20
750	13	9.8	48	32
1000	13	13	65	41
750	16	12	62.5	38
300	18	5.4	32	20
500	18	9	49	32
500	24	12	62.5	38
300	24	7.2	not measured	not measured

FIGURE 8.1

The controls of the Walton Five anaesthetic machine and the experimental arrangement used for measurement of the concentration of oxygen delivered under steady flow conditions.

FIGURE 8.2

The experimental arrangement used for measurement of the concentration of oxygen delivered under conditions of simulated respiration.

EMERGENCY OXYGEN CONTROL

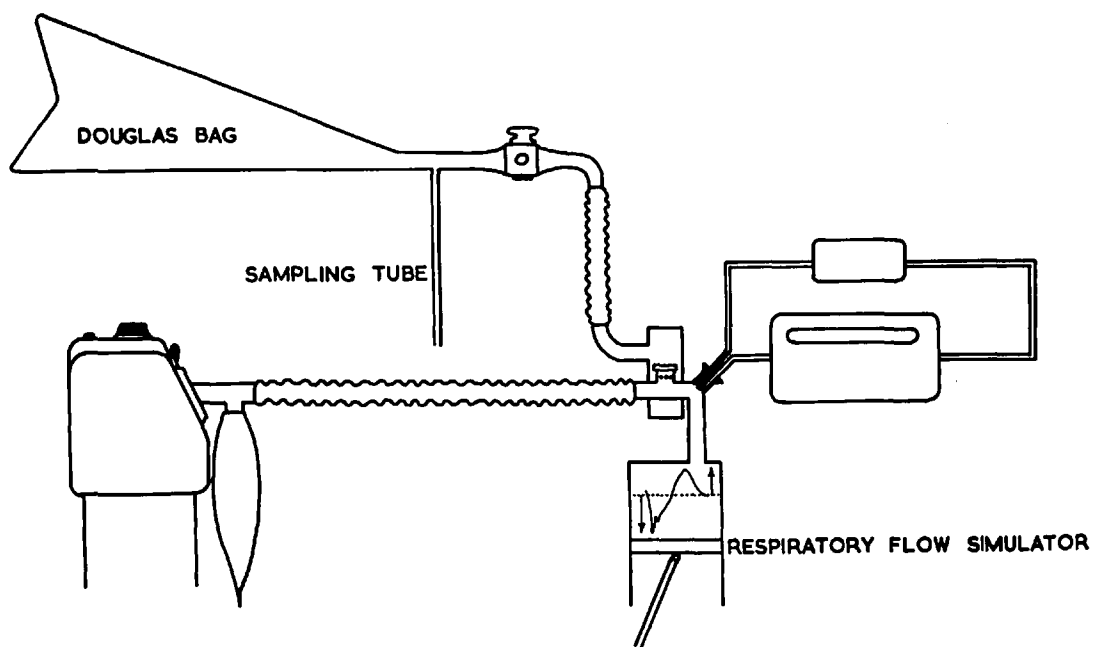
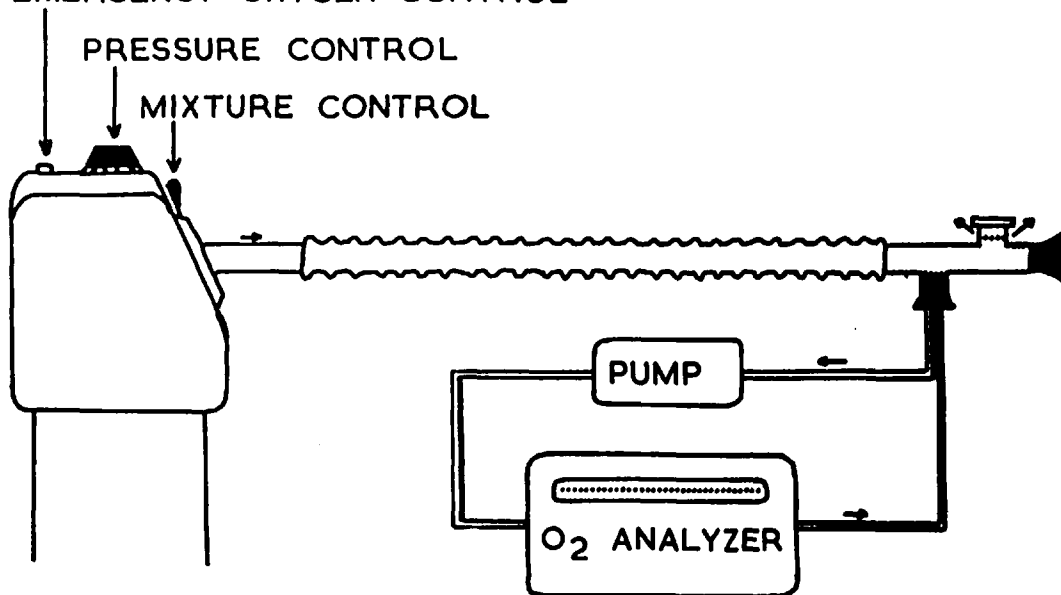


FIGURE 8.3

The experimental arrangements used for measurement of the pressure-flow relationships of the Walton Five anaesthetic machine under steady flow conditions.

The flow transducer (upper diagram) was used during free unobstructed flow.

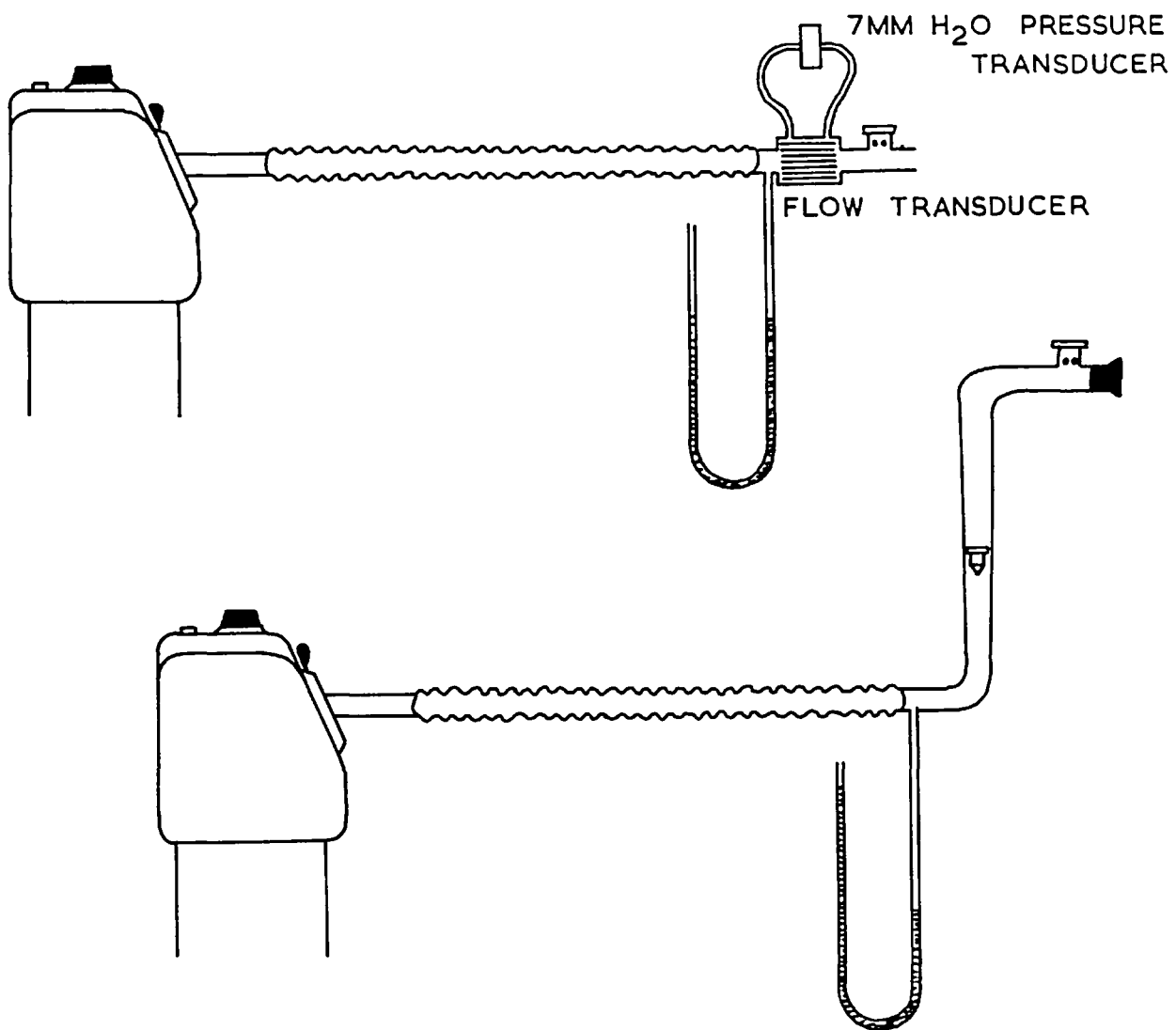


FIGURE 8.4

The experimental arrangement used for measurement of the pressure-flow relationships of the Walton Five anaesthetic machine under conditions of simulated respiration.

FIGURE 8.5

The experimental arrangement used for measurement of volume back-flow into the Walton Five anaesthetic machine during conditions of simulated respiration. Corrugated and non-expansile tubing were used alternately, with and without the reservoir bag.

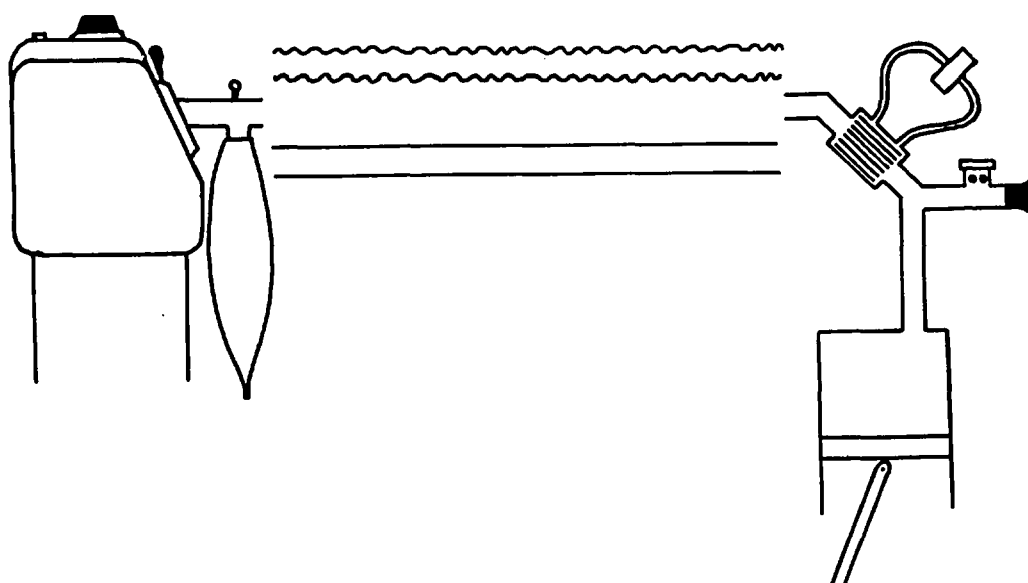
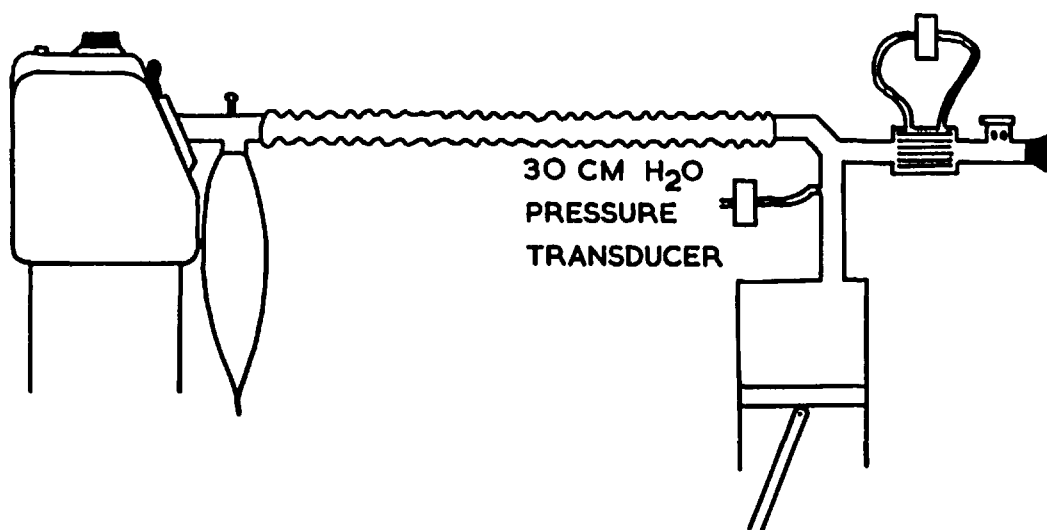


FIGURE 8.6

The flow resistance characteristics of the Heidbrink valve used for testing the Walton Five anaesthetic machine. Note that the pressure across the valve during the passage of gas at low flow rates was less when 80 per cent nitrous oxide was used than when air was used (the viscosity of nitrous oxide is less than that of air, so flow was presumably laminar). At higher flow rates the reverse was the case (the density of nitrous oxide is greater than that of air, so flow was presumably turbulent).

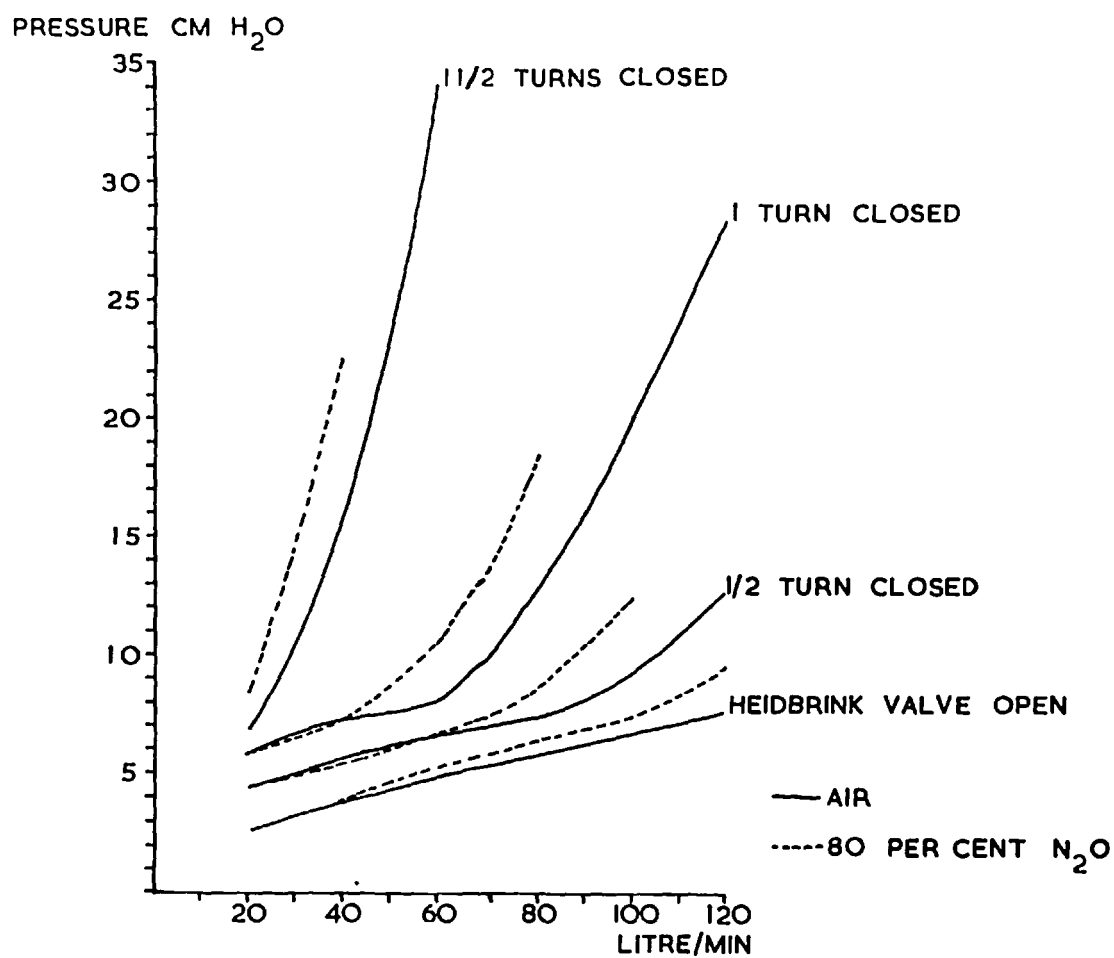


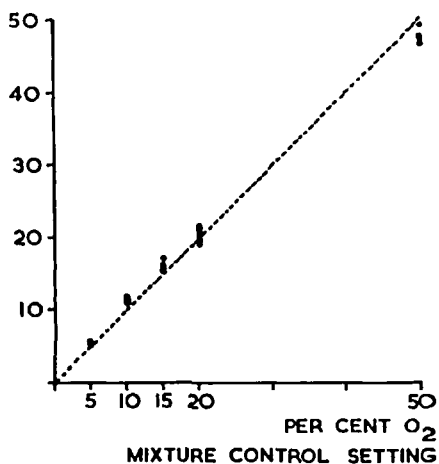
FIGURE 8.7

The concentrations of oxygen delivered, using different settings of the mixture control under all the conditions of test described in the text.

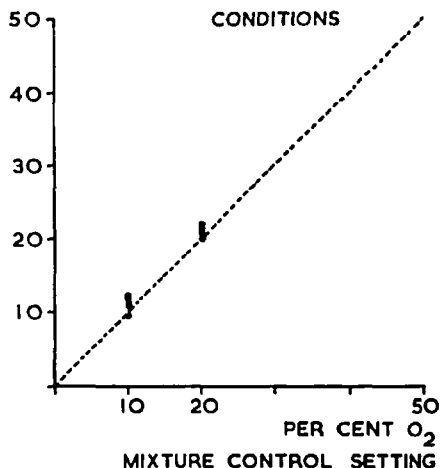
FIGURE 8.8

The concentration of oxygen delivered against the resistance of the open Heidbrink valve while the emergency oxygen control was depressed.

PER CENT O_2 DELIVERED
STEADY FLOW CONDITIONS



PER CENT O_2 DELIVERED
SIMULATED RESPIRATORY FLOW
CONDITIONS



PER CENT O_2 DELIVERED
WHILE EMERGENCY O_2 BUTTON DEPRESSED
• 0 MM HG

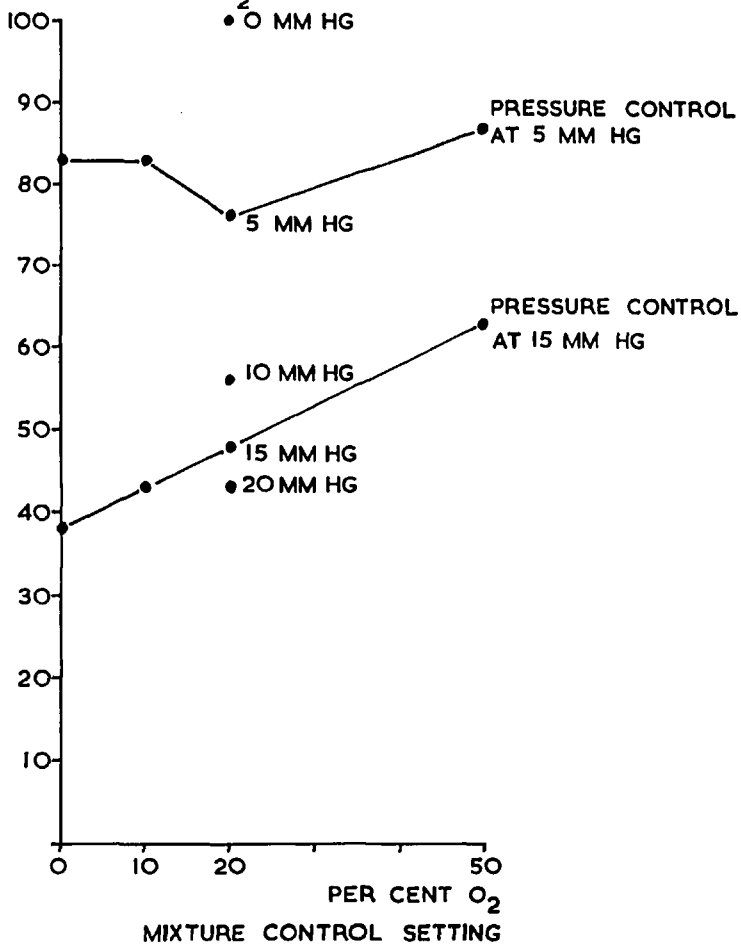


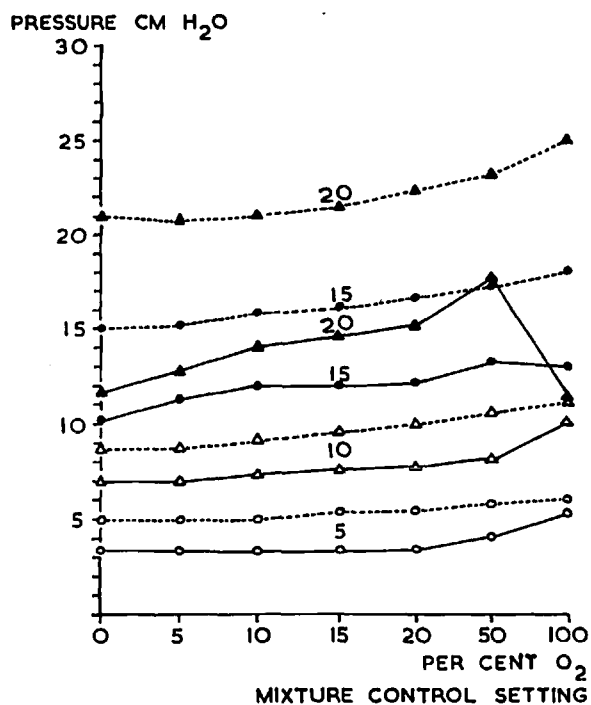
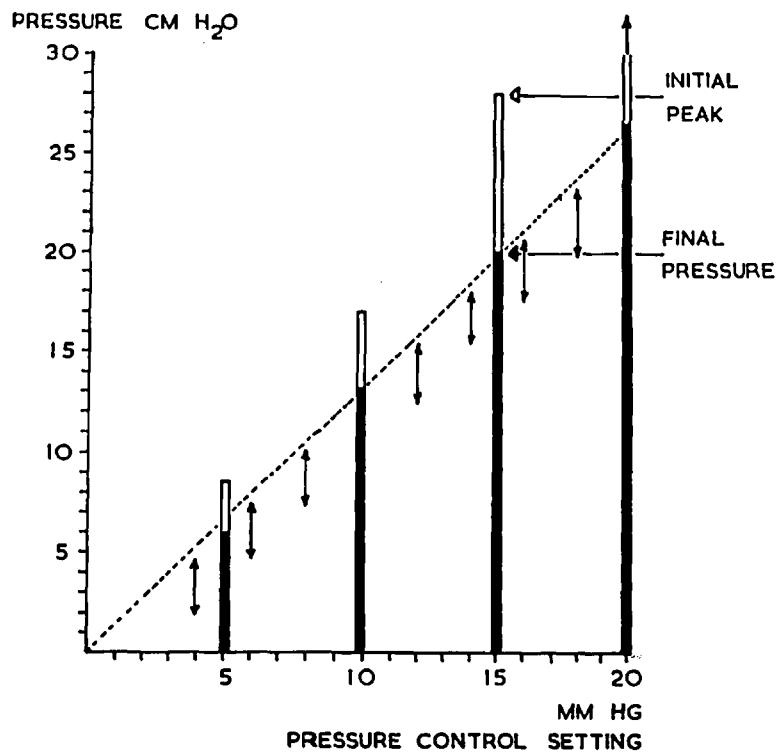
FIGURE 8.9

The calibration of the pressure control. Vertical arrowed lines indicate the pressure oscillations observed during maintained occlusion of the outlet.

A pressure transducer was used for measuring the initial peak pressures.

FIGURE 8.10

The effect of the setting of the mixture control upon the pressure generated under conditions of steady flow.



PRESSURE CONTROL

AT 5 MM HG ○

10 MM HG △

15 MM HG ●

20 MM HG ▲

HEIDBRINK VALVE

OPEN —

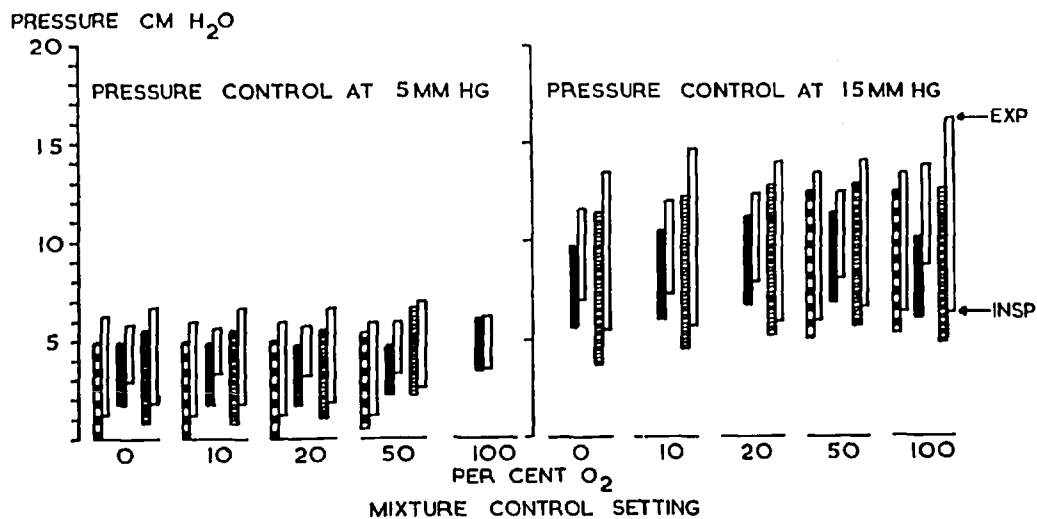
1 1/2 TURNS CLOSED - - - -

FIGURE 8.11

The pressure swings occurring during various conditions of simulated respiration, the Heidbrink valve being open.

FIGURE 8.12

The effect of varying the resistance of the expiratory valve, and of the setting of the pressure control, during set conditions. (Tidal volume - 750 ml; rate - 13 per minute. Mixture control set to deliver 20 per cent oxygen).



■ 500 ML 24/MIN ■ 500 ML 13/MIN ■ 1000 ML 13/MIN □ PRESSURE SWINGS WHILE O₂ BUTTON DEPRESSED

■ PRESSURE CONTROL AT 5 MM HG
 ▨ PRESSURE CONTROL AT 10 MM HG
 □ PRESSURE CONTROL AT 15 MM HG

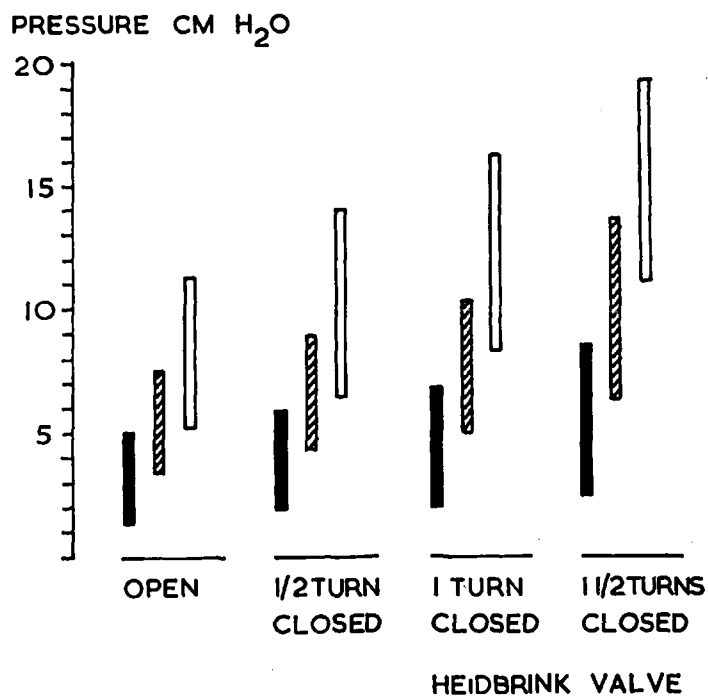


FIGURE 8.13

The pressure-supply-flowrate characteristics of the Walton Five anaesthetic machine (solid lines, labelled according to the setting of the pressure control), related to the flow-resistance characteristics of the Heidbrink valve (broken lines) under conditions of steady flow. The arrow-points indicate the pressure-supply-flowrate characteristics while the emergency oxygen button is depressed.

N.B. Mixture control set to deliver 20 per cent oxygen with nitrous oxide.

FIGURE 8.14

Solid lines - pressure-supply-flowrate characteristics of Walton Five machine under conditions of steady flow.

Broken lines - pressure-supply-flowrate characteristics of the Walton Five machine under conditions of simulated respiration.

Dotted lines - flow-resistance characteristics of the twin supply tubing for a nasal inhaler, when used alone, and when used with the nose-piece and its incorporated expiratory valve - for a mixture of 20 per cent oxygen with nitrous oxide.

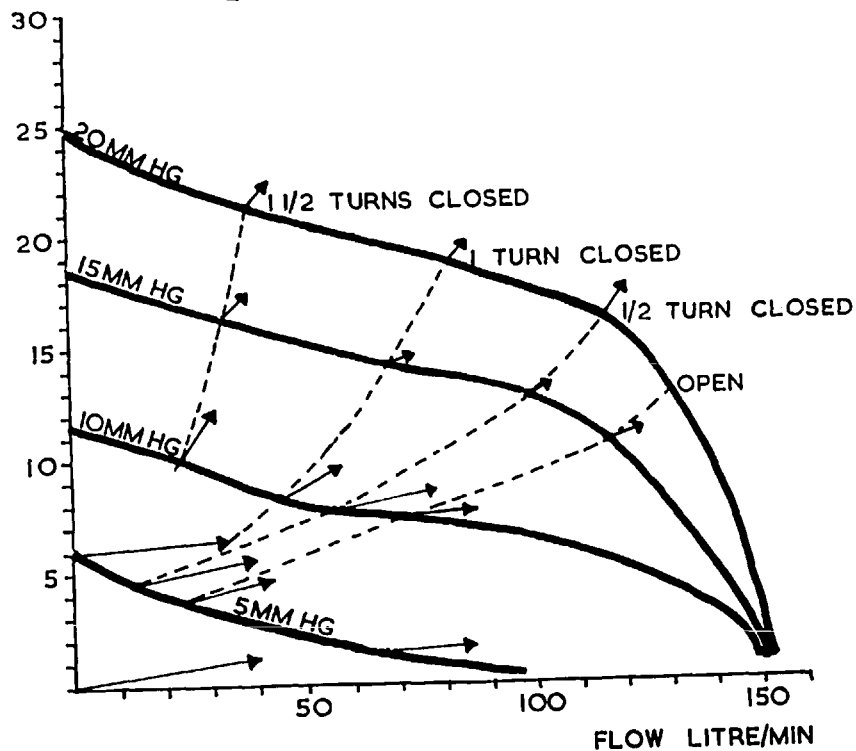
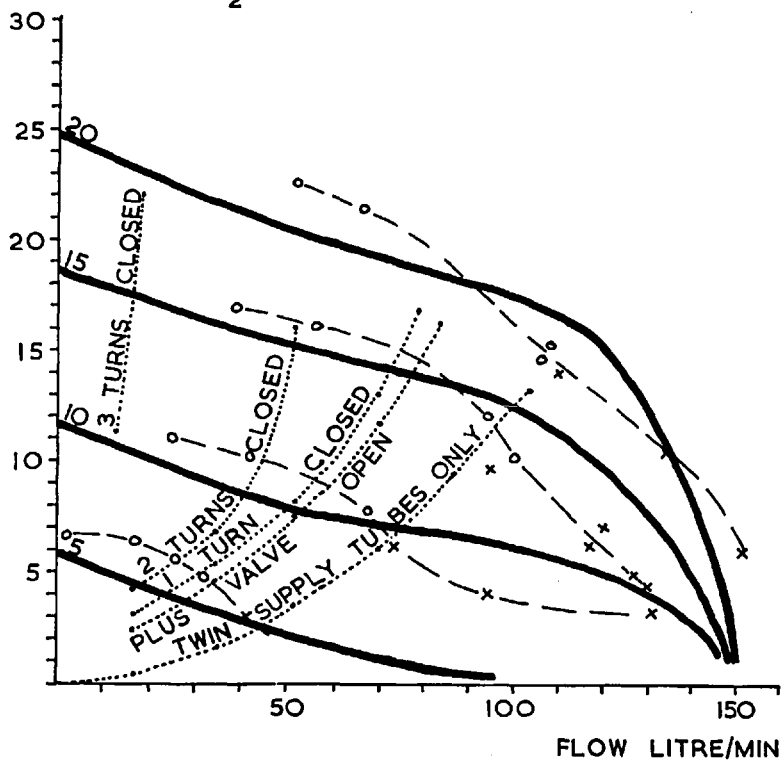
PRESSURE CM H₂OPRESSURE CM H₂O

FIGURE 8.15

The back-flow measured during conditions of simulated respiration, using corrugated and non-expansile tubing alternately, with and without the reservoir bag. The pressure control was set to the 5 mm Hg position.

RATE/MINUTE

24

24

24

13

13

13

13

VALVE CLOSURE
IN TURNS

1

1 1/2

1 1/2

1

1 1/2

1

1 1/2

TIDAL VOLUME

300

500

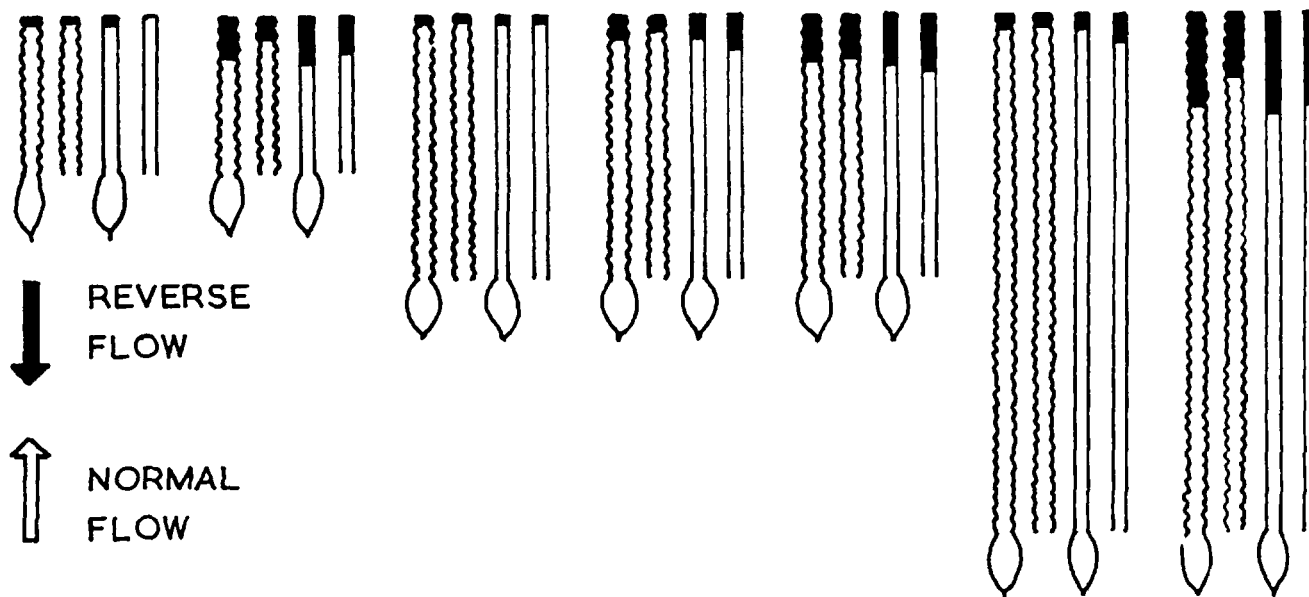
1000



REVERSE
FLOW



NORMAL
FLOW



CHAPTER 9

DELAYS IN ANAESTHETIC BREATHING SYSTEMS

The contents of this chapter have not been published. The work was started in 1964, while holding a Geigy Research Fellowship in the Research Department of Anaesthetics, the Royal College of Surgeons of England. It was continued in the Department of Anaesthesia, University of Leeds, where Dr. Klaus Siebold assisted with the final experiments.

There can be no doubt about the desirability of knowing the dose of any drug prescribed for a patient. When an anaesthetist administers an inhalation anaesthetic, however, he is usually unaware of its dose, although he should have some idea of its concentration (see chapter 16).

Goldman (1959) advocated the administration of 100 per cent nitrous oxide for the induction of anaesthesia in the dental chair. Once "automatic" respiration was established, he recommended the administration of 10 per cent oxygen for two or three minutes, and then the addition of 1 per cent of oxygen for every minute of anaesthesia, so that at the end of five minutes the patient would be getting at least 15 per cent oxygen. Recently (Goldman, 1965) he laid more stress on the intravenous induction of anaesthesia, but made the same recommendations with regard to the gas mixtures to be administered for maintenance.

Walsh (1960), discussing the choice of anaesthetic machines for dental anaesthesia, commented: "In dental anaesthesia the mixture breathed by the patient must be critically and accurately adjusted and requires several fine alterations during the anaesthetic, if possible anticipating changes in the depth of anaesthesia. There is not the time to make the necessary mental arithmetic involved in calculating what changes are necessary, say, in a gas mixture of 10 litres of nitrous oxide and one litre of oxygen, to alter the mixture to contain say 7% oxygen; whereas in an intermittent-flow machine the mixture is read in percentage direct from a dial".

Evidence was provided in chapter 8 to suggest that one ought to be able to place a fair degree of confidence in the calibration of the mixture control of the Walton Five anaesthetic machine, and it was mentioned that the mixture control is marked in 1 per cent divisions between 0 and 15 per cent oxygen. This machine, therefore, is designed

to cater for the above requirements, which are probably fairly representative for an appreciable number of dental anaesthetists.

What is more important than the amount of oxygen delivered by the anaesthetic machine at any one moment, however, is the amount of oxygen reaching the heart and the central nervous system; or, considering the other component of the gas mixture, the partial pressure of nitrous oxide reaching the central nervous system is of more immediate significance than that leaving the anaesthetic machine. It takes time for a change in anaesthetic mixture delivered by an anaesthetic machine to be reflected by a corresponding change in the brain, and this is what Walsh (1960) would have had in mind when he referred to the need to make "several fine alterations during the anaesthetic, if possible anticipating changes in the depth of anaesthesia". It takes time for a change in anaesthetic mixture to become established, first throughout the breathing system, and secondly throughout the lungs. Further delays are related to the lung-brain circulation time, and to the rate of perfusion and the volume (i. e. the time constant) of the brain itself.

The delays in transport in both the apparatus and the patient should be considered in relation to the usual duration of dental anaesthetics, and in relation to the number of times that it is considered necessary to change the gas mixture delivered during a single anaesthetic. The average duration of 300 dental anaesthetics observed by Walsh (1958) at the Royal Dental Hospital of London was about two and a half minutes. In Part IV an average duration of just over three minutes is reported for the same hospital in 1961. The frequency distribution curve of anaesthetic duration against numbers of patients anaesthetised showed its main peak at two minutes (see chapter 13, figure 13.6) in both series. The average duration in series reported

by Bourne (1960) and Goldman (1964) is even shorter. If only three "fine alterations" have to be made within two minutes, this allows, on average, only about 30 seconds for each change to become effective. Allowing 10 seconds for transport from lungs to brain, and assuming that there is no delay in the apparatus, this leaves about 20 seconds for the mixture to reach the alveoli. In this time the alveolar concentration is unlikely to register more than about 60 per cent of the change in gas composition introduced at the mouth (see also the end-expired nitrous oxide "wash-in" curves for two volunteers, presented in chapter 20. These indicate a change of about 50 per cent of the inspired concentration in the first 20 seconds).

Delays in the transport of nitrous oxide within the patient were mentioned in chapter 2, and they are mentioned again in chapter 12 and in Part V. This chapter is concerned with delays arising within apparatus.

THEORETICAL ANALYSIS

Symbols

V_T	Tidal volume (inspiratory) in ml.
V_B	Volume of gases contained in the reservoir bag at the change from expiration to inspiration, in ml.
V_{App}	Apparatus volume - excluding the reservoir bag - in ml. (In this instance the apparatus volume is accounted for largely by the capacity of a standard length of corrugated tubing used in anaesthesia. This is usually about 500 ml when new. After softening and stretching it may be nearer 700 ml).
$\dot{V}_I$	Inspired minute volume in l/min.

$\dot{V}_g$	Flow rate of fresh gases in l/min
f	Respiratory rate in c.p. min.
$\bar{F}_{I_{N_2O}}$	Fractional concentration of nitrous oxide in mixed inspired gases.
$\bar{F}_{I_{Air}}$	Fractional concentration of air in mixed inspired gases.
$\bar{F}_{I_{O_2}}$	Fractional concentration of oxygen in mixed inspired gases.
t	Time interval in seconds.

Demand systems

An economical demand system, used without a reservoir bag, would supply the patient's peak inspiratory flow requirements at atmospheric pressure (i. e. under conditions of free flow - see chapter 8), and it would supply no fresh gases during expiration.

From figure 8.14 (chapter 8) it can be seen that by setting the pressure control of the Walton Five anaesthetic machine to the 5 mm Hg position, a free flow of 100 l/min can be obtained; in other words the patient can inspire fresh gases at instantaneous flow rates up to 100 l/min without having to develop a subatmospheric pressure in the mask. (It is shown in chapter 15 that peak flow rates of 100 l/min can easily occur during dental anaesthesia). In order to stop the flow of fresh gases during expiration, the opening pressure of the relief valve in the breathing system would have to be adjusted to 5 mm Hg (6.8 cm H₂O). This arrangement would impose a positive pressure in the mask according to the difference between the instantaneous inspiratory flow rate and 100 l/min, and it would impose an excessive pressure throughout expiration. This could be unpleasant during induction of anaesthesia, and undesirable (see chapters 3 and 12). It would have the advantage that any leaks would be outwards, from the

breathing system into the room.

The above analysis assumes negligible flow resistance between the anaesthetic machine and the patient. In the face of a high flow resistance, the pressure control would have to be turned up to an even higher setting. Using narrow bore twin tubes having the flow resistance characteristics indicated in figure 8.14; for example, the pressure control would have to be turned up to about the 14 mm Hg position, (for 100 l/min peak flow), and unless the anaesthetist screwed down the expiratory valve so that corresponding expiratory pressures were developed, fresh gases would flow to waste during expiration.

By adding a reservoir bag and using a "Magill" system with corrugated tubing having negligible flow resistance, it would be possible to reduce the setting of the pressure control so that free flow would be sufficient to supply the patient's inspiratory tidal volume during inspiration (i.e. the supply flow rate during inspiration would be about twice the inspired minute volume, if inspiration and expiration were of equal duration). The opening pressure of the relief valve could be reduced correspondingly. Supply of fresh gases would cease during expiration, as above, so the "Magill" system would not be working in the customary manner (its operation is usually considered in relation to a continuous flow anaesthetic machine, such as the "Boyle"). A diagrammatic analysis of the events during a single respiration is shown in figure 9.1.

Whether a reservoir bag is or is not used, however, if a demand system is working economically, the average flow rate of fresh gases, taken over a complete respiration, is equal to the patient's inspired minute volume. Only expired gases go to waste. If a reservoir bag is not used, the average transit time of fresh gas from the anaesthetic machine to the patient will then depend upon the volume

of the apparatus (excluding the reservoir bag) and the inspired minute volume. Leaving aside any rebreathing and mixing of inspired and expired gases, the delay in delivery of a new gas mixture from the anaesthetic machine to the patient will be given by:

$$t = \frac{V_{App}}{\dot{V}_I} \times \frac{60}{1000}$$

Example: Suppose $V_{App} = 500$ ml., and $\dot{V}_I = 10$ l/min., then the average delay will be 3 seconds. The actual delay will depend upon the phase of respiration when the change is made. If $V_T = 1000$ ml. ($\dot{V}_I$ being 10 l/min), and if inspiration and expiration are of equal duration, there will be no flow at all for the 3 seconds of expiration. Thus it will take more than the average 3 seconds for an altered gas mixture to reach the patient if the change is made near the end of inspiration or the beginning of expiration. On the other hand the actual transit time will be less than 3 seconds if the change is made during peak inspiratory flow.

If a reservoir bag is used, prediction of the delay in delivering a new gas mixture becomes more difficult. The sequence of events can be followed in figure 9.2. Suppose a patient, who has been pre-oxygenated, is supplied with 100 per cent nitrous oxide, which is turned on at the start of inspiration. Up to the time "a", nitrous oxide will pass directly into the corrugated tubing. Between times "a" and "b", the corrugated tubing will receive nitrous oxide from the anaesthetic machine and oxygen from the reservoir bag. The unshaded area between "a" and "b" indicates the volume of oxygen coming from the reservoir bag, and the shaded area indicates the volume of nitrous oxide coming from the anaesthetic machine. Between times "b" and "c", only nitrous oxide will enter the corrugated tube, but it will also enter the reservoir bag. Between times "c" and "d", which is now in the beginning of expiration, nitrous oxide will continue to enter the reservoir bag from the anaesthetic machine, but gases will also enter

the reservoir bag from the corrugated tubing, due to the rebreathing that takes place between the start of expiration and the opening of the relief valve. In a Magill system which is working efficiently, the volume of gas flowing from the corrugated tubing back into the reservoir bag will be equal to the patient's anatomical dead space. The first part of it will be nitrous oxide, and the last part may be a mixture of nitrous oxide and oxygen, depending upon the amount of rebreathing. From the time "d" to the start of the next inspiration, expired gases will escape from the relief valve.

Whether any nitrous oxide at all reaches the patient during the first breath depends upon the relative magnitudes of V_T and V_{App} . The gas mixture remaining in the reservoir bag will depend upon its initial volume V_B relative to the tidal volume V_T . During the second inspiration the patient will inhale the gases left in the corrugated tubing by the end of the first expiration, and gases will enter the corrugated tubing in the same manner as during the first breath - except that at the start of the second inspiration the reservoir bag will contain a mixture of nitrous oxide and oxygen instead of just oxygen. The patient will not receive 100 per cent nitrous oxide until all the oxygen has been extracted from the reservoir bag. The delay will depend appreciably upon V_B . "Dumping" the bag at the end of the first inspiration would reduce the ultimate delay, although the contents of the second breath would be mainly the previous contents of the "dumped" reservoir bag. "Dumping" the reservoir bag immediately before changing the composition of the gases supplied would be more effective.

Non-rebreathing systems

Given a non-rebreathing system (for example, such as that used by Young and Whitwam, 1964), the setting of the pressure control

could be reduced further, so that free flow would be sufficient to supply the patient's minute volume (instead of twice the minute volume described above), because flow into the reservoir bag would continue during expiration. The events during a single cycle are indicated in figure 9.3, which may be compared with figures 9.1 and 9.2.

Analysis of a non-rebreathing system may be simplified by making the following assumptions:

- i) that at the start of inspiration, the inspiratory flow rate reaches the supply flow rate instantaneously (cf. Mapleson, 1954b).
- ii) that at the end of inspiration, the inspiratory flow rate falls from the supply flow rate to zero instantaneously;
- iii) that inspiration and expiration are of equal duration.

For the first analysis let $V_T = V_{App}$.

Suppose the mixture control is moved from the 100 per cent oxygen position to the 100 per cent nitrous oxide position at the start of inspiration. Then, by the end of inspiration, the patient will have inhaled the oxygen which previously filled the corrugated tube, and the corrugated tube will contain $\frac{V_T}{2}$ of nitrous oxide from the anaesthetic machine, and $\frac{V_T}{2}$ of oxygen from the reservoir bag.

By the end of the expiration, the $\frac{V_T}{2}$ of oxygen withdrawn from the reservoir bag will have been replaced by an equal volume of nitrous oxide from the anaesthetic machine. The concentration of nitrous oxide in the reservoir bag will depend upon V_B and the 'mixed' concentration of nitrous oxide in the corrugated tube will be 50 per cent.

Although the concentration of nitrous oxide inhaled from the corrugated tube will vary from moment to moment (as indicated in figure

9.3), the mixed inspired concentration of nitrous oxide during the second breath will be 50 per cent ($\frac{V_T}{2}$ of nitrous oxide from the anaesthetic machine and $\frac{V_T}{2}$ of oxygen from the reservoir bag). This will be replaced by 75 per cent of nitrous oxide, and by the end of the second breath the reservoir bag will contain 88 per cent nitrous oxide - and so on.

Calculations, along the above lines, using values for V_B of $\frac{V_T}{2}$, V_T and $2 V_T$, ($V_{App} = V_T$), are summarised in table 9.1. This indicates the breath by breath rise in mixed inspired concentration of nitrous oxide under each set of circumstances.

If V_T is greater than V_{App} , theoretical analysis becomes difficult because allowance has to be made for the inspiratory flow pattern, and this has not been attempted.

EXPERIMENTAL ANALYSIS

The foregoing theoretical analysis was put to the test of a series of laboratory experiments, using, in the first instance, the experimental arrangement shown in figure 9.4.

Supplies of air (from a pump) and nitrous oxide were passed through individual Rotameters to a multi-way tap which connected one gas to the breathing system under test, and the other to a Heidbrink valve which was adjusted to have the same flow resistance as the breathing system. Turning the multi-way tap changed the gas supply to the breathing system, directed the other gas to another Heidbrink valve, and provided a marking signal on one channel of a four channel Ediswan pen recorder.

The breathing system consisted of a reservoir bag connected to a standard length of corrugated tubing (about 1 metre long) which terminated in a Heidbrink valve to form a Magill system; or, in a pair

of non-return valves to form a non-rebreathing system; or, the far end was left open to permit free flow.

A versatile piston-type variable flow generator (Hill, Hook and Bell, 1961) was used to simulate a patient breathing into the system, as in chapter 8. This was adjusted so that the only contribution to the "F.R.C." was the connection between the cylinder and the breathing system. The gases "expired", therefore, could be taken as having almost the same composition as the "mixed inspired" gases. A sine waveform was generated.

A Vickers Research Limited flow transducer was interposed between the "patient" and the breathing system (see chapter 6) to provide a "respired volume" write-out on the second channel of the Ediswan pen recorder.

The "respired" gases were sampled continuously, at a rate of 300 ml/min., from a sampling point between the flow transducer and the breathing system, and analysed for nitrous oxide using a prototype solid state transistorised infra-red analyser (Hill and Stone, 1964). This was calibrated using mixtures of nitrous oxide and air obtained from appropriate Rotameters. An alternative sampling point was provided between the breathing system and the gas supply.

Free flow

The flows of nitrous oxide and of air were adjusted to 2.5 l/min, and the multi-way tap was turned to supply nitrous oxide to the breathing system. The gases were sampled between the gas supply and the reservoir bag, which was excluded from the system. The multi-way tap was then turned abruptly so that air was supplied to the system. The interval (t_0) between the signal marking the turning of the tap, and the time at which the infra-red record first registered a change in concentration of nitrous oxide, was noted. The experiment

was then repeated while the gases were sampled at the "patient" end of the system. The interval (t_p) between the marking signal and the first recorded change in concentration of nitrous oxide was again noted. The transit time of air (t) between the sampling points is given by $t = t_p - t_o$. This sequence was repeated with the reservoir bag included in the system.

The whole experiment was repeated using flow rates of 5, 10, 20, 40, 80 and 150 l/min.

As $V_{App} = t \times \dot{V}_S \times \frac{1000}{60} \text{ ml}$, $\frac{1}{\dot{V}_S}$ has been plotted against t in figure 9.5. This should produce a straight line of slope $\frac{t}{\frac{1}{\dot{V}_S}} = V_{App} \times \frac{60}{1000}$

V_{App} was measured by filling the system with water. It was found to be 550 ml, and the corresponding slope has been indicated as a broken line. This is consistent with the results obtained.

There was no consistent difference between the results obtained with the reservoir bag in and out of the system, from which it is concluded that under conditions of free steady flow there is little mixing between the gas in the reservoir bag and the gas supplied to the system - provided that there are no pressure changes. This was confirmed by filling the whole system with nitrous oxide, and then supplying air. One minute after 0 per cent nitrous oxide was registered by the infra-red analyser, the reservoir bag was squeezed, and then a reading of 100 per cent nitrous oxide was obtained for a few seconds.

Tidal flow

In the following experiments the patient simulator was used with both the non-rebreathing and the Magill breathing systems. There was some doubt about V_B , but the reservoir bag was kept "clinically" full at end-expiration and its measured volume in this state was about 1800 ml. When using a non-rebreathing system, $\dot{V}_S$ was adjusted so

that the reservoir bag neither filled nor emptied. $\dot{V}_S$ was slightly greater than $f \times V_T \approx \frac{60}{1000}$ because of the continuous sampling for the infra-red analyser. The same value for $\dot{V}_S$ was used when the Magill system was tested in place of the non-rebreathing system, all else being equal.

Theoretical calculations of the expected breath by breath changes in "mixed inspired" concentrations of air and nitrous oxide, for comparison with the experimental results, were not made because of the uncertainty about V_B .

The general procedure was similar to that described above for free flow conditions, except that the reservoir bag was always incorporated; that tidal flows were used instead of steady flows; and that only the "respired" gases were sampled.

Respiratory rate kept constant

The "breath by breath" changes in "mixed inspired" gas composition following a change in composition of the gases supplied (from nitrous oxide to air), using a non-rebreathing system, and tidal volumes of 400 ml and 600 ml, and the same rate of 15 c.p.m., are shown in figure 9.6. As expected, the change was slower using the lower values for V_T and $\dot{V}_I$.

Tidal volume kept constant

When the tidal volume was kept at 600 ml, and the rate was adjusted to 15 c.p.m. and to 25 c.p.m., using a non-rebreathing system, fewer "breaths" were required to achieve a given change in composition when the lower rate was used. This is shown in figure 9.7. Five "breaths" at a rate of 25 c.p.m. were required for an 80 per cent change, as against 6 "breaths" when a rate of 15 c.p.m. was used. From the theoretical analysis one might have expected the two conditions to have produced the same results on a "breath by breath" basis.

When the change is related to time rather than to numbers of "breaths", the change is shown to have been more rapid with the high rate and minute volume, as expected. An 80 per cent change was achieved after 14.5 seconds using the higher rate, and after 20 seconds using the lower.

The findings were similar when a tidal volume of 1000 ml was chosen, using rates of 9 c.p.m. and 15 c.p.m. See figure 9.8.

Minute volume kept constant

Keeping the minute volume approximately constant at 15 l/min, but altering the tidal volume and rate, using a non-rebreathing system, it was shown that the larger the tidal volume the fewer the breaths required to achieve a given change in composition - see figure 9.9. (14.4 l/min was used when the tidal volume was 400 ml; and about 300 ml/min was added in all the experiments, to allow for the sampling rate). Four "breaths" were required for an 80 per cent change in composition when V_T was 1000 ml, 6 "breaths" were quite adequate when V_T was 600 ml, and 6 "breaths" were marginally adequate when V_T was 400 ml. Plotting the change against time, however, it was shown that an 80 per cent change was achieved sooner using the lower tidal volumes and the higher rates: 10 seconds being required when V_T was 400 ml ($f = 36$), 14.5 seconds when V_T was 600 ($f = 25$), and 16 seconds when V_T was 1000 ml ($f = 15$).

Comparison of non-rebreathing and Magill systems

Comparison between the rate of change of "mixed inspired" gas composition achieved using non-rebreathing and Magill systems under comparable conditions is shown in figures 9.7, 9.8, and 9.9. In every case the change was slower when the Magill system was used, as might be expected. Figure 9.7 shows that five more "breaths" (12 seconds) were required to achieve an 80 per cent change when the Magill system

was used with $V_T = 600$, $f = 25$, and $V_I = 15$. Two extra "breaths" (13 seconds) were required with $V_T = 1000$, $f = 9$, and $V_I = 9$ (figure 9.8). Six extra "breaths" (10 seconds) were required with $V_T = 400$, $f = 36$ and $V_I = 14.4$ (figure 9.9).

The effect of "dumping" the reservoir bag

The effect of "dumping" the reservoir bag immediately after changing the composition of the fresh gas supply is shown in figure 9.10. As expected, the effect was to slow the immediate rise in "mixed inspired" concentration of the new gas mixture delivered to the patient, which is clinically undesirable, although the ultimate rise was more rapid.

The influence of the volume of the reservoir bag

There was no certainty as to the "full" capacity of the reservoir bag in any of the above experiments. In the following experiments, in order to be able to record its size, the reservoir bag was placed in a bottle, and this was connected to a spirometer, as shown in figure 9.11.

The patient simulator of Hill, Hook and Bell (1961) was not available when these experiments were carried out, so a Beaver Respirator was used instead. The disadvantage of this was that the Beaver Respirator had an "F.R.C." of about 700 ml. It was therefore connected to the bottle of a second bag-in-bottle system, the bag of which took the place of a patient's lungs. Even with this arrangement, however, an "F.R.C." of about 150 ml had to be accepted. Attempts to reduce it resulted in pressure changes in the system which made the control and the measurement of tidal volumes difficult.

The infra-red analyser used was a commercial version (Sir Howard Grubb Parsons Ltd., Med 1 Infra-red Analyser) of the prototype used for the earlier experiments. It was calibrated against a previously checked Servomex OA 150 paramagnetic oxygen analyser,

using mixtures of nitrous oxide and oxygen. The output from the Med 1 analyser was recorded using a 'Mingograf' ink jet recorder (Elema-Schonander AB). A sampling rate of 400 ml/min was used and the sample was returned to the "lungs" as shown in figure 9.11.

The multi-way tap used previously was not available, so three separate taps were used in its place; one to control the supply of oxygen (which was used instead of air), a second to control the supply of nitrous oxide, and a third which, when open, allowed nitrous oxide to be diverted into the room so that its flow rate could be adjusted just before the change over (see figure 9.11).

Because of the errors introduced by pressure changes in small bag-in-bottle systems, no attempt was made to investigate the influence of the capacity of the reservoir bag on the operation of the Magill system. The arrangement was used only with a non-rebreathing system.

The procedure was to supply nitrous oxide to the system, and to adjust its flow rate to match $\dot{V}_I$ (taps 1 and 3 being closed and tap 2 being open). The requisite flow was noted, and the nitrous oxide was turned off. Oxygen was substituted (taps 1 and 3 being open and tap 2 being closed). The flow of oxygen was adjusted to match $\dot{V}_I$. Then, watching the spirogram, either the Beaver respirator or the oxygen supply, as appropriate, was turned off momentarily, until the required V_B was recorded on the spirogram. The nitrous oxide supply was turned on again and adjusted to the necessary flow rate. At the end of "expiration", tap 1 was closed, and immediately afterwards tap 2 was opened and tap 3 was closed (the latter operations being carried out simultaneously), and marks were made on the spirogram and the 'Mingograf' record.

Experiments were carried out using a tidal volume of 500 ml, a rate of 12 c.p.m., and reservoir bag volumes of 750 ml and 1300 ml.

The results obtained under the two sets of conditions are compared in figure 9.12. The smaller volume in the reservoir bag enabled an 80 per cent change to be achieved one "breath" (5 seconds) sooner, although the results would have been distorted slightly due to the "F.R.C." of the "lungs". The results to be expected, allowing for an "F.R.C." of 150 ml and a V_{App} of 500 ml (this was measured as 520 ml) have been calculated, and they are indicated in broken lines in figure 9.12. They indicate a difference of two "breaths" (10 seconds) in achieving an 80 per cent change under the two sets of conditions.

DISCUSSION

Considering the difficulty in obtaining precise control over all the variables in these experiments (despite their superficial appearance of simplicity), there is tolerable agreement between theory and experiment.

All the variables which were considered have some effect on the delay in delivering a new gas mixture from an anaesthetic machine to a patient. In a clinical context, however, so far as delays are concerned, there is little point in making an issue of any one of them. In relation to a long anaesthetic the delays can be ignored; but they can assume importance during the induction of inhalation anaesthesia or during brief outpatient anaesthetics.

If a "fine alteration" is made to the gas mixture delivered by an anaesthetic machine, little change in the patient's response can be expected for at least half a minute. (Gross alterations are another matter.) Because of the mechanical and biological delays in conveying an inhalation anaesthetic to a patient's brain, "fine alterations" only make sense if their need is anticipated, and this implies considerable clinical experience. There are, however, four other approaches to the problem.

The first approach is to use high supply flow rates. This will reduce delays in the breathing system, but it will not help over the

delays occurring within the patient. It also has the potential disadvantages of being wasteful of anaesthetic gases and of introducing unwanted pressures in the breathing system.

Another approach which will help to reduce delays in the breathing system, but which will do nothing to counteract delays occurring in the patient, is to "dump" the contents of the reservoir bag immediately before adjusting the gas mixture delivered by the anaesthetic machine; but clinically this may present practical difficulties.

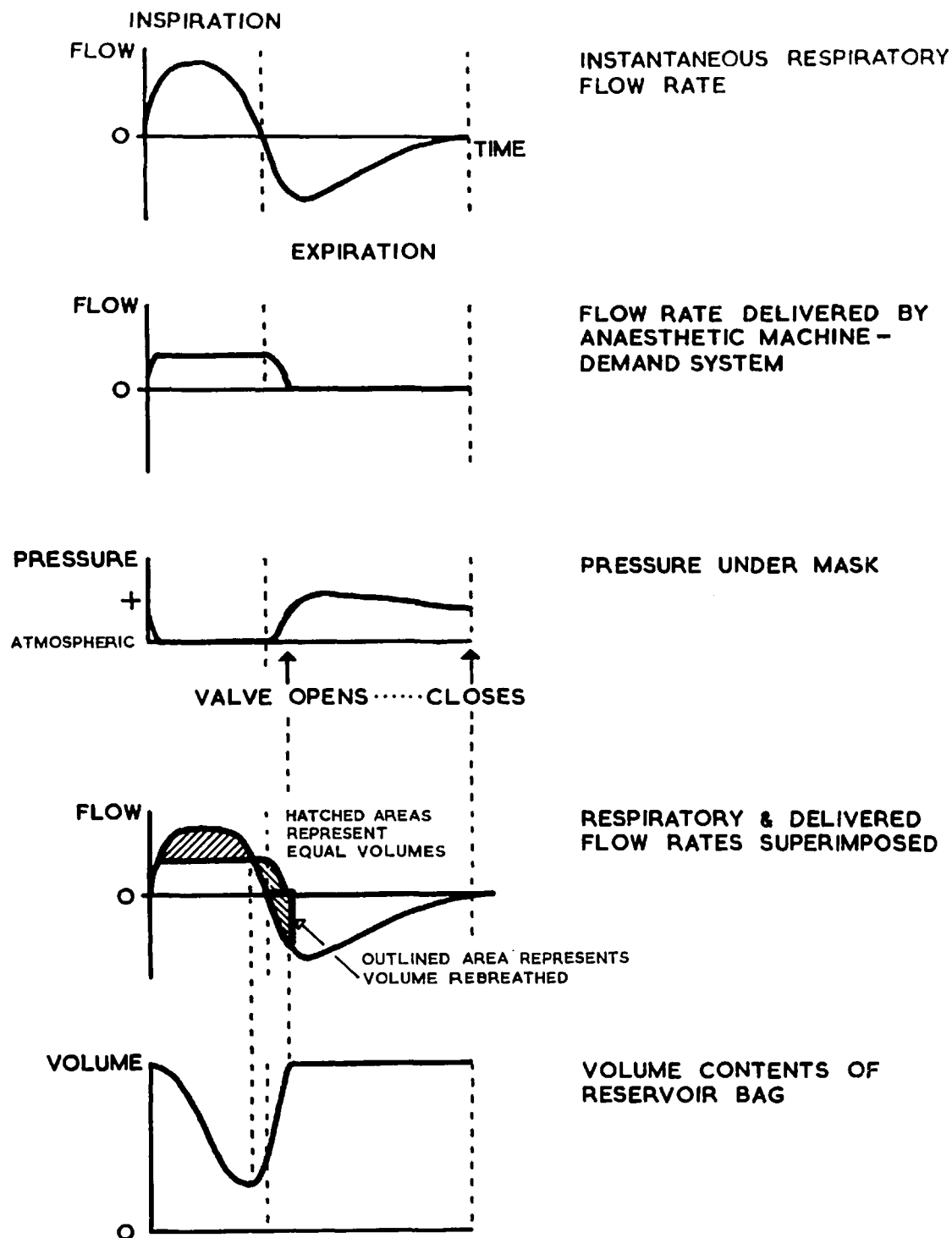
The third approach is to start by delivering a higher concentration of anaesthetic from the anaesthetic machine, than is required ultimately by the patient. The concentration can then be reduced as the anaesthesia deepens. This is done when starting the induction of anaesthesia by administering 100 per cent nitrous oxide, but in this case it involves restriction of oxygen. Using this approach with other inhalation anaesthetics there is the possibility of "overshooting", and then there will be a delay before corrective action can become effective.

Finally, so far as nitrous oxide is concerned, the delays can be ignored by making no "fine alterations" to the mixture delivered, using 80 per cent nitrous oxide throughout, and admitting a supplementary anaesthetic as required. This, of course, does not remove the delays. In the context of dental anaesthesia, it may, in fact accentuate them, by avoiding the hypoxic drive to hyperventilation. The concentration of the supplementary anaesthetic may be adjusted in accordance with the third approach described above.

TABLE 9.1

Mixed inspired concentration of nitrous oxide - per cent Non-rebreathing system. $V_T = V_{App}$			
$V_B =$	$2V_T$	V_T	$\frac{V_T}{2}$
Breath 1	0	0	0
Breath 2	25	50	100
Breath 3	44	75	
Breath 4	58	88	
Breath 5	68	94	
Breath 6	77		
Breath 7	82		
Breath 8	87		
Breath 9	90		
Respiratory rate	27	15	
and $\dot{V}_I$ for 90% change in 20 secs ($V_{App} = 500$ ml)	13.5	7.5	

Calculated breath by breath rise in $\bar{F}_{I_{N_2O}}$ when using a non-rebreathing system.



Events during a single respiratory cycle while using a 'demand' anaesthetic machine supplying a reservoir bag, corrugated tube, an expiratory valve and a mask

FIGURE 9.1

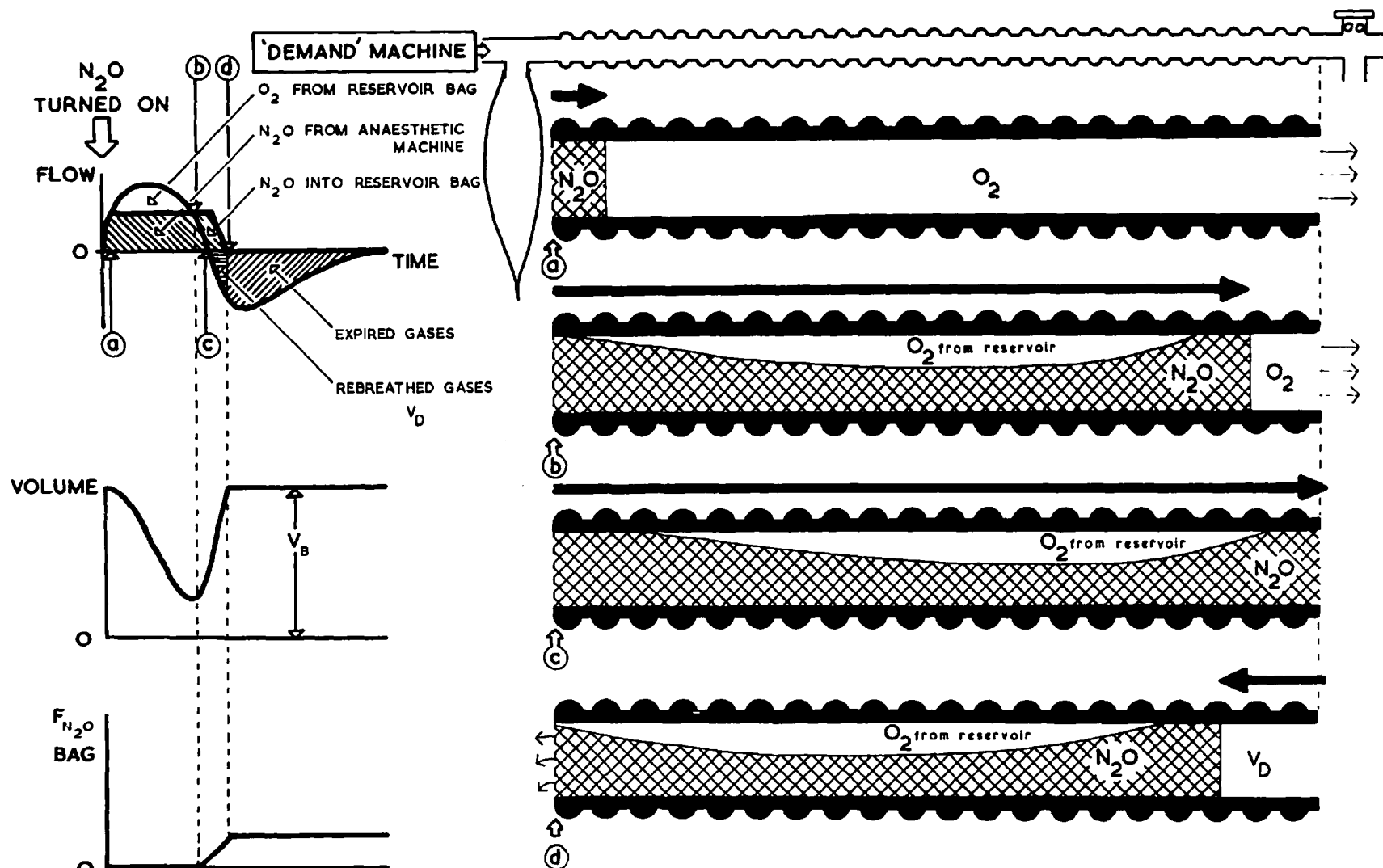


FIGURE 9.2

Relative contributions from the anaesthetic machine and the reservoir bag during inspiration and reversal of flow during early expiration

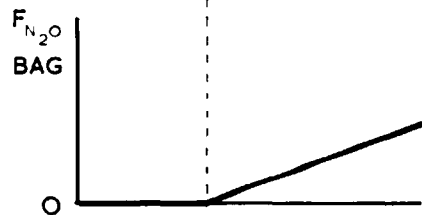
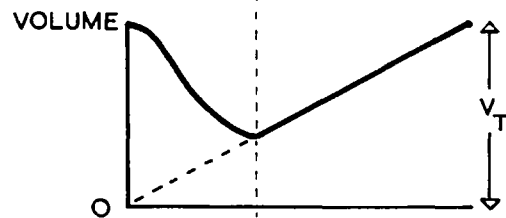
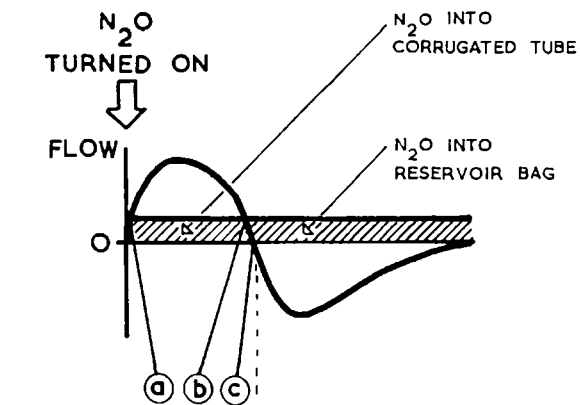
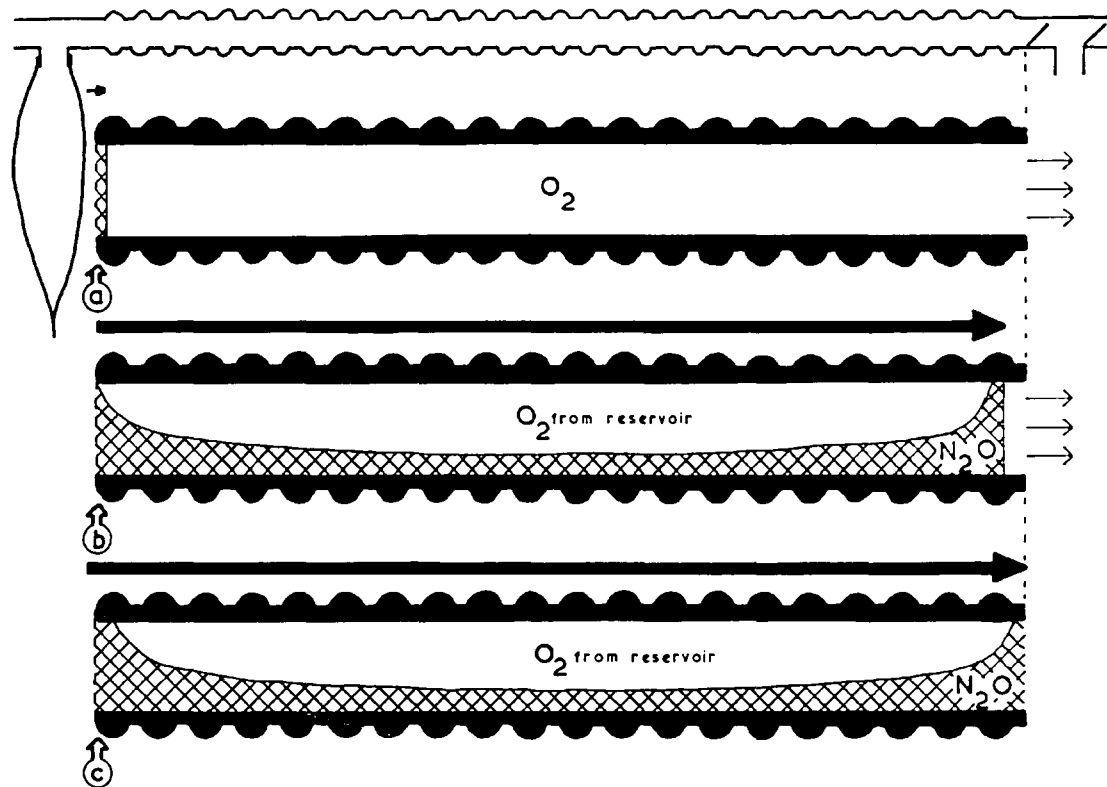
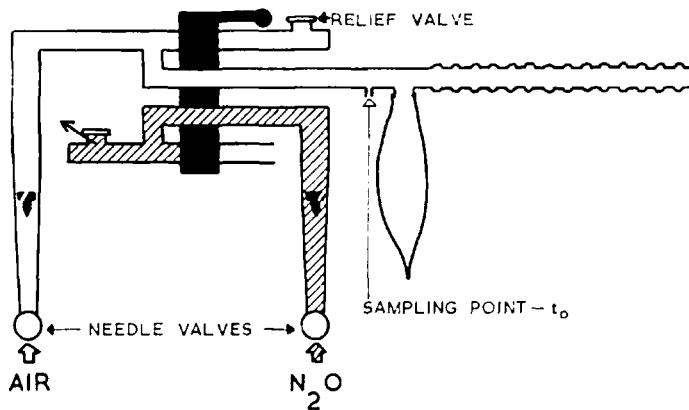


FIGURE 9.3

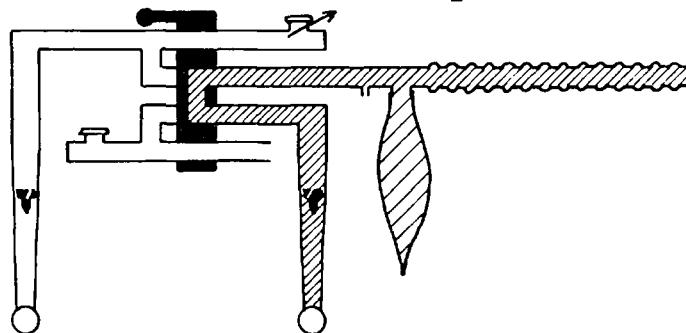


Relative contributions from the anaesthetic machine and the reservoir bag during inspiration — no rebreathing
'DEMAND' MACHINE

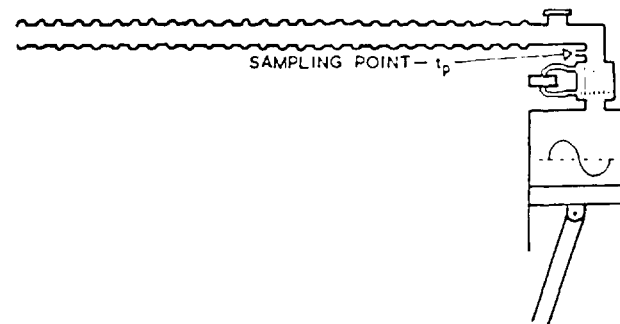
TAP POSITIONED TO SUPPLY AIR



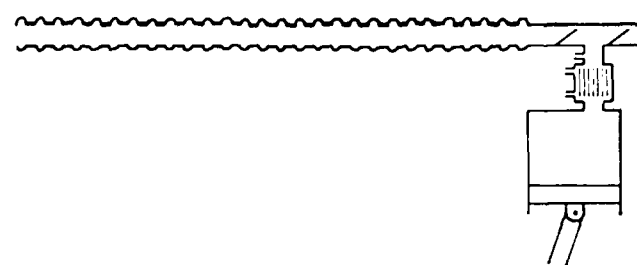
TAP POSITIONED TO SUPPLY N_2O



'MAGILL' SYSTEM



'NON-REBREATHING' SYSTEM



FREE FLOW

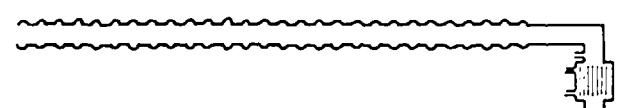


FIGURE 9.4

LEFT—arrangement for suddenly changing the gas mixture supplied to the alternative experimental 'breathing' systems on the RIGHT

The needle and relief valves can be adjusted for equal flow rates of the two gas mixtures and for equal loading of the supply systems

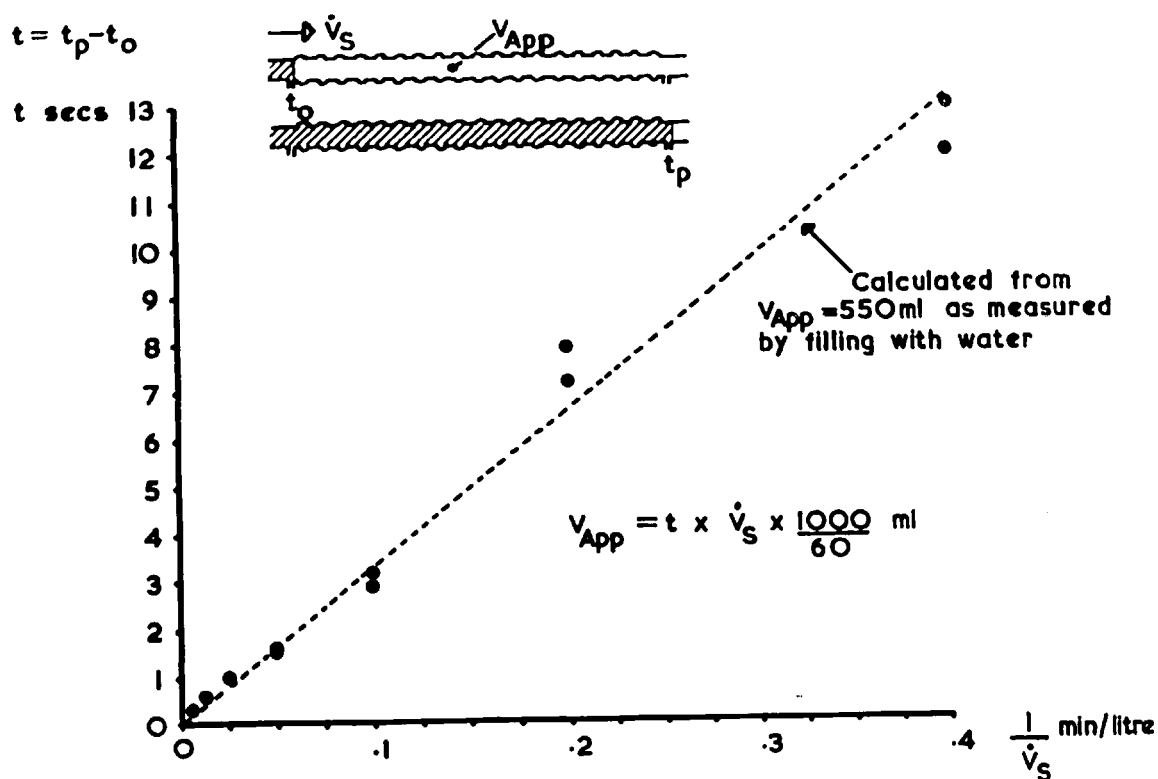


FIGURE 9.5

RATE CONSTANT 15 'BREATHS'/MIN
 'NON-REBREATHING' $\times V_T = 600 \text{ ML}$ $\circ V_T = 400 \text{ ML}$

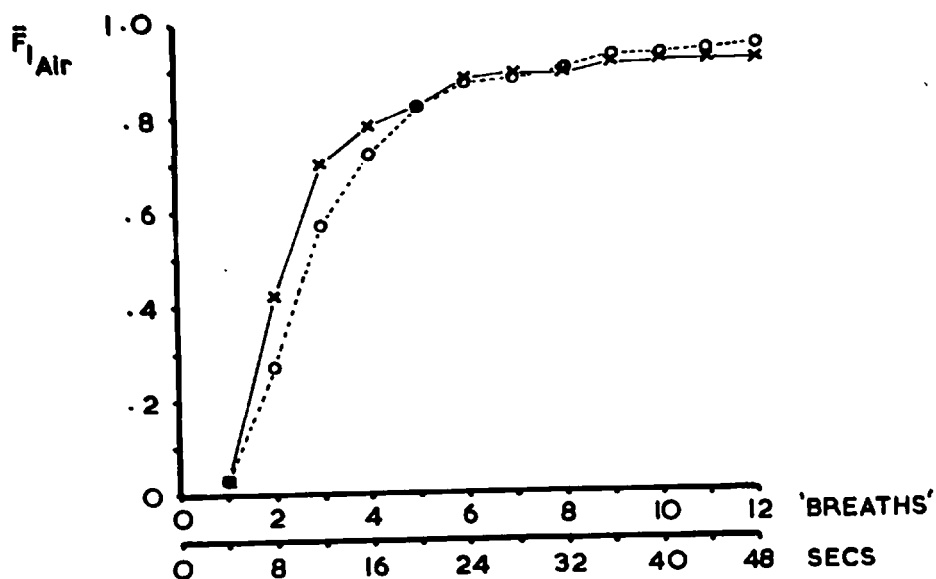


FIGURE 9.6

V_T CONSTANT 600 ML

$\times$ $f = 15$ 'breaths/min' } 'NON-REBREATHING'
 $\circ$ $f = 25$ " " }
 $\triangle$ $f = 25$ 'breaths/min' 'MAGILL'

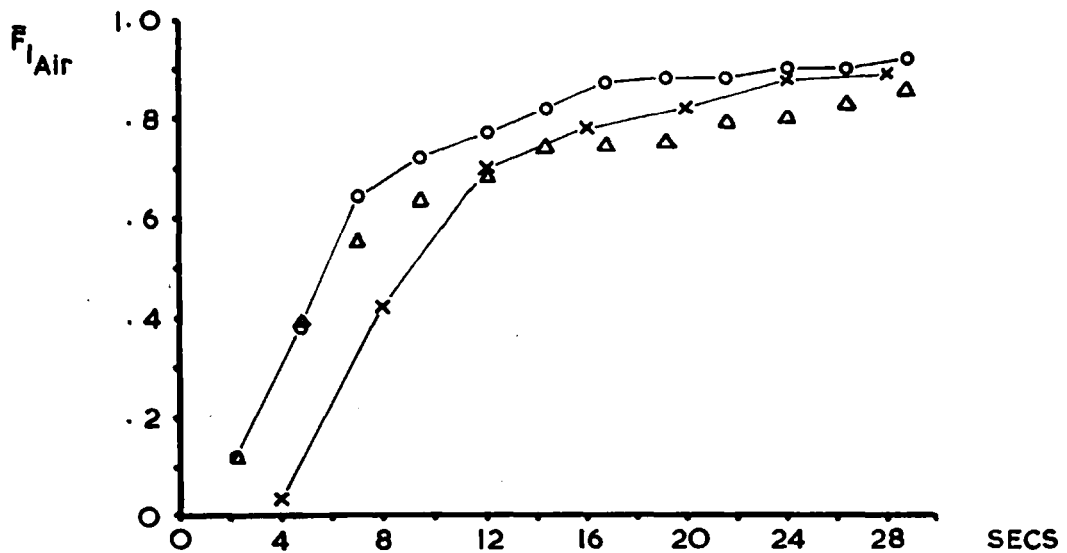
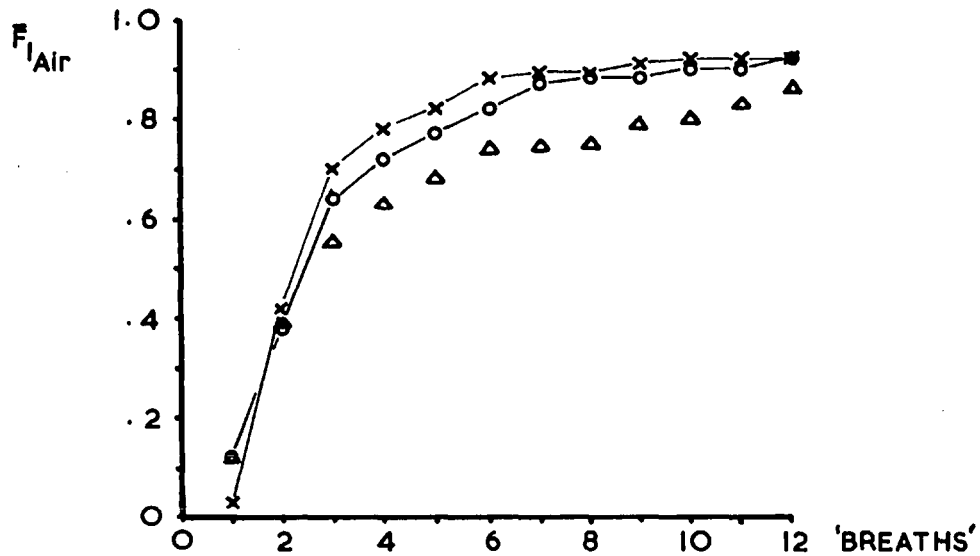


FIGURE 9.7

V_T CONSTANT 1000 ML

$+$ $f = 9$ breaths/min } 'NON-REBREATHING'
 $\square$ $f = 15$ " " }
 ∇ $f = 9$ breaths/min 'MAGILL'

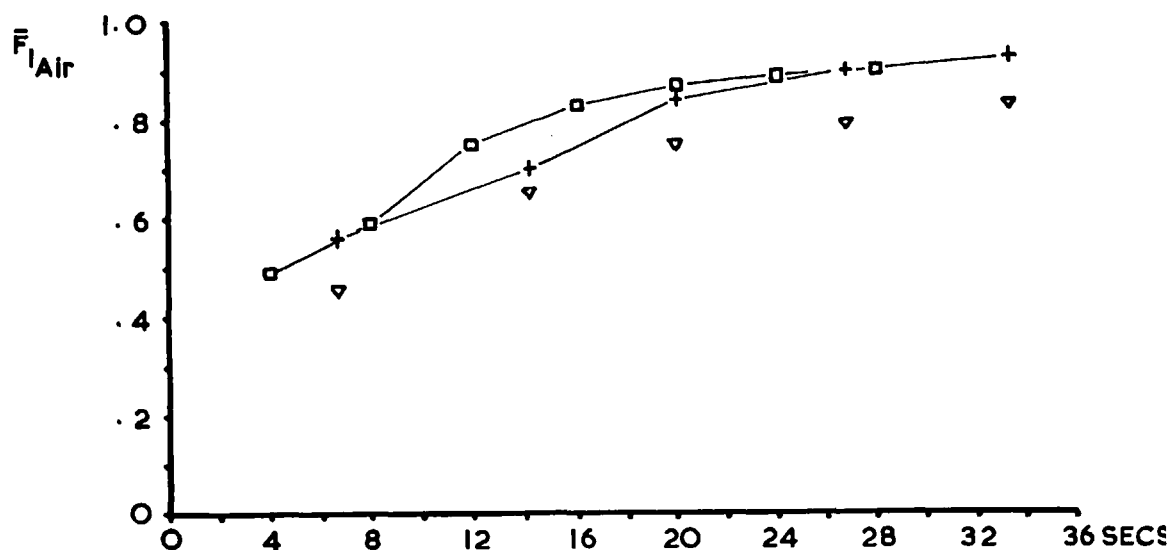
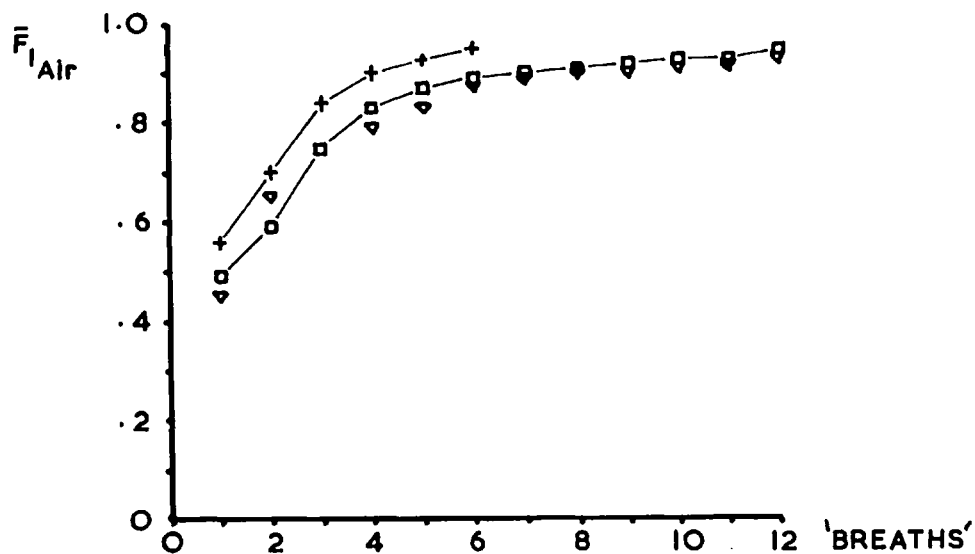


FIGURE 9.8

$\dot{V}$ CONSTANT 15 LITRE/MIN

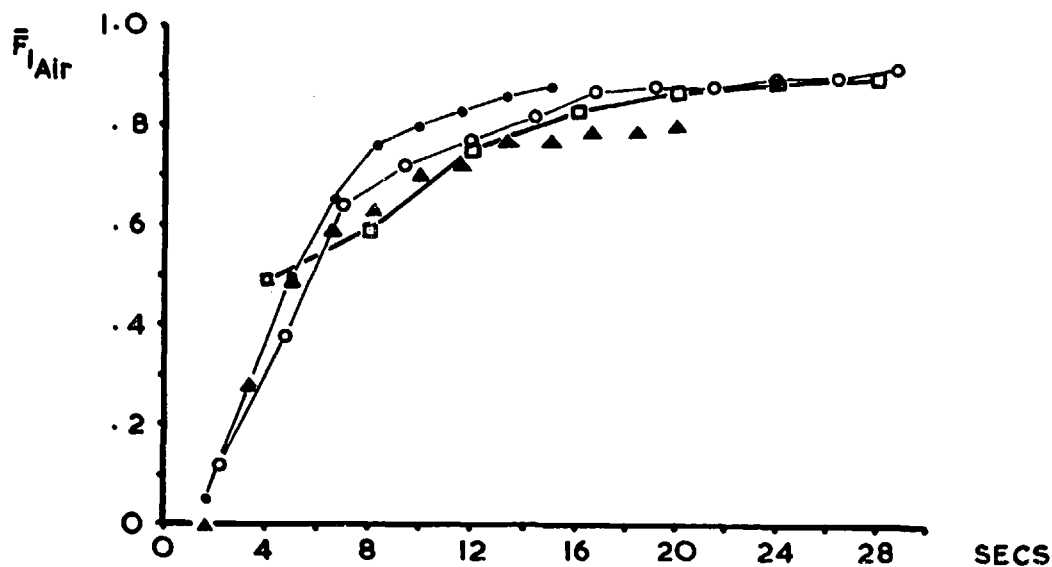
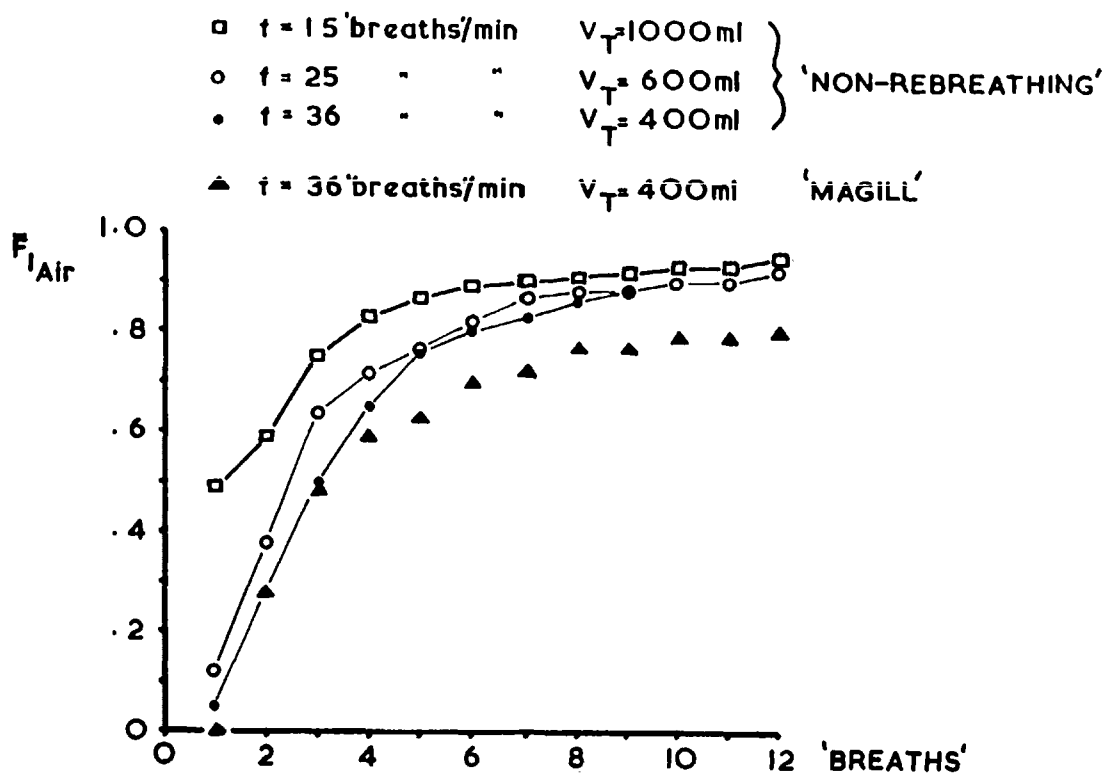


FIGURE 9.9

WITH & WITHOUT 'DUMPING' BAG

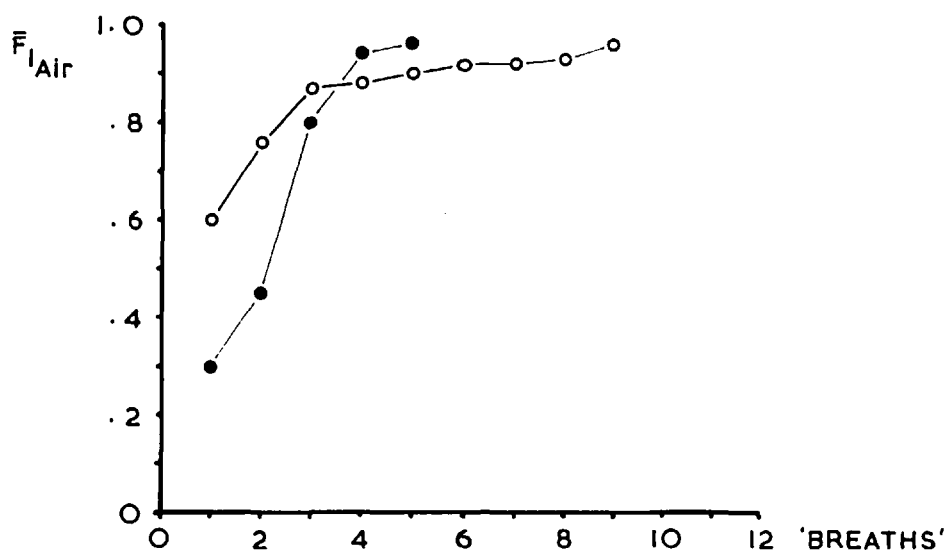
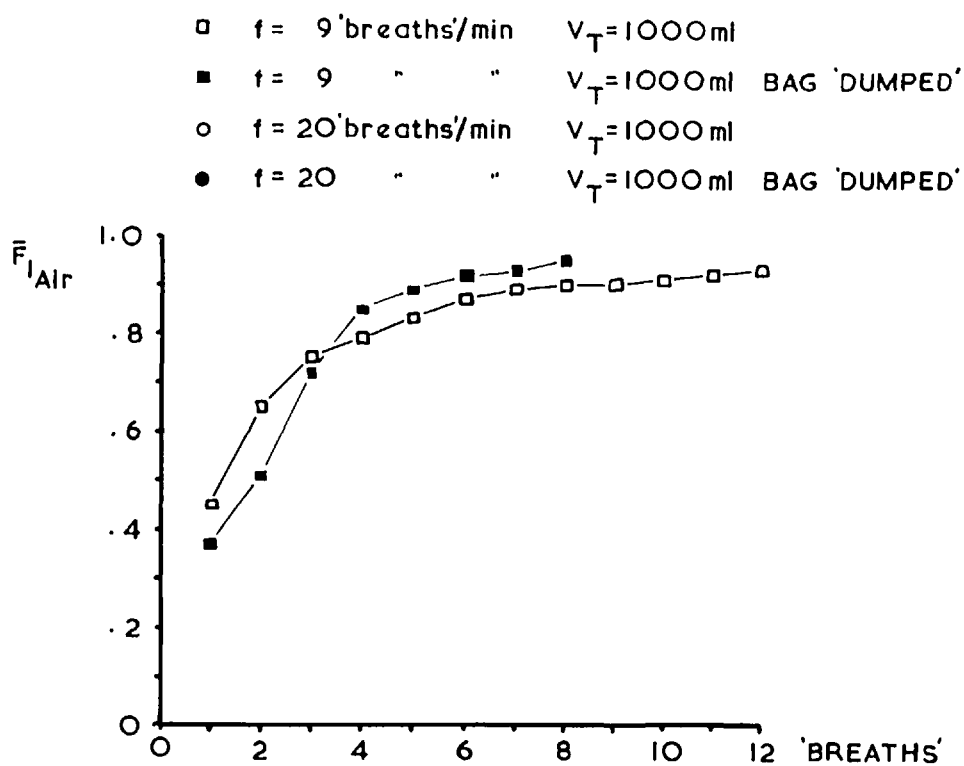


FIGURE 9-10

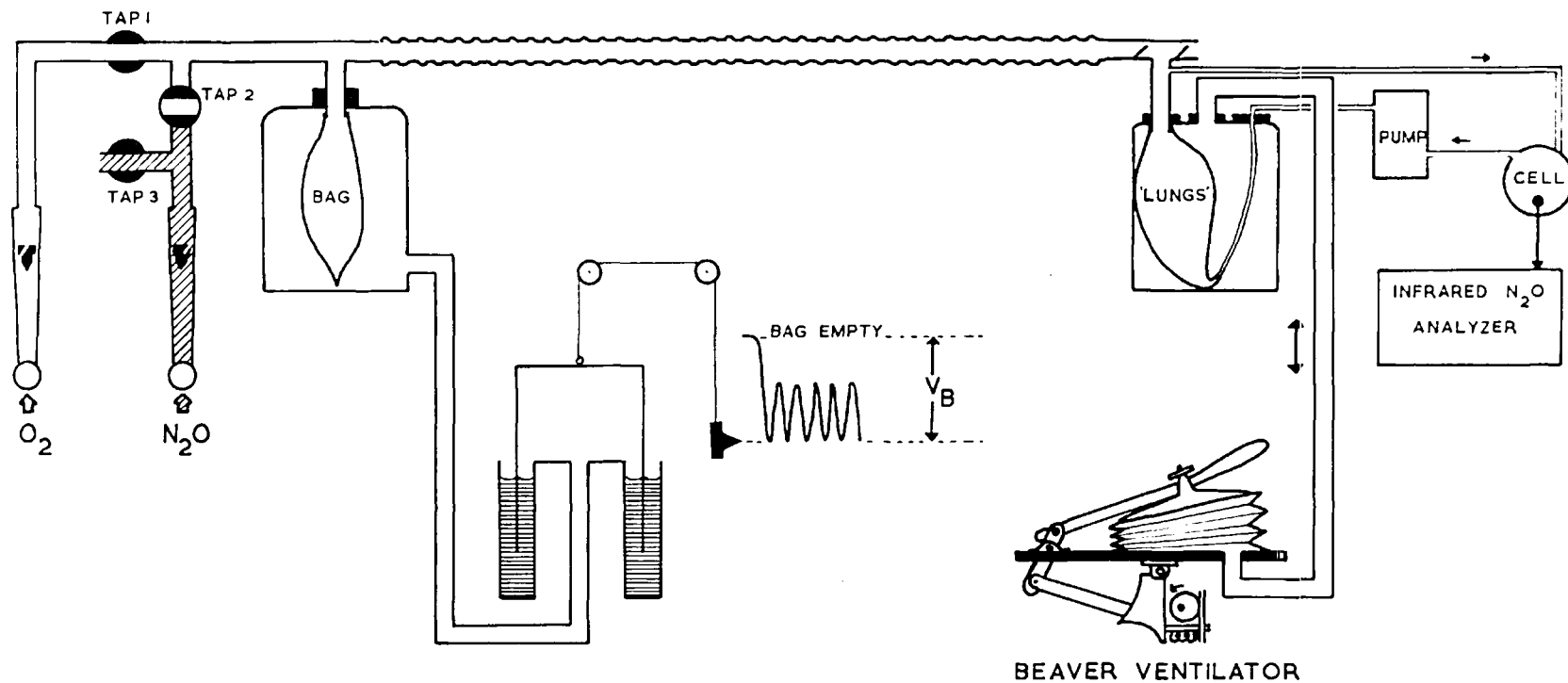


FIGURE 9-11

Experimental set up for recording the volume of the reservoir bag while measuring the change in composition of gases 'respired' after a sudden change in the gas mixture supplied to a 'non-rebreathing' system

RATE CONSTANT 12 'BREATHS'/MIN
 V_T CONSTANT 500ML
 'NON-REBREATHING'

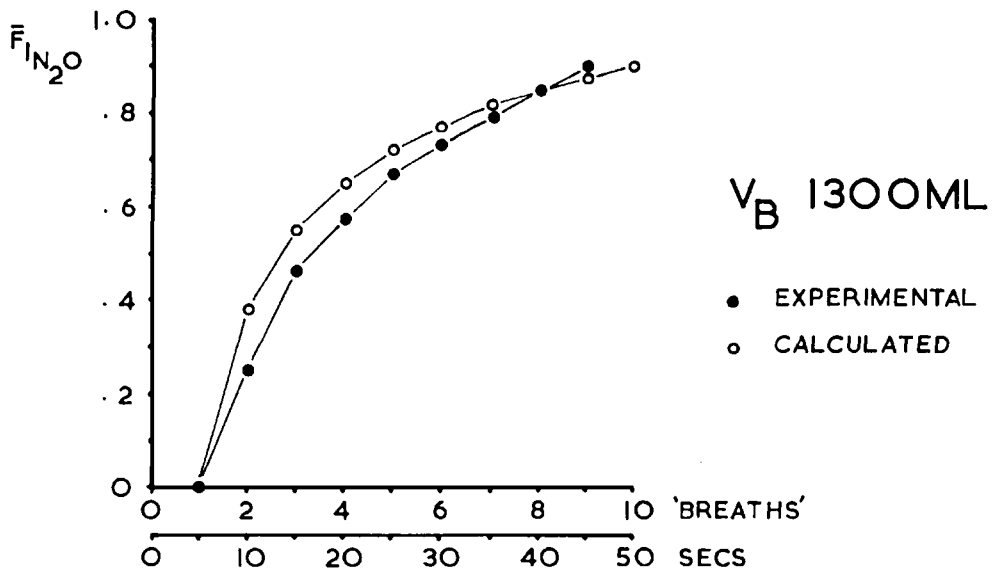
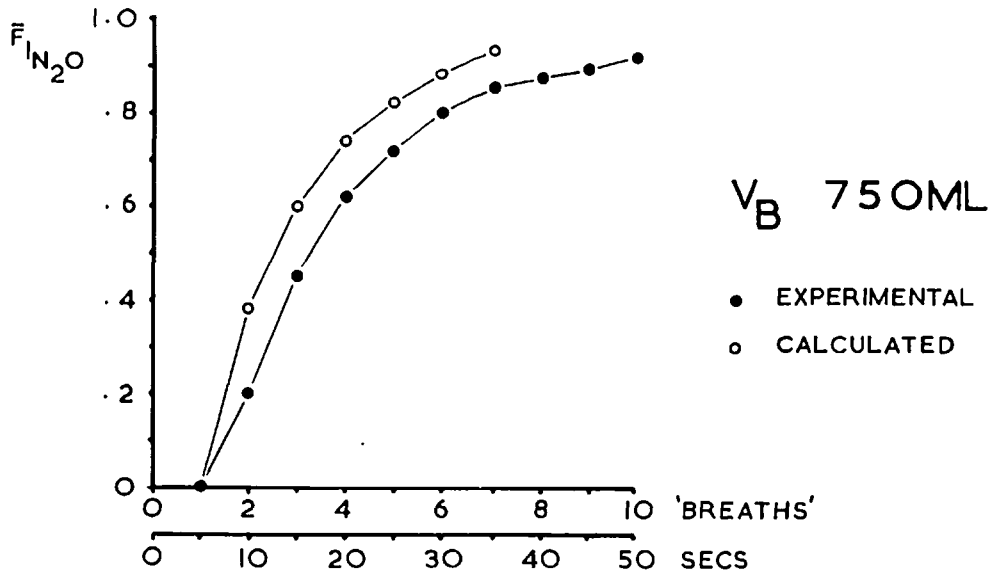


FIGURE 9.12

PART III: PRELIMINARY STUDIES USING VOLUNTEERS

CHAPTER 10

Methods of exploring the effects of expiratory resistance, oxygen and hypoxia on sitting volunteers. 266

CHAPTER 11

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CHAPTER 12*

The effects of different nitrous oxide and oxygen mixtures, and of pressure, upon speed of induction. 345

CHAPTER 10

METHODS OF EXPLORING THE EFFECTS OF
EXPIRATORY RESISTANCE, OXYGEN AND HYPOXIA
ON SITTING VOLUNTEERS

The work described in this chapter was carried out while holding a Wellcome Research Fellowship in the Research Department of Anaesthetics, Royal College of Surgeons of England. It has been published (Smith, W.D.A. (1962) A method of recording systolic blood pressure. *Brit.J.Anaesth.* 34, 136. Smith, W.D.A. (1962) A dead weight expiratory resistance. *Brit.J.Anaesth.* 34, 290. Smith, W.D.A. (1963) The effects of expiratory resistance, oxygen and hypoxia in relation to dental anaesthesia. Part II: an experimental study with conscious subjects. *Brit.J.Anaesth.* 35, 64).

Wing Commander J. Ernsting very kindly provided details of the multi-electrode manometer designed by him and of the pulse detector designed by Chief Technician A. W. Cresswell. The multi-electrode mercury manometer described in this chapter was made by Mr. J. C. Hook, who also constructed the dead weight expiratory resistance.

The study of routine dental anaesthesia (see Part IV) required that measurements be made with as little disturbance of the patients, and of the staff of the Dental Hospital, as possible. This imposed limitations on the methods of measurement used, and made it desirable that the apparatus chosen should be reliable and well tried. The preliminary study on volunteers, described in chapters 10 and 11, was carried out as a means of testing and gaining facility with the apparatus; and of exploring the effects of expiratory resistance, oxygen and hypoxia, upon the systolic blood pressure, pulse rate and respiration of conscious sitting subjects, under circumstances related to those existing during dental anaesthesia. The possible relevance of these measurements has been discussed in chapter 3.

The experimental plan

Each subject sat with his face resting in an anaesthetic mask which was connected to a non-rebreathing system. The left arm was used for measurement of pulse rate and indirect systolic blood pressure. The right arm was free for making notes and the subject was asked to write down any relevant subjective experiences and to note their times. A bookrest was also provided.

The conditions of respiration were changed at approximately 5-minute intervals. The planned sequence, which was usually followed, is indicated in table 10.1. Some volunteers went through the complete sequence at a single session, but usually the experiment was spread over two or three sittings. At the end of these, some of the earlier sequences were sometimes repeated or, alternatively, the effects of low concentrations of nitrous oxide, or of periods of induction using 80 per cent nitrous

oxide, were observed.

Each complete experiment was divided into three main parts. During the first, except for 5 minutes breathing oxygen, the subject breathed air, but an expiratory resistance was imposed throughout alternative 5-minute periods. During the second part, the subject breathed 10 per cent oxygen with nitrogen throughout alternate 5-minute periods but an expiratory resistance was not introduced. During the third, inspiration of 10 per cent oxygen was combined with the use of an expiratory resistance.

Referring to the 5-minute periods as numbered in table 10.1, periods 1, 2 and 3 taken in sequence might be considered as providing conditions similar to those imposed upon a patient coming from room air, being given a non-hypoxic anaesthetic using apparatus imposing resistance to expiration, and then being returned to room air again. Periods 3, 4 and 5 might be considered as representative of a similar anaesthetic being terminated with 100 per cent oxygen, and periods 5, 6 and 7 as representative of a similar anaesthetic following pre-oxygenation. Periods 8 to 14 may be grouped correspondingly to represent anaesthetics entailing some hypoxia but being administered from apparatus offering negligible resistance to respiration. Periods 15 and 16 were included to show up any effects of 100 per cent oxygen. Periods 17 to 23 cover conditions of combined hypoxia and expiratory resistance. Periods 24 and 25 were included to show up any effects of inhaling oxygen following hypoxia while still breathing against expiratory resistance.

One subject was denied food and sleep and another was subjected to a short period of acute anoxia using 100 per cent nitrogen. Some volunteers also inhaled nitrous oxide with oxygen.

The breathing system

The breathing system is shown diagrammatically in figure 10.1. A Vickers Research Ltd. flow transducer (see chapter 6) was interposed between the mask and the stem of a wide bore Y-piece. This introduced a deadspace of about 40 ml in addition to that contained in the mask. The Y-piece was connected to the inspiratory and expiratory limbs of a non-rebreathing system. In the inspiratory limb a reservoir bag and a light non-return valve were connected in series. This non-return valve could be supplied either with room air or with gas mixtures from a Walton Five anaesthetic machine. The expiratory limb was terminated by a dead weight flow resistance (see below) which also acted as a non-return valve. When the expiratory resistance was not required, it could be by-passed through a light non-return valve by opening a tap. The various components of the non-rebreathing system were connected together by wide-bore non-expansile tubing.

The control of gas mixtures

A Walton Five anaesthetic machine was used to provide the various gas mixtures. The reliability and the performance of this machine had previously been checked (see chapter 8). The mixture control was also calibrated for mixtures of oxygen and nitrogen. While the Walton Five machine was being used, the air intake on the inspiratory non-return valve was occluded. Room air could be supplied by turning off the anaesthetic machine and leaving the air inlet open.

A diaphragm pump circulated a continuous gas sample through a Beckman D.2 oxygen analyser in order that the oxygen content of the delivered gas mixtures might be checked from time to time.

The expiratory resistance and the measurement of pressure within the mask

The intention was to impose an expiratory resistance of about 11 mm Hg (15 cm H₂O) which would remain constant regardless of changes in respired gas composition and regardless of the subject's respiratory flow pattern. This was achieved during the later experiments (four subjects of this series) using a weighted lever type of dead weight flow resistance (see below). During the earlier experiments of the series, however, this constancy was not achieved when using the prototype cylindrical weight type of dead weight resistance (see below) (three subjects) nor when using a Coxeter valve (four subjects). (The Coxeter valve offered a resistance of 11 mm Hg to a steady flow of 20 l./min when its control knob was set to position 3.)

For measurement of the pressure fluctuations within the mask a tapping was inserted and connected to a pressure transducer (Vickers Research Ltd., capacitance type, ± 15 cm H₂O, see chapter 6). This was used in conjunction with a Respiratory Analyser (Scott and Williams, 1960; Williams, 1960) and an Ediswan four-channel pen recorder. A typical pressure record is shown in the fourth trace of figure 10.2.

The dead weight expiratory resistance and its development

It was hoped that an expiratory flow resistance based on the principle of breathing against the opposition of a column of water of known height would meet the requirement of a flow resistance which would remain constant regardless of changes in respiratory flow pattern and in the composition of the gases respired. In its simplest form such a resistance might consist of a wide bore tube inserted vertically, to a known depth, into water contained

in a suitable vessel. The hydraulic pressure at the lower end of the tube would be equal to its depth. When breathing into it, this pressure would have to be generated before air could emerge from the lower end and bubble upwards through the water.

Disturbances of water level due to large bubbles might be avoided by arranging for the dispersal of the air as it emerged, and by keeping the surface area and the total volume of the water large. In practice, however, measurement revealed that the pressures generated when breathing through such a device were not independent of respiratory flow pattern. It was found that initially the pressure required before air would flow was greater than the hydraulic pressure at the lower end of the tube. It was also found that this initial pressure increased as ventilation increased. The effect was due to the need to expel the column of water contained within the tube before air could escape. Both the inertia of the column of water being expelled, and the fluid resistance between it and the inner surface of the tube, had to be overcome. The possibility of using non-return valves was considered but discarded.

Another basic approach to the problem would be to interpose between the expiratory limb of a breathing circuit and the atmosphere a known weight resting upon and occluding an outlet of known area. Such a device is illustrated in figure 10.3. The open tube projecting horizontally from the base of the device was for connection to the expiratory limb of a breathing circuit. The other end of this tube was connected to a wide circular outlet lying in a horizontal plane. The margin of the outlet was machined into a circular knife edge, and upon this rested a hollow cylinder of slightly larger diameter. This cylinder was filled

with water to the depth appropriate to the expiratory pressure required. Eight free-running wheels rotating about horizontal axes were arranged around the cylinder in order to keep it vertical. Theoretically the pressure which must be generated in the expiratory circuit before air can escape through the outlet equals the weight of the cylinder divided by the surface area of the outlet, plus the pressure required to overcome the inertia of the cylinder, plus the pressure required to overcome the resistance to flow through the annular orifice between the outlet and the cylinder. The area of the orifice is given by the product of the height through which the cylinder is raised off the knife edge and the circumference of the outlet. Since the resistance to flow through an orifice varies with gas density it is desirable to keep this as small as possible by making the outlet large. This also reduces the height by which the cylinder is raised. Two such devices were constructed and used in the breathing experiments. The first was made of perspex, its outlet diameter being 9.5 cm. The second, illustrated in figure 10.3, was made of duralumin except for the wheel bearings which were made of PTFE. The outlet diameter was 7.8 cm. Both the perspex and the duralumin cylinders were 14 cm. high. These dead weight expiratory resistances had excellent characteristics for flow rates greater than about 30 l./min, but the expiratory resistance achieved at lower flows tended to be inadequate. This was due to the difficulty in adjusting the wheel bearings so that they neither pressed against the cylinder tightly enough to cause added friction nor were left slack enough to permit the cylinder to tilt slightly. In practice the latter usually occurred so that at low flows the cylinder tended to rest

one edge upon the outlet while air escaped from the opposite side.

These difficulties were overcome by reducing the size of the outlet so that the weight was lifted clear of the knife edge at lower flow rates, and by designing the dead weight in the form of a weighted, pivoted lever. This avoided the necessity for wheel bearings. The device finally constructed and used in the majority of the experiments is illustrated in figure 10.4. The port shown projecting from the righthand side of the base was for connection to the expiratory limb of a breathing circuit. Within the box it was connected by wide bore tube to the circular knife edge outlet which projected upward from the box. The lever terminated in a horizontal flat plate which rested upon and occluded the outlet. The plane of the outlet could be adjusted to coincide with the plane of the under surface of the plate by means of three screws. The force opposing escape of air from the outlet could be varied by adjusting the position of the weight along the arm of the lever. The orifice, the lever, the fulcrum and the adjustable weight were made of brass. The diameter of the knife edge was 2.7 cm. The length of the arm was 20 cm, the distance from the pivot to the centre of the plate being 15.3 cm.

With all three devices there was a tendency for the breathing system to oscillate at critical flow rates. This tendency was reduced by using nonexpansile rather than corrugated tubing, and sometimes it was avoided by slight adjustment of the opening pressure.

The weighted lever type of dead weight resistance had excellent characteristics and these are illustrated in the upper record of figure 10.5. The record should be read from right to left. The upper trace recorded the flow rate through a non-

rebreathing circuit, the dead weight resistance being connected to the expiratory limb. The lower trace recorded the pressure within the breathing circuit. On the right can be seen the effect of connecting a continuous flow generator to the system. It can be seen that no air flowed until a pressure of about 5 cm H_2O was reached and that this pressure then remained almost constant while the flow rate was increased slowly to 100 l./min and then reduced stepwise by decrements of 10 l./min. The time marker operated at 1-second intervals. The remainder of the trace shows the effect of breathing first slowly and then rapidly into the non-rebreathing circuit while varying the tidal volume and the peak expiratory flow rate. Again the expiratory resistance remained almost constant. The lower record shows the pressure developed when a water resistance was tested under comparable circumstances. The characteristics under steady flow conditions might be considered as acceptable, but the very high initial expiratory pressures developed while breathing into the system are well illustrated. By lining up a setsquare against the start of expiratory flow on this record, it can also be seen that expiratory flow did not start until the high initial pressure has been reached. (By completely enclosing the dead weight resistance within a suitable container, but leaving the port open to atmosphere and the container connected to the inspiratory limb of a breathing circuit, the device can be used as an inspiratory resistance.)

The measurement of indirect systolic blood pressure and pulse rate

Ideally, direct measurement of intra-arterial blood pressure should have been employed for these experiments, with determination of systolic, diastolic and mean blood pressures.

As this would be impracticable during routine dental anaesthesia, indirect systolic blood pressure was recorded. The method used was a slight modification of a method developed at the Institution of Aviation Medicine, Farnborough (Ernsting, personal communication, 1961).

A piezo-electric crystal pulse detector was placed over the brachial artery above the elbow joint. It was then overlapped by the lower margin of a standard sphygmomanometer cuff which was wrapped round the arm in the usual way. Signals from the pulse detector and the pressure within the cuff were recorded simultaneously using an Ediswan four channel pen recorder.

The cuff was connected to a mercury manometer, the tube of which was made of perspex (fig. 10.6). Platinum electrodes passed through the perspex at regular intervals and projected a short distance into the lumen of the tube. Resistors were connected between adjacent electrodes and these were short-circuited in turn as the column of mercury was within the tube. By incorporating these resistors in a suitable bridge circuit, movement of the mercury meniscus was represented by a series of "step" deflections of the pen recorder, each complete step being equivalent to the movement of the meniscus between two adjacent electrodes. The width of individual steps on the record was varied by suitable choice of resistance values, and by this means steps, recognizable by their width, were arranged at key positions for identification purposes. Two such identification steps are shown in figure 10.9, between 140 and 150 mm Hg.

The electrodes were placed at intervals corresponding to pressure increments of 2.5 mm Hg. Two additional electrodes were inserted at the 100 mm Hg and the 200 mm Hg

positions. These actuated two relays which were so connected that the full sweep of the recorder pen could be used for each of the three ranges 0-100 mm Hg, 100-200 mm Hg and 200-300 mm Hg. This arrangement ensured that the step deflections were of readable size, despite the large number of electrodes used. The circuit diagram is given in figure 10.7.

A modified Acos type 43-1 (Cosmocord Ltd.) crystal microphone was used as a pulse detector. Details of construction are indicated in figure 10.8. A hole of approximately 2.2 cm diameter was cut out of the centre of the perforated plate which normally protects the light alloy cone. The cone was discarded. In its place sorbo rubber was used to transmit impulses from the brachial artery to the crystal. Three sorbo discs, 0.5 cm thick and of approximate diameters 0.5 cm, 2 cm, and 3 cm were stuck together and mounted so that the smallest disc pressed against the central corner of the crystal (in place of the apex of the cone); so that the middle disc lay within the hole cut in the perforated plate; and so that the margin of the largest disc overrode the perforated plate, to which it was stuck. A small wedge of sorbo rubber was introduced between the central corner of the crystal and the base of the microphone. This prevented overloading. The assembly was then mounted in a suitable container, the outer surface of the largest sorbo disc being left exposed. The microphone lead was anchored so that no mechanical strain was put on the solder tag connections. When using this pulse detector it is important to place it accurately over the site of the brachial artery. During the course of the observations made during dental anaesthesia (see Part IV) it was found to be advantageous to stick an

additional button of sorbo rubber to the centre of the outer surface of the largest sorbo disc.

An Ediswan e. e. g. amplifier, with the gain control turned to minimum, was used for amplifying the signals from the pulse detector because this happened to be available. A simpler amplifier could have been used.

Blood pressure recordings were taken by inflating the cuff rapidly to a pressure greater than the systolic pressure and then deflating it slowly. The cuff was inflated with oxygen from a regulated reducing valve and deflated through an adjustable leak by rotation of a two-position lever. This opened and closed appropriate pinch-cocks. When the lever was in the "leak" position it was possible to increase the cuff pressure by means of a standard sphygmomanometer bulb.

The systolic blood pressure may be taken as not less than the cuff pressure indicated by the step write-out at the instant when the brachial arterial pulse is first detected and recorded. A sample record is shown in figure 10.9. This should be read from right to left. The top record was obtained using a paper speed of about 0.5 cm/sec, which is the speed that has usually been selected. The bottom record was obtained using a paper speed of 6 cm/sec. From above downwards the pens recorded the cuff pressure; the signals obtained from the crystal pulse detector over the brachial artery; a pneumotachograph trace to indicate phase of respiration; and pulse signals derived from a photo-electric pulse detector applied to the lobe of an ear. The top cuff pressure trace shows the cuff being inflated and then released slowly. Note the two wide identification steps between 140 and 150 mm Hg. The crystal pulse detector and the pneumo-

tachograph traces reveal the variation of systolic blood pressure which occurs with respiration, the systolic blood pressure usually being greatest towards the tail of expiration. In this instance the systolic blood pressure during expiration is indicated as being not less than 136 mm Hg. It could be argued that the brachial pulse might have been detected when the pressure within the cuff was 140 mm Hg if this had coincided with the end of expiration.

It can be said, therefore, that the maximum systolic pressure during expiration lies somewhere between the cuff pressure at the instant at which the brachial pulse is first detected, and the pressure within the cuff towards the end of the previous expiration. Upon further deflation of the cuff it can be seen that the last pulse which failed to get past the cuff to the pulse detector occurred when the pressure within the cuff was 126 mm Hg. This coincides with inspiration. The difference between the systolic pressures occurring during inspiration and during expiration may be increased when the subject breathes against resistance. It follows that the rate of deflation of the cuff should be adjusted according to the respiratory rate, especially when accurate measurements are being attempted. This limits the number of blood pressure readings that can be taken within a given time. In addition to the variations in systolic blood pressure which occur during a single respiratory cycle, some subjects show a superimposed cyclical variation over about two or three breaths.

A very small pulse signal, transmitted through the cuff, was usually detected while the cuff was inflated to a pressure above the systolic pressure. Whether a very small pulse is being

recorded while the cuff is inflated above the systolic pressure, or whether a large pulse is being recorded while the cuff is deflated below the systolic pressure, it can be seen from the bottom record with the faster paper speed, in figure 10.9, that the start of the recorded pulse always bears a constant time relationship with the pulse signal detected at the ear. The maximum response, however, usually occurs after a variable delay. This fact should be considered when deriving the pulse rate from the time of only a few pulses.

The amplitude and the form of the pulses recorded vary from person to person. Some of the obvious factors involved are the accuracy with which the crystal detector is placed, the anatomical relations of the brachial artery and the precise anatomy and bulk of the related structures, the tone of the arterial wall, the arterial pulse volume and waveform and the arterial blood pressure. In a few subjects the pulse signal was very small and difficult to read. A smaller pulse detector would be needed for use with children. It has been noted that during long experiments there may be a progressive reduction in the amplitude of the pulse recorded. This was most evident with a volunteer who found the repeated blood pressure determinations to be rather unpleasant. This observation could be explained by arterial spasm. It may not be possible to read the pulse record during movements of the arm, but normal recording is resumed immediately the disturbance ceases. This is one of the advantages of using a piezo-electric crystal for pulse detection.

Throughout these experiments both the upper and lower limits of the possible values of the peak systolic blood pressure

were determined and they have been analysed separately, except in the final analysis where the mean of their changes has been taken. When the cuff was deflated slowly in relation to the respiratory rate, these upper and lower limits of systolic blood pressure approached each other. When the cuff was deflated rapidly in relation to the respiratory rate, the upper and lower limits diverged and less accurate blood pressure readings were obtained. The results of trial experiments had to be discarded because this fact had not been appreciated and the cuff had been deflated too quickly.

The upper limit of the lowest systolic blood pressure which occurs during inspiration may be determined if deflation of the cuff is continued slowly. It is the lowest cuff pressure at which the crystal fails to detect the brachial arterial pulse.

The measurement of respiratory flow rate and of ventilation

There were two reasons for including the flow transducer (pneumotachograph) in the breathing system. One was to relate the upper and lower limits of systolic blood pressure to the phase of respiration as explained above. The other was to measure the changes in ventilation that occurred in response to the different breathing conditions. It was originally planned to record respired volume (electronically integrated flow rate), as distinct from flow rate. This would have covered both requirements. In practice, however, the drift of the volume record was more than could be controlled satisfactorily by an unaided experimenter. Except during two experiments, therefore, and then only while no expiratory resistance was used, respiratory flow rate was recorded rather than respired volume. A typical record is shown in figure 10.2. A Vickers Research

Ltd. flow transducer was used in conjunction with the Respiratory Analyser and an Ediswan pen recorder.

In order to determine the changes in ventilation it was necessary to measure the areas contained between the flow rate records and the base line. To do this by planimetry for about 1,000 feet of record was out of the question. The Data Centre of the de Havilland Aircraft Co., however, generously made their computer facilities available for this purpose. For reasons of economy, minute volumes were determined only for the 2 minutes immediately before and immediately after each change of the breathing conditions. Furthermore, only the inspiratory half of the flow rate records was analysed (the chances of errors arising due to leaks were less during inspiration than during expiration. Also, since the composition of inspired gas mixtures was known, the correction factors appropriate to their viscosities could be applied (see chapter 6). The analysis of the flow rate records entailed two processes. The first consisted of defining the points of inflection of the curves in terms of co-ordinates and of recording these on punched cards. The second process entailed feeding the punched cards into a machine which computed the required volumes. These processes would not have eliminated errors due to drift.

TABLE 10.1

The planned sequence of breathing conditions which were changed every 5 minutes.

R denotes expiratory resistance

PART I Alternate periods with expiratory resistance but no hypoxia		PART II Alternate periods with hypoxia but no expiratory resistance		PART III Alternate periods with expiratory resistance and hypoxia	
5-min periods	Overlapping 10-min periods	5-min periods	Overlapping 10-min periods	5-min periods	Overlapping 10-min periods
1. Air	} A	8. Air	} G	17. Air	} AG
2. Air and R		9. 10% O ₂		18. 10% O ₂ and R	
3. Air	} C	10. Air	} I	19. Air	} CI
4. Air and R		11. 10% O ₂		20. 10% O ₂ and R	
5. Oxygen	} E	12. Oxygen	} K	21. Oxygen	} EK
6. Air and R		13. 10% O ₂		22. 10% O ₂ and R	
7. Air	} F	14. Air	} M	23. Air	} O
		15. Oxygen		24. 10% O ₂ and R	
		16. Air	} N	25. Oxygen and R	} Q
				26. Air	

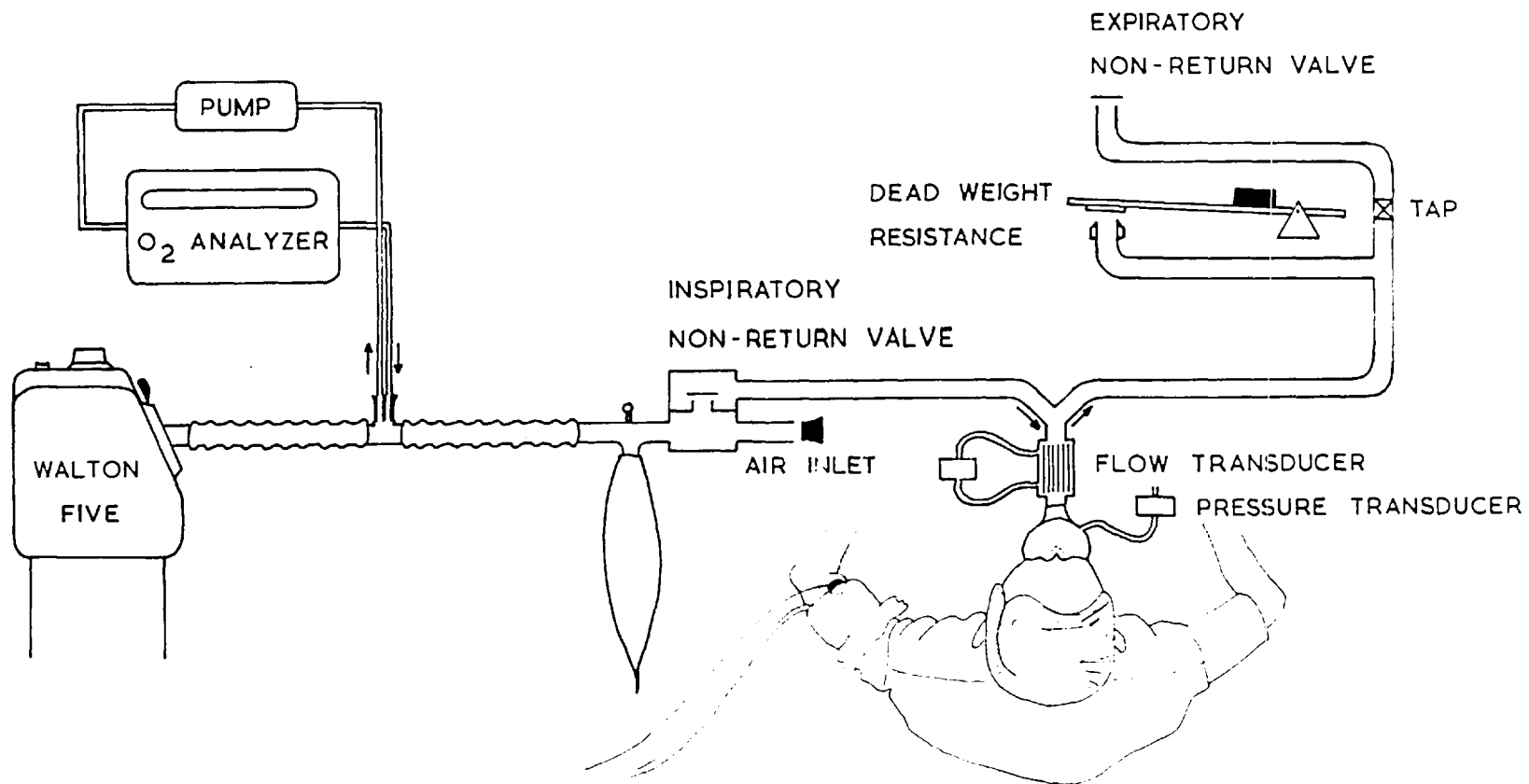


FIGURE 10.1

FIGURE 10.2

Read from right to left.

A record of sphygmomanometer cuff pressure (see also figures 10.7 and 10.9), brachial pulse, respiratory flowrate and mask pressure, taken during a change of breathing conditions from breathing air without resistance to breathing air against an expiratory resistance.

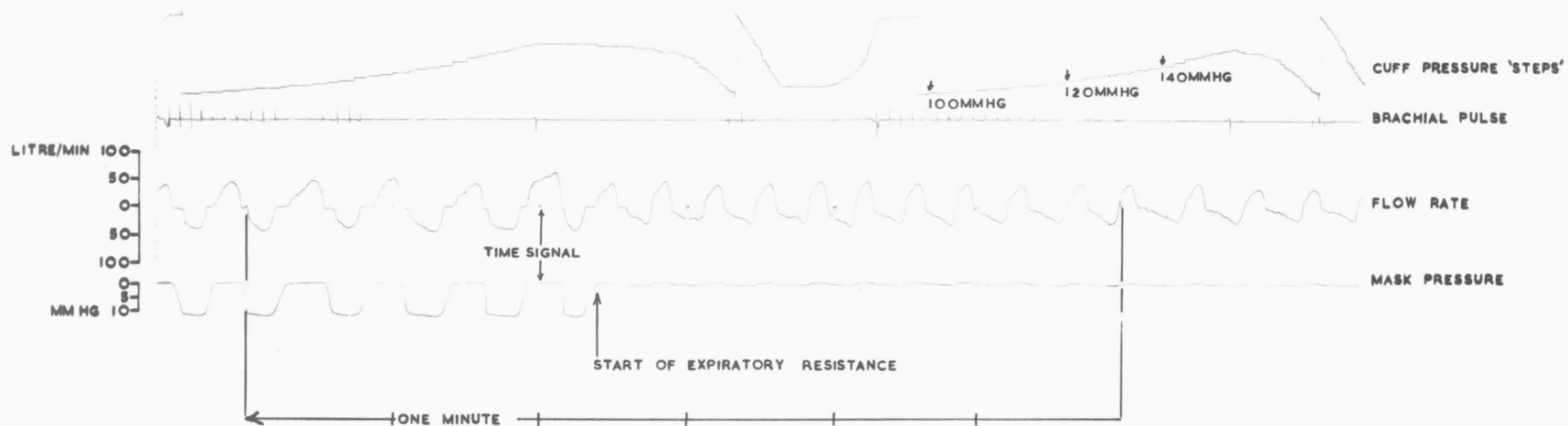


FIGURE 10.3

A prototype dead weight expiratory resistance in which the dead weight was a hollow vertical cylinder containing water. It rested upon a circular knife edge and it was kept vertical by means of eight free running wheels.

FIGURE 10.4

The final form of dead weight expiratory resistance which was used. The dead weight was a weighted lever which terminated in a horizontal flat plate. This rested upon and occluded a circular knife edge. The position of a weight along the lever governed the magnitude of the resistance to expiration.

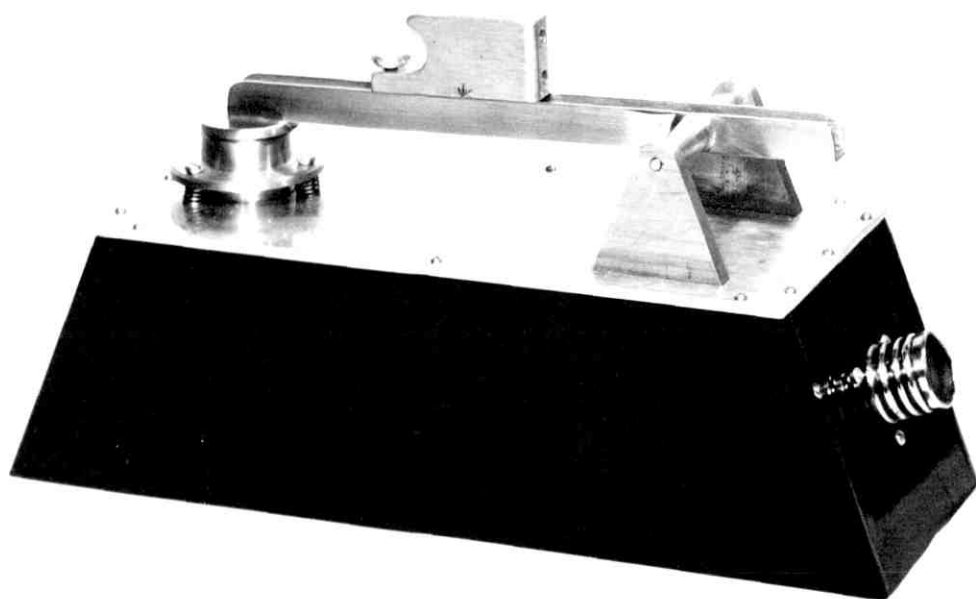
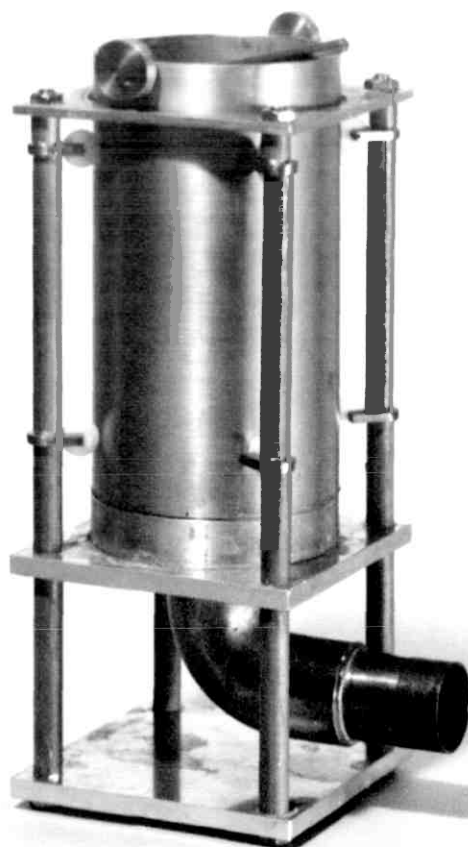
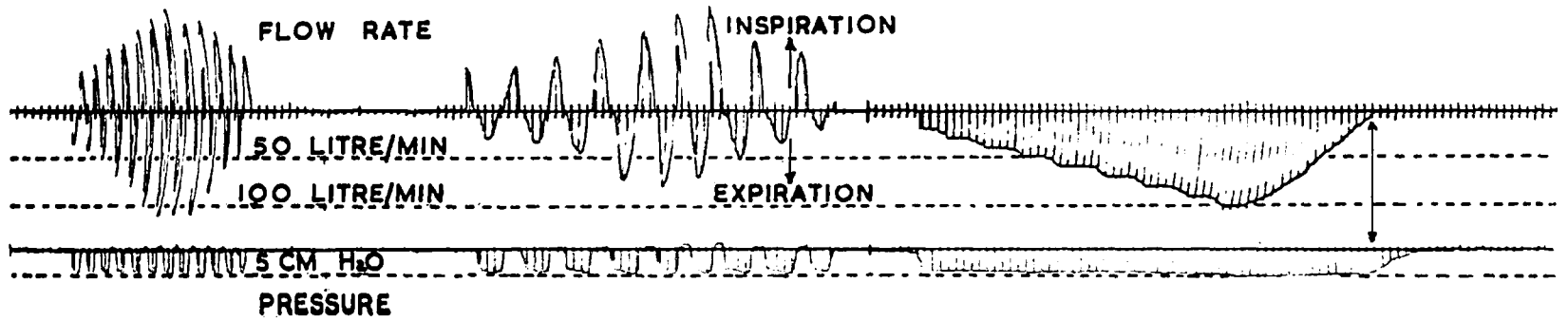


FIGURE 10.5

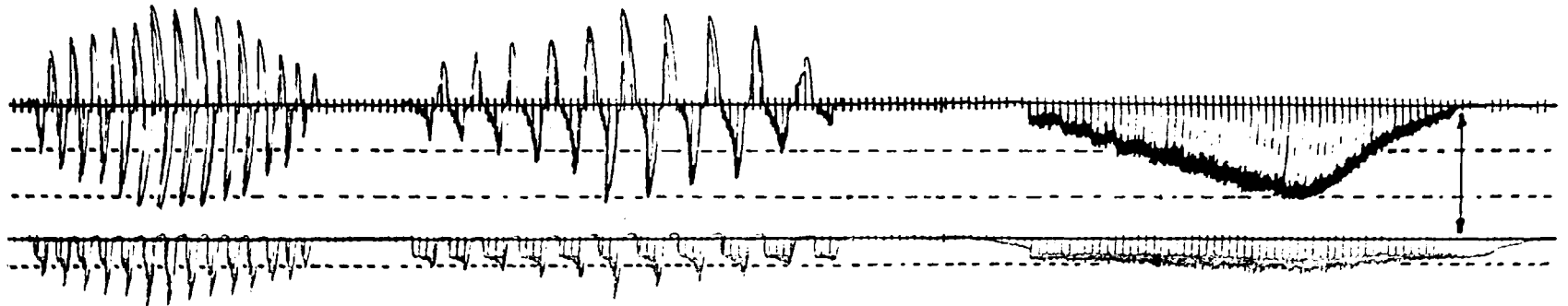
Read from right to left.

A comparison of the pressure-flowrate characteristics of the weighted lever type of dead weight expiratory resistance (figure 10.4) and of an "under-water" resistance. The upper trace of each record indicates the flowrate into and out of a non-rebreathing system, while the lower trace indicates the pressure within the system.

DEAD WEIGHT EXPIRATORY RESISTANCE



WATER RESISTANCE



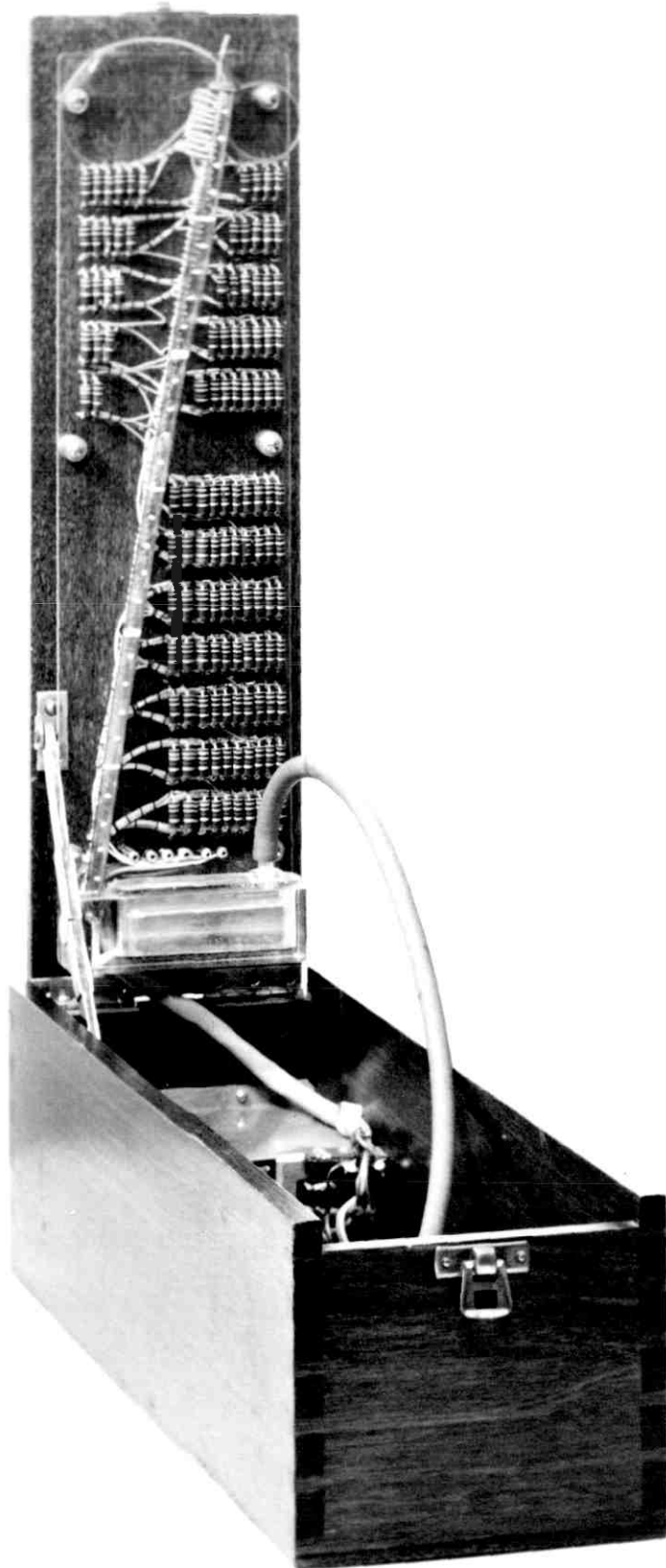


FIGURE 10.6

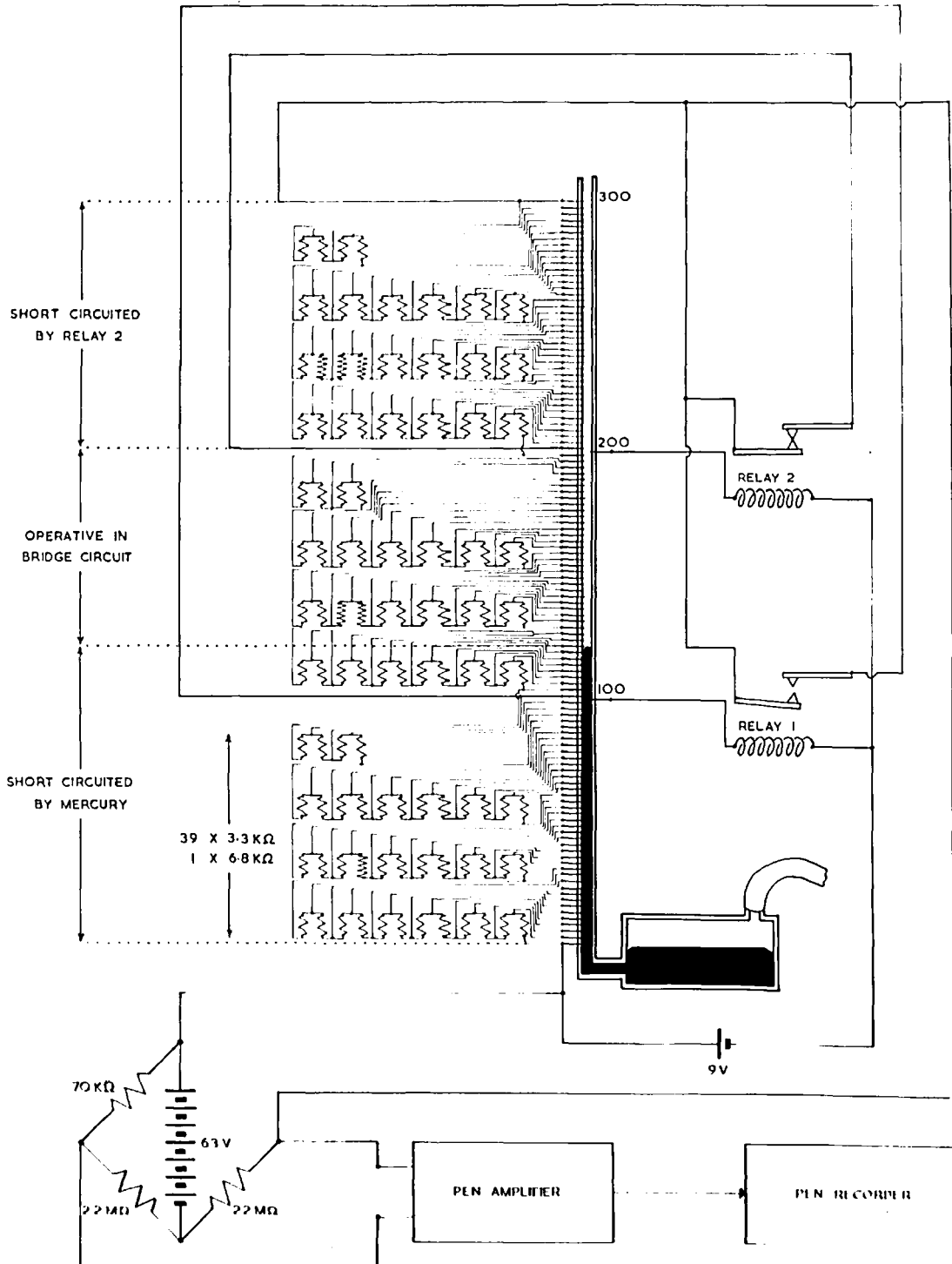


FIGURE 10.7

CRYSTAL PULSE DETECTOR

OUTER CASING NOT SHOWN

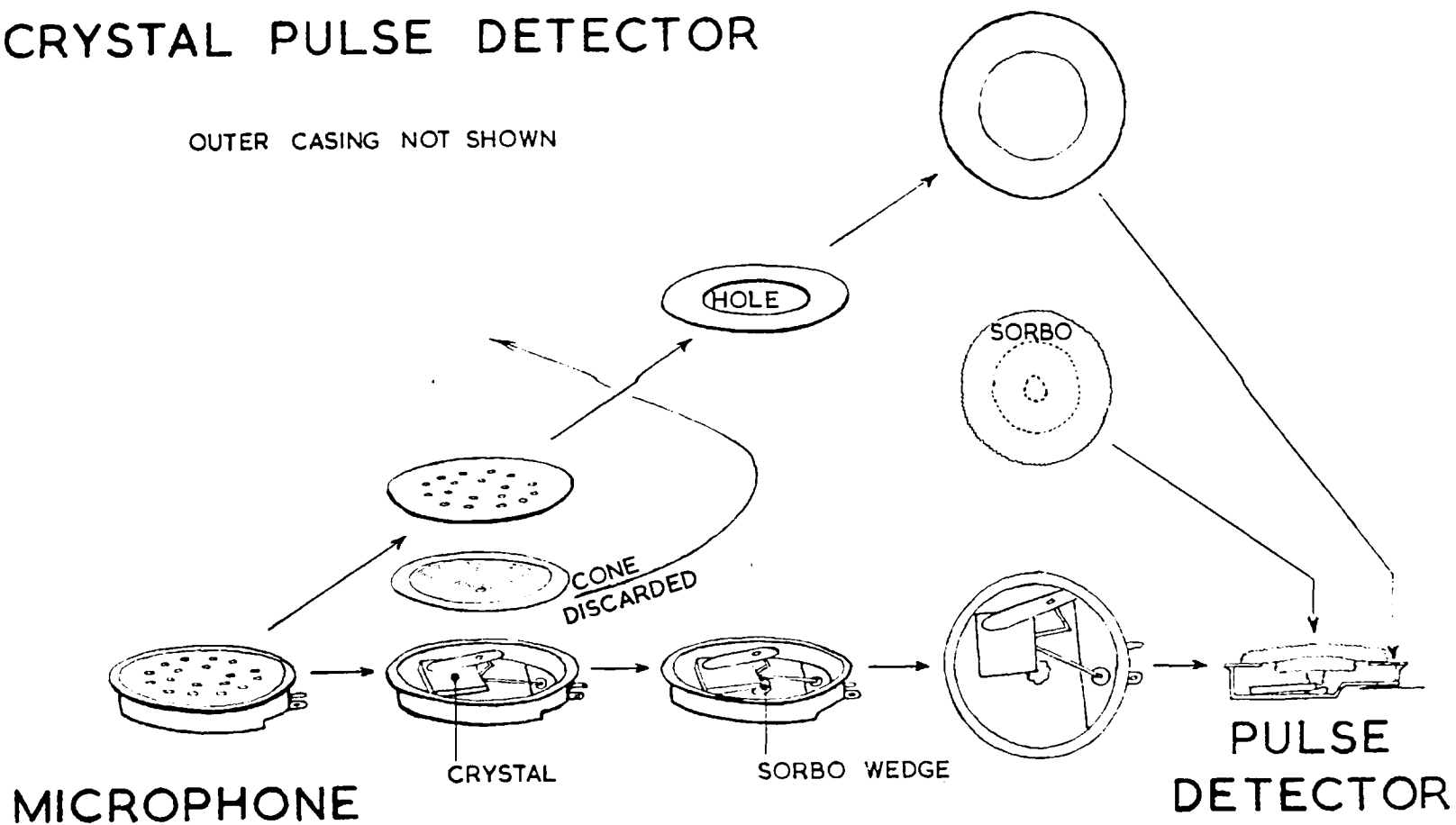


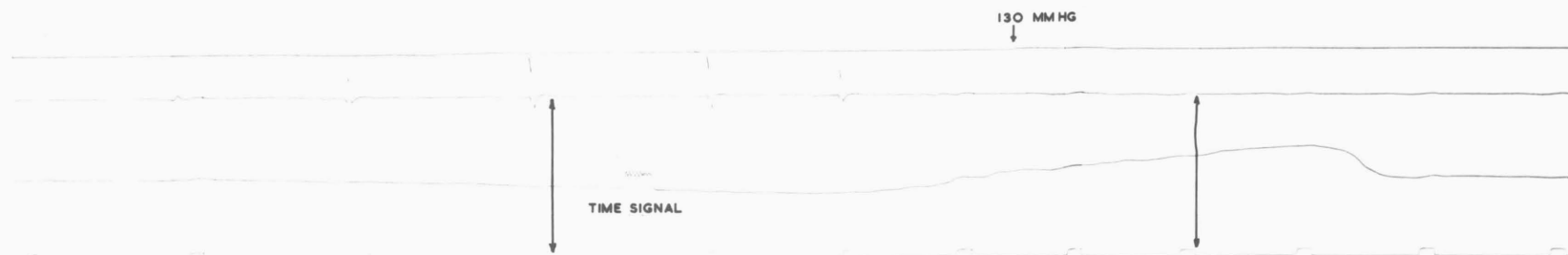
FIGURE 10.8

FIGURE 10.9

Records of:

1. (Top trace) Cuff pressure. Note the two wide identification "steps" between 140 and 150 mm Hg.
2. Pulse, as obtained from the piezo-electric pulse detector placed over the brachial artery and overlapped by the lower margin of a sphygmomanometer cuff.
3. Respiratory flowrate (pneumotachogram with 10 second time signal superimposed).
4. Pulse, as obtained from a photoelectric pulse detector attached to the lobe of an ear.

Paper Speed: Top record - 0.5 cm/sec: Bottom record - 6 cm/sec.



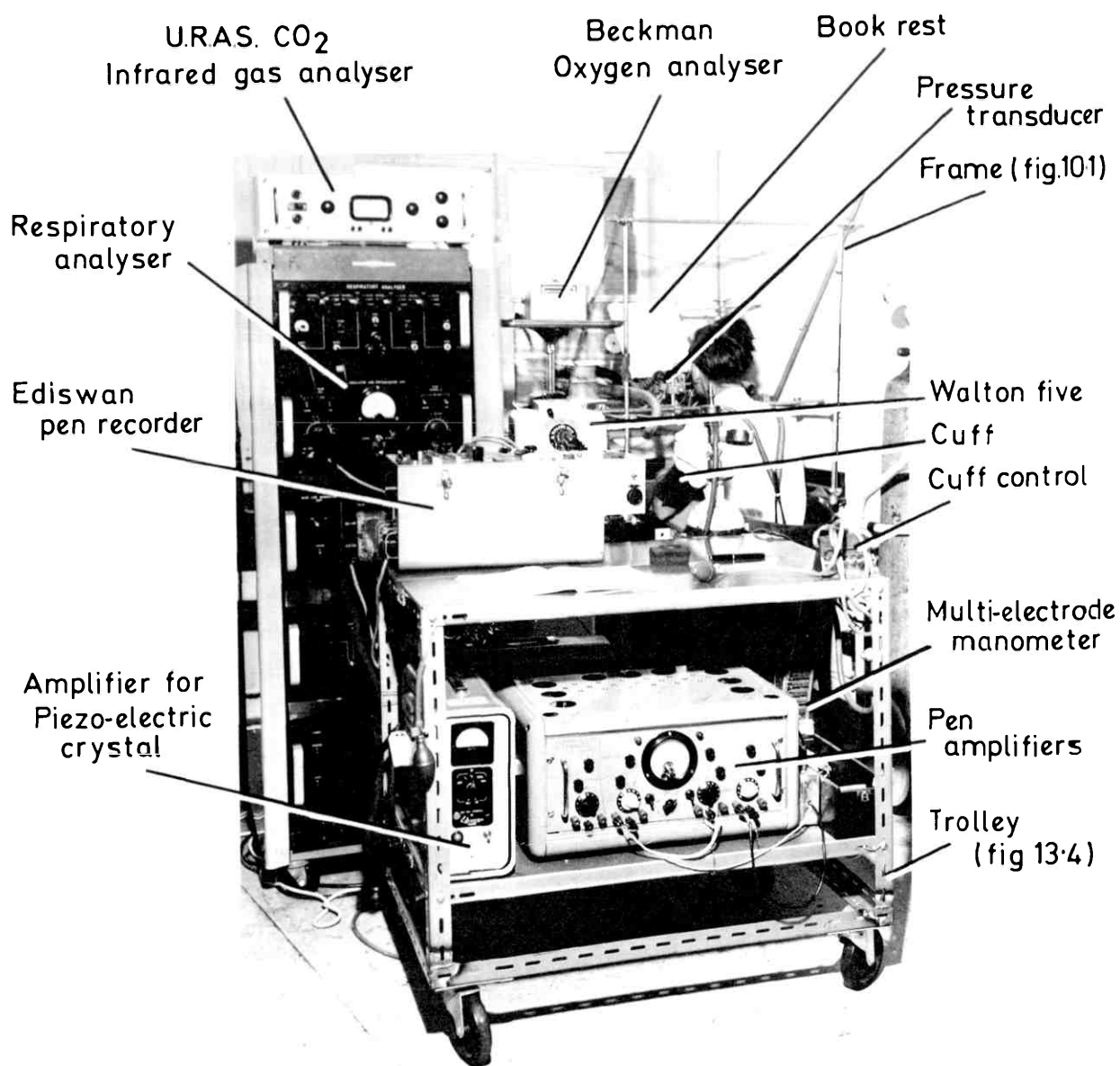


Fig. 10.10

CHAPTER 11

THE EFFECTS OF EXPIRATORY RESISTANCE,
OXYGEN AND HYPOXIA ON SITTING VOLUNTEERS

This work was carried out while holding a Wellcome Research Fellowship in the Research Department of Anaesthetics, the Royal College of Surgeons of England. It has been published (Smith, W.D.A. (1963). The effects of expiratory resistance, oxygen and hypoxia in relation to dental anaesthesia. Part II: an experimental study with conscious subjects. *Brit.J.Anaesth.* 35, 64).

At one time or another nearly all members of the Research Department of Anaesthetics became involved as subjects, and help was given with the operation of the apparatus on those occasions when the author was the subject. Representatives of the Departments of Anatomy, Dental Surgery and Physiology of the Royal College of Surgeons also "volunteered". The de Havilland Aircraft Company and Mr. C. C. Williams and Mr. J. Heyes assisted with the analysis of the respiratory records.

This investigation was carried out in order to obtain background information against which to assess the results of a study of routine outpatient dental anaesthesia which had been planned (see chapters 13 and 14); and to assess whether the methods used with conscious subjects in the laboratory would be suitable for application to the proposed clinical study, without interfering unduly with the patients, the anaesthetists or the dentists. These methods, and the plan of investigation, have been described in chapter 10.

In this chapter the effects are reported of expiratory resistance, and the administration of various mixtures of oxygen and nitrogen, on the systolic blood pressure, pulse rate and respiration of eleven normal subjects. Their ages ranged from 17 to 53 years. Their average age was 33 years and there were nine males and two females.

CARDIOVASCULAR CHANGES

Individual experiments

Pulse rate and the upper and lower limits of systolic blood pressure recorded at peak expiration during the earlier experiments are shown in figures 11.1, 11.2, 11.3 and 11.4. The sex and the ages of the subjects are indicated in figure 11.1. (The readings plotted for subject 1 were in fact the last to be obtained during this early series. They were recorded during a repetition of earlier experiments, the results of which were discarded.) The upper margin of the thick line representing the systolic blood pressure during the peak of expiration indicates the upper limit of the measurement. The lower margin indicates the lower limit. The thickness of the line indicates

the difference between the upper and lower limits (see figure 11.1, subject 2). In general, the greater the frequency with which the readings of indirect systolic blood pressure are taken, the more rapid is the rate of deflation of the sphygmomanometer cuff in relation to the respiratory rate, and the less the accuracy of the measurement (see chapter 10).

Breathing against an expiratory resistance without hypoxia, was accompanied by a rise in systolic blood pressure and sometimes by a slight rise in pulse rate. This is shown in figure 11.1. During inspiration of 10 per cent oxygen there was little change in systolic blood pressure, but there was a consistent rise in pulse rate which is shown in figure 11.2. Figure 11.3 shows the effects of combining inspiration of 10 per cent oxygen with expiration against resistance. There were increases in both systolic blood pressure and in pulse rate.

Figure 11.4 shows the results of a series of experiments performed with subject 9 on six different occasions. This subject received particular attention because he used to faint easily as a boy and twice during the last 5 years experienced post-micturitional syncope. The routine experimental sequences were repeated using an expiratory resistance of only 5 mm Hg (15. 6. 61. and 16. 6. 61.). In addition, periods of breathing 8.5 per cent oxygen were included. The final experiment was carried out in the afternoon, the subject having deliberately remained up and awake throughout the previous night and having had nothing to eat since the evening. The general pattern of results was the same as those presented in figure 11.3. It is interesting to note that while he was breathing against an expiratory pressure of 5 mm Hg, the systolic blood pressure

appeared to rise almost as much as when an expiratory pressure of 11 mm Hg was used. In the absence of expiratory resistance, this subject showed a slightly greater blood pressure rise when breathing 8.5 per cent oxygen than when breathing 10 per cent oxygen, though both were small. There was also a slight fall in blood pressure when inspiring 100 per cent oxygen and still breathing against the expiratory resistance. No dramatic events were recorded during the final experiment.

The presentation of the results obtained from eleven subjects

If direct intra-arterial blood pressure had been measured continuously using electromanometry, the results would have been more accurate and easier to interpret. The method used gave only an intermittent indication of the limits between which the peak systolic blood pressure lay. Analysis and presentation of the results were further complicated by the variable number of blood pressure readings taken during each minute, and by the variable duration of the "5-minute" periods. As can be seen from figures 11.1 to 11.4, these did not always last precisely 5 minutes, so that the relative times at which breathing conditions were changed varied from subject to subject. The following section describes the methods which have been used for analysing the results and for presenting them collectively.

One of the purposes of these experiments was to find out the changes in systolic blood pressure and in pulse rate brought about by making known changes in the breathing conditions. In analysing the results, therefore, attention has been focused upon the changes in systolic blood pressure and upon the changes in pulse rate, rather than upon their absolute values.

The changes associated with each alteration of the breathing

conditions have been analyzed by considering successive overlapping periods of 10 minutes. Each of these embraced two consecutive 5-minute periods, so that there was an alteration of the breathing conditions in the middle of each 10-minute period. The events occurring within each 10-minute period were timed in relation to this midpoint, that is in minutes before or after the instant at which the breathing conditions were altered. For ease of reference the 10-minute periods have been allotted letters which are given in table 10.1 (chapter 10). Ten-minute periods A to F covered Part I, G to N covered Part II, and A.G. to Q covered Part III. Reference to figure 11.5 should make this clear.

Another purpose of the experiments was to test the suitability of the apparatus for use during a study of dental anaesthesia. The use of a pneumotachograph, however, was not planned for the clinical investigation, so it would not be possible to define the upper limits of systolic blood pressure - only the lower limits would be obtainable. For this study with conscious subjects, therefore, the changes in the upper and lower limits of systolic blood pressure have been analysed separately in the first instance, so that they can be compared. In the final analysis the mean of the changes in the upper and lower limits of systolic blood pressure has been taken, and the changes found during consecutive 10-minute periods have been related to each other in order to indicate the trends during each main part of the experiment (see figure 11.11).

The method of analysis of changes in systolic blood pressure and pulse rate

The record obtained with each subject was first examined

in detail. For each 10-minute period, as described above, the position on the record corresponding with the instant at which the breathing conditions were changed was identified. Such a point of change is indicated on figure 10.2 (chapter 10) as "Start of expiratory resistance". The record was then marked off into 1-minute intervals before and after the time at which the breathing conditions changed. The measurements of pulse rate and of the upper and lower limits of systolic blood pressure falling within each of these 1-minute intervals were averaged, so that there was one set of readings (upper and lower limits of systolic blood pressure and pulse rate) for each subject for each minute of the experiment. Then, starting from the first minute of each 10-minute period (in other words starting from 5 minutes before each change of the breathing conditions), the changes in the mean values, from each minute to the following minute, were obtained by subtraction.

Having found the minute-to-minute changes shown by each subject, the average of the changes shown by all eleven subjects during each minute of each 10-minute period was calculated. These collective results are shown in figures 11.5 to 11.7. The changes in the upper and lower limits of systolic blood pressure have been superimposed. The thickness of the lines representing changes in systolic blood pressure indicates the discrepancy between the minute-to-minute changes as derived from the upper and lower limits of systolic blood pressure respectively. No consistency was in fact shown in the relative magnitudes of the changes obtained from the upper and lower limits.

Figures 11.5 to 11.7 do not present the same information as does a standard chart of blood pressure and pulse rate. They

indicate the changes which occur between consecutive minutes, or the rate of change. This may be understood by reference to period A (figure 11.5). The first minute of the period is taken as the starting point (the fifth minute before the change). Between the first and second minutes (the fifth and fourth minutes before the change) one limit of the systolic blood pressure increased slightly and the other fell slightly. The pulse rate did not change. Between the fifth and sixth minutes (between the minutes immediately before and after the change) both the upper and the lower limits of systolic blood pressure showed a definite increase, whereas the average pulse rate rose by only 2 b.p.m. Between the sixth and seventh, seventh and eighth, and eighth and ninth minutes the systolic blood pressure continued to rise slightly.

There are discrepancies between the results plotted for the first half of each 10-minute period and the second half of the previous (and over-lapping) 10-minute period. For example, the changes shown in figure 11.5 for the first half of period B are not identical with those for the second half of period A. These discrepancies arise because of the slight differences in the duration of the "5-minute" periods (differences between consecutive periods with a given subject and between comparable periods with different subjects); and because the minutes referred to within each 10-minute period are related to the time at which the breathing conditions were changed in the middle of that period. (A reading obtained during the second minute after a change of conditions would fall within the fourth minute before the following change if the intervening period lasted for exactly 5 minutes; but if the intervening period lasted for 6 minutes, the reading

would fall within the fifth minute before the following change).

The results plotted during the first half of each 10-minute period are timed in relation to the following change of breathing conditions - an event which had not happened. The results plotted during the second half of each 10-minute period are timed in relation to the previous change of breathing conditions - an event which had just happened. The latter obviously have greater significance.

The minute-to-minute changes in systolic blood pressure and pulse rate

The average minute-to-minute changes when an expiratory resistance was imposed without accompanying hypoxia are shown in figure 11.5. During the minute immediately following the application of the expiratory resistance (A, C and E) there was a sudden rise in systolic blood pressure which equalled or exceeded the mask pressure during expiration. (The pressure in the mask, relative to atmospheric pressure, is indicated by the height of the vertically hatched areas in the figures). The systolic pressure continued to rise from minute to minute during the following 3 minutes, except when the expiratory resistance was introduced for the third time (E) following the inspiration of 100 per cent oxygen. During the first minute following the removal of the expiratory resistance (B, D and F) the blood pressure fell by an amount equal to or slightly less than the initial rise recorded when the resistance was previously introduced. The fall in systolic pressure, however, was not progressive during subsequent minutes, and there was a suggestion of an overshoot during the second or third minutes following removal of the resistance. The changes in pulse rate were small.

The average minute-to-minute changes recorded during periods of breathing different concentrations of oxygen are shown in figure 11.6. The blood pressure changes were small. The pulse rate rose throughout each period of breathing 10 per cent oxygen, the rate of rise being greatest during the third minute when room air had been breathed previously (G and I), and during the fourth minute of hypoxia following the inspiration of 100 per cent oxygen (K). The rate of fall of pulse rate upon the removal of the hypoxic conditions tended to be steeper than the initial rise (H and J, but not so obvious in L). This fall was greatest when 100 per cent oxygen was breathed (J). Changes in pulse rate on breathing 100 per cent oxygen following air (M) were small but on breathing air again (N) there appeared to be a slight rise in pulse rate during the first minute followed by a fall during the second minute.

The effects of introducing and removing a combination of hypoxic and resistive breathing conditions are shown in figure 11.7. There were changes in both systolic blood pressure and pulse rate. The patterns of blood pressure change were similar to those shown in figure 11.5. The magnitude of the systolic blood pressure changes occurring while breathing against an expiratory resistance (AG, CI, EK and C), however, were less, and the blood pressure fall on removing the expiratory resistance (BH, DJ, FL and Q) continued beyond the first minute.

The cumulative changes of systolic blood pressure and pulse rate during each 10-minute period

The cumulative changes of systolic blood pressure and of pulse rate, from the beginning to the end of each 10-minute period are shown in figures 11.8 to 11.10. They have been

obtained by progressive summation of the minute-to-minute changes shown in figures 11.5 to 11.8. Figure 11.8, for example, shows the cumulative changes derived from the results presented in figure 11.5. Whereas figures 11.5 to 11.7 show the changes between successive minutes, figures 11.8 to 11.10 show the changes from the start of each 10-minute period. The profiles shown in figures 11.8 to 11.10 may be regarded as equivalent to the profiles of standard charts of blood pressure and pulse rate.

The same general comments may be made as for figures 11.5 to 11.7. Certain features, however, become clearer. In figure 11.8 the steady rise in blood pressure during the latter parts of periods A and C, and the smaller blood pressure falls during the latter parts of the periods B and D are well shown. The slight rise in pulse rate that occurred while breathing against an expiratory resistance, without hypoxia, becomes more obvious, and although the subsequent fall in pulse rate when 100 per cent oxygen was breathed (D) was steeper, its final value was not significantly lower than when air was breathed (B) following resistance breathing. In figure 11.9 there is a suggestion of a slight rise in blood pressure when 10 per cent oxygen was breathed. During the latter part of period J, when 100 per cent oxygen was breathed following 10 per cent oxygen, it can be seen that not only was the fall in pulse rate steeper than when air was breathed (H), but the pulse rate also fell below the initial absolute value recorded before hypoxia was introduced. The same effect is seen with period DJ in figure 11.10. The pronounced fall in blood pressure following breathing an hypoxic mixture against an expiratory resistance (DJ and FL) relative

to the smaller initial rise on introducing those conditions (CI and EK) is well shown in this figure. It can also be seen that the effect of introducing 100 per cent oxygen following 10 per cent oxygen, while still breathing against an expiratory resistance (F), was mainly to produce a fall in pulse rate, but not to a level lower than at the start of the experiment. This fall did not take place until the second minute following the introduction of oxygen, and then, during the fourth minute, the pulse rose slightly.

The changes of systolic blood pressure and pulse rate throughout each main part of the experiment

The changes throughout Parts I, II and III of the main experiment (see table 10.1; chapter 10) have been derived from the data given in figures 11.8 to 11.10. For clarity, the means of the changes in the upper and the lower limits of systolic blood pressure were first determined. The figures were then redrawn so as to show only the changes during the second half of each 10-minute period. Finally, the plots for each of these 5-minute periods (the second halves of the 10-minute periods) were shifted vertically so that the first plot of each 5-minute period coincided with the last plot of the previous 5-minute period. The final result is shown in figure 11.11. The hatched areas represent an expiratory resistance of 11 mm Hg and they have been included to facilitate comparison of the magnitude of the blood pressure changes with the magnitude of the expiratory pressures applied. (As mentioned above, a steady expiratory resistance of 11 mm Hg was achieved with four subjects only. No attempt has been made to determine the average mask pressure for all eleven subjects, but the value

would usually have been a little less than 11 mm Hg and the change in intrathoracic pressure would have been smaller still.)

During Part I, when an expiratory resistance was introduced without hypoxia, the blood pressure rose by more than the rise in intrathoracic pressure, and the discrepancy between the two became less with the second and third periods of resistance breathing (periods 4 and 6, table 10.1). During the intervening periods it did not fall quite back to the level which existed before the previous resistance breathing started. As a result, there was an overall tendency for the absolute value of the systolic blood pressure to rise progressively with each successive period of resistance breathing. This effect was not shown by every subject. The mean rise of the pulse rate did not appear to be more than 10 b.p.m. during resistance breathing, and during the intervening periods it did not fall below the starting value.

The systolic blood pressure during Part II fluctuated within 5 mm Hg above and below the starting level. The average pulse rate increase while breathing 10 per cent oxygen was up to 16 b.p.m. and there was a tendency to undershoot the starting level during the intervening periods, especially while breathing 100 per cent oxygen, when the greatest average fall below the starting level was 10 b.p.m.

The changes during Part III are shown compared with the arithmetical sum of the cumulative changes during Parts I and II. The effects of hypoxia and of expiratory resistance do not appear to be strictly additive. Of greater interest, however, are the apparent tendencies for the systolic blood pressure to

be less well maintained during each successive period breathing against an expiratory resistance while hypoxic, and for the blood pressure fall during the intervening periods to be greater than the previous rise. There appeared to be an overall tendency for the systolic blood pressure to fall progressively, although this fall was small and was not shown by all subjects. The increase in pulse rate while breathing under these conditions appears to have been slightly greater than when breathing 10 per cent oxygen alone. The fall in pulse rate during the intervening periods appears to have been the same.

RESPIRATORY CHANGES

The respiratory responses to the different breathing conditions were not analysed in as much detail as the cardiovascular changes. The respiratory changes were less constant and the methods used to investigate them were open to greater error. The changes in minute volume, tidal volume and respiratory frequency expressed in general terms, however, are of interest.

Minute volume

During Part I the overall tendency was for the minute volume to be increased while breathing air against an expiratory resistance and most of the subjects followed this pattern. Three subjects, however, did the reverse. Two of these expired against the resistance of a Coxeter valve. The resistance of this valve is flow-dependent and subjects appeared to find the discomfort of breathing against it reduced by breathing slowly. The reduction in minute volume which occurred on removing the expiratory resistance was no greater when oxygen was breathed instead of air.

Most of the individual records covering Part II showed a tendency for the minute volume to rise very slowly during the period of hypoxia and to fall during the first minute of the following period. The fall was greater when breathing oxygen instead of air.

The average trend during Part III was for the minute volume to rise when inspiring 10 per cent oxygen and expiring against resistance, and for this rise to be more maintained than when breathing against an expiratory resistance without deliberate hypoxia. There was a greater reduction in minute volume when breathing oxygen following the combination of hypoxia and expiratory resistance than when breathing air. Two of the subjects who showed the reverse of the usual pattern during Part I, showed small and inconsistent changes during Part III.

Tidal volume and respiratory frequency

In almost every instance the subjects responded to the imposition of an expiratory resistance while breathing air by increasing their tidal volume. The changes in respiratory rate were not so constant. Only two subjects showed a consistent increase, one subject showed either no change or a slight rise, and the remainder showed a decrease in respiratory rate. In those instances in which a reduction of minute volume was recorded in the presence of an expiratory resistance while breathing air, this was due to a fall in respiratory rate large enough to offset any increase in tidal volume.

Whereas nearly all the records revealed a tendency towards an increase in minute volume while breathing 10 per cent oxygen during Part II, the relative contributions of changes

in tidal volume and respiratory rate were variable, even with a given subject. A sudden fall in minute volume immediately following a period of hypoxia almost always involved a reduction in both respiratory rate and in tidal volume; but even here one subject showed a consistent rise in respiratory rate accompanying the reduction in minute and tidal volumes.

In all cases there was an increase in tidal volume while breathing 10 per cent oxygen and expiring against resistance. The respiratory rate under these circumstances was consistent with the findings while breathing air against resistance. One of the subjects who showed a reduction in minute volume while breathing air against resistance, and an increase in minute volume while breathing 10 per cent oxygen without resistance, showed very little change in minute volume while inspiring 10 per cent oxygen and expiring against resistance.

ADDITIONAL OBSERVATIONS

Cyanosis

The degree of cyanosis observed while subjects breathed 10 per cent oxygen was variable. Sometimes it was obvious and sometimes barely noticeable.

Subjective impressions

More than half the volunteers experienced the full sequence of routine experimental breathing conditions without recording their sensations. Five of the eleven subjects made a total of twenty-eight notes. Twenty of these recorded "muzziness", "difficulty in concentrating", "dizziness", "narcosis", "faintness", or "lack of interest". Only one was recorded while breathing air against resistance but four were recorded when

first breathing 100 per cent oxygen following a period of breathing air against resistance. (None was recorded while breathing air following a period of breathing air against resistance.) Three were noted while breathing 10 per cent oxygen without an expiratory resistance and two when first breathing 100 per cent oxygen following a period of hypoxia. (None was recorded while breathing air following a period of breathing 10 per cent oxygen without resistance.) Four were recorded while inspiring 10 per cent oxygen and expiring against resistance; and four while breathing air and two while breathing 100 per cent oxygen following these conditions. The high incidence of "muzziness", etc., while breathing 100 per cent oxygen and upon release from expiratory resistance breathing, especially when this was combined with hypoxia, is of interest. One subject actually fell asleep while breathing 100 per cent oxygen during the trial experiments.

The subjective effects during inhalation of 8.5 per cent oxygen were more pronounced and unpleasant than during the routine experiments when 10 per cent oxygen was used. One subject, after breathing 8.5 per cent oxygen against resistance, raised the query "Does venous pooling increase with time during pressure breathing?" This was based upon the subjective impression of an increasing fullness of the legs. While breathing 100 per cent oxygen and expiring against resistance, following a period of inspiring 8.5 per cent oxygen and expiring against resistance, the same subject recorded "Time seems to be going very slowly.....thought I was falling asleep".

The inhalation of 100 per cent nitrogen

One subject was also given 100 per cent nitrogen to breathe for 50 seconds following a 5-minute period breathing air against resistance. The subject was seen to pick up a pencil as if to write a note but consciousness was lost before anything could be written and before there was any obvious peripheral cyanosis when viewed from one side. The record is shown in figure 11.12. The moment of loss of consciousness was not noted, and there was a gap in the blood pressure recording, but the rapidly rising pulse rate, pulse amplitude and respiratory rate and depth are well shown. Systolic blood pressure and pulse rate readings for the 10 minutes before and after the inhalation of pure nitrogen are plotted in figure 11.13. Just over 2 minutes after the subject began breathing air following the acute anoxia, the pulse rate had returned to normal levels, but the systolic blood pressure was still 30 mm Hg above the starting level. It had probably been very much higher during the period of acute anoxia. The time of return of consciousness was not noted, but recovery appeared to be sudden and complete. Quite suddenly the subject said "What's happened?" and then appeared to be awake and normal. There were no subjective sequelae and the only objective observation immediately following recovery was the raised blood pressure already described.

DISCUSSION

The secondary purpose of this study - to test the suitability of the methods used for application to a clinical study during routine outpatient dental anaesthesia, without interfering unduly with the patients, the anaesthetists or the

dentists - was satisfied. Some people may experience slight discomfort from repeated inflation of a blood pressure cuff but usually this is acceptable by adults. When changes of systolic blood pressure are being measured, as distinct from absolute values, it appears to make little difference whether the upper or the lower limits of peak systolic blood pressure are used.

Before discussing the overall results, this study should be considered in the context of its relationship to anaesthesia in the dental chair. Although the experiments were designed to present circumstances to some extent comparable with those existing during nitrous oxide and oxygen dental anaesthesia, the subjects were conscious. Any conclusions drawn from the results, therefore, are not necessarily directly applicable to the circumstances of anaesthesia; and they should be accepted with appropriate reserve. A similar investigation of the effects of the same variables while using nitrous oxide, instead of nitrogen, during alternate 5-minute periods would provide a valuable companion study.

In relation to the practice of dental anaesthesia, only a moderate reduction of the inspired oxygen concentration was used in these experiments. During dental anaesthesia the inhalation of 10 per cent oxygen is often preceded by an induction using 100 per cent nitrous oxide which may be continued until the start of automatic respiration, and hypoxia may also be increased by respiratory obstruction during dental surgery. On the other hand, the reduction of arterial oxygen tension brought about by an induction of anaesthesia using 10 per cent oxygen with nitrous oxide may be less than that produced by

inhalation of 10 per cent oxygen with nitrogen. This is to be expected because the rate of uptake of nitrous oxide during the induction of anaesthesia is greater than the rate of elimination of nitrogen. The proportion of oxygen remaining in the alveoli increases and its partial pressure is raised accordingly. Too few measurements have been made to justify any reliance on this phenomenon as a safeguard during induction of anaesthesia. Heller and Watson (1962) using arterial polarography have shown that the arterial oxygen tension may increase during induction of anaesthesia with 79 per cent nitrous oxide and 21 per cent oxygen. Eighty-six per cent nitrous oxide and 14 per cent oxygen produced a moderate fall in arterial oxygen tension.

Although there were no dramatic subjective or objective consequences of inspiring 10 per cent oxygen for 5 minutes, the series was too small to justify the conclusion that the use of 10 per cent oxygen for corresponding periods during dental anaesthesia is without risk.

The variability of the cyanosis observed while inspiring a standard mixture of 10 per cent oxygen with nitrogen during these experiments illustrates the well-known unreliability of this sign as a guide to the degree of hypoxia imposed when using dental anaesthetic machines of uncertain calibration.

The changes in systolic blood pressure in response to the inspiration of 10 per cent oxygen were small (figure 11.11). Under these conditions both the systolic blood pressure and the pulse rate changes were consistent with the findings of previous workers (Schneider, 1918; Abramson, Landt and Benjamin, 1943; Dripps and Comroe, 1947 (blood pressure not recorded); Motley

et al., 1947). The pulse rate changes while breathing 10 per cent oxygen were only slightly increased by the inclusion of an expiratory resistance.

The increase in systolic blood pressure in response to the introduction of an expiratory resistance while breathing air tended to be greater than the corresponding increase in mask pressure. This is consistent with the findings in conscious sitting subjects reported by Dern and Fenn (1947). The pattern of change in figures 11.8 and 11.11 shows that during the first two periods of resistance breathing (periods 2 and 4, table 10.1; chapter 10) there was an initial sudden rise in systolic blood pressure. This could be explained by the combination of a reflex peripheral vasoconstriction and the mechanical effects of an increase in intrathoracic pressure, which has been discussed in chapter 3. After the initial sudden rise in systolic blood pressure in response to the introduction of an expiratory resistance during Part I, there followed a further slow rise. This could also be reflex in origin and there could be a humoral element. Watson (1961a) found that the distensibility of the hand began to decrease about 10 seconds after the intrathoracic pressure was increased and had usually attained a steady state within 2 minutes, but the circumstances of positive pressure pulmonary inflation in paralysed patients are not quite the same as those of positive pressure expiration in spontaneously breathing fit subjects.

It is interesting to note that the systolic blood pressure measured during the intervening periods of breathing without resistance showed a tendency to rise throughout Part I, whereas Fenn and Chadwick (1947) found that vasoconstriction outlasted

pressure breathing by only 20 to 30 seconds, and Watson (1961a) found that the distensibility of the capacity vessels of the hand returned to normal within 2 minutes upon removal of positive pressure.

During the third period of breathing against resistance (period 6, table 10.1; chapter 10) the blood pressure rose rapidly to a plateau. This change in pattern could be related to the previous period of breathing 100 per cent oxygen, or to the previous periods of resistance breathing and the steady rise in systolic blood pressure throughout Part I. It could be fortuitous.

The pattern of systolic blood pressure change measured during Part III (figure 11.11), when inspiration of 10 per cent oxygen was combined with expiration against resistance, shows that the measured systolic blood pressure tended to fall progressively during the intervening periods. In terms of absolute blood pressure the changes are small, but this overall trend during Part III contrasts strikingly with the reverse trend during Part I. Although Watson (1961b) found that the distensibility of the capacity vessels in normal subjects decreased during hypoxia, which is consistent with the results obtained during Part II, he did not report on the effects of imposing and removing the combination of hypoxia and raised intrathoracic pressure. The blood pressure changes recorded during Part III suggest that the compensatory increase in vasomotor tone during pressure breathing may, after a time, become less efficient during hypoxia; and that following this combination the peripheral vascular tone may become less than normal. It may be relevant that one subject had the impression

of an increasing fullness of the legs while inspiring 8.5 per cent oxygen and expiring against resistance. With the indirect method of measuring systolic blood pressure used, however, one cannot have confidence in the reality of these trends. There might be a case for repeating some of these measurements using continuous intravascular measurement of arterial blood pressure.

The high incidence of subjective observation noted, and the greater reduction in minute volume found on breathing oxygen rather than air following the combination of hypoxia plus resistance, also suggest that there may be something particularly significant about sudden release from these conditions. These observations may be related to the oxygen paradox mentioned in chapter 3.

The increase in minute volume recorded while breathing 10 per cent oxygen in Part II is consistent with the findings of previous workers (Schneider, 1918; Abramson, Landt and Benjamin, 1943; Dripps and Comroe, 1947; Motley et al., 1947).

Davies, Haldane and Priestley (1919) found that the introduction of resistance during both phases of respiration usually resulted in a slowing and a deepening of breathing. The findings in Part I of the present study are, in general, consistent with theirs. They also found that with excessive resistance the breathing, after a time, suddenly became shallow and rapid. The resistance required for this to happen varied from subject to subject, and in a given subject it was produced more easily in the presence of anoxaemia. They also found a rise in alveolar carbon dioxide tension which implies a reduction in minute volume. Similar results were obtained by Cain and Otis (1949) using laminar flow resistances with five trained subjects.

McIlroy et al. (1956) found that the effects of added inspiratory and expiratory resistance in four subjects varied between different subjects and in different experiments on the same subject. Out of ten experiments the alveolar ventilation was reduced in seven, virtually unchanged in one and increased in two. Little attention appears to have been paid to the effects of resistance applied only during expiration. In the present study the use of an expiratory resistance during Part I did result in a reduction in minute volume in three subjects but usually the minute volume increased. This may be related to the absence of an inspiratory resistance or to the nature of the expiratory resistance used. Neither laminar flow nor threshold resistance conditions (as with a dead weight resistance) apply to the expiratory resistance occurring during dental anaesthesia when turbulent flow may be expected in the expiratory valve. Inspiratory resistance can occur during dental anaesthesia if inadequate supply flow rates are used. This is most likely if narrow-bore tubing is used or if the reservoir bag is excluded.

The effects of expiratory resistance are of particular interest in relation to dental anaesthesia. An increase in tidal volume was almost invariable. There was often a decrease in respiratory rate. In some instances the reduction in respiratory rate was sufficient to cause a reduction in minute volume. One subject who increased his minute volume during hypoxia without resistance, showed very little change in minute volume while inspiring 10 per cent oxygen and expiring against resistance. This indicates that a desirable compensatory increase in minute volume in response to hypoxia may be counteracted by the introduction of an expiratory resistance.

The results of this study suggest that an inspired oxygen concentration of not less than 10 per cent and an expiratory resistance of not more than 11 mm Hg are not, either singly or together, likely to cause a rise in systolic blood pressure of more than 15 to 20 mm Hg. Goldman, Cornwell and Lethbridge (1958), however, who recorded a rise in blood pressure in 94 out of 100 unselected patients, found the rise to be less than 20 mm Hg in only 46 of them. Walsh (1958) found a rise of more than 15 mm Hg in 126 patients and a rise of more than 25 mm Hg in 63 patients in a series of 300 dental anaesthetics. (Either trichloroethylene or halothane was used to supplement nitrous oxide and oxygen in 200 of these.) The use of an expiratory resistance of more than 11 mm Hg during dental anaesthesia is unlikely except for short periods when anaesthetizing resistant patients. It is probable that in many instances the rise in blood pressure occurring during dental anaesthesia is an expression of the degree of hypoxia to which the patients are subjected, or of surgical stimulation under very light anaesthesia.

The increases in systolic blood pressure, pulse rate and ventilation which can occur during a 50-second exposure to acute anoxia are illustrated in figures 11.12 and 11.13. In the context of dental anaesthesia these should be regarded as compensatory changes tending to facilitate the transport of any available oxygen to vital tissues, even if at a reduced partial pressure, rather than as a built-in protection against hypotension in the dental chair. A patient may appreciate the lack of unpleasant sensations during induction of "anaesthesia" by acute anoxia using nitrous oxide, provided that the surgical procedure for which the "anaesthetic" is given is brief. If the

incident is not complicated in any way he may both lose consciousness and recover quickly. Induction of anaesthesia using nitrous oxide without hypoxia, on the other hand, is likely to take much longer, consciousness will be lost more gradually, and, since more nitrous oxide will have entered the body during the longer induction, recovery may be a little slower. Superficially the former type of anaesthetic might, in expert hands, appear to be the more impressive to a casual observer in a dental clinic. Provided that adequate anaesthesia is obtained (and if necessary a supplement can be added) the latter type of anaesthetic is likely to have a greater margin of safety.

CONCLUSIONS

This study achieved its object of proving the reliability of the apparatus and methods used, and their suitability for use during routine dental anaesthesia. It confirmed that expiratory resistance was associated with an increase in systolic blood pressure, and hypoxia with an increase in pulse rate. It suggested that compensatory mechanisms normally stimulated by pressure breathing may become less efficient in the presence of hypoxia; that the changes occurring upon the sudden relief of hypoxia may be important, especially where hypoxia has been combined with an expiratory resistance; and that in some subjects an adequate compensatory increase in minute volume, in response to hypoxia, may be prevented by the imposition of an expiratory resistance. These conclusions apply to conscious sitting subjects. It does not necessarily follow that they all apply to anaesthetised sitting patients.

FIGURE 11.1

The upper and lower limits of peak expiratory systolic blood pressure, the pulse rate and the mask pressure recorded during experiments with five subjects while breathing against an expiratory resistance during alternative 5-minute periods without hypoxia.

(See table 10.1; chapter 10. Part I.)

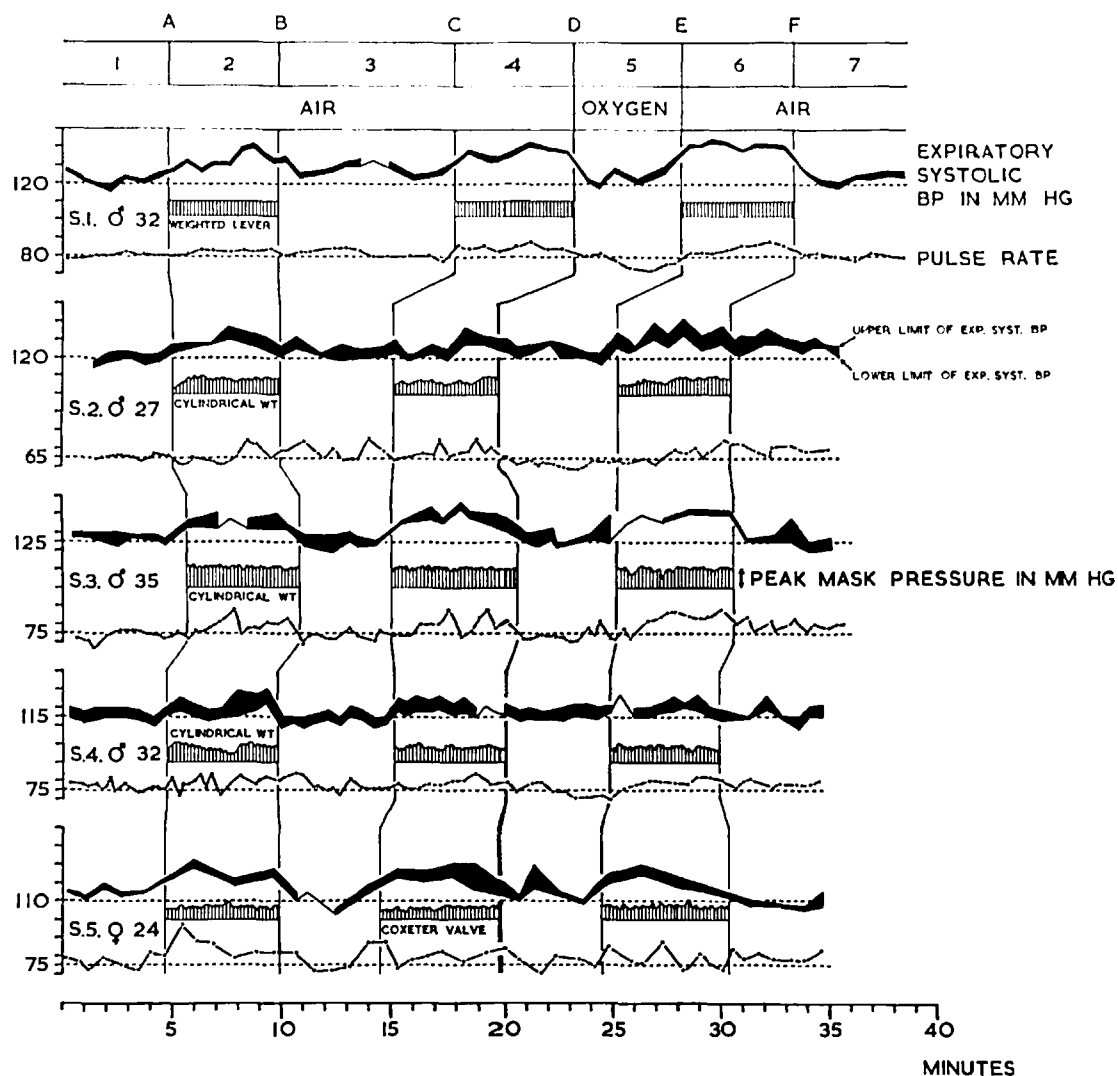


FIGURE 11.2

The upper and lower limits of peak expiratory systolic blood pressure, and the pulse rate recorded during experiments with the same five subjects as in figure 11.1, while breathing 10 per cent oxygen with nitrogen during alternate 5-minute periods. (See table 10.1; chapter 10. Part II.)

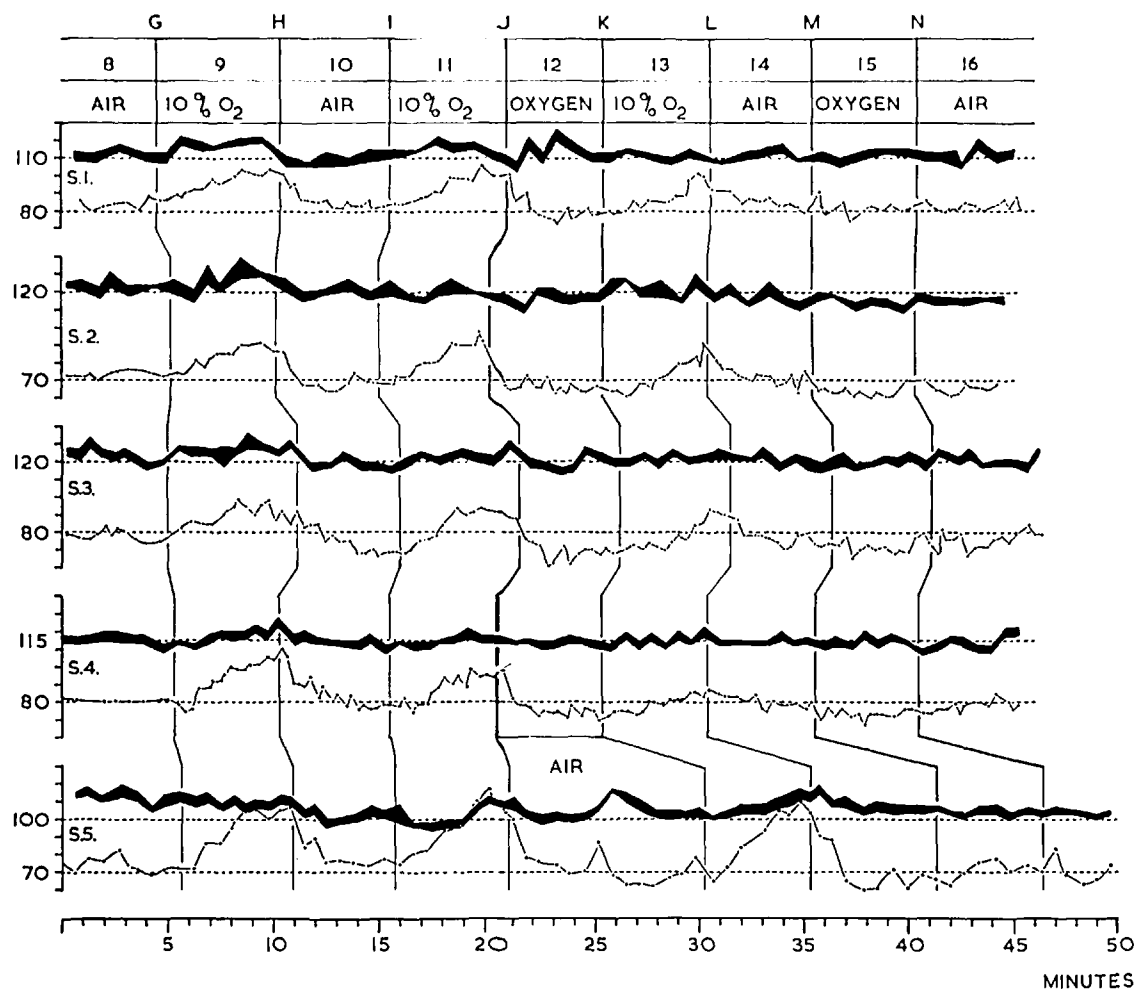


FIGURE 11.3

The upper and lower limits of peak expiratory systolic blood pressure, the pulse rate and the mask pressure recorded during experiments with five subjects while breathing 10 per cent oxygen and at the same time against an expiratory resistance during alternate 5-minute periods. (See table 10.1; chapter 10. Part III.)

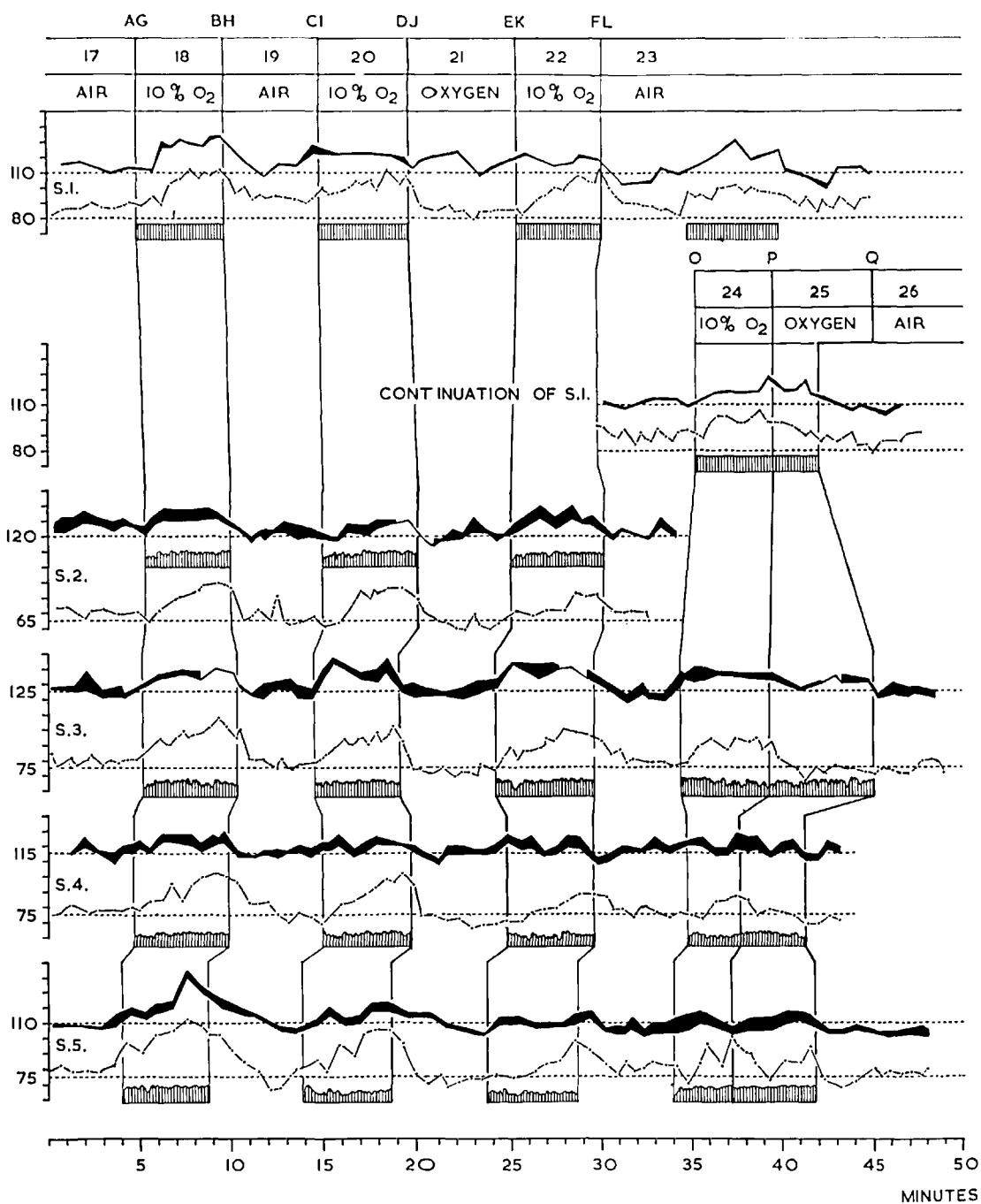


FIGURE 11.4

The upper and lower limits of peak expiratory systolic blood pressure, the pulse rate and the mask pressure recorded during six experiments carried out with the same subject (male aged 43 years). The upper limits of the lowest systolic blood pressure recorded during inspiration have been indicated thus $\wedge$.

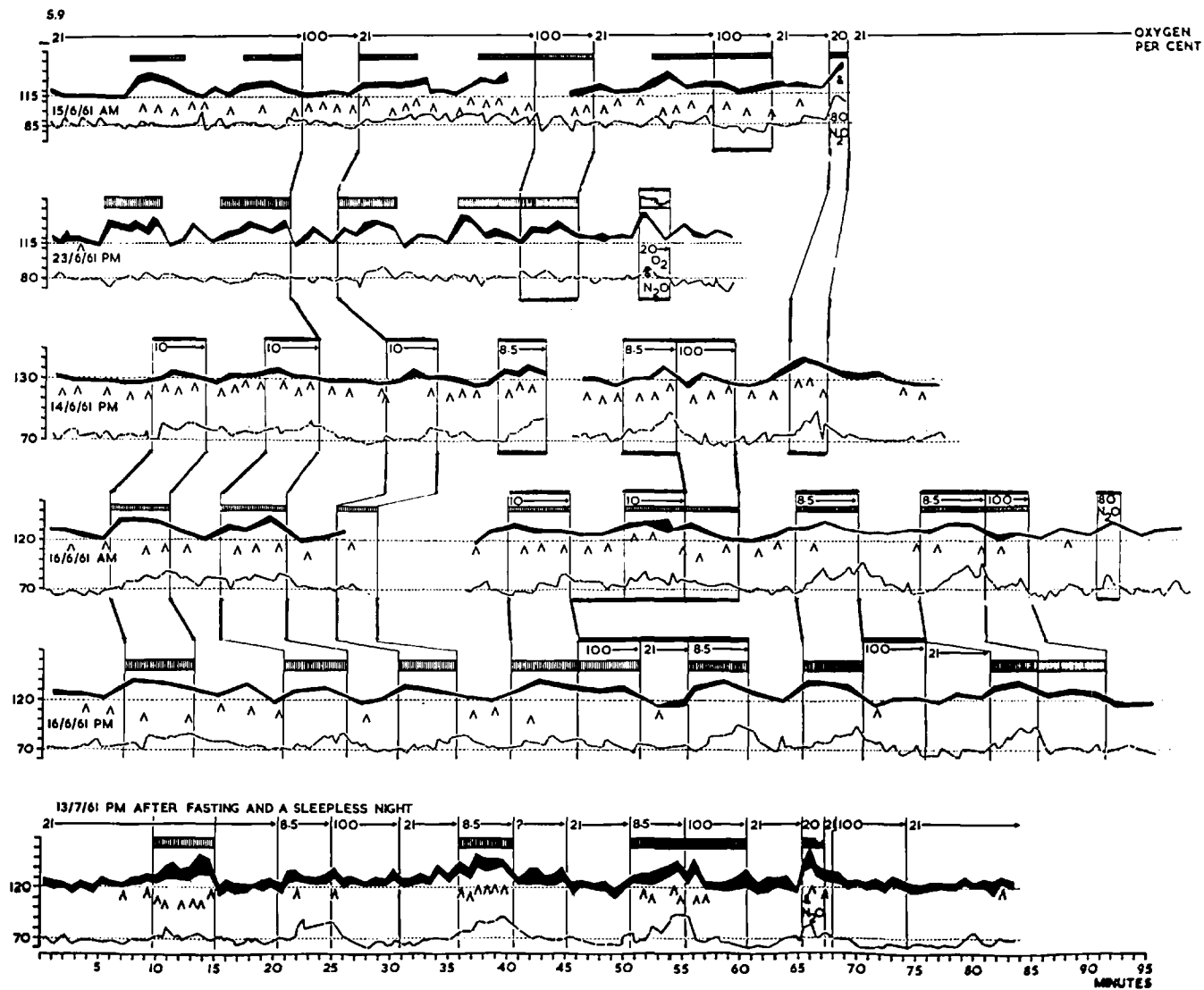


FIGURE 11.5

The averaged results obtained with 11 volunteers, showing the changes from minute to minute (i.e. the rate of change) of systolic blood pressure at peak expiration (above - the average changes in the upper and lower limits being analysed separately and superimposed), and of pulse rate (below), during overlapping 10-minute periods. The 10-minute periods are labelled with capital letters to correspond with table 10.1, A to F (Chapter 10). An expiratory resistance (indicated by vertical hatching) was applied throughout one half of each 10-minute period, but there was no hypoxia. The start of each 10-minute period was taken from 5 minutes before the time at which the conditions of the experiment were changed.

(In the first instance the S.D.'s of the minute to minute changes were shown as broken lines on this diagram. These suggested that little confidence can be placed on the smaller changes, which is what might be expected when using an indirect method of measuring systolic blood pressure. Indication of the S.D.'s in this way added confusion to the diagrams, so they have been omitted from the figures shown here).

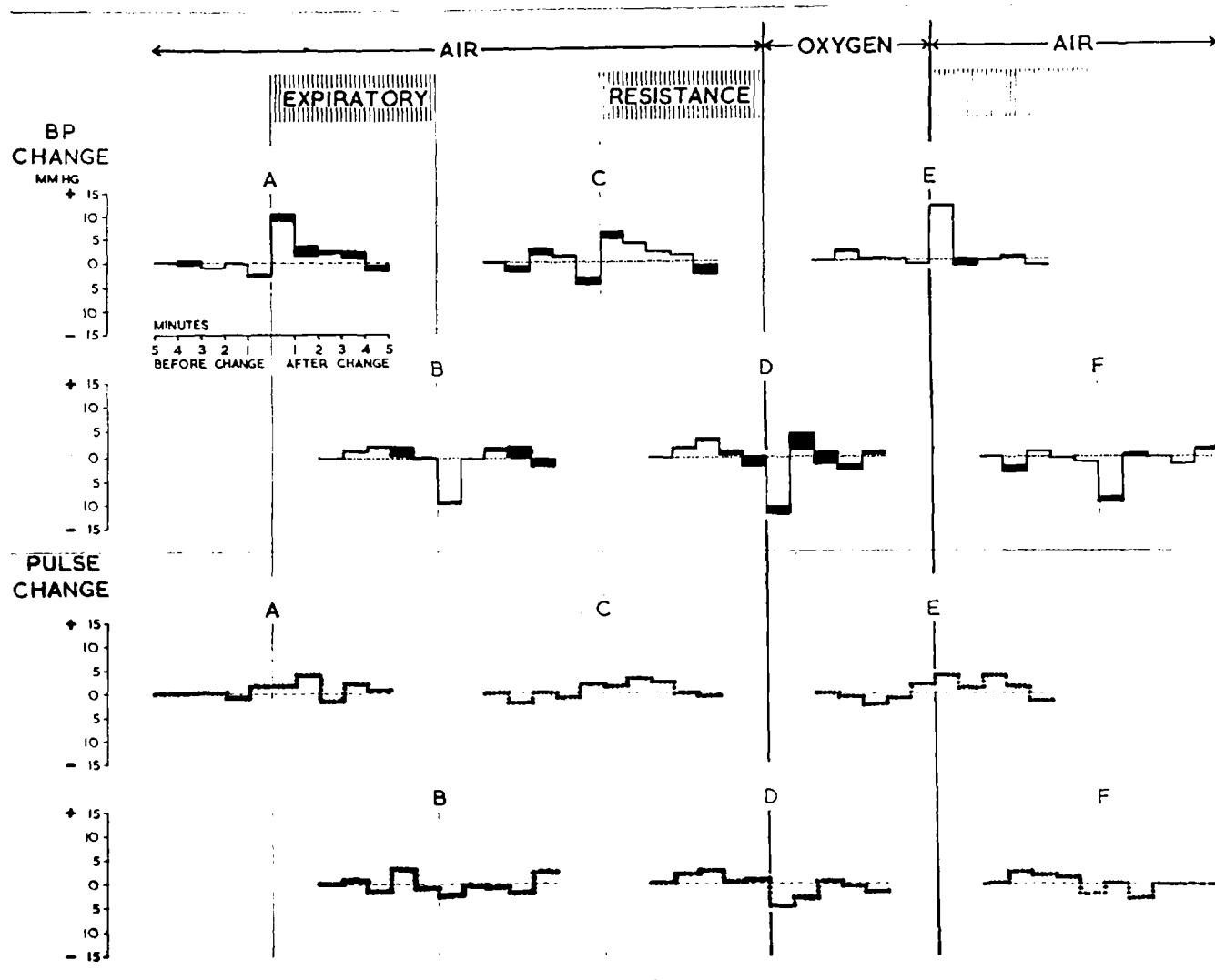
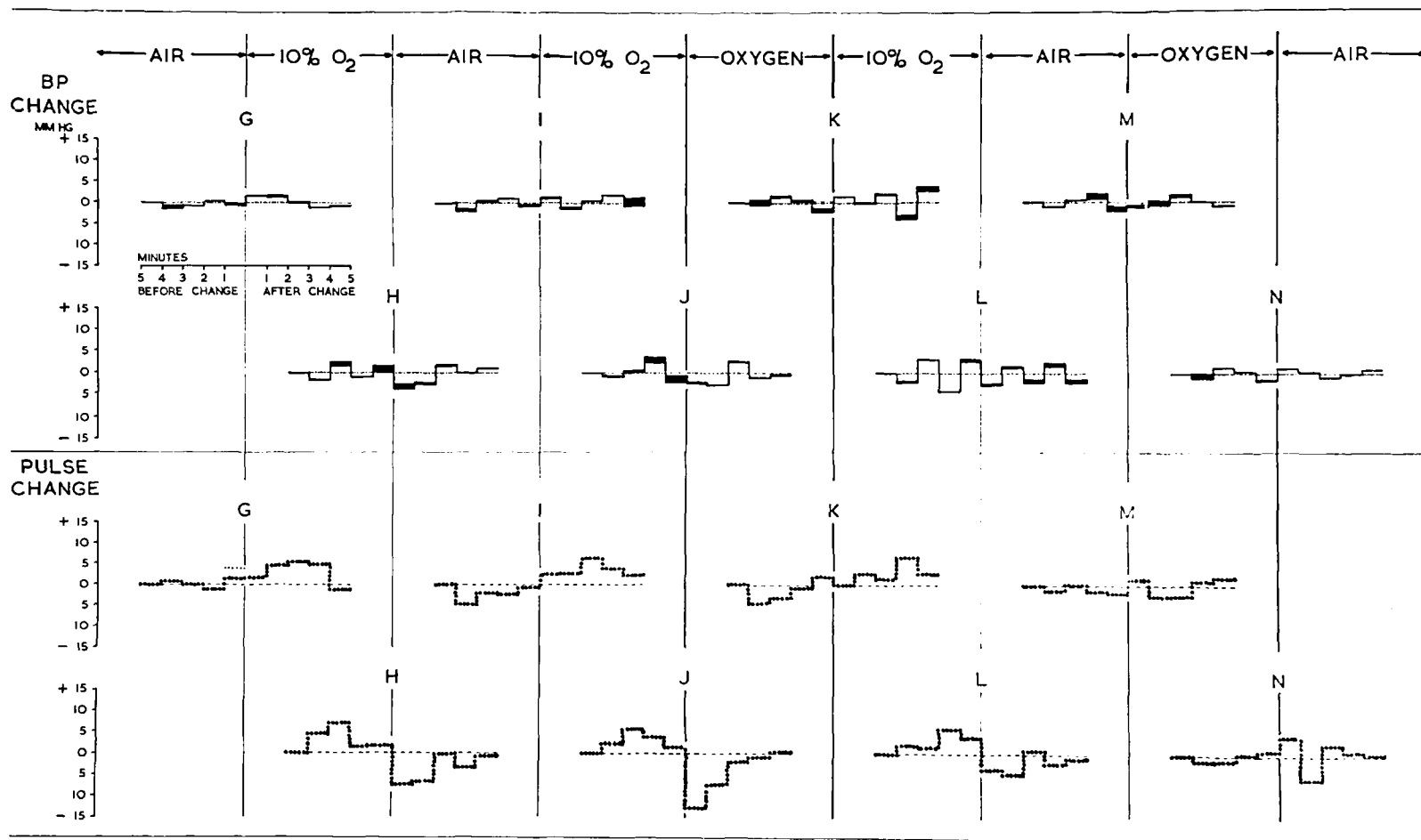


FIGURE 11.6

As figure 11.5, but for the 10-minute periods G to N. 10 per cent oxygen was breathed during this part of the experiment, but there was no expiratory resistance.



CHAPTER 11.7

As figure 11.5, but for 10-minute periods AG to Q. During this part of the experiment hypoxia was combined with breathing against an expiratory resistance.

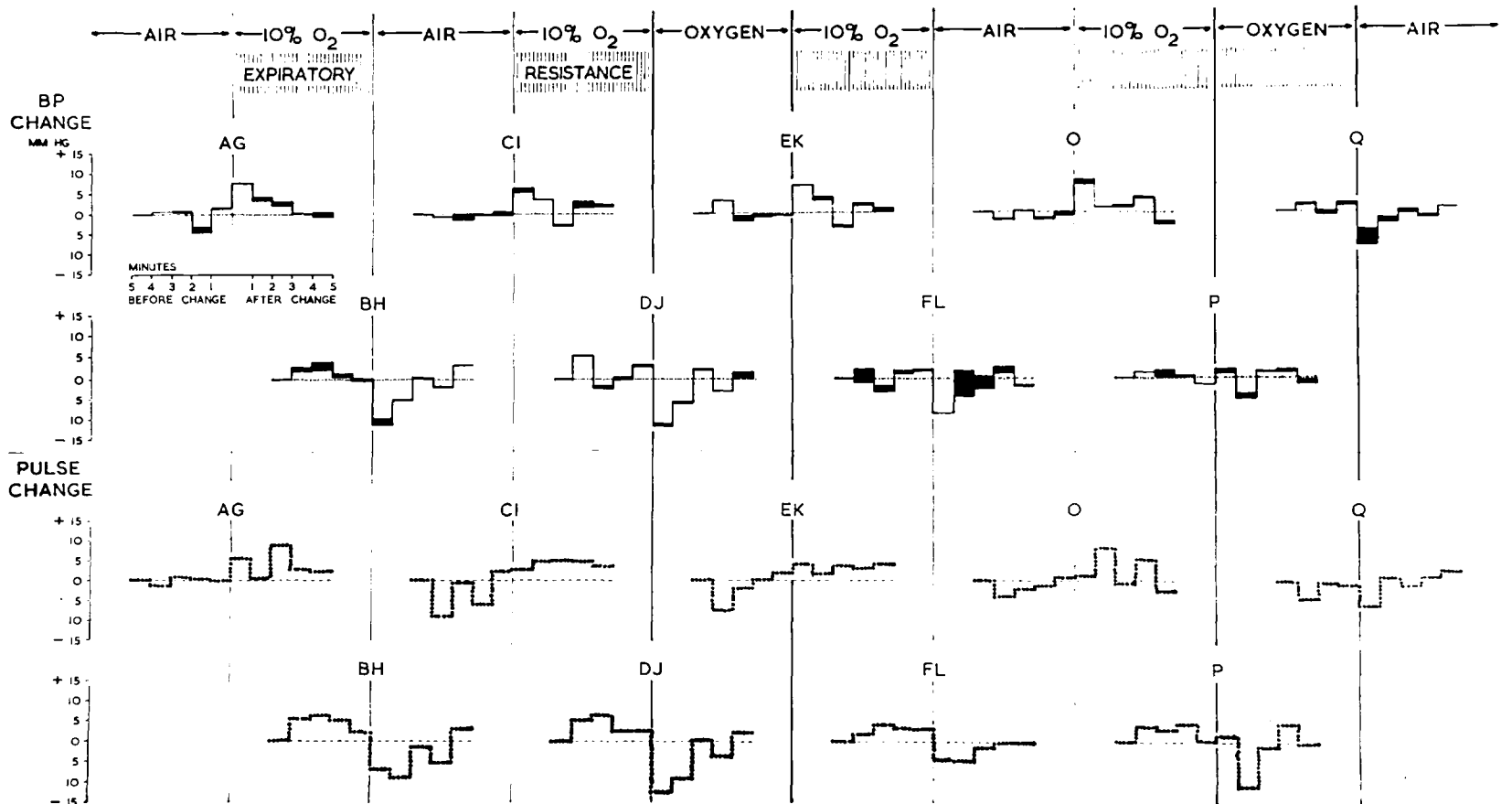


FIGURE 11.8

The averaged results obtained with 11 volunteers, showing the change from the start of each 10-minute period (derived by progressive summation of the minute to minute changes shown in figure 11.5) of systolic blood pressure at peak expiration (above - the average changes in the upper and lower limits being analysed separately and superimposed), and of pulse rate (below), during 10-minute periods A to F. (Expiratory resistance but no hypoxia.) The profiles obtained for each 10-minute period may be regarded as equivalent to the profiles of standard charts of systolic blood pressure and of pulse rate.

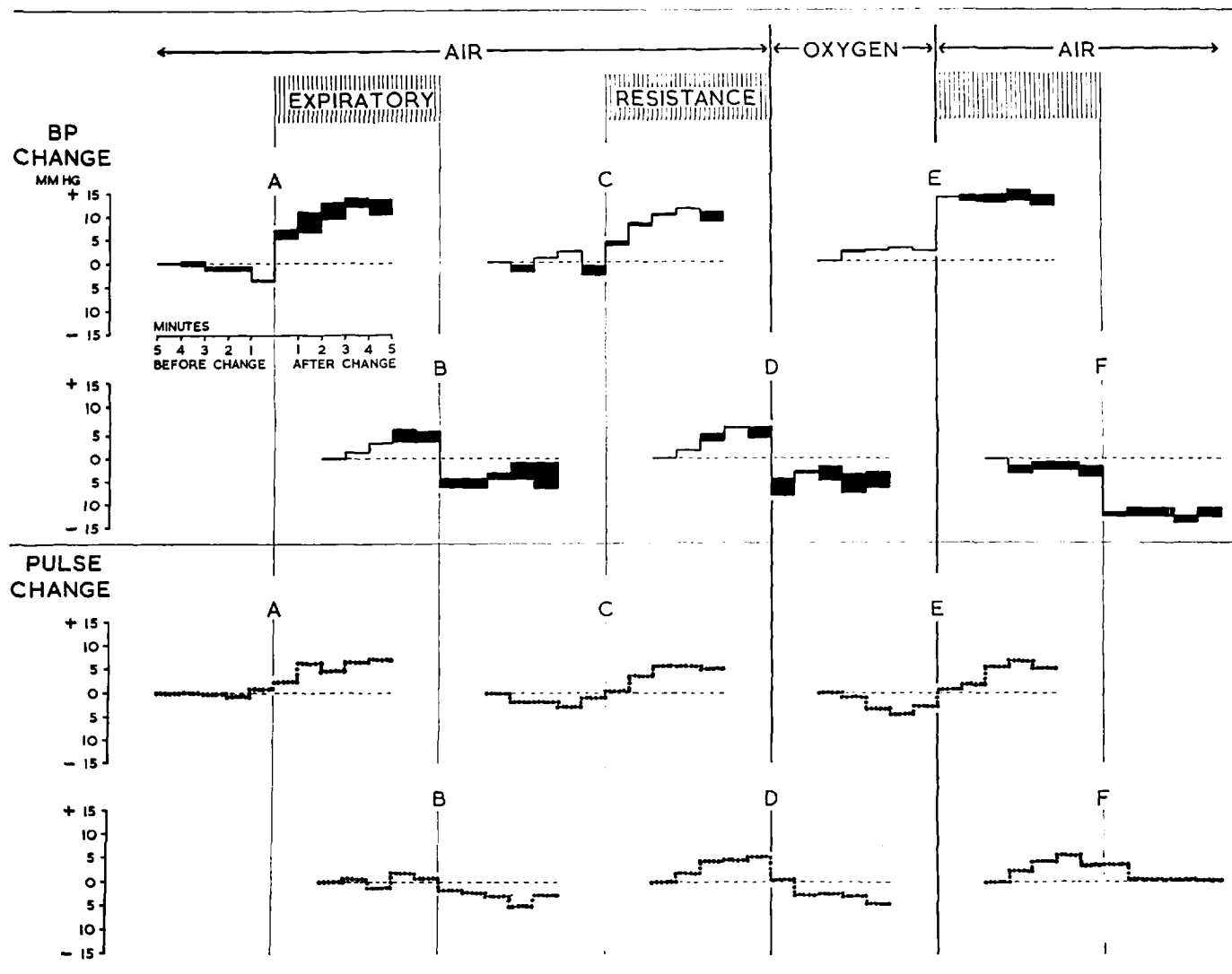


FIGURE 11.9

As figure 11.8, but derived from figure 11.6.

(Periods G to N - hypoxia but no expiratory resistance.)

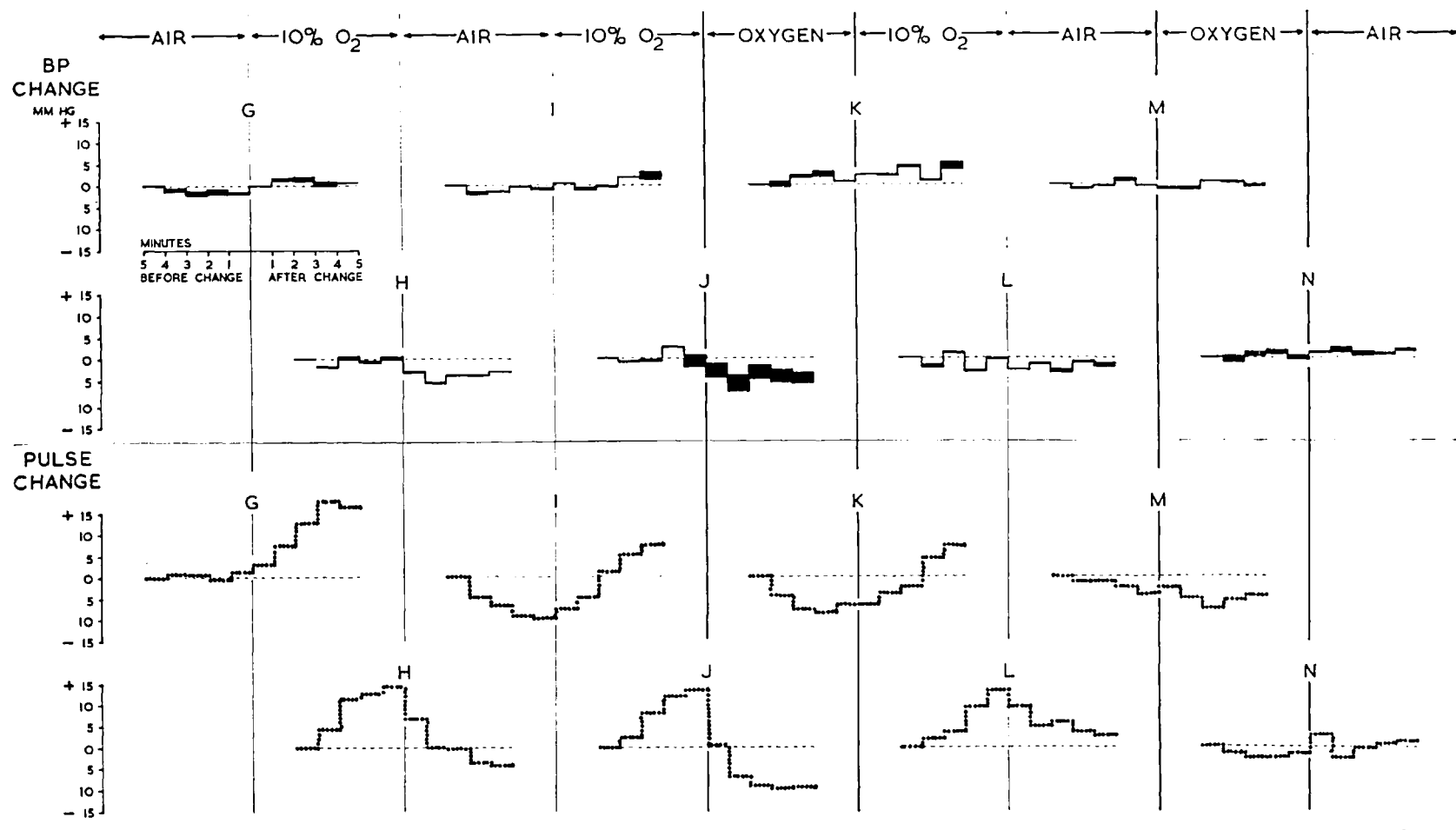


FIGURE 11.10

As figure 11.8, but derived from figure 11.7.

(Periods AG to Ω - hypoxia combined with expiratory resistance.)

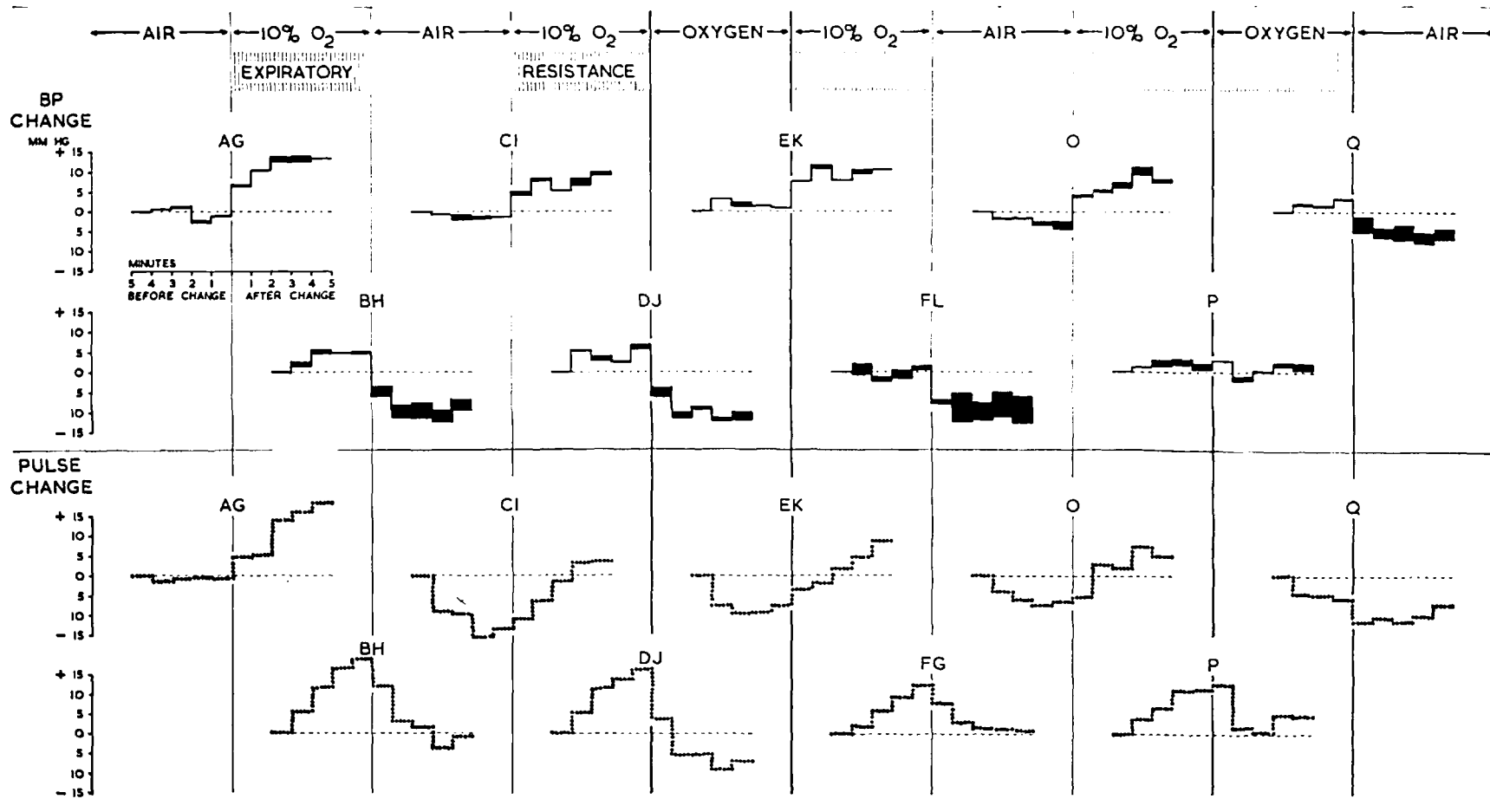


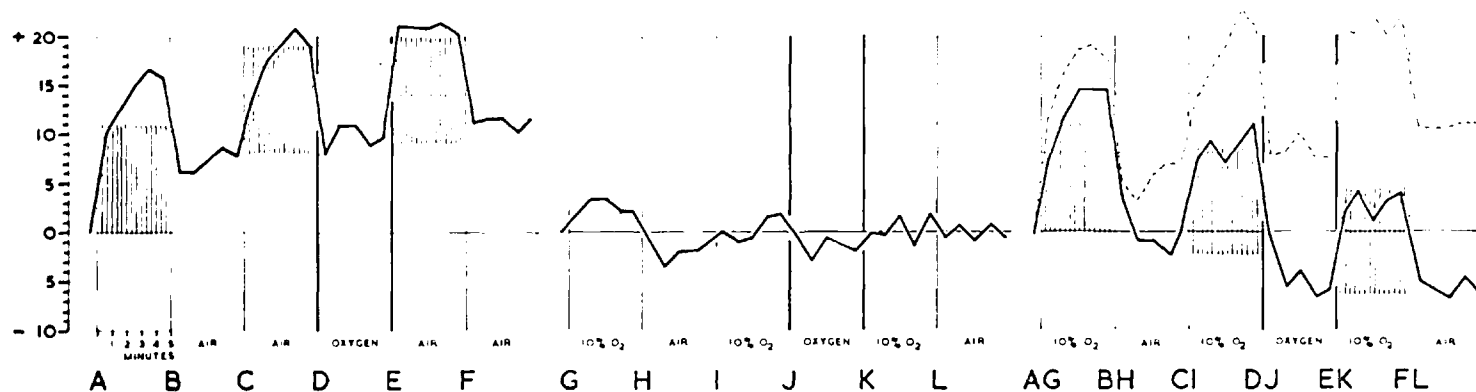
FIGURE 11.11

The averaged results obtained with 11 volunteers, showing trends of the systolic blood pressure measured at peak expiration (the average of the upper and lower limits has been used in this figure), and of the pulse rate, throughout each of the three main part of the experiment (I - alternate periods breathing against an expiratory resistance (the timing and magnitude of which is indicated by the vertically hatched areas); II - alternate periods breathing 10 per cent oxygen; III - alternate periods during which breathing 10 per cent oxygen was combined with breathing against an expiratory resistance).

This figure was derived from figures 11.8, 11.9, and 11.10, by taking the results from the second half of each 10 minute period, and lining them up to give a continuous chart.

The long-term trends of the measured systolic blood pressure at peak expiration should be interpreted with caution (see text).

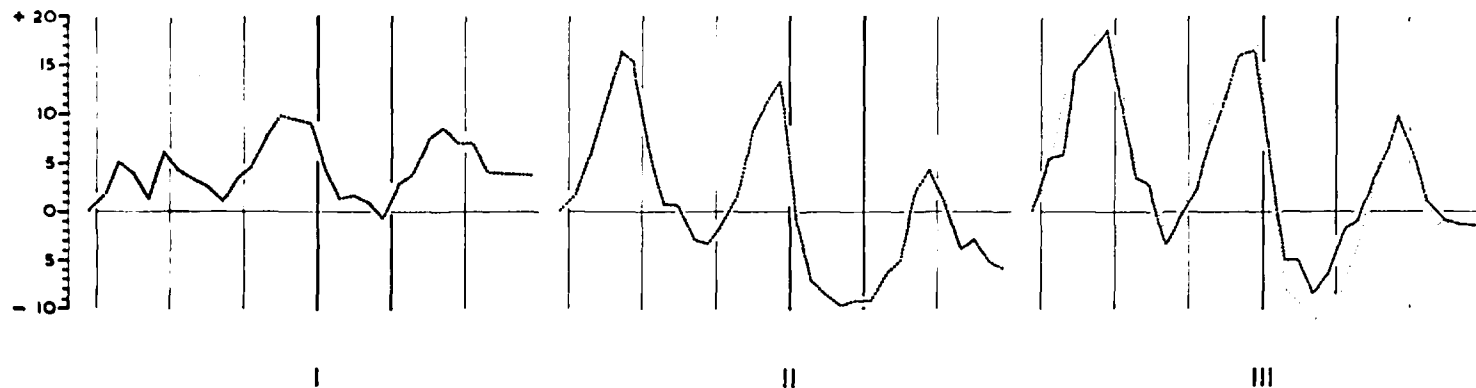
BP
CHANGE
MM HG



PULSE CHANGE
ALTERNATE PERIODS BREATHING AGAINST
EXPIRATORY RESISTANCE

ALTERNATE PERIODS BREATHING TEN PER CENT
OXYGEN

ALTERNATE PERIODS BREATHING TEN PER CENT
OXYGEN AND AGAINST EXPIRATORY RESISTANCE



ELEVEN CONSCIOUS SITTING SUBJECTS

FIGURE 11.12

This record, taken while a subject changed from breathing air against an expiratory resistance to breathing 100 per cent nitrogen without resistance, should be read from right to left.

Top Trace. "Step" write out of cuff pressure. The systolic blood pressure at end-expiration just before stopping pressure breathing was between 111 and 113.5 mm Hg.

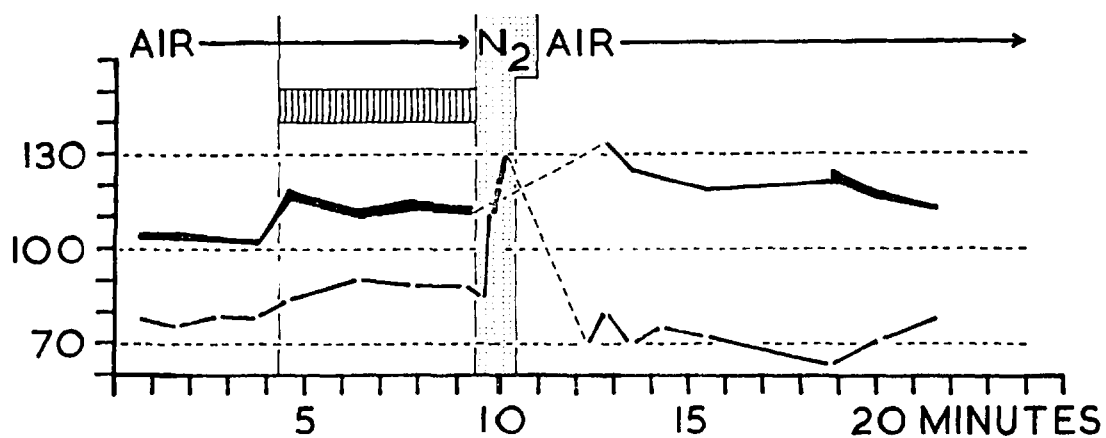
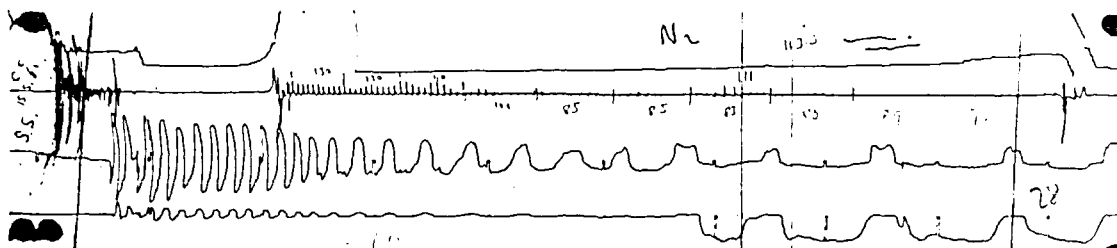
2nd Trace. Brachial pulse (figures indicate pulse rate).

3rd Trace. Pneumotachogram with 10 second time signal superimposed.

Bottom Trace. Pressure in the mask with 10 second time signal superimposed.

FIGURE 11.13

Chart of systolic blood pressure and pulse rate derived from a record obtained when a subject changed from breathing air against an expiratory resistance to breathing 100 per cent nitrogen without resistance. A part of the actual record is shown in figure 11.12.



CHAPTER 12

THE EFFECTS OF DIFFERENT NITROUS OXIDE AND
OXYGEN MIXTURES, AND OF PRESSURE, UPON
SPEED OF INDUCTION

This work was carried out while holding a Wellcome Research Fellowship in the Research Department of Anaesthetics, the Royal College of Surgeons of England, in 1963-64. It has not been published. It was done in collaboration with Dr. M. Bookallil while he was working on the design of a proportional respiratory sampling apparatus, at the suggestion of the author (see Bookallil, M. and Smith, W.D.A. (1964). A proportional respiratory sampling apparatus. *Brit. J. Anaesth.*, 36, 527). The concept of the experiments described in this chapter was the author's, and it was mentioned in an unpublished paper on Oxygen and Outpatient Anaesthesia read at the Royal College of Surgeons on 6th November, 1963, on the occasion of a televised symposium between London and Chicago which was relayed by "Telstar". (This paper was not part of the televised programme). The author acted as subject throughout this series of experiments, and Dr. Bookallil acted as anaesthetist, using the set-up associated with his proportional sampling apparatus.

It was mentioned in chapter 2 that the administration of 83.5 per cent nitrous oxide with oxygen, following six breaths of 100 per cent nitrous oxide, produced inadequate anaesthesia in 45 per cent of patients anaesthetised in a Casualty Department; and that Mostert (1958) suggested that anaesthesia could be induced more effectively, and without hypoxia, using 100 per cent nitrous oxide for a whole minute following efficient pre-oxygenation for three minutes. A theoretical comparison between the former technique, [which was essentially that of Tom (1956)] and the technique of Mostert (1958), was also provided: but what is really required is a direct comparison between different techniques of inducing and maintaining outpatient anaesthesia, in the same patients. The opportunity for anaesthetising the same patient several times in an outpatient department, however, arises only infrequently. The series of experiments described in this chapter was planned as a first step towards making a comparison in the laboratory.

METHODS

Different mixtures of nitrous oxide and oxygen were administered to a male subject, 43 years old, on different days but at the same time of day. He breathed into a non-rebreathing system offering negligible resistance to respiration, except during one experiment when a pressure of 15 cm H₂O was imposed during expiration, using a dead weight expiratory resistance (see chapter 10)

This resistance to expiration was introduced in order to mimic the practice of increasing the supply flowrate and screwing down the expiratory valve, which has been used as a means of "quelling the resistant patient".

The mixtures used were:-

1. 80 per cent nitrous oxide after the subject had been breathing room air;
2. 100 per cent nitrous oxide after the subject had been breathing room air.
3. 80 per cent nitrous oxide after the subject had been breathing 100 per cent oxygen for 3 minutes.
4. 100 per cent nitrous oxide after the subject had been breathing 100 per cent oxygen for 3 minutes.
5. 80 per cent nitrous oxide while a pressure of 15 cm H_2O was applied during expiration, after the subject had been breathing room air.

In each case the interval between the start of the administration and the time at which the subject ceased to respond to auditory stimuli was taken as a measure of the speed of induction.

Auditory stimuli were provided in the form of pre-recorded spoken numbers which were played back from a tape recorder during the induction of anaesthesia. They were spoken at irregular intervals - about 25 per minute. The subject responded by pressing a morse key. The audio signals from the tape recorder and the signals generated on pressing the morse key were superimposed on one channel of a 4 channel Ediswan pen recorder (the bottom trace of each record shown in figure 12.1).

In all except the fifth record shown in figure 12.1, the other three channels of the Ediswan pen recorder were used to record from above downwards: 1) The withdrawal of the Bookallil sampling syringe during inspiration. (Note how the top trace conforms accurately with the inspiratory phase of the second trace - see Bookallil and Smith, 1964); 2) The inspired and expired tidal volumes

(integrated pneumotachograms); and 3) The output from a photo-electric pulse detector.

Unfortunately the calibration of the record of respired volume was not retained. The integrated pneumotachograph signals were digitalised and recorded on punched tape for analysis by computer, together with other data obtained while using the sampling apparatus. The final results, however, were not obtained for all the experiments, so it has been impossible to make full use of the records of respired volume.

In the fifth record, obtained while the subject breathed against an expiratory resistance, the pressure in the breathing system was measured in place of the withdrawal of the Bookallil syringe, using a Vickers Research Ltd. pressure transducer; and the concentrations of nitrous oxide in the gases respired was recorded instead of respired gas volume, using a prototype infra red analyser set up for nitrous oxide (Hill and Stone, 1964).

RESULTS

The speeds of induction of anaesthesia and the average pulse rates over the first 50 seconds are indicated in Table 12.1.

The left hand arrows on figure 12.1 indicate the start of the induction of anaesthesia. (The top five arrows are placed correctly. The bottom arrow is placed at the beginning of expiration; it should be moved a little to the left so as to coincide with the start of inspiration). The right hand arrows indicate the time of no response. The stippled areas indicate a preliminary disturbance of the subject's contact with his environment.

DISCUSSION

Time of "no-response"

In all except the second experiment (administration of 100 per cent nitrous oxide after breathing room air), the end point of "no-response" was not sharply defined. The lack of definition arose from this subject's tendency to press the morse key repeatedly as he began to lose contact with his environment, regardless of the numbers being spoken. This phenomenon is not observed with all subjects. Over a number of experiments some insight was gained into the causes of this effect. One cause was an uncertainty as to whether the morse key was depressed in response to the previous number, which led to it being pressed again - to make sure. Another cause arose from over-eagerness to press the morse key in response to the next number, with the result that it was anticipated. Sometimes the subject was aware that he was pressing the morse key rapidly, without knowing why. On other occasions he knew that he had failed to press the morse key at the appropriate time because he was distracted by some object, activity or thought. Because he could remember these incidents, and had a certain amount of insight into them, the time of "no-response" was taken as the time of the first number after which there was no appropriate response, and by which repetitive pressing of the morse key had ceased. Even then confusion could arise from the subject's hand resting upon the morse key after loss of consciousness.

Administration of 100 per cent nitrous oxide

The fact that the end-point was more clearly defined, and occurred sooner, when 100 per cent nitrous oxide was breathed after breathing room air, than after preoxygenation, suggests that

an hypoxic induction may be speedier and less likely to be associated with the disturbances of the so-called "excitement" stage of anaesthesia. It does not follow, however, that this apparent advantage is gained solely by a direct effect of hypoxia on "consciousness".

It can be seen from the integrated pneumotachograms (even in the absence of calibration) that hypoxia-induced hyperventilation, which would have increased the rate of entry of nitrous oxide into the lungs. The tachycardia recorded implies that the cardiac output was probably increased, which would have increased the rate of uptake of nitrous oxide from the lungs, but, because 100 per cent nitrous oxide was being administered, this uptake would not have made an appreciable reduction in the rate of rise of the partial pressure of nitrous oxide in the alveoli (see chapter 16). One might expect the administration of 100 per cent nitrous oxide to result in a rapid rise in the arterial tension of nitrous oxide because of the high partial pressure administered and because of the hyperventilation.

The hyperventilation would also have resulted in a reduction of the arterial tension of carbon dioxide, which, in turn, could be expected to produce some cerebral vasoconstriction. On the one hand this might have tended to accelerate loss of consciousness by increasing the cerebral hypoxia, and on the other hand a reduction in cerebral blood flow would have tended to reduce the transport of nitrous oxide to the brain.

There is no doubt that acute hypoxia can, by itself, produce loss of consciousness. Observation of the case cited in chapter 11 (figures 11.12 and 11.13), however, suggests that initially hyperventilation and increased cardiac output supply sufficient oxygen

to the brain to maintain consciousness, and that when the supply of adequate oxygen ultimately fails, loss of consciousness is sudden. The precise moment at which that subject lost consciousness was not recorded, but the experiment was terminated 52 seconds from the start of the administration of nitrogen. The subject lost consciousness, therefore, within 50 seconds, which was within the time it took the present subject to lose consciousness when breathing 100 per cent nitrous oxide. It is arguable whether he lost consciousness because of the presence of an adequate tension of nitrous oxide in the brain or because of an inadequate tension of oxygen. Neither comparison of the two subjects, nor comparison of the two experiments in which 100 per cent nitrous oxide was administered with and without pre-oxygenation, really help to decide the issue.

The subject who breathed 100 per cent nitrogen was a female aged 24. One might have expected her to have been more resilient, but she may have had a higher metabolic rate at the time. Furthermore, all else being equal, a more acute hypoxia is produced by breathing nitrogen than by breathing nitrous oxide, because the net volume uptake is much less when breathing nitrogen (see chapter 16).

The absence of a marked tachycardia when breathing 100 per cent nitrous oxide after pre-oxygenation suggests that acute hypoxia was not a factor on that occasion. Consciousness was retained for at least 12 seconds longer, yet inspection of the integrated pneumotachograms suggests that the total volume of nitrous oxide inhaled after pre-oxygenation was no more, and possibly less, than the volume inhaled without pre-oxygenation.

Pre-oxygenation before the administration of 80 per cent nitrous oxide

Pre-oxygenation does not appear to have effected time to no-response when breathing 80 per cent nitrous oxide. It would be rash to jump to conclusions from a single comparison, but it may be noted that repetitive operation of the morse key was absent from the third experiment recorded in figure 12.1, whereas it was present in the first. The initial pulse-rate was slower (Fig. 12.2).

The imposition of expiratory pressure breathing

The prolongation of the period of response by imposing a pressure of 15 cm H_2O during expiration came as a surprise. The experiment was repeated with similar result. The cause of this effect is open to question and cannot be decided without further evidence. Some delay in the rise of the tension of nitrous oxide in the lungs may have resulted from a compensatory increase in Functional Residual Capacity, although this is not obvious from the record obtained from the infra red analyser. The effect of the expiratory resistance on the cardiac output and its distribution is unknown. Nor is it known whether breathing under these slightly uncomfortable circumstances had any effect on the tension of nitrous oxide required in the brain to produce narcosis.

It may be noted that the amplitude of the recorded pulse rose to higher levels in this experiment compared with all the others, even at corresponding times. (Figure 12.2).

One should not have expected the increase in tension of nitrous oxide to have had any effect on the speed of induction. An increase in pressure of nitrous oxide of 15 cm H_2O would increase its partial pressure by an amount equivalent to increasing its concentration from 80 to 81.5 per cent. In the experiment this increased pressure was applied only during expiration.

The success of the manoeuvre of increasing the supply flow rate and screwing down the expiratory valve in clinical practice probably arises from the circumstances of its use. Potent causes of difficulty in the induction of inhalation dental anaesthesia are leaks in the system and mouth breathing. Under these circumstances the manoeuvre will tend to reduce inward leaks, and when they do occur during inspiration, the atmosphere "leaked" is likely to contain nitrous oxide from corresponding outward leaks during the previous expiration.

Absence of response after breathing 50 per cent nitrous oxide

The fact that the subject ceased to respond to auditory stimuli after 160 seconds, while breathing 50 per cent nitrous oxide, does not mean that he would not have responded if the intensity of the auditory stimuli had been increased, or if another form of stimulus had been substituted. There is even some doubt as to whether he can really be said to have lost consciousness at 160 seconds. The morse key was still being held down, either "deliberately" or by the weight of the hand.

The significance of "Time-to-No-Response"

When inducing inhalation anaesthesia in an outpatient the anaesthetist wants to know when his patient is unlikely to respond to auditory stimuli, and when he is unlikely to respond to surgical stimulation. These experiments have been concerned with the former and they give no guide to the latter.

If these experiments were to be repeated with decreasing concentrations of nitrous oxide, a concentration would be found at which the subject would just lose consciousness, if anaesthetised for long enough. It is unlikely, however, that surgical anaesthesia would ever be achieved when using the minimum concentration

required to produce unconsciousness.

It can be argued, although it may be over-simplifying the problem, that while breathing 80 per cent nitrous oxide, consciousness is lost when the partial pressure of nitrous oxide in the brain reaches the same level as that which is eventually reached when breathing the minimum concentration required to produce unconsciousness. Unconsciousness will not be produced, however, as soon as the partial pressure of nitrous oxide in the alveoli has risen to this value. It will be delayed because of the lung-brain circulation time, and because uptake of nitrous oxide by the brain itself causes a reduction in its tension in the blood perfusing it, until equilibrium has been reached. The inhalation of nitrous oxide may also effect the lung-brain circulation time and cerebral perfusion.

If the administration of 80 per cent nitrous oxide is continued after unconsciousness has been produced, in about 45 per cent of subjects at least, induction of surgical anaesthesia can be expected. The assessment of surgical anaesthesia, however, presents problems. No sane volunteer would agree to being subjected to repeated incisions during the induction of anaesthesia, and there can be no guarantee that results obtained using repeated pin pricks, for example, would be relevant to the clinical situation. What is required is a means of producing intensely painful stimuli at short intervals without causing any damage to tissues. It is possible that electrical stimuli generated by an oscillator and applied through a constant current amplifier, as used by Clutton-Brock (1966) could be used for this purpose, but if so, it is quite possible that the application of painful stimuli during the induction of anaesthesia might influence the time of loss of consciousness.

An alternative might be to withhold painful stimuli until after loss of consciousness, and to continue them until some objective response (such as movement, change in pulse rate, change of pupil size, change in peripheral blood flow, etc.) was no longer elicited. Problems would arise due to the time lag between stimulus and response, and perhaps due to persistence of the response. It might be necessary to allow appreciable intervals between successive stimuli. Another possibility would be to withhold painful stimuli, in the first instance, until after surgical anaesthesia had been achieved, and then, at each repeat experiment, to introduce the painful stimuli a little sooner until a time was found when the subject just responded. This approach would have the disadvantage of requiring a large number of anaesthetics in the same subject.

Given a suitable technique for determining the time of onset of surgical anaesthesia, one would expect the time interval between the time of no-response to auditory stimuli and the time of no-response to painful stimuli to increase as the concentration of nitrous oxide administered was decreased. One would also expect to find a range of concentrations of nitrous oxide administered within which surgical anaesthesia could not be achieved even if the subject lost consciousness. When administering more than 80 per cent nitrous oxide at ambient pressure one would expect the relationship between the times to no-response to auditory and to painful stimuli to be complicated by factors related to hypoxia. The administration or the accumulation of carbon dioxide could also be expected to effect the induction of anaesthesia: and so could various clinical procedures, such as that recommended by Tom (1956) of administering first 100 per cent nitrous oxide for six

breaths, and then 85 per cent nitrous oxide; or the administration of sub-anaesthetic concentrations of nitrous oxide during a preliminary period of pre-oxygenation.

The series of experiments described in this chapter suffered from being undertaken as a side issue to the main project in hand. Its reconsideration as a definitive study might prove fruitful.

TABLE 12.1

Gas Respired Before Anaesthesia	Mixture Respired During Induction of Anaesthesia	Conditions of Respiration	Time to "no-response"	Average Pulse** Rate During First 50 Secs.
Air	80 per cent N ₂ O	Low Resistance	72 secs	96 b.p.m.
Air	100 per cent N ₂ O	Low Resistance	50 secs	124 b.p.m.
Oxygen	80 per cent N ₂ O	Low Resistance	73 secs	79 b.p.m.
Oxygen	100 per cent N ₂ O	Low Resistance	approx. 62 secs (?68)*	94 b.p.m.
Air	80 per cent N ₂ O	Imposed Expiratory Pressure	approx. 98 secs *	108 b.p.m.
Air	50 per cent N ₂ C	Low Resistance	160 secs	83 b.p.m.

* The administration of nitrous oxide was stopped a little prematurely.

** Pulse rate changes during each experiment are shown in figure 12.2.

FIGURE 12.1

Records obtained while inducing anaesthesia in the same subject on six different occasions, but at the same time of day. They should be read from left to right. The mixtures of nitrous oxide and oxygen administered are stated to the left of each record. In each case anaesthesia started at the time indicated by the heavy arrow on the left (top five records) or at the start of the following inspiration. The arrow on the right indicates the time of no-response (see text). In all the records except the fifth from the top, the uppermost trace indicated the linear movement (downward deflections) of the Bookallil sampling syringe while it was withdrawn during expiration. This movement was directly proportional to the volume expired, as may be seen by comparison with the second trace which recorded inspired and expired tidal volumes (integrated pneumotachograms). Upward deflections for inspiration and downward deflections for expiration. The trace was automatically returned to zero with each change of phase of respiration - see Chapter 17). The third trace recorded the output from a photoelectric pulse detector.* On the bottom trace of each record the output from the tape recorder (each black "smudge" represents a spoken number), and the signals generated by pressing the morse key (downward deflections) were superimposed. On the fifth record from the top, the uppermost trace indicated the pressure in the breathing system (upward deflections for expiration), and the second trace recorded the output from an infrared analyser for nitrous oxide which continuously sampled the gases respired at the mouth.

* Pulse rates are shown in figure 12.2.

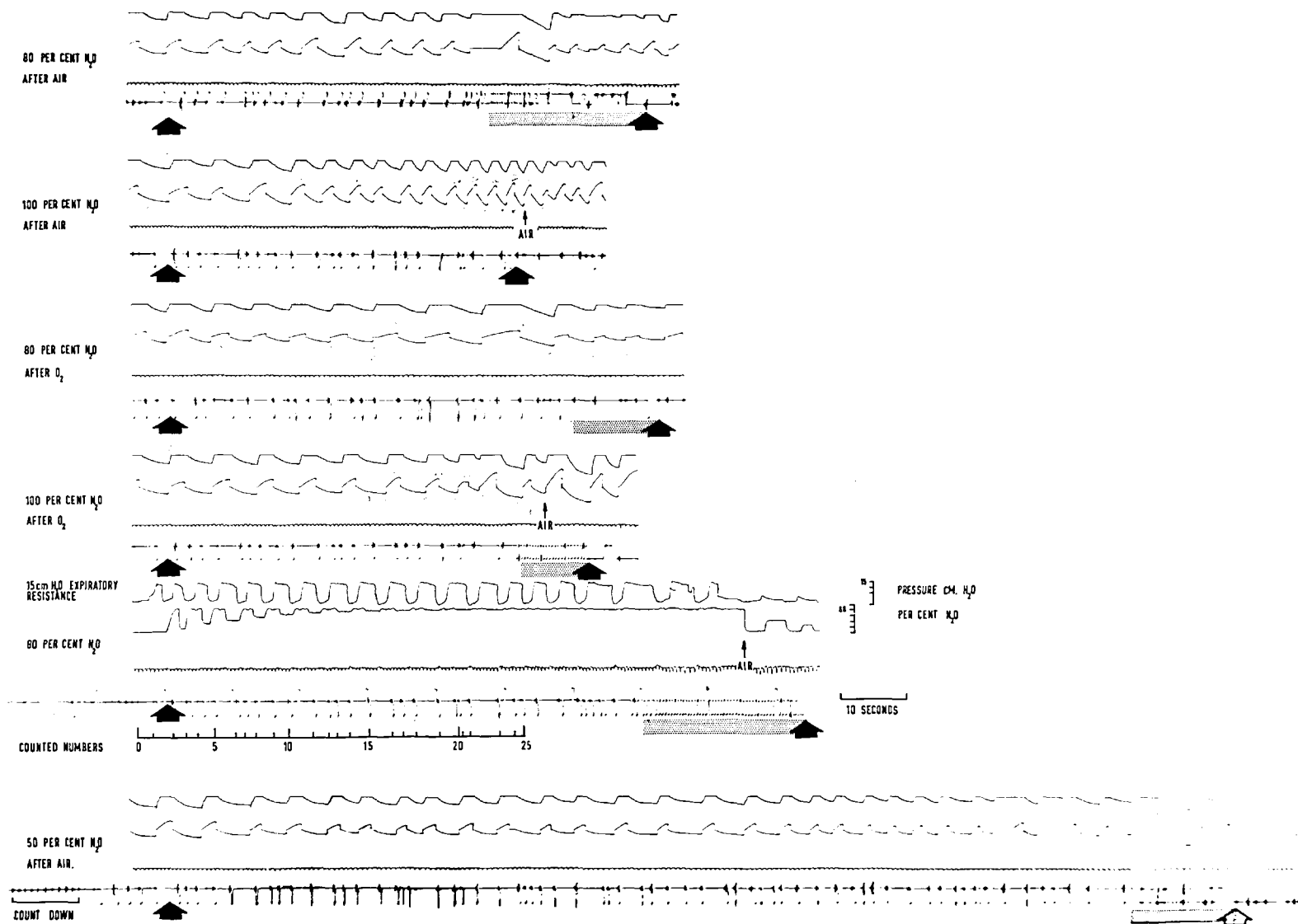


FIGURE 12.2

The changes in pulse rate derived from the records shown in figure 12.1.

Despite the differences in pulse rate recorded at the start of each experiment, except where there was frank hypoxia or an expiratory resistance, the pulse rate fell to about 80/min after 65 seconds.

It may be noted in figure 12.1 that the greatest change in the amplitude of the photo-electrically recorded digital pulsations occurred during and immediately after breathing against an expiratory resistance.

PULSE RATE

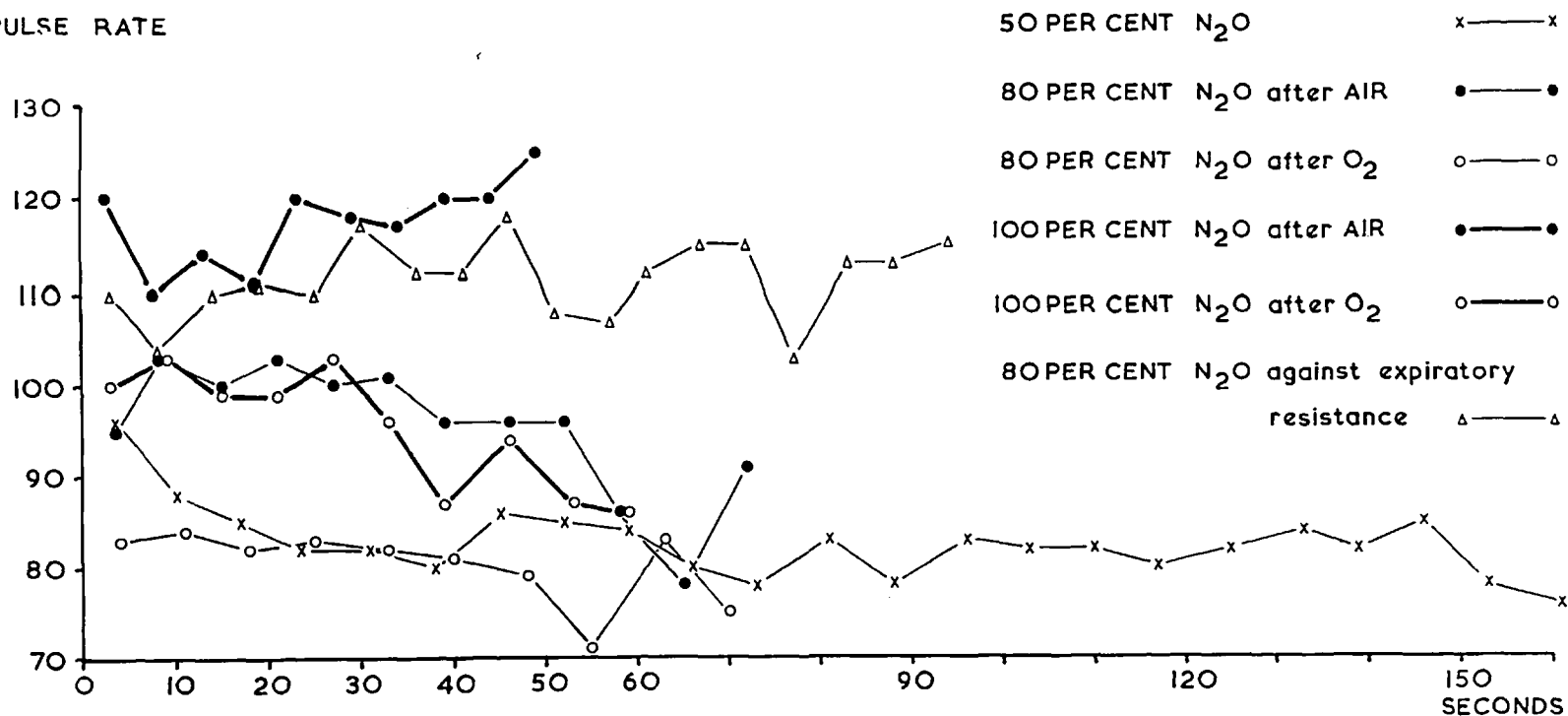


FIGURE 12.2

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