Monitoring of heart and lung function in cardiac surgery

PROEFSCHRIFT

ter verkrijging van de graad van Doctor in de
Geneeskunde
aan de Erasmus Universiteit Rotterdam
op gezag van de rector magnificus
Prof. Dr. J. Sperna Weiland
en volgens besluit van het college van dekanen.
De openbare verdediging zal plaatsvinden op
woensdag 1 oktober 1980 des namiddags
te 2.00 uur

door
OM PRAKASH
geboren te Gorakhpur (India)

1980
Drukkerij Verweij B.V. – Mijdrecht

Promotoren : Prof. P. G. Hugenholtz
Prof. Dr. D. H. G. Keuskamp
Co-referenten: Prof. Dr. J. Nauta
Prof. Dr. B. Jonson

To Anna-Marie
Sangeeta
Ursula

Het verschijnen van dit proefschrift is mede mogelijk gemaakt door steun van de Nederlandse Hartstichting.

ACKNOWLEDGEMENTS

The author wishes to state at the outset that this thesis could only be written thanks to the help of many in the operating room and elsewhere throughout the Thorax Centre. First of all I am greatly indebted to my promotors, Prof. P. G. Hugenholtz and Prof. Dr. D. H. G. Keuskamp. It was also the exciting and stimulating environment of engineers, physiologists, and physicians working together which made it possible to document the study material.

Dr. W. Hekman, Prof. Dr. J. Nauta, and Prof. Dr. E. Bos are thanked for their invaluable guidance and advice, and for providing the facilities necessary for carrying out the clinical research in the operating room and the post-operative intensive care unit.

Gratitude is extended to my co-authors for their criticisms and co-operation, to my anaesthesia and surgery colleagues, and to Prof. Dr. K. Bom and Prof. Dr. C. Hilvering. Special appreciation is felt for Prof. Dr. B. Jonson, M. D., Clinical Physiology Department, University of Lund, Sweden, for his enthusiasm and guidance throughout this study.

The close collaboration of the Siemens Corporation deserves acknowledgement, especially Mr. S. G. Olsson of Siemens-Elema AB, Solna, Sweden, and Mr. J. van der Belt of Siemens Nederland B.V., Amsterdam.

Mr. J. van der Kolk provided invaluable technical help in the initial phase of the study.

I am indebted to Bas van der Borden and Simon Meij for their thorough involvement in the project, their determined efforts, the several innovations they made in the field of instrumentation, and their contributions to the betterment of the "Methodological Platform". The computer group and the M.I.T. engineers are thanked for their kind assistance, particularly Mr. T. van Dalen and Mr. C. Zeelenberg.

I wish to express gratitude to P. van der Schelde and J. A. J. Koopmans and others of the anaesthesia nursing staff, the operating room staff for their helpfulness, the post-operative nurses for assistance in acute circumstances while measurements were being made, Mr. D. de Jong and his staff who made practical contributions, and the laboratory staff, headed by Jeannet Veelbehr, who are fondly appreciated for their contributions.

For the typing and the final co-ordination of all the many details involved in the completion of this thesis, I wish to express my particular appreciation to Carla Vermeulen, Louise van Solkema, and Margreet Blaauw-Koch.

Lastly, I would like to thank all the members of the Thorax Centre not already mentioned, and my family, for their continued support.

CONTENTS

CHAPTER 1
Overview of this thesis

The aim of the study described was to develop and evaluate monitoring of cardiovascular and respiratory functions during and immediately after the administration of anaesthesia in the operating room for open-heart surgery. Also, monitoring techniques for the period of time the patient was in the intensive care unit were developed. All studies were made at the Thorax Centre of the University Hospital in Rotterdam.

The work started in 1974. At that time, we were well aware that monitoring techniques did not allow an adequate appraisal of the patient's condition. Hence, the condition of some patients deteriorated "inexplicably" during the first few hours after surgery. It was felt that detailed measurement of cardiopulmonary function during this critical period might provide data from which an immediate prognosis could be derived and which would also allow rational decisions as to whether respiratory support should be continued. Concurrent developments in the world and the advent of modern technology made it particularly appropriate to study these problems at that time.

A brief outline is here given of each of the following eight chapters.

The second chapter contains a review of the literature on pulmonary function monitoring during anaesthesia and open-heart surgery. The need for further research in this field is made obvious.

In chapter three, the instrumentation that had to be developed for this purpose is discussed in detail and the integration of respiratory and cardiovascular function measurements is emphasized. The term "Methodological Platform" was coined to describe this complex of interrelated measurements.

Technical and clinical documentation of the Elema carbon dioxide analyser is presented in chapter four. The chapter is based on data that were previously published elsewhere; the original text is reproduced.

In chapter five, criteria for early extubation after open-heart surgery are presented. The study shows that very few patients who meet the criteria have to be re-intubated during the subsequent post-operative course. Currently, 85 to 90% of patients undergoing open-heart surgery in the Thorax Centre are extubated while still on the operating table. Again, part of the data in this chapter is based on material published earlier. Evidence is provided that early extubation is beneficial to the patient. Also, it simplifies post-operative management.

Another example of the application of the Methodological Platform is provided in chapter six. Continuous measurement of expired carbon dioxide during cooling obviates the need for frequent arterial blood sampling. The

carbon dioxide production is not allowed to fall below 45% of the value at normothermia. The physiology of acid-base balance during surface cooling to very low temperatures is explained. The data on which this work is based have also been published elsewhere.

In chapter seven, data are provided which show that studies of the efficacy of new anaesthetic agents for cardiac patients can be made by means of the Methodological Platform. Such clinical research may at times have to be done in the human rather than in the animal, and the Platform provides the means.

Chapter eight is actually the companion paper of chapter three. It describes haemodynamic and metabolic changes in a series of 33 patients who were extubated in the post-operative intensive care unit a few hours after surgery. The chapter also contains a number of case histories in which the Platform has been particularly helpful.

Chapter nine, the final chapter, contains the summary and conclusions.

CHAPTER 2

Development of pulmonary function monitoring during anaesthesia for open-heart surgery and in the intensive care unit

A review of history and literature

2.1. Historical development of mechanical ventilation

John Snow, who will be remembered as being the first physician to apply science to anaesthesia, was probably the first person to monitor the vital function of respiration when he noticed "ascending respiratory paralysis during deepening of ether anaesthesia". This observation led Guedel[1] to use the sequential changes which occur in the pattern of spontaneous respiration as the basis for his classification of the stages and planes of ether anaesthesia. Long before these two pioneers, however, Vesalius[2] in 1555 introduced the first physical method of inflating the lungs with air, by "inserting a tube or hollow cane through an opening cut in the trunk of the trachea". Matas[3], as long ago as 1899, realized that "artificial inflation of the lungs, and rhythmic maintenance of artificial respiration by a tube in the glottis directly connected to a pair of bellows" were prerequisites for thoracic surgery. Intermittent Positive Pressure Ventilation (IPPV), as it was termed, was accepted in the U.S.A. early in the 1900's, and equipment for connecting a patient to a breathing circuit was constructed by Elsberg[4] in 1910, and used clinically in 1913 by Meltzer[5] and Janeway.[6]

Automatic equipment (as opposed to the "hand-squeezing" type) for the administration of IPPV to patients was not invented until 1934, when Frenckner[7] introduced his Spiropulsator for artificial rhythmic lung inflation during thoracic surgery; his apparatus was subsequently modified by a number of pioneers.[8,9] This history of thoracic anaesthesia and the role of IPPV in its development has been fascinatingly described by Rendell-Baker.[10]

In 1950, an experimental model of a mechanical IPPV ventilator which delivered a predetermined volume (instead of being controlled by airway pressure) was constructed by Engström in Sweden.

During the severe epidemic of poliomyelitis in Denmark in 1952, Lassen,[11] Anderson and Ibsen,[12] and Astrup et al.[13] introduced and organized treatment of respiratory paralysis by manual ventilation of the lungs, as it had been done during anaesthesia. This method replaced treatment in a tank respirator. It was the first example of manual ventilation for the treatment of respiratory paralysis, and the first example of long-term ventilation outside the operating

room. When the outbreak of poliomyelitis spread to Sweden in 1953, Engström used his prototype ventilator to replace the relay of hands which had been necessary for prolonged manual positive pressure ventilation of the lungs. During the period of this poliomyelitis outbreak in Western Europe, many types of mechanical ventilators came to be constructed.[14]

Meanwhile, following the discovery of curare, investigations by Gray[15] and others demonstrated the numerous advantages of controlled respiration with paralysis of the respiratory muscles during surgical procedures. The use of manual ventilating methods was quickly superseded by the mechanical ventilator, and the technique was then extended to routine thoracic surgery,[16] and hence to many other branches of surgery.

Despite its intra-operative benefits, the post-operative use of mechanical ventilation with patients was not generally adopted until 1955, when Björk and Engström[16] demonstrated the considerable advantages of using the Engström ventilator after extensive pulmonary resection. Their initial series consisted of only 3 patiënts, 2 of whom had widespread infiltration of a single functioning lung following previous post-operative chest infection; however, their results were so impressive that they were convinced of the efficacy of this life-saving technique and continued to use it. By 1957, they had treated 61 patients by this regime, with 44 survivals.[17] In the same year, Swensson[18] became the first anaesthetist to use the Engström ventilator post-operatively in patients with pulmonary complications and peritonitis. He subsequently used the same methods in patients developing acute renal failure following surgery or trauma.[19]

With the recognition of the significance of post-operative mechanical ventilation in the recovery of the critically ill patient, elective post-cardiac surgery ventilation was also introduced, with very favourable results.[20-25] Indeed, it has played no small part in the tremendous advances which have occurred in cardiac surgery.

These, in turn, have been accompanied by development in cardiovascular monitoring techniques during the intra- and post-operative phases. Unfortunately, although mechanical ventilation has continued to play a role in this, respiratory monitoring techniques have not been applied in anything like a parallel fashion to corresponding cardiovascular techniques. Indeed, it is only in the last three or four years that the value of respiratory monitoring has begun to be appreciated.

2.2. Cardiovascular and respiratory problems caused by mechanical ventilation

In 1935, Moore, Humphreys and Wreggit[26] reported a marked decrease in cardiac output in thoracotomized dogs, both during Constant Positive

Pressure Ventilation (CPPV) and Intermittent Positive Pressure Ventilation (IPPV). Other investigators subsequently confirmed this in man, in closed-chest studies.[27-29] The decrease in cardiac output was considered to be caused by a reduction in venous return as a result of elevated intrathoracic pressure.

The circulatory effects of IPPV by different systems of pressure ventilation were comprehensively evaluated by Motley et al in 1948.[30] Similarly, in 1947, Werkö[31] investigated the relationship between intermittent positive pressure respiration and its untoward circulatory effects. He found that IPPV does produce an elevation in the intrathoracic pressure and that this does impede the venous return, at least temporarily. This in turn lowers cardiac output, and thereby reduces the mean arterial pressure. However, in 1946, Otis, Rahn and Fenn[32] performed elegant experimental work which demonstrated that the increase in venous pressure shown by Moore et al.[26] was in the end equal to the rise in intrathoracic pressure. Their work showed that at this later stage in cardiovascular response, the venous return and cardiac output were largely restored to normal, unless the cardiovascular response was compromised by blood loss, or by paralysis of the vascular musculature by neurological disease or vasoplegic drugs.

In experiments on animals, the changes which occur in the lung and thorax during anaesthesia with controlled ventilation have aroused interest, especially in the relationship between the reduced oxygen content in arterial blood and the observed decrease in lung elasticity.[33]

In 1946, Rahn et al.[29] described a method for continuous measurement of pressure-volume data of the lungs of conscious subjects. When, in 1955, Nims, Conner and Comroe Jr.[34] applied the same measurement technique to anaesthetized patients, they discovered that the lungs became less compliant than when the patients were simply asleep.

Clinical observations of a similar nature were made in 1963 by Egbert, Laver and Bendixen.[35] These correlations have not been confirmed by later studies,[36-38] but many anaesthetists still consider anaesthesia with controlled ventilation to be associated with a progressive reduction in lung compliance.[39]

These contradictory results may perhaps be explained by variations in anaesthetic and surgical management and in rules for maintenance of fluid balance in various centres.

Norlander[40] found no major deviations in compliance during and after extracorporeal circulation, whilst making continuous automatic recordings of certain pulmonary mechanics data. The same results were obtained by Blair et al.[41] in 1967. However, Patterson et al.[42] demonstrated in the same year that under conditions of extracorporeal circulation, the composition of the ventilatory gases administered did significantly affect the mechanics of respiration.

2.3. Modern requirements for mechanical ventilation and pulmonary function monitoring

2.3.1. Alarm systems based upon measurements of ventilation

Originally, artificial ventilation during surgery was always performed manually by sqeezing a bag in the ventilatory circuit. The main reasons for replacing manual methods were: 1) to free the anaesthetist for other important tasks; and 2) to provide stable and optimal ventilation. The shift in anaesthetic opinion towards mechnical ventilators was probably accelerated by the ever-increasing number of tasks which the modern anaesthetist is required to perform, not only as regards increasingly large numbers of operations to be supervised, but particularly in relation to the complexity of surgery and of anaesthesia. The vast experience and alertness needed to give adequate manual ventilation to patients could not possibly be guaranteed to every patient.

But the benefits of ventilators were obtained at a high initial price. Bag squeezing is, in itself, an efficient alarm system against potential catastrophes, such as disconnection of tubings or severe obstruction. In such an event the squeezing hand is always there to recognize the problem and to take proper action. Everyone who has worked long enough with mechanical ventilators knows that without efficient and properly used alarm systems, patients may suffer severe damage and sometimes die due to malfunction or incorrect setting-up. Alarm systems based upon measurements of ventilation may therefore be considered vital.

2.3.2. Clinical monitoring of pulmonary mechanics parameters

Peters and Hilberman[43] set up an intensive care unit system for computerized respiratory monitoring of 4 patient beds. The system was designed to produce data on respiratory mechanics, respiratory work and flows, and transpulmonary pressures, with maximum accuracy, speed, and convenience, by means of a P.D.P. 8 digital computer system. The Fleisch pneumotachograph head was used for intermittent measurement of airflow in the patient's airway, while intrathoracic pressure was measured with an intra-oesophageal balloon catheter and a differential pressure transducer; thus, the intrathoracic pressure could be compared with airway pressure. Parameters such as tidal volume, minute volume, compliance, resistance, total work per breath, resistive work per litre/min of gas flow were then calculated for 16 breaths. The mean concentration of expired gas (for gas exchange computation) was obtained by first passing the expired gases through an appropriate mixing box. Gas passing out of this box was then sampled and fed to slow response instruments such as the Godard infra-red carbon dioxide analyser and the Westinghouse oxygen analyser. With the data obtained from these investiga-

tions, the authors (together with Proctor et al.[44]) derived a series of criteria for the interpretation of respiratory data obtained in the post-operative period. These criteria enable them to be alerted when a patient's respiratory status was deteriorating and also gave them an objective indication of when respiratory assistance was required.

Saklad et al.[45] employed both analogue and digital computers on-line for the measurement and display of airflow and pressure changes which took place in the lungs during anaesthesia. Secondary data were then calculated and displayed either instantaneously or within a few seconds. Tidal volume was measured with a pneumotachograph and with the values obtained breath-by-breath compliance and work of breathing were calculated. There was also a digital display of the duration of inspiratory flow, inspiratory pause, expiratory flow and expiratory pause of each breath. This was one of the earliest attempts to monitor pulmonary function in the operating theatre.

2.3.3. Monitoring of gas exchange in the lungs

There are two distinct requirements for gas measurements. In the first place, it is important to know what concentration of fresh gases are being administered to the patient in order to provide adequate respiratory gas exchange and to guard against hypoxia. This aspect is relatively easily achieved by monitoring the inspired oxygen concentration (FiO_2). In addition, the inhaled concentrations of anaesthetic gases and volatile agents need to be under control. Here, too, simple methods such as nitrous oxide and oxygen rotameters, calibrated vaporisers, etc. may be perfectly adequate, except in the special case of "closed-circuit" configurations.

Secondly, it is important to know the concentrations of gases being exhaled by the patient, especially the gases exhaled at the end of expiration. In reasonably healthy lungs, the so-called "end-expired" gases approximate fairly closely the partial pressure of appropriate constituents in arterial blood. Thus, reliable estimations of the rate of excretion of carbon dioxide can be made. It provides a fairly accurate, non-invasive measure of arterial pCO_2.

In 1977, Osborn[46] described an alternative system in his paper "Cardiopulmonary monitoring in the respiratory intensive care unit". These measurements were performed in an 8-bed cardiac intensive care unit, and, once again, intensive respiratory monitoring was conducted for a period lasting from several hours to a few days post-operatively. Airway flows were measured in intubated patients, with a special differential pressure pneumotachograph which did not change its calibration characteristics when water passed through it. For oxygen measurement, a heated ceramic type of polarographic oxygen electrode was successfully employed, whilst for carbon dioxide measurement an infra-red gas analyser was utilized.

Of more than 30 respiratory parameters which were monitored by this computer-based system, the most informative one in mechanically ventilated patients proved to be the end-tidal carbon dioxide. This is because it is the direct measurement of whether the preset minute volume ventilation is matched to the patient's needs. In the hypoventilated patient, the end-tidal carbon dioxide will rise, whereas in the hyperventilated patient it will fall. Any maladjustment, leak, or faulty function in the ventilator is likely to show up promptly as a change in end-tidal carbon dioxide.

Management by means of routine end-tidal carbon dioxide monitoring led to fewer cardiac dysrhythmias, presumably because those caused by incorrect volume settings were avoided. Prior to the introduction of end-tidal carbon dioxide monitoring, this cause of dysrhythmias had not been frequently recognized as such.

The normal gradient between end-tidal carbon dioxide and arterial p_{CO_2} was found to average .67 kPa. Because of the constant observation of the end-tidal carbon dioxide, tidal volume and minute volume, many blood gas determinations were avoided, especially when patients were weaned off the ventilator. A patient who is unable to sustain his own breathing will show a characteristic rise in end-tidal carbon dioxide, together with clinical signs of increasing physical exhaustion. What is more important, the rise in end-tidal carbon dioxide often substantially antecedes the appearance of exhaustion, giving an invaluable "early warning" of critical respiratory insufficiency.

The monitoring system was also employed by Osborn for other simple pulmonary function tests, such as vital capacity, lung compliance, and pressure-flow-volume loops. As a result of this, he reported that when immediate post-operative lung compliance values were low they were associated with a poor post-operative prognosis (table 2.1).

In this brief, selective review of the literature relevant to the development of

Table 2.1

Pulmonary compliance values in a series of 80 patients following open-heart surgery

number of cases	status	maximum inspired pressure (cm H_2O)*	compliance (litres/cm H_2O)*
52	did well	22 ± 6.7	0.047 ± 0.0095
17	did poorly	27 ± 9	0.036 ± 0.0130
11	died	34 ± 11	0.035 ± 0.0150

* mean ± standard deviation. A compliance of 0.03 had a 50% mortality rate.

Reproduced with the author's permission from: Osborn JJ: Cardiopulmonary monitoring in the respiratory intensive care unit. Med Instrum 11: 278, 1977.

peri-operative pulmonary function monitoring, it has been shown that the application of monitoring of respiratory physiology has become a science of which John Snow would have been justly proud. One might summarize, in the words of Osborn,[46] that "respiratory monitoring is emerging as another example in medicine of how data can substitute for guesswork in making clinical diagnoses and in managing patients". However, we must not lose sight of the fact that at the present time, the availability of equipment and skilled personnel still varies from unit to unit, which must inevitably lead to considerable differences in the extent to which these techniques can be applied generally. The quality of monitoring, and therefore, of the control of pulmonary function, needs further improvement in many laboratories.

2.4. References

1. Guedel A: Inhalation anesthesia; a fundamental guide. 2nd Edition. New York, Macmillan, 1951
2. Vesalius A: De Corporis Humanis Fabrica. Some observation on the dissection of living animals. Vol. 7, Ch. 19 (p.824). Basel, 1555.
3. Matas R: On the management of acute traumatic pneumothorax. Ann Surg 29: 409, 1899.
4. Elsberg CA: Clinical experiences with intratracheal insufflation (Meltzer), with remarks upon the value of the method for thoracic surgery. Ann Surg 52: 23, 1910.
5. Meltzer SJ, Auer JL: Meltzer & Auer insufflation apparatus. 17th Int. Congr. Med., London, Sub-section VII (b), 1913.
6. Janeway HH: Intratracheal Anaesthesia. A. By nitrous oxide and oxygen. B. By nitrous oxide and oxygen under conditions of differential pressure. Ann Surg 58: 927, 1913.
7. Frenckner P: The technique in bronchospirometry and bronchial catheterization. Preliminary report. Acta Oto-Laryng 20: 404, 1934.
8. Anderson E, Crafoord C, Frenckner P: A new and practical method of producing rhythmic ventilation during positive pressure anaesthesia. Acta Oto-Laryng 28: 95, 1940.
9. Crafoord C: Pulmonary ventilation and anesthesia in major chest surgery. J Thorac Surg 9: 237, 1940.
10. Rendell-Baker L: The history of thoracic anaesthesia· In: Mushin WW (Ed): Thoracic Anaesthesia (p. 598). Oxford, Blackwell, 1963.
11. Lassen HCA: A preliminary report on: The 1952 epidemic of poliomyelitis in Copenhagen, with special reference to the treatment of acute respiratory insufficiency. Lancet I: 37, 1953.
12. Andersen EW, Ibsen B: The anaesthetic management of patients with poliomyelitis and respiratory paralysis. Br Med J 1: 786, 1954.
13. Astrup P, Gøtzche H, Neukirch F: Laboratory investigations during treatment of patients with poliomyelitis and respiratory paralysis. Br Med J 1: 780, 1954.

14. Crampton Smith A, Spalding JMK, Russell WR: Artificial respiration by intermittent positive pressure in poliomyelitis and other diseases. Lancet I: 939, 1954.
15. Gray TC, Nunn JF, Utting JE (Eds.): General anaesthesia. 4th Edition. London, Butterworths, 1980.
16. Björk VO, Engström C-G: The treatment of ventilatory insufficiency after pulmonary resection with tracheostomy and prolonged artificial ventilation. J Thorac Surg 30: 356, 1955.
17. Björk VO, Engström C-G: The treatment of ventilatory insufficiency by tracheostomy and artificial ventilation. A study of 61 thoracic surgical cases. J Thorac Surg 34: 228, 1957.
18. Swensson SA: Artificial respiration in general surgery. Acta Chir Scand 113: 417, 1957.
19. Swensson SA: Respiratorbehandling. Nord Med 60: 1957, 1958.
20. Erlanson P, Lindholm T, Lindqvist B et al: Artificial respiration in severe renal failure with pulmonary insufficiency. Acta Med Scand 166: 81, 1960.
21. Norlander OP, Björk VO, Crafoord C et al: Controlled ventilation in medical practice. Anaesthesia 16: 285, 1961.
22. Holmdahl MH:son: The respiratory care unit. Anesthesiology 23: 559, 1962.
23. Björk VO, Holmdahl MH:son: Respirator treatment for hypoventilation following thoracic surgery. Ann NY Acad Sci 121: 920, 1965.
24. Björk VO, Grenvik Å: Principes et indications de la trachéotomie et du traitement par respirateur en chirurgie thoracique. Les Bronches 15: 119, 1965.
25. Holmdahl MH:son, Westerholm C-J: Postoperative respirator treatment. Symp. Anaesthesiologiae Internationale. Abstracta Prague, CSSR, 54, 1965.
26. Moore RL, Humphreys GH, Wreggit WR: Studies on the volume output of blood from the heart in anesthetized dogs before thoracotomy and after thoracotomy and intermittent or continuous inflation of the lungs. J Thorac Surg 5: 195, 1935.
27. Otis AB, Rahn H, Brontman M et al: Ballistocardiographic study of changes in cardiac output due to respiration. J Clin Invest 25: 413, 1946.
28. Motley HL, Cournand A, Eckman M et al: Physiological studies on man with the pneumatic balance resuscitator, "Burns Model". J Aviation Med 17: 413, 1946.
29. Rahn H, Otis AB, Chadwick LE et al: The pressure-flow diagram of the thorax and lung. Am J Physiol 146: 161, 1946.
30. Motley HL, Cournand A, Werkö L et al: Intermittent positive pressure breathing: a means of administering artificial respiration in man. JAMA 137: 370, 1948.
31. Werkö L: The influence of positive pressure breathing on the circulation in man. Acta Med Scand Suppl 193: 1, 1947.
32. Otis AB, Rahn H, Fenn WO: Venous pressure changes associated with

positive intrapulmonary pressures; their relationship to the distensibility of the lung. Am J Physiol 146: 307, 1946.
33. Mead J, Collier C: Relation of volume history of lungs to respiratory mechanics in anesthetized dogs. J Appl Physiol 14: 669, 1959.
34. Nims RG, Conner EH, Comroe JH: The compliance of the human thorax in anesthetized patients. J Clin Invest 34: 744, 1955.
35. Egbert LD, Laver MB, Bendixen HH: Intermittent deep breaths and compliance during anesthesia in man. Anesthesiology 24: 57, 1963.
36. Askrog VF, Pender JW, Smith TC et al: Changes in respiratory dead space during halothane, cyclopropane and nitrous oxide anaesthesia. Anesthesiology 25: 342, 1964.
37. Nunn JF, Bergman NA, Coleman AJ: Factors influencing the arterial oxygen tension during anaesthesia with artificial ventilation. Br J Anaesth 37: 898, 1965.
38. Martinez LR, Norlander OP: Arterial oxygen tension during nitrous oxide-oxygen-halothane anaesthesia in patients with cardiovascular and pulmonary disease. Acta Anaesthesiol Scand 11: 353, 1967.
39. Sykes MK: Pulmonary compliance and airway resistance during anaesthesia. In: Evans FT and Gray TC (Eds.): Modern trends in anaesthesia. Vol. 3 Aspects of metabolism and pulmonary ventilation (p. 56). London, Butterworths, 1967.
40. Norlander O, Herzog P, Nordén I et al: Compliance and airway resistance during anaesthesia with controlled ventilation. Acta Anaesthesiol Scand 12: 135, 1968.
41. Blair E, Hedstrand U, Westerholm C-J et al: Effect of total cardiopulmonary bypass on human lung elastic properties. Circulation 35, Suppl I: 206, 1967.
42. Patterson RW, Sullivan SF, Malm JR et al: Effect of airway hypocapnia on mechanics of breathing during cardiopulmonary bypass. Circulation 35, Suppl I: 212, 1967.
43. Peters RM, Hilberman M: Respiratory insufficiency: Diagnosis and control of therapy. Surgery 70: 280, 1971.
44. Proctor HJ, Ballantine TVN, Broussard ND: An analysis of pulmonary function following non-thoracic trauma, with recommendations for therapy. Ann Surg 172: 180, 1970.
45. Saklad M, Paliotta J, Weyerhaeuser RM: On-line monitoring of ventilatory parameters. In: Dornette EHL (Ed.): Clinical anesthesia (p. 333). Philadelphia, Davis, 1973.
46. Osborn JJ: Cardiopulmonary monitoring in the respiratory intensive care unit. Med Instrum 11: 278, 1977.

CHAPTER 3

Computerized monitoring of lung and heart function in the operating room: a description of a "Methodological Platform" Part I: Instrumentation*

O. PRAKASH, M.D.**, senior anaesthetist
B. JONSON, M.D.***, clinical physiologist
S.H. MEIJ, M.Sc.**, computer engineer
S.G. VAN DER BORDEN, B. Sc.**, research assistant
P.G. HUGENHOLTZ, M.D.**, professor of cardiology

3.1. Introduction

In the operating theatre, it has been commonplace since 1950 to monitor the elementary functions pertaining to the heart electronically, with the electrocardiogram, the arterial blood pressure and the pulse as the essential guidelines.

However, measurement of pulmonary function may be as vital as that of cardiac function, not only to enhance the safety of the patient, but also to enable ventilation with controlled gas exchange to be achieved. If this is done, the result will be maintenance of the all-important carbon dioxide tension within normal limits. If, however, the pulmonary function is not monitored, vital disturbances in ventilation or gas exchange (which may give more rapid or early, accurate information concerning a developing crisis) may be missed.

In addition to allowing accurate control of gas exchange and stabilisation of desired arterial carbon dioxide tensions, monitoring of pulmonary function has a number of other important applications. For example, by accurately predicting the future respiratory performance of a sick patient, it helps in the correct timing of the decision to replace controlled by spontaneous respiration as the patient's condition improves. Moreover, establishment by monitoring of the physiological status of the patient also enables controlled deviations from the normal to be undertaken, as with progressive hypothermia in small infants undergoing cardiac surgery. Adequate monitoring also permits study of the effects of various physiological "insults" sometimes imposed on the human body; for example, the effects of anaesthetic drugs, of transfusions, of surgery

* Accepted for publication C.C.C.P.M. proceedings May, 1979, Norwalk, Plenum Books, New York (N.Y.).

** From the Thorax Centre, Erasmus University and University Hospital, Rotterdam, The Netherlands.

*** From the Department of Clinical Physiology, University of Lund, Lund, Sweden.

or accidental trauma. Post-operative threatening complications can be recognised early and the effect of treatment against them studied.

3.2. An outline of the results of having inadequate monitoring facilities

The anaesthetist must constantly monitor the depth of anaesthesia when he uses inhalational anaesthetic agents. Variations in anaesthetic depth may lead to serious disturbances in the patient's tidal and minute volume ventilation (if breathing spontaneously) or in blood and airway gas composition (whether ventilation is spontaneous or artificially maintained). This in turn can lead to critical disturbances in the patient's cardiovascular status.

Thus, a knowledge of the patient's ventilatory performance and the composition of inhaled and exhaled gases is very important to the anaesthetist. However, in the vast majority of anaesthetic procedures, patient monitoring is restricted to a few simple cardiovascular and pulmonary parameters like pulse rate, blood pressure, capillary bed colour, and perhaps the electrocardiogram, which will reveal the end-results of ventilatory disturbances.

In 1976, a report was published in the Journal of the American Medical Association entitled "Unexpected cardiac arrest during anaesthesia and surgery".[1] In this report, 41 cases of cardiac arrest (in 30 adults and 11 children) which occurred during surgery were classified according to the most likely primary causative mechanism. Cardiac arrest was thought to have resulted from anaesthetic or ventilatory mismanagement in two-thirds of the cases. In 19 of the patients, hypoxia was listed as the cause of the arrest, and it appeared to be primarily due to hypoventilation. In 9 patients, the arrest was attributed to anaesthetic mismanagement, whilst in a further 9 patients, severe bradycardia occurred which might have been secondary to other events. Four others had hypotension associated with hypovolaemia.

Of the total of 41 patients, 13 were dark-skinned, representing 31.7% of the group studied. This is interesting, since many anaesthetists depend only upon the repetitive observation of skin colour as an index of adequate oxygenation and adequate peripheral perfusion. As a result of such a limited monitoring regimen, non-white patients may be at significantly greater risk. This report subsequently came to the attention of a major liability insurance company, a development spurred on by the fact that an earlier report[2] had already found an incidence of cardiac arrest in the operating area of 1 case in every 3400 operations.

In this recent article entitled "Monitoring in the operating room: Current techniques and future requirements", Hilberman (1977)[3] reviews the J.A.M.A. report and the subsequent lawsuit, and agrees that ventilatory problems appear to be a major source of intra-operative morbidity and mortality.

Obviously, monitoring of ventilation could prevent most accidents of ventilatory origin. Furthermore, some circulatory problems with a fall in cardiac output are detected earlier from the monitoring of gas exchange than from electrocardiograms and intravascular pressure.

3.3. Modern requirements for the practice of peri-operative pulmonary control

Hilberman's assessment of the present situation shows that equipment is needed which not only monitors cardiovascular parameters, but also ventilation and airway gas concentrations. He states that it is a fundamental necessity in modern anaesthetic practice. However, in order to be acceptable by the majority of potential users (mainly anaesthetists and intensive care doctors), such equipment must also be unobtrusive, simple, and convenient to use. Also, it must be trustworthy, accurate, and relatively inexpensive.

Such requirements are not easy to combine into a practical piece of commercial apparatus.

The modern requirements for control of anaesthetic pulmonary ventilation may be considered under two headings: the efficiency of gas exchange, and the stability of pulmonary mechanics.

3.3.1. Monitoring the efficiency of gas exchange

Until the second World War, accurate knowledge of this composition of expired gas could only be provided by chemical analysis. With the Haldane apparatus it took some 20 minutes for the analysis of a sample to be performed by an accomplished operator. The method had an accuracy of 0.1 mol% in skilled hands. By 1950, methods based upon various types of thermal conductivity changes, infra-red absorption (carbon dioxide and nitrous oxide), paramagnetic susceptibility (oxygen) and spectral emission (nitrogen) were in use.[4] Nearly all of these instruments had a long response time, with the exception of Lilly's nitrogen meter.[5] It was also recognized at that time that mass spectrometry was a promising analytic method for respiratory gases, since it is specific for gases of different molecular weights. In 1947, Siri[6] scanned the mass range of medical gases with a simple and compact instrument and showed that single peaks could be recorded with response times of little more than one second. Hunter, Stacey and Hitchcock (1949)[7] made an instrument with a sample transport system showing a quarter-second response time, and with three fixed collectors aligned to receive nitrogen, oxygen and carbon dioxide simultaneously. In 1950 a single-channel conventional instrument was modified by the addition of a short sampling system with a response time of under 100 ms and used in a number of respiratory studies in the University of Pennsylvania.[8]

Although mass spectrometry has seen increasing use in respiratory research work and clinical investigation, its use in the operating theatre remains limited by serious drawbacks. The sheer size and high capital cost of a mass spectrometer generally makes it impractical for use in the operating room; it is often severely affected by volatile anaesthetic agents, and it is technically difficult for the "clinical" mass spectrometer to distinguish between nitrous oxide and carbon dioxide, since both have the same molecular weight (N_2O = N+N+O = 14+14+16=44, CO_2 = C+O+O = 12+16+16=44).

Based on the work of Peters and Hilberman, whose elaborate I.C.U.-based computerized pulmonary function monitoring system was reported in 1971,[9] Osborn (1977),[10] developed a more refined system for respiratory monitoring in the intensive care unit, using a computer to handle the processing of all the data he had acquired, just as Peters and Hilberman did. Of the more than 30 parameters measured, the conclusion arrived at was that the most useful one in the mechanically ventilated patient was the end-tidal carbon dioxide. This was simply because it is a direct measurement of whether the preset minute volume ventilation is adequately "clearing" pulmonary arterial blood of its carbon dioxide load. In the hypoventilated patient, this "clearing" process becomes inadequate, and the end-tidal carbon dioxide will rise; by contrast, hyperventilation leads to a "washing-out" of carbon dioxide, and hence the end-tidal carbon dioxide falls. Thus, any maladjustment, leak, or faulty function in the ventilator is likely to show up promptly as a change in end-tidal carbon dioxide. Thus, this measurement is an extremely helpful one in routine clinical practice.

3.3.2. Monitoring of pulmonary mechanics

Although it is over 50 years since Fleisch first described the pneumotachograph, it is only in recent years that this technique has become widely accepted. This delay has been caused by the many practical problems which exist with the use of Fleisch heads, especially the deposition of water from humid gases (which upsets the characteristics of the particular instrument) and the changing physical constitution of the gas mixture passing through it (which changes the pressure/flow relationship of the instrument). Even today, Fleisch's equipment has some limitations to its usefulness in routine clinical circumstances. However, the evaluation of lung function is based upon measurements of parameters such as expiratory and inspiratory flow rates, airway pressures, and respiratory gas concentrations.

In a lung function laboratory, studies of lung function can be made using large and complicated instruments, operated by specially trained technicians and laboratory assistants. Conventional equipment of this sort, as well as being

bulky, generally involves the use of extra tubing and pumps, and frequently still relies on the use of non-electronic calibration systems.

3.4. The instrumentation employed in the "Methodological Platform"

3.4.1. Introduction

A comprehensive monitoring system developed at the Thorax Centre in Rotterdam allows accurate study and control of pulmonary and cardiovascular functions during anaesthesia and in the immediate post-operative period. It has been called the "Methodological Platform".

The discussion in the previous section attached an importance to respiratory monitoring considerably greater than that normally considered necessary by clinicians. It is perhaps not surprising, therefore, that much attention has been given to an efficient respiratory control system. Additional data are collected from oxygen analysers, intravascular pressure transducers, E.C.G. equipment, and temperature probes. Blood gas analysis, and, in many cases, measurement of cardiac output, are also performed.

A unified and consistent approach produces data which may be regarded as a basis upon which clinical decision-making can be based, and from which many different rational treatment strategies can be devised and pursued. Hence, it may truly be said to constitute a "Methodological Platform". The success or failure of such a concept depends not only on the quality of data, but also on its relevance and on how they are presented to the clinician.

3.4.2. The central role of the Servo 900 B ventilator and its monitors

Knowledge of blood gas composition and acid-base status is of central importance in critical care patient management. Upon this rests decisions regarding the respiratory management of the patient. Also resting upon it is the control of blood chemistry during any abnormal physiological excursion which may be imposed upon the patient; for example, deep hypothermia.

3.4.3. The ventilator

The central unit is the Servo 900 B ventilator, which is a sophisticated electronic servo-controlled machine allowing great flexibility and precision of ventilatory control. It incorporates pneumotachograph transducers, specially designed to overcome most of the drawbacks of previous designs which monitor both inspiratory and expiratory flow rates. The pneumotachograph in the inspiratory limb is the vital factor in a feedback chain which regulates inspiratory flow. There is also a transducer which monitors airway pressure. Thus, the machine gives the clinician direct control over a large number of ventilator parameters, viz.:

i) airway pressure
ii) respiratory frequency

iii) inspiratory time
iv) pause time
v) maximum expiratory flow
vi) inspired minute volume
vii) expired minute volume

The parameters ii to vi are set directly on the machine, while parameters i and vii are monitored continuously on analogue meters. The ventilator also has settings for Intermittent Mandatory Ventilation (I.M.V.) and for spontaneous respiration. If the last-mentioned setting is selected, the patient breathes fresh gas which has been humidified by the ventilator. The expired gas is measured by the ventilator. There is also a comprehensive alarm system incorporated.

The Servo 900 B ventilator thus represents, in our view, an almost ideal and flexible means of maintaining proper lung function both in ventilated and spontaneously-breathing patients. It is small, quiet, and easy to set up and use. It uses electronic transducers instead of mechanical systems for the measurement of pressure and flow, so that these parameters are readily available for control, analysis, and display. Finally, it has a readily available and comprehensive alarm system built into it.

3.4.4. The carbon dioxide analyser

As has already been pointed out, the main function of the lungs is respiratory gas exchange. Hence, it appears much more logical to control the gas tensions achieved by a given ventilatory regime than simply to control the ventilator settings themselves in some arbitrary "rule-of-thumb" fashion, with perhaps occasional blood-gas analysis. Osborn (1977)[10] discussed results which demonstrated that in all normal clinical circumstances, the end-tidal carbon dioxide concentration ($P_{et}CO_2$) provides an accurate reflection of arterial carbon dioxide tension ($PaCO_2$).

The expired carbon dioxide concentration ($FeCO_2$) is measured through a highly selective, miniaturized infra-red analyser unit (SE930). This analyses the whole of the patient's flow, since it scans across the ventilatory Y-piece itself; this avoids all the problems and potentially dangerous complications which can arise from the withdrawal of gas samples from the main air-flow. The infra-red radiation passes across the Y-piece via sapphire windows, which are easy to keep clean. The radiation then passes via a narrow-band optical filter to a Gallium-Arsenide solid-state detector (Fig. 3.1). The moment-by-moment expired carbon dioxide is immediately available as a continuous signal. In addition, by utilising the timing pulses from the ventilator, the unit is able to display a breath-by-breath value for the end-tidal carbon dioxide.

As mentioned, the 900 B ventilator also yields an expiratory flow signal

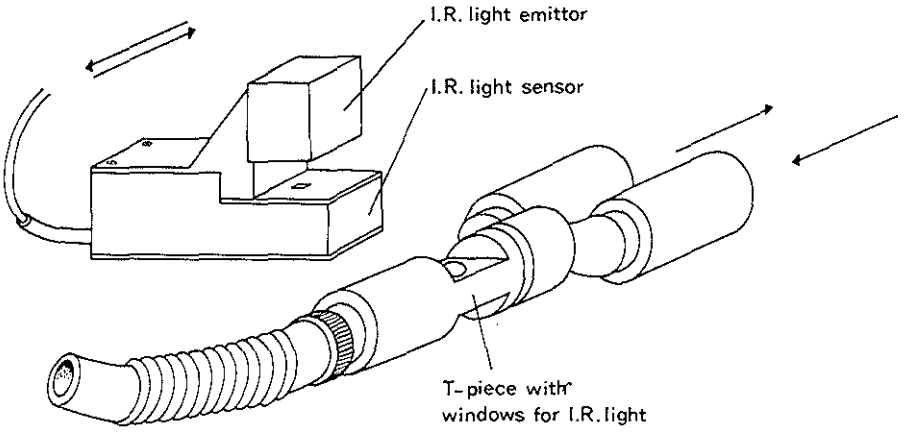


Fig. 3.1. The "Cuvette" constitutes a Y-piece connecting the expiratory and inspiratory lines with the patient. The cuvette is attached to the photometer so that one window in its wall faces an infra-red emitter and the opposite window an infra-red sensor.

which, by multiplication with the instantaneous carbon dioxide signal, will give the instantaneous expired flow of carbon dioxide. By integration, the expired volume of carbon dioxide is obtained. The carbon dioxide unit also "divides" the tidal volume into two parts, namely the initial carbon dioxide-free "ineffective" volume and the carbon dioxide-carrying "effective" volume.

All in all, the carbon dioxide unit provides information on:

i) end-tidal carbon dioxide concentration
ii) tidal carbon dioxide production
iii) minute carbon dioxide production
iv) ineffective tidal volume
v) effective tidal volume
vi) effective minute volume

3.4.5. The lung mechanics calculator

It will be remembered that in the Servo 900 B ventilator, the airway pressure is measured by an electronic pressure transducer, while the gas flows into and out of the patient are measured by pneumotachograph heads. These signals are available on the output socket of the ventilator, together with timing signals. The Lung Mechanics Calculator (LMC) connects directly to this output socket, and calculates six different lung mechanics parameters.[11]

The parameters calculated by the Unit 940 are as follows:

i) peak inspiratory pressure
ii) inspiratory pause pressure
iii) end-inspiratory resistance

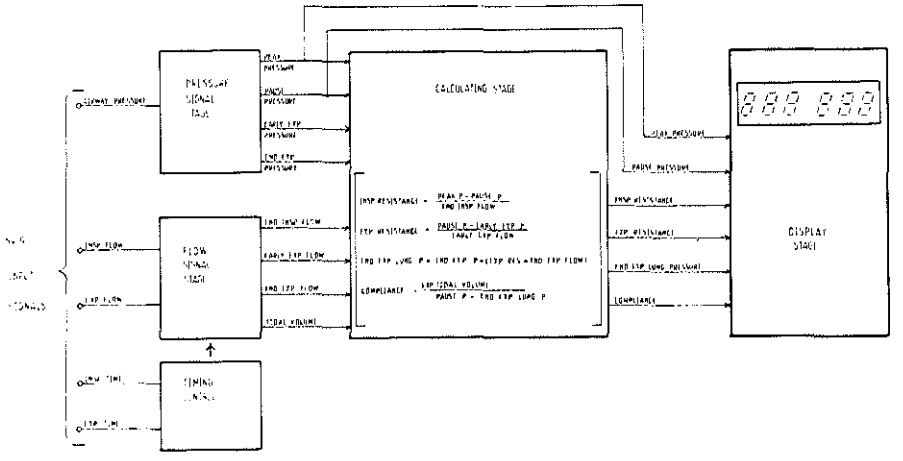
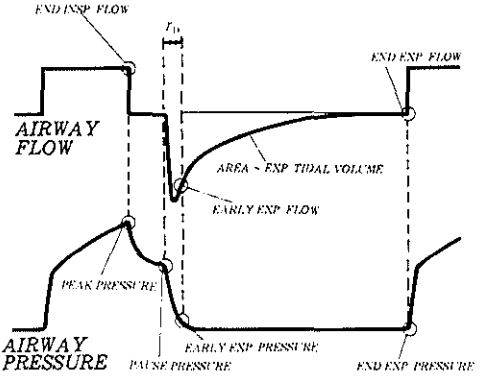


Fig. 3.2. Servo 900 B input signals and derived parameters. Reproduced from: Siemens-Elema Lung Mechanics Calculator 940 Operating Manual.



$$\text{INSP. RESISTANCE} = \frac{\text{PEAK PRESSURE} - \text{PAUSE PRESSURE}}{\text{END INSP. FLOW}}$$

$$\text{EXP. RESISTANCE} = \frac{\text{PAUSE PRESSURE} - \text{EARLY EXP. PRESSURE}}{\text{EARLY EXP. FLOW}}$$

$$\text{END EXP. LUNG PRESSURE} = \text{END EXP. PRESSURE} + (\text{END EXP. FLOW} \times \text{EXP. RESISTANCE})$$

$$\text{COMPLIANCE} = \frac{\text{EXP. TIDAL VOLUME}}{\text{PAUSE PRESSURE} - \text{END EXP. LUNG PRESSURE}}$$

Fig. 3.3. Schematic pressure and flow curves, together with a summary of the method of derivation of the various parameters mathematically. Reproduced from: Siemens-Elema Lung Mechanics Calculator 940 Operating Manual. T_D denotes the time taken for the decompression of gas and depends upon the volume of gas in the tubings and humidifier.

iv) early-expiratory resistance
v) pulmonary compliance
vi) end-expiratory airway pressure

The parameters are presented in pairs, the appropriate pair being selected by a switch on the front of the unit. The peak and pause pressures are values of the pressure signal sampled at the end of inspiration and at the end of the inspiratory pause plateau (see Fig. 3.2 and Fig. 3.3). The flow and pressure signals are also available for direct recording on external devices.

3.4.6. Operating the Servo 900 B system

Because of the carbon dioxide analyser, adjustment of the ventilator settings becomes very straightforward in most cases. A suitable respiratory rate is chosen and then the minute volume ventilation is adjusted until a desired end-tidal carbon dioxide level is reached. However, in the presence of severe lung disease, this approach may have limitations, since end-tidal carbon dioxide will not approximate arterial pCO_2 levels.[12] The lung mechanics unit and the shape of the expiratory carbon dioxide curve may help to identify such patients.[13]

The minute volume ventilation necessary to maintain a "normal" $PaCO_2$ can be obtained from Nomograms;[14-16] once it has been decided that the patient's ventilatory requirements appear to lie well outside his predicted values, the data from the carbon dioxide unit is used in a logical search for the underlying cause. The carbon dioxide production may be chosen as a starting point. If this is higher than expected, the need for ventilation will have correspondingly increased. Further research should be directed towards factors influencing aerobic metabolic rate such as pain, anxiety, shivering, and fever.

In other cases, the alveolar ventilation, $\dot{V}_A$, is found to be low. In the presence of normal total ventilation, $\dot{V}_T$, the physiological dead space, $\dot{V}_D$, must therefore be increased; this can be calculated from available data (see below). An increased $\dot{V}_D$ may be caused by a high ineffective ventilation (absolute dead space);[17] for example, an increased compressed volume in the tubing or humidifier, caused by high airway pressures. This problem is of course of much greater importance in children, especially in infants.[18] The lung mechanics calculator will give additional information about lung compliance and resistance, which may be the cause of an increased airway pressure.

If the reason for the dysfunction has still not been found, increased intrapulmonary or alveolar dead space must be present. As is well known, such dead space can be caused by several factors: ventilation-perfusion mismatching, pulmonary embolism and venous admixture (i.e. right to left shunt) may all contribute.

Various forms of dead space can be derived from the unit alone or in combination with arterial pCO_2. Hence, physiological dead space is calculated

as:

$$V_{D\ physiol} = V_T - \frac{V_{CO_2}}{PaCO_2 \times K}$$

V_T, V_{CO_2} represent tidal volume and carbon dioxide volume expired per breath and are obtained from the CO_2 unit; K is a constant converting $PaCO_2$ to fraction of carbon dioxide.

A "single breath curve" is obtained by plotting the carbon dioxide concentration against expired volume during a single breath, and can be done on an oscilloscope. The shape of the single breath curve gives information about ventilation/perfusion mismatching, since emptying lung compartments with different ventilation-perfusion relationships yields a poorly-defined alveolar plateau. This type of pathological response is often found in obstructive lung disease, even when other relevant signs are missing. The carbon dioxide analyser, therefore, also offers the opportunity for study of these factors.

Other phenomena, such as venous admixture or synchronous emptying of lung compartments with different carbon dioxide contents, yield a different pattern with a flat alveolar plateau that is lower than that corresponding to $PaCO_2$. This pattern has been observed in conjunction with lung embolism (non-perfusion of lung compartments), and with variable right-left shunt.[19] The usefulness and limitations of the single breath curve in detailed diagnosis of lung failure remain largely to be explored.

3.4.7. Other instrumentation

Other gas analysers

Where necessary, the inspired and mixed expired oxygen fractions, FiO_2 and $F\bar{E}O_2$, were measured at the patient's airway connection (mouth or endotracheal tube) using a Servomex paramagnetic analyser (Taylor-Sybron, England). With the analyser used, an accuracy of ± 0.05% oxygen can be achieved. A system in the analyser line for drying the gases causes some mixing of the gases, and also introduces a time-delay in the display of the results. Thus only the mixed-expired concentration can be displayed.

After 1976, a Perkin-Elmer clinical Mass Spectrometer was used for the measurement of oxygen concentrations; with this instrument, nitrous oxide or carbon dioxide concentrations could also be measured simultaneously.

Cardiovascular monitoring

Fluid-filled catheters in a systemic artery, in the right and left atria, and often also in the pulmonary artery, allowed comprehensive monitoring of the various vascular pressures and cardiac performance parameters.

The cardiac output could be measured directly using the Fick principle.

Blood samples were taken from the catheters for blood-gas analysis, biochemical and hematological investigations. The presence of the right and left heart catheters also allowed detection of left-to-right or right-to-left shunts. The pulmonary venous admixture ($\dot{Q}_s/\dot{Q}_t$) was calculated from the equation:

$$\frac{\dot{Q}_s}{\dot{Q}_t} = \frac{Cc'O_2 - CaO_2}{Cc'O_2 - C\bar{v}O_2}$$

where:
$Cc'O_2$ = end-pulmonary capillary oxygen content
CaO_2 = arterial oxygen content
$C\bar{v}O_2$ = mixed venous oxygen content

End-capillary oxgyen saturation ($Sc'O_2$) was calculated from the "ideal" alveolar pressure (P_AO_2), the arterial carbon dioxide tension ($PaCO_2$) and the pHa, with the approach suggested by Kelman.[20] The "ideal" alveolar oxygen pressure was first calculated from the equation:

$$P_AO_2 = PiO_2 - \frac{PaCO_2}{R.Q.} \{ 1 - FiO_2 \times (1\text{-}R.Q.)\}$$

The oxygen content (vol%) was derived from the equation:

$$C_{O_2} = \frac{S_{O_2}}{100} \times Hb \times 1.39 + (0.0031 \times pO_2)$$

Oxygen saturation was also to be determined from a Hemoreflector (American Optical Company), and in some instances continuously by means of a Fibre-Optic Haemoreflector (Schwarzer Company, Munich).

From these data calculation of the right and left ventricular stroke work and estimation of the perfusion resistances in the pulmonary and systemic circulations was carried out. Left atrial pressure was measured directly by inserting a catheter in the left atrium after opening of the chest; the right atrial pressure was taken to be equal to the central venous pressure.

Information regarding the quality of peripheral systemic perfusion was obtained by using a series of thermocouple temperature probes (Ellab) positioned in the rectum or oesophagus (for core temperature) and on the skin of the big toe. The skin probes were kept covered by gauze wrappings, so as to minimise air-draught effects.

3.5. Record keeping

Manual record keeping, although essential, is often unsatisfactory, simply

due to the fact that constant attention to the patient is frequently diverted. Automatic multi-channel recording machines are bulky and expensive. Although central, fully computer-based record keeping has great attraction, it requires a high initial outlay and is subject to intolerable drawbacks in cases of system break. At the Thorax Centre, at the present time, a dual system based upon manual as well as automated record keeping is in use.

In the post-operative care unit in particular, the previously described intensive care computer monitoring system – the ICPM system[21] – allows record keeping of physiological signals over 24 hours. The data inputs into the system include cardiac rhythm, various intravascular pressures, and the signals from the Ventilator/Lung Mechanics/Carbon Dioxide Computation System. All calculations (like cardiac output studies and trends) are performed on a Digital Equipment Corporation P.D.P. 9 computer and became available via a lineprinter or plotter at a later time. Current efforts being made are to decentralize this form of bookkeeping to render it in a condensed form under the control of the nursing staff.[22,23]

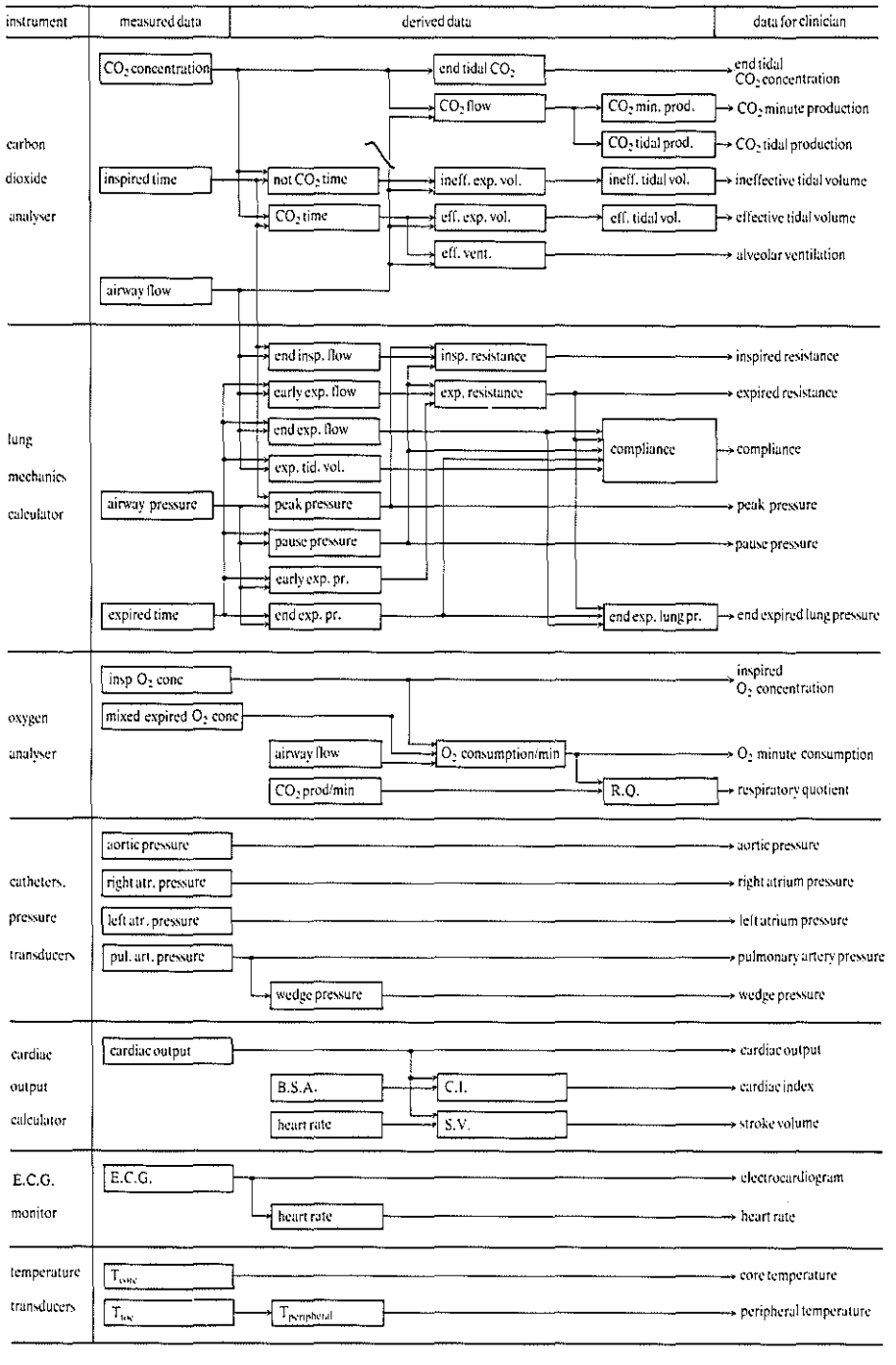
3.6. Discussion

The introduction of multiple, miniaturised, sophisticated monitoring devices opens up considerable possibilities. Numerical, graphical, or digital presentation of data relating to ventilation, pulmonary mechanics, pulmonary gas exchange and cardiovascular performance allows the continuous monitoring of the main vital functions. Because of this, early detection and analysis of technical or organic malfunction becomes possible. Several workers have, of course, pointed out various applications of modern diagnostic techniques both during and after surgery, but the field has only been explored to a very limited extent.

The present system has been built up in response to an increasingly felt need for continous and detailed information concerning cardiopulmonary status during and after open-heart surgery. Elaborate measurement systems may, however, convey problems of all kinds: cabinets full of knobs for calibration procedures and settings; tubing, pumps, chart recorders, computers – space fully taken up by equipment and personnel, leaving little room over for anything except a caricature of a patient deserted in a sea of technology! In contrast to this picture, the comprehensive use of miniaturisation and of electronic processing techniques has enabled the present monitoring hardware to remain small, simple to set up and use, and clear in its presentation of the important data. Because of this, the welfare of the patient has remained the focus of clinical attention.

In a unified and consistent approach all data must be combined to provide a "Platform" upon which clinical decision-making can be based and from which

Table 3.1 **Summary of the Methodological Platform**



rational treatment strategies can be devised and pursued. The success or failure of such a concept depends not only on the quality of each signal but also on the *relevance* of the data. Finally there is the factor of the display and of the ease with which data obtained can be interpreted.

A brief summary of the various parameters which were monitored routinely, and of the derivations of the processed data which are then available, is shown schematically in table 3.1. The aim of the "Platform" is to permit successful monitoring of all these parameters, with clear and concise data display; when this aim has been realized in practice, then a truly quantitative interface may be said to exist between the patient and his clinician.

A number of specialised clinical studies have been performed, with a view to trying to establish just such a quantitative clinical interface using the "Methodological Platform". Studies have been performed on early post-operative extubation,[24] metabolic changes during deep hypothermia,[19] and haemodynamic and biochemical variables after induction of anaesthesia with fentanyl/nitrous oxide in patients undergoing coronary artery bypass surgery.[25] Some interesting observations have also been made on the occurrence of various intra- and post-operative complications. As a result of these studies, problems in cardiac surgery, cardiac anaesthesia and post-operative care have been reduced, indeed, in some cases this has turned out to represent an unexpectedly large improvement in patient welfare. Moreover, the ability of the "Platform" to furnish data which allows strategic manipulation of the patient's physiology has led to the discovery of a number of novel solutions to well-known clinical problems.

3.7. References

1. Taylor G, Larson CP Jr, Prestwich R: Unexpected cardiac arrest during anesthesia and surgery. An environmental study. JAMA 236: 2758, 1976.
2. McClure JN, Skardasis GM, Brown JM: Cardiac arrest in the operating area. Am Surgeon 38: 241, 1972.
3. Hilberman M: Monitoring in the operating room: Current techniques and future requirements. Med Instrum 11: 283, 1977.
4. Lilly JC: Physical methods of respiratory gas analysis. Meth in Med Res 2: 133, 1950.
5. Lilly JC: Mixing of gases within respiratory system with a new type nitrogen meter. Am J Physiol 161: 342, 1950.
6. Siri W: A mass spectroscope for analysis in the low mass range. Rev Sci Instrum 18: 540, 1947.
7. Hunter JA, Stacey RW, Hitchcock FA: A mass spectrometer for continuous gas analysis. Rev Sci Instrum 20: 333, 1949.
8. Comroe JH Jr.: The functions of the lung. Harvey Lec 48: 110, 1952.
9. Peters RM, Hilberman M: Respiratory insufficiency: Diagnosis and control of therapy. Surgery 70: 280, 1971.

10. Osborn JJ: Cardiopulmonary monitoring in the respiratory intensive care unit. Med Instrum 11: 278, 1977.
11. Jonson B, Nordström L, Olsson SG et al: Monitoring of ventilation and lung mechanics during automatic ventilation. A new device. Bull Physiopath Resp 11: 729, 1975.
12. Fletcher R, Jonson B: Skattning av arteriell pCO_2 genom mätning av CO_2 i expirationsluft. Svenska Läkeresàllskapets Riksstämma (p. 84). Stockholm, Hygiea, 1978.
13. Fletcher R, Jonson B, Cumming G et al: The concept of dead space with special reference to the single breath test for CO_2. Submitted for publication to the Br. J Anaesth, 1980.
14. Engström C-G, Herzog P: Ventilation nomogram for practical use with the Engström respirator. Acta Chir Scand Suppl 245: 37, 1959.
15. Engström C-G, Herzog P, Norlander OP et al: Ventilation nomogram for the newborn and small children to be used with the Engström respirator. Acta Anaesthesiol Scand 6: 175, 1962.
16. Radford EP: Ventilation standards for use in artificial respiration. J Appl Physiol 7: 451, 1955.
17. Bartels J, Severinghaus JW, Forster RE et al: The respiratory dead space measured by single breath analysis of oxygen, carbon dioxide, nitrogen or helium. J Clin Invest 33: 41, 1954.
18. Okmian LG: Artificial ventilation by respirator for newborn infants during anaesthesia. Acta Anaesthesiol Scand 7: 31, 1963.
19. Prakash O, Jonson B, Bos E et al: Cardiorespiratory and metabolic effects of profound hypothermia. Crit Care Med 6: 340, 1978.
20. Kelman GR: Digital computer subroutine for the conversion of oxygen tension into saturation. J Appl Physiol 21: 1375, 1966.
21. Hugenholtz PG, Miller AC, Krauss ZH et al: Automation in the management of data in intensive care. Proc. Eight Pfizer Int. Symp., Edinburg, 1973.
22. Deutsch LS, Engelse WAH, Zeelenberg C et al: The Unibed patient monitoring system: A new approach for a new technology. Med Instrum 11: 274, 1977.
23. Zeelenberg C, Engelse WAH, Deutsch LS: A hierarchical patient monitoring computer network. In: Computers in Cardiology (p. 439). Long Beach, Cal, IEEE Computer Society, 1977.
24. Prakash O, Jonson B, Meij S et al: Criteria for early extubation after intracardiac surgery in adults. Anesth Analg 56: 703, 1977.
25. Prakash O, Verdouw PD, De Jong JW et al: Haemodynamic and biochemical variables after induction of anaesthesia with fentanyl/ nitrous oxide in patients undergoing coronary artery by-pass surgery. Can Anaesth Soc J 27: 223, 1980.

CHAPTER 4

Br. J. Anaestl. (1980), 52, 491

CLINICAL STUDIES OF GAS EXCHANGE DURING VENTILATORY SUPPORT—A METHOD USING THE SIEMENS–ELEMA CO_2 ANALYZER

S. G. OLSSON, R. FLETCHER, B. JONSON, L. NORDSTRÖM AND O. PRAKASH

SUMMARY

We describe a new portable infra-red analyser for use with the Siemens–Elema Servo ventilator. The sensor head constitutes a Y-piece connecting the patient to the ventilator tubing, and gives instant carbon dioxide determination. It is based upon simple principles that can be realized with modern techniques, offering for instance freedom from interference by anaesthetic gases, and eliminating the need for calibration. A non-zero inspired carbon dioxide concentration interferes with the measurements. Integration of the carbon dioxide signal with the flow signal from the Servo ventilator yields data about carbon dioxide excretion, and additional calculation yields V_D/V_T if Pa_{CO_2} is known. The accuracy of determination of end-tidal carbon dioxide and carbon dioxide elimination was found to be adequate for research purposes, and that of V_D/V_T for clinical purposes. The device is considered to be of value in the operating theatre and intensive care unit, for monitoring, as a guide to ventilatory needs, and for the investigation of the magnitude and causes of increased deadspace.

When ventilatory support is required, control of gas exchange is at least as important as ventilation itself. The following equations show some factors that govern the maintenance of Pa_{CO_2}:

$$Pa_{CO_2} = \frac{\dot{V}CO_2}{\dot{V}_A} \times k \qquad (1)$$

$$\dot{V}_A = \dot{V}_T - \dot{V}_D \qquad (2)$$

It is assumed that equilibrium occurs between alveolar and arterial PCO_2. $\dot{V}CO_2$ = carbon dioxide production, $\dot{V}_A$ = alveolar ventilation, $\dot{V}_T$ = total ventilation and $\dot{V}_D$ = ventilation of physiological deadspace. k is a factor converting carbon dioxide fraction to PCO_2.

In the absence of lung disease, end-tidal PCO_2 ($P_E'CO_2$) closely reflects Pa_{CO_2} (Galdston, Benjamin and Hurewitz, 1951; Collier, 1955; Dahlgren and Symreng, 1974), and adequate Pa_{CO_2} is generally maintained with ordinary ventilation. When this is not the case the analysis of mechanisms involved is aided by knowledge of VCO_2 and the various fractions of deadspace. Suitable systems for measurement of $P_E'CO_2$, $\dot{V}CO_2$ and $\dot{V}_D$ have in the past been bulky, cumbersome and expensive. This paper presents an unobtrusive device for making these measurements in the intensive care unit and operating theatre. The basis of the measurements is the integration of signals for carbon dioxide concentration of expired gas, and expiratory flow. This yields much additional information, and the CO_2 Analyzer also offers advantages over previous devices in compactness, ease of handling, accuracy and freedom from errors caused by anaesthetic gases.

S. G. OLSSON, Siemens-Elema Company, Solna, Sweden. R. FLETCHER, F.F.A.R.C.S.; L. NORDSTRÖM, M.D.; Department of Anaesthesia, University Hospital, Lund, Sweden. B. JONSON, M.D., Department of Clinical Physiology, University of Lund, Sweden. O. PRAKASH, M.D., Thoraxcenter, Erasmus University, Rotterdam, The Netherlands.

0007–0912/80/050491–09 $01.00

APPARATUS AND WORKING PRINCIPLES

The Servo ventilator 900 or 900 B (Ingelstedt et al., 1972) produces an expiratory flow signal and the carbon dioxide signal comes from the CO_2 Analyzer 930 described below (both from Siemens-Elema AB, Solna, Sweden). The CO_2 Analyzer is designed to operate with the ventilator, which provides a flow signal and power and timing pulses.

The carbon dioxide sensor (fig. 1) works on the principle of absorption of infra-red radiation from a broad spectrum IR emitter (fig. 2). The radiation passes via sapphire glass windows through a Y-piece connecting the patient to the ventilator tubing. The Y-piece offers a negligible resistance to flow (0.8 cm H_2O litre^{-1} s) at a flow rate of 0.5 litre s^{-1} and 1.6 at 1 litre s^{-1}). Its deadspace is smaller than that of the ordinary Y-piece that it replaces. Part of the radiation is absorbed by the windows which are thereby heated, preventing condensation. Carbon dioxide molecules in the gas cause further absorption

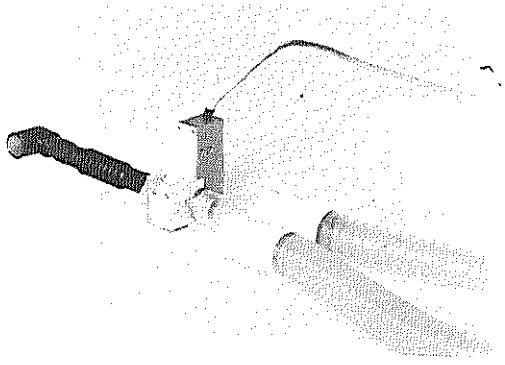


FIG. 1. Carbon dioxide sensor and cuvette.

of IR radiation of specific wavelengths. The radiation is then mechanically chopped at a frequency of 180 Hz. An interference filter transmits only light with a wavelength of 4.2 μm at which carbon dioxide has a main absorption peak. The band-width is 0.07 μm. The chopped and filtered radiation is received by a photoelectric Ge-As-sensor, the signal of which is amplified.

The signal oscillates between one value when the chopper is closed and another when it is open. Thus the chopper generates a carrier frequency that is modulated by the transmitted radiation. In this way problems inherent in detection of small signals superimposed upon large drifting ones are solved.

The amplitude of the oscillations generated by the chopper reflects transmitted pulsed light, which is a function of carbon dioxide absorption within the gas. Irrelevant factors such as the amount of emitted radiation, its absorption within the windows and the temperature of the IR detector also affect the signal. This problem is eliminated by the signal processor to which the signal is transmitted after amplification.

The signal processor (fig. 2) demodulates the signal by an amplifier that is phase-locked to the chopper signal. After demodulation a signal U corresponds to the amount of light received. At the end of inspiration there is no carbon dioxide in the sensor head. The signal at this moment (U_I) is sampled and held, to be used as a reference for the following expiration. An analog divider gives the quotient U/U_I. In the absence of carbon dioxide, when $U = U_I$, the output signal is standardized to 1 arithmetic unit. The division by U_I corrects for changes in the amount of emitted light, absorption in the windows, the sensitivity of the IR detector and primary amplification of the signal. If for example dirt, or a droplet of sputum, lands on one of the windows, this will only influence the current expiration. For the following expiration a new U_I will restore correct amplification.

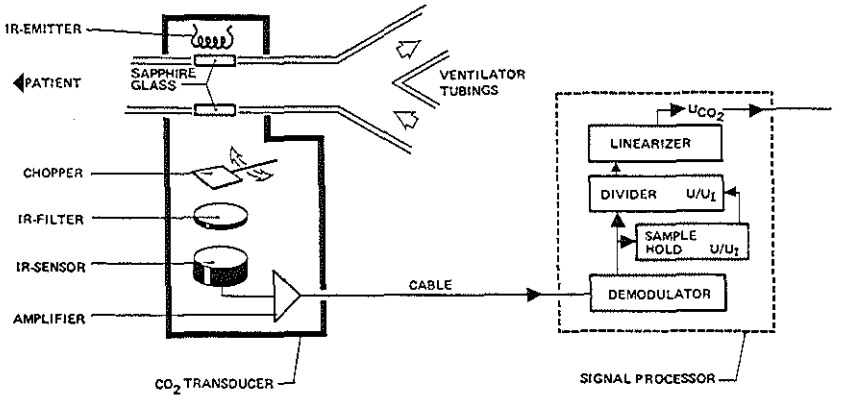


FIG. 2. The carbon dioxide transducer and initial part of circuitry within the CO_2 Analyzer 930. A beam of infra-red radiation passes through the expired gas via sapphire windows in a detachable Y-piece connecting the patient to the ventilator tubing. The beam is mechanically chopped, filtered and sensed by a photoelectric sensor. The signal is amplified and transmitted to the Analyzer. The original signal is processed to yield a signal, U_{CO_2}, that is proportional to carbon dioxide irrespective of drift of the carbon dioxide transducer (see text).

The signal U/U_I will only be influenced by carbon dioxide molecules in the pathway of radiation within the sensor head. The length of this pathway is the only critical factor, and this can be well controlled at manufacture. After the divider the signal level is high and the electronics operate under optimal conditions at which drift of amplification or base-line is negligible. The features described explain why the equipment does not need any zero adjustment or recalibration: there are no exterior controls for such procedures. The signal U/U_I is a strict, nearly logarithmic function of expired carbon dioxide concentration. After further processing, mainly linearization, a signal proportional to carbon dioxide concentration is obtained (1 V = 1% carbon dioxide). Apart from the chopping there is no delay in the analysis. One hundred per cent response to a change of carbon dioxide is obtained within 6 ms.

Interference with other gases such as water vapour and nitrous oxide is avoided by the use of a very narrow band-width of infra-red radiation, carefully selected for optimum separation. A contributory factor is that the CO_2 Analyzer measures differences between expired and inspired gases. However, even during induction of nitrous oxide anaesthesia when there are great differences between inspired and expired nitrous oxide (measured with a mass spectrometer), the carbon dioxide signal remains unaffected. When carbon dioxide is added to the inspired gas the Analyzer measures the increase of carbon dioxide over that concentration. Added carbon dioxide should be delivered in a way that ensures that the inspired carbon dioxide concentration, serving as a new base-line, is stable. If this is achieved, then the values for carbon dioxide production are still valid, and the stated end-tidal carbon dioxide becomes the excess

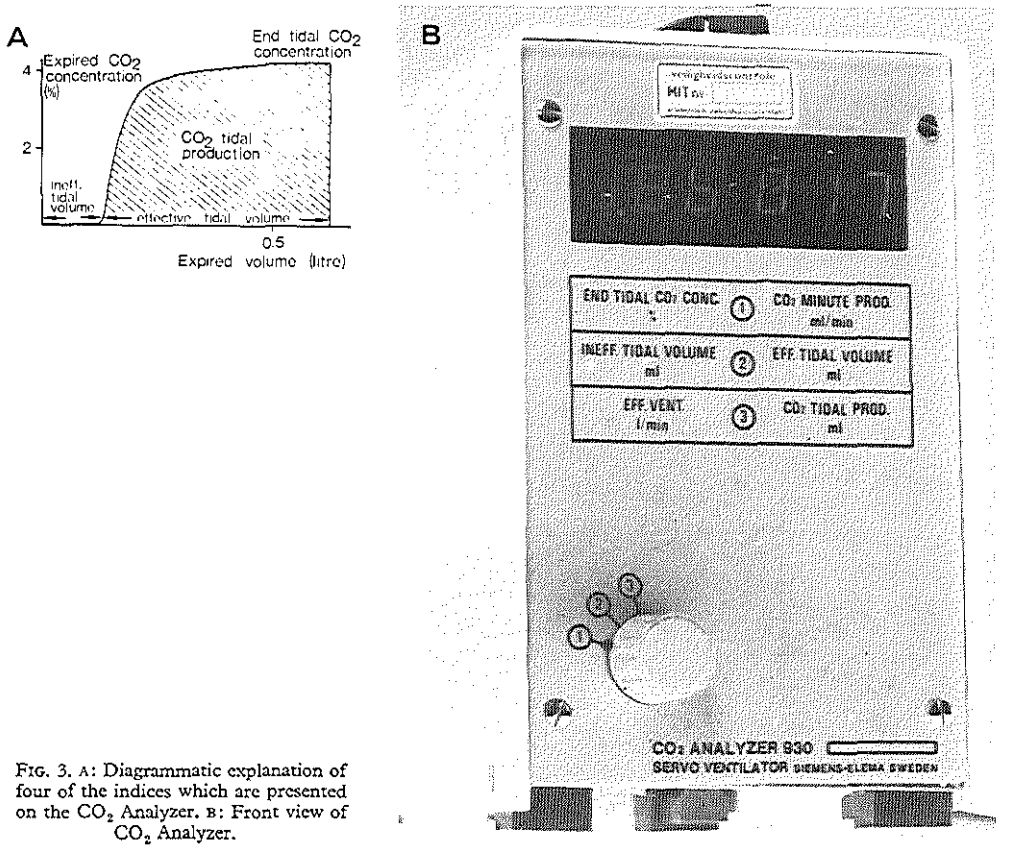


FIG. 3. A: Diagrammatic explanation of four of the indices which are presented on the CO_2 Analyzer. B: Front view of CO_2 Analyzer.

over the inspired value. If the inspired carbon dioxide concentration varies, the Analyzer can give misleading results.

Pressure dependence. With a given gas in the sensor head an increase of pressure will cause an increasing carbon dioxide signal for two reasons. First, the number of carbon dioxide molecules increases in proportion to pressure—a 1% increase causes a 1% increase of the number of radiation-absorbing carbon dioxide molecules. Second, intermolecular forces that increase with pressure will enhance absorption by carbon dioxide. This factor will cause an additional increase of the carbon dioxide signal by 0.8%. In all, a 1% increase of pressure in the sensor head will increase the signal by 1.8%. If the CO_2 Analyzer is calibrated at a barometric pressure of 100 kPa (750 mm Hg) and tested with 4% carbon dioxide at 101 kPa (758 mm Hg) a reading of $4 \times 1.018 = 4.07$ will be obtained. As the concentration is 4% an error of 0.07% will appear if the reading is regarded as concentration. In conjunction with estimates of arterial blood-gas tensions, it is preferable to regard the reading as P_{CO_2} (kPa) and not per cent carbon dioxide as stated on the Analyzer. In this case the true value at a barometric pressure of 101 kPa (758 mm Hg) is 4.04 kPa (40 mm Hg), and the error of the reading is only 0.03 kPa (0.2 mm Hg). In studies in which precision is needed, correction for variations in barometric pressure may be useful. A similar correction should then also be made when very great expiratory airway pressures are applied. In routine clinical use corrections appear to be unnecessary.

Presentation of data. The carbon dioxide signal is processed with the expiratory flow signal to provide further digital and analog information. Figure 3B shows the front panel of the instrument from which six values can be read, four of which are explained in figure 3A.

End-tidal carbon dioxide concentration. The initial carbon dioxide-free part of the expired tidal volume represents gas compressed in the ventilator tubing and humidifier, and gas from conducting airways (*ineffective tidal volume*); the carbon dioxide-containing part is the *effective tidal volume*. As soon as the carbon dioxide concentration exceeds 5% of the previous end-tidal carbon dioxide, the effective part of the tidal volume is recognized. (Ineffective tidal volume is therefore less than the anatomical dead-space.) Averaging of this volume provides a measure of *effective minute ventilation*. Integration of the product carbon dioxide concentration × instantaneous expiratory flow yields the *carbon dioxide tidal production* which is also averaged to *carbon dioxide minute production*. A more appropriate label on the carbon

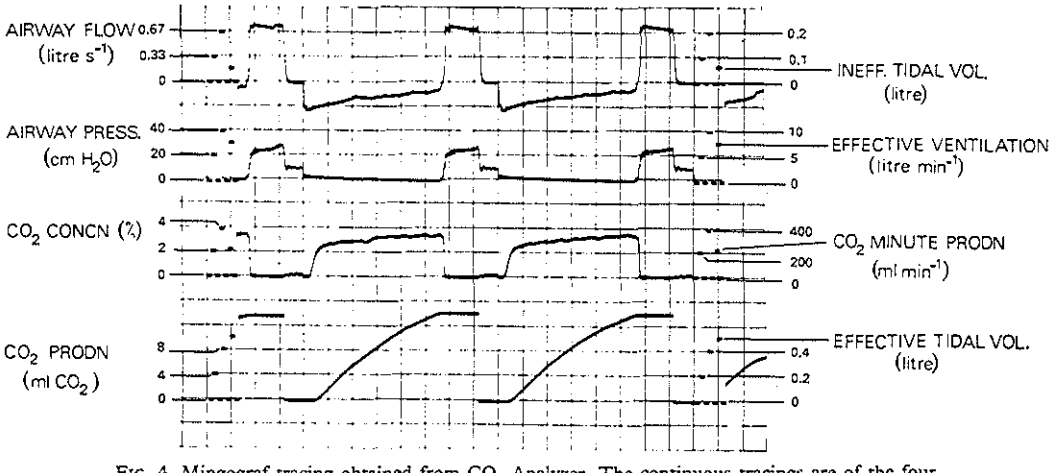


FIG. 4. Mingograf tracing obtained from CO_2 Analyzer. The continuous tracings are of the four signals named on the left, and the calibrations are given by the labelled dots. The values named on the right can be obtained from the penultimate (labelled) dot in the calibration complex which also serves as a scale for these values. For instance, on the uppermost tracing the dots give the calibrations for both the continuous tracing (airway flow) and for ineffective tidal volume. Inspiratory flow is 0.7 litre s^{-1} and ineffective volume 0.06 litre.

dioxide unit would be carbon dioxide elimination which is equal to the carbon dioxide production in the tissues only at steady state.

A simple testing device is available for checking calibration of the carbon dioxide signal against a gas mixture of known carbon dioxide concentration.

Figure 4 shows a tracing from the CO_2 Analyzer recorded on a multi-channel recorder (Mingograf 61, Siemens-Elema AB). Airway pressure, flow rate, carbon dioxide concentration and tidal expired carbon dioxide volume are shown. Every 10 s the recording is interrupted by an automated procedure that prints calibrated scales on each channel. The end-tidal carbon dioxide and $\dot{V}CO_2$ can be read directly. Immediately after the three dots of each scale a fourth dot represents one of the other four data available.

The single breath test for carbon dioxide and determination of V_D/V_T

Although the above method of obtaining carbon dioxide tracings is convenient for clinical use, more information can be obtained from the single breath test for carbon dioxide (SBT-CO_2) in which the *x*-axis represents volume instead of time. Analog signals available from the Analyzer make it possible to present SBT-CO_2 on an *XY* oscilloscope or recorder, directly or via a computer, in one of two ways. In the standard presentation (Comroe, 1962), carbon dioxide concentration is recorded against expired volume (fig. 3A). In the presentation suggested by Langley and others (1975), expired carbon dioxide volume is recorded against expired volume. (A separate cable, in which the signals are not interrupted by calibration dots as in figure 4, is used for this purpose.)

With the latter presentation, mixed expired carbon dioxide fraction or partial pressure ($P\bar{E}_{CO_2}$) can be calculated by dividing the volume of carbon dioxide per breath by the tidal volume. V_D/V_T can therefore be calculated if Pa_{CO_2} is measured simultaneously, by substituting in the Bohr equation (Bohr, 1891):

$$V_D/V_T = 1 - \frac{P\bar{E}_{CO_2}}{Pa_{CO_2}}$$

$P\bar{E}_{CO_2}$ can also be calculated from the digital displays during controlled ventilation, by dividing "carbon dioxide tidal production" by the tidal volume—ineffective plus effective tidal volume. This method is unreliable during spontaneous breathing since tidal volume and carbon dioxide tidal production are obtained at different positions of the control knob on the Analyzer and therefore cannot be obtained for the same breath.

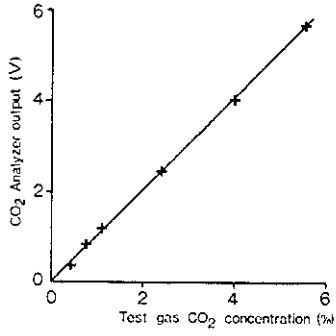


FIG. 5. Output of CO_2 Analyzer (volts) plotted against standard test gas mixtures.

CLINICAL TESTS

The linearity of the CO_2 Analyzer was checked repeatedly with gases analysed with the Scholander apparatus (Scholander, 1947). Figure 5 shows a typical result.

End-tidal carbon dioxide concentration (%) from the infrared Analyzer (IR) and a Perkin Elmer mass spectrometer MGA 1300 A (MS) were compared in anaesthetized patients. The mass numbers used were 12 and 44 for nitrous oxide–oxygen and oxygen–air mixtures respectively. With oxygen–air mixtures (78 observations on 18 individuals) we found: end-tidal carbon dioxide (%) (IR) = 0.218 + 0.927 × end-tidal carbon dioxide (MS) (r = 0.987, SD = 0.22 (residual SD about the regression), SEM of intercept = 0.119, SEM of slope = 0.028).

In oxygen–nitrous oxide mixtures (91 observations on 22 individuals): end-tidal carbon dioxide (%) (IR) = 0.156 + 0.9783 × end-tidal carbon dioxide(MS) (r = 0.987, SD = 0.15, SEM of intercept = 0.068, SEM of slope = 0.017).

A t test showed that the differences in intercept and slope between oxygen–air and oxygen–nitrous oxide mixtures were not significant ($P > 0.05$).

Carbon dioxide production ($\dot{V}CO_2$) (ml min^{-1}) obtained digitally from the CO_2 Analyzer was compared with values obtained from mass spectrometry by multiplying mixed expired carbon dioxide concentration with expired gas volume as measured by the Servo ventilator. Mixed expired gas was obtained by leading the expired gases to a mixing chamber before admission to the mass spectrometer.

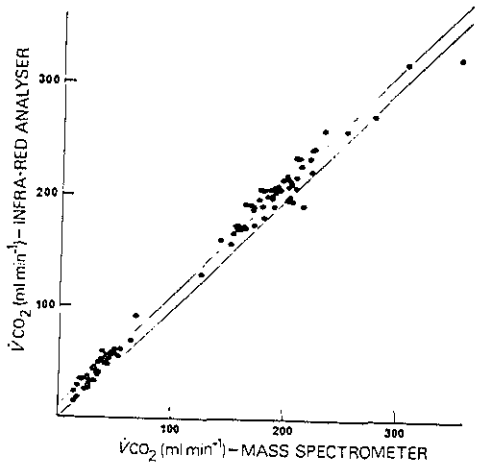


FIG. 6. Comparison of CO_2 Analyzer with mass spectrometer. Nitrous oxide–oxygen mixture.

For oxygen–air mixtures (73 observations on 18 individuals): $\dot{V}CO_2$ (IR) $= -0.649 + 1.047 \times \dot{V}CO_2$ (MS) ($r = 0.991$, SD = 14.0, SEM of intercept = 2.84, SEM of slope = 0.0147).

For oxygen–nitrous oxide mixtures (91 observations on 22 individuals) (fig. 6): $\dot{V}CO_2$ (IR) $= 10.56 + 1.006 \times \dot{V}CO_2$ (MS) ($r = 0.993$, SD = 10.1, SEM of intercept = 2.728, SEM of slope = 0.0174).

A t test showed that the difference in slope between oxygen–air and oxygen–nitrous oxide mixtures was not significant ($P > 0.05$). The difference in the intercepts was significant ($0.01 > P > 0.005$).

The physiological deadspace : tidal volume ratio was measured during spontaneous breathing by the single breath method. At steady state, mixed expired gas was collected for analysis (Scholander, 1947), arterial blood was sampled and the single breath profile was recorded. The mixed expired carbon dioxide fraction was obtained from a single tidal breath. In 10 patients with lung disease the following regression was obtained: V_D/V_T (SBT-CO_2) $= 0.028 + 0.8599 \times V_D/V_T$ (Scholander) ($r = 0.949$, SD = 0.024, SEM of intercept = 0.041, SEM of slope = 0.106).

DISCUSSION

The operating theatre or intensive care unit make special demands on technical equipment with respect to size, maintenance and safety. The CO_2 Analyzer is compact and silent and has only one cable running with the ventilator tubing. The analysis of carbon dioxide within the airway is instant and makes a gas withdrawal system unnecessary. This makes the device simple to use, and safety is not compromised by the potential for creating a subatmospheric pressure in the airway.

The features that eliminate the need for daily calibration were described in some detail to illustrate how simple principles can be realized by modern electronics. The price of achieving this simplicity is limited usefulness in systems with carbon dioxide in the inspired gas, and that the Analyzer can only be used in conjunction with the Servo 900 ventilator.

The results show that the measurement of $\dot{V}CO_2$ and end-tidal carbon dioxide is sufficiently accurate for research purposes.

The carbon dioxide measurement was not affected by nitrous oxide. The signal representing $\dot{V}CO_2$ showed similar results in adults with and without nitrous oxide. The significant difference in intercept should not be regarded as implying that the CO_2 Analyzer yields a positive carbon dioxide reading at zero $\dot{V}CO_2$ values. Thus the relationship between the two $\dot{V}CO_2$ estimates is non-linear and is not adequately described by the regression equation. It is, however, difficult to see why non-linearity should be confined to the nitrous oxide–oxygen mixture. In the presence of nitrous oxide, the mass spectrometer was used in the anaesthetic mode, which made the accuracy of carbon dioxide determination less, but did not introduce a systematic error. The difference in the intercepts should not be overemphasized, for in view of the complexity of both methods the extent of the agreement was reassuring.

Estimation of V_D/V_T during spontaneous breathing is acceptable for clinical use.

Greater accuracy for V_D/V_T would be expected during controlled ventilation, because of the smaller breath-to-breath variation in tidal volume and carbon dioxide content. Apart from Pa_{CO_2} all the data needed for calculation of V_D/V_T can be obtained from the carbon dioxide unit itself. For example, mixed expired carbon dioxide concentration can be obtained from either $\dot{V}CO_2/\dot{V}E$ or from carbon dioxide tidal production/(ineffective + effective tidal volume).

The most common application of the analysis of expired carbon dioxide is control of ventilation to maintain suitable end-tidal and arterial PCO_2 values (Collier, 1955; Dahlgren and Symreng, 1974; Prakash et al., 1978). However, although useful under most circumstances, the use of end-tidal carbon dioxide has limitations in the presence of lung disease

(Fletcher and Jonson, 1977). The present CO_2 Analyzer yields information that can reveal subclinical lung disease (see below), and we are studying how this information can be used to improve the usefulness, and to avoid the pitfalls, of end-tidal measurements in the control of ventilation.

A rough guide to ventilatory needs may be obtained from a nomogram (Radford, 1955; Engström and Herzog, 1959; Engström et al., 1962). However, our experience with the CO_2 Analyzer suggests that large variations in $\dot{V}_{CO_2}$ and, to a lesser extent, V_D/V_T, are commonplace during surgery.

When a standard ventilator setting does not give an acceptable Pa_{CO_2}, the information from the CO_2 Analyzer should be used in a logical search for the reason. The carbon dioxide production may be chosen as the starting point. If, at steady state, this is greater than expected, the need for ventilation is correspondingly increased. Further search should be directed towards non-pulmonary factors, such as fever, pain, anxiety and shivering.

In other cases the alveolar ventilation is low. In the presence of normal or high total ventilation this implies increased deadspace. Total "physiological" deadspace ventilation can be calculated and the physiological deadspace (ml) by division with the frequency. Increased V_D can result from a high ineffective ventilation (absolute deadspace) (Bartels et al., 1954). Increased compressed volumes in the tubings or humidifier may be caused by increased airway pressures or inadequate levels of water in some humidifiers. This problem is of course of importance in children and especially in infants (Okmian, 1963). The lung mechanics calculator 940 (Jonson et al., 1975) (Siemens–Elema AB) gives additional information about compliance and resistance, possible causes of an increased airway pressure.

If the reason for dysfunction is still not obvious, increased intrapulmonary or alveolar deadspace must be present. This can be caused by several factors: ventilation–perfusion mismatching, pulmonary embolism and venous admixture may all contribute. The CO_2 Analyzer offers some possibilities for further analysis. Sequential emptying of lung compartments with different ventilation–perfusion relationships yields SBT-CO_2 with a poorly defined, steeply sloping alveolar plateau (fig. 7, left). This may be found in obstructive lung disease, even when other signs are missing.

Non-sequential phenomena, such as venous admixture or synchronous emptying of lung compartments with different carbon dioxide contents, yield another pattern (fig. 7, right). This pattern has been observed in conjunction with hypovolaemia and pulmonary embolism (non-perfusion of lung compartments) and congenital heart disease with variable right to left shunts (Prakash et al., 1978).

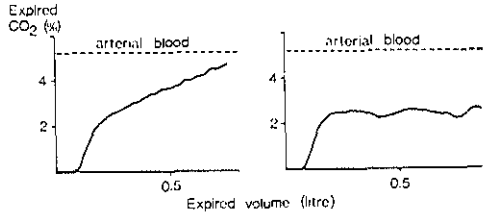


FIG. 7. Left: carbon dioxide single breath test from a 73-yr-old man with emphysema. Note the steeply sloping, poorly defined alveolar plateau. This is caused by sequential emptying of lung compartments with greatly differing carbon dioxide concentrations. The arterial–end-tidal difference is indicative of alveolar deadspace. Right: carbon dioxide single breath test from a 72-yr-old man with massive pulmonary emboli. The alveolar plateau is clearly defined and shows marked cardiogenic oscillations. The simultaneous emptying of well-perfused and underperfused lung compartments causes a large alveolar deadspace and a large arterial–end-tidal carbon dioxide difference. The horizontal plateau suggests the absence of pre-existing obstructive lung disease.

The usefulness and limitations of SBT-CO_2 as a diagnostic tool in lung disease remain to be explored.

Monitoring of the electrocardiogram (e.c.g.) and ventilation may continue undisturbed in spite of even circulatory arrest. As gas exchange is the immediate vital function of both ventilation and circulation, monitoring of carbon dioxide elimination or oxygen uptake offers a more fundamental guarantee against unobserved life-threatening malfunction of vital organs. Any sudden severe malfunction depresses the carbon dioxide elimination via the lungs (Smalhout and Kalenda, 1975). Such an observation should lead to a systematic search for the reason, starting with control of ventilation and the e.c.g. A common cause for circulatory depression during thoracic surgery in the presence of undisturbed e.c.g. and ventilation is temporary interference with venous return. It is important to be able to recognize such events before, for example, hypoxic arrhythmias occur. Continuous monitoring of aerobic metabolism probably offers the best prospects of early discovery of malignant hyperthermia.

Apart from ventilating the lungs in response to end-tidal P_{CO_2}, the control of other routine procedures

may be based on information from gas analysis. Profound hypothermia during anaesthesia for cardiac surgery in infants may be performed with guidance from carbon dioxide analysis (Prakash et al., 1978). At extubation of the trachea it has been found useful to check the ability to maintain adequate gas exchange during a spontaneous ventilation test (Prakash et al., 1977). The efficiency of ventilation is, in some patients, dependent upon the breathing pattern produced by the ventilator; this aspect of the use of instant analysis of the gas exchange is largely unexplored.

Note added in proof: New evidence indicates that the balance of gases influences the reading of the CO_2 Analyzer (A. v. Bijnen, Department of Hospital Engineering, University Hospital, Leyden, The Netherlands, personal communication). Nitrous oxide should cause increased, and oxygen decreased readings. A 65% nitrous oxide:35% oxygen mixture should result in carbon dioxide values that are slightly too great. Although the comparison between different mixtures of gases presented in the article does not show significant differences in slopes, a trend towards higher readings in the presence of nitrous oxide can be observed. The error is not related to absorbtion of infra-red radiation of nitrous oxide, but rather to intermolecular interaction between gases. Its nature and magnitude require further studies.

ACKNOWLEDGEMENTS

This study was supported by the Swedish Medical Research Council, grant 14X-02872 and by the Swedish National Association against Chest and Heart Diseases.

REFERENCES

Bartels, J., Severinghaus, J. W., Forster, R. E., Briscoe, W. A., and Bates, D. V. (1954). The respiratory dead space measured by single breath analysis of oxygen, carbon dioxide, nitrogen or helium. *J. Clin. Invest.*, **33**, 41.

Bohr, C. (1891). Ueber die Lungenathmung. *Skand. Arhiv. Physiol.*, **2**, 236.

Collier, C. R. (1955). Continuous rapid infrared CO_2 analysis. *J. Lab. Clin. Med.*, **45**, 526.

Comroe, J. H. (1962). *The Lung*, 2nd edn, p. 107. Chicago: Year Book Medical Publishers.

Dahlgren, B. E., and Symreng, T. (1974). Instant control of the alveolar P_{CO_2} in neurosurgical operations by the use of Godart–Statham capnograph. *Opusc. Med.*, **19**, 271.

Engström, C.-G., and Herzog, P. (1959). Ventilation nomogram for practical use with the Engström respirator. *Acta Chir. Scand.* (Suppl.), 245, 37.

—— —— Norlander, O. P., and Swensson, S. A. (1962). Ventilation nomogram for the newborn and small children to be used with the Engström respirator. *Acta Anaesthesiol. Scand.*, **6**, 175.

Fletcher, R., and Jonson, B. (1977). Skattning av arteriellt P_{CO_2} genom mätning av CO_2 i expirationsluft. *Sven. Läkaresällsk. Riksstäm.*, p. 84. Stockholm: Hygiea.

Galdston, M., Benjamin, B., and Hurewitz, M. (1951). "Alveolar air" and arterial blood-gas tension studies in normal and chronic lung disease patients. *Fed. Proc.*, **10**, 47.

Ingelstedt, S., Jonson, B., Nordström, L., and Olsson, S.-G. (1972). A servo-controlled ventilator measuring expired minute volume, airway flow and pressure. *Acta Anaesthesiol. Scand.* (Suppl.), **47**, 7.

Jonson, B., Nordström, L., Olsson, S.-G., and Åkerback, D. (1975). Monitoring of ventilation and lung mechanics during automatic ventilation. A new device. *Bull. Physiopathol. Respir.*, **11**, 729.

Langley, F., Even, P., Duroux, P., Nicolas, R. L., and Cumming, G. (1975). Ventilatory consequences of unilateral pulmonary artery occlusion. *Colloques Instit. Nat. Santé Rech. Méd.*, **51**, 209.

Okmian, L. G. (1963). Artificial ventilation by respirator for newborn infants during anaesthesia. *Acta Anaesthesiol. Scand.*, **7**, 31.

Prakash, O., Jonson, B., Bos, E., Meij, S., Hugenholtz, P. G., and Hekman, W. (1978). Cardiorespiratory and metabolic effects of profound hypothermia. *Crit. Care Med.*, **6**, 340.

—— —— Meij, S., Bos, E., Hugenholtz, P. G., Nauta, J., and Hekman, W. (1977). Criteria for early extubation after intracardiac surgery in adults. *Anesth. Analg. (Cleve.)*, **56**, 703.

Radford, E. P. (1955). Ventilation standards for use in artificial respiration. *J. Appl. Physiol.*, **7**, 451.

Scholander, P. F. (1947). Analyzer for accurate estimation of respiratory gases in one-half cubic centimeter samples. *J. Biol. Chem.*, **167**, 235.

Smalhout, B., and Kalenda, Z. (1975). *An Atlas of Capnography*, p. 28. Zeist: Kerckebosch.

ETUDES CLINIQUES SUR L'ECHANGE DE GAZ PENDANT L'USAGE D'UN SYSTEME VENTILATOIRE D'APPOINT—METHODE BASEE SUR L'ANALYSEUR DE CO_2 SIEMENS-ELEMA (SIEMENS-ELEMA CO_2 ANALYZER)

RESUME

Nous décrivons dans cet article un nouvel analyseur portatif à infrarouges que l'on utilise avec le Servoventilateur Siemens-Elema. La tête du système sensible est en forme d'Y; elle relie le patient au tuyau du ventilateur et permet de déterminer instantanément la quantité de gaz carbonique. Cet appareil est basé sur des principes simples qui peuvent être réalisés grâce aux techniques modernes. Il permet par exemple d'éviter toute interférence de la part des gaz anesthésiants et élimine la nécessité de procéder à des étalonnages. Toute concentration de gaz carbonique inspiré, d'une valeur autre que zéro, gène les mesures. L'intégration du signal gaz carbonique dans le signal du débit émanant du Servoventilateur permet d'obtenir des données sur l'excrétion de gaz carbonique, et en faisant quelques calculs complémentaires on peut obtenir la V_D/V_T, lorsqu'on connaît la Pa_{CO_2}. On a trouvé que la précision de la détermination du gaz carbonique en fin d'expiration ainsi que celle de l'élimination du gaz carbonique étaient adéquates pour les

besoins de la recherche, et qu'il en était de même pour la V_D/V_T du point de vue clinique. Cet appareil est considéré comme ayant son utilité dans les salles d'opérations et les salles de soins intensifs, pour la surveillance générale, pour la détermination des impératifs ventilatoires, et pour faire des recherches sur l'importance et les causes de l'augmentation de l'espace mort.

KLINISCHE STUDIEN DES GASAUSTAUSCHES BEI KÜNSTLICHER BELÜFTUNG—EINE METHODE MIT VERWENDUNG DES SIEMENS-ELEMA CO_2 ANALYZER

ZUSAMMENFASSUNG

Wir beschreiben einen neuen, transportablen Infrarot-Analysator zur Benutzung mit dem Siemens-Elema-Servoventilator. Der Sensorkopf stellt ein Y-förmiges Stück dar, das den Patienten an den Ventilator anschliesst, und sofortige Kohlendioxydbestimmung ermöglicht. Es beruht auf einfachen Prinzipien, die durch moderne Methoden realisiert werden können, und bietet z.B. Freiheit von Störung durch Anästhesiegase, und eliminiert die Notwendigkeit einer Kalibrierung. Ein Vorhandensein von angesaugten Kohlendioxydkonzentrationen beeinträchtigt die Messungen. Integrierung des CO_2-Signals mit dem Durchflusssignal vom Servoventilator ergibt Daten über CO_2-Ausscheidung, und zusätzliche Berechnungen ergeben V_D/V_T, wenn Pa_{CO_2} bekannt ist. Die Genauigkeit der Endausatmung von Kohlendioxyd und von dessen Ausscheidung hat sich als ausreichend für Forschungszwecke erwiesen, und die Genauigkeit von V_D/V_T für klinische Zwecke. Das Gerät ist wertvoll in Operationssaal und Intensivstation—für Überwachung, für eine Richtlinie der Belüftungserfordernisse und für die Untersuchung von Grösse und Ursachen vergrösserten Totraums.

ESTUDIOS CLINICOS DEL INTERCAMBIO DE GASES DURANTE APOYO VENTILATORIO—UN METODO EN QUE SE USA UN SIEMENS-ELEMA CO_2 ANALYZER

SUMARIO

Describimos un nuevo analizador infra-rojo portátil para uso con el ventilador Siemens-Elema. La cabeza detectora constituye una pieza en Y que conecta al paciente con la tubería del ventilador y arroja una determinación instantánea del dióxido de carbono. Se basa en principios sencillos que se pueden poner en práctica con técnicas modernas que ofrecen por ejemplo una independencia con respecto a los gases anestéticos y eliminan la necesidad de calibración. Una concentración de dióxido de carbono inspirado sin cero interfiere con las mediciones. La integración de la señal de dióxido de carbono con la señal del flujo del Servo-ventilador arroja datos sobre la excreción de dióxido de carbono y un cálculo adicional suministra el V_D/V_T si se conoce el Pa_{CO_2}. La exactitud de la determinación del dióxido de carbono respiratorio-terminal y de la eliminación del dióxido de carbono se consideró adecuada con respecto a los fines de la investigación y la del V_D/V_T para fines clínicos. Se considera que el aparato es valioso en la sala de operación y en el servicio de cuidados intensivos, para el control así como para guía respecto de las necesidades ventilatorias, al igual que para la investigación de la magnitud y de las causas del creciente espacio muerto.

CHAPTER 5

The role of controlled ventilation in cardiac surgery

5.1. Introduction and background

Controlled ventilation after cardiac surgery[1-9] is routine in most centres. The rationale is that extra work of breathing should not be imposed on a patient with a limited cardiac reserve.

On the other hand, controlled ventilation involves risks and disadvantages such as pulmonary infection, life-threatening airway obstruction, discomfort, and the need for heavy sedation. In the last few years, therefore, there has been a trend towards shorter periods of controlled ventilation following cardiac surgery.[10] Moreover, recent progress in both surgical and anaesthetic techniques has rendered long-term post-surgical ventilation much less of a necessity than previously.

The object of the study was to identify patients who could safely be extubated shortly after cardiac surgery.[11] Extubation of the trachea was defined as "early" if it were done within 3 hours after chest closure. For reasons outlined above, we wanted to employ early extubation on as many patients as possible. A total of 142 consecutive adult patients were studied.

5.2. Review of previous work

In the fit individual at rest, the cost of respiratory work represents some 1 to 3% of the total oxygen consumption.[12-17] However, the work of breathing in a patient suffering from respiratory and/or circulatory difficulties often represents a heavy extra burden, which is liable to become an acute problem in the period immediately after cardiac surgery. In such patients, the oxygen cost of spontaneous respiration may be equivalent to an increase in total oxygen consumption of as much as 36%.[18] Controlling the respiration may thus result in a useful reduction in oxygen consumption, as shown by Holmdahl,[19] Björk et al.,[20] Thung et al.,[3] Gerbode et al.,[15] and Clowes et al.[21] Grenvik,[22] for example, observed an 8-20% increase in oxygen consumption after resumption of spontaneous respiration at the end of 24 hours of post-operative controlled ventilation.

In a study of patients undergoing open-heart surgery,[23] significant post-operative changes from pre-operative levels were found in compliance and gas exchange values. In 41 open-heart surgery patients with total cardiopulmonary bypass, the compliance was shown to be decreased for up to six months post-operatively. The oxygen uptake was also significantly altered in the post-

operative period with an increase from pre-operative levels of 159 ml. $min^{-1}.m^{-2}$ to 176 ml. $min^{-1}.m^{-2}$ on the first post-operative day. A negative correlation was found between compliance and oxygen uptake; i.e. a decrease in compliance was associated with an increase in oxygen consumption. Thung and Norlander[24] demonstrated an increase of 32% in oxygen consumption measured in patients in the period immediately after open-heart surgery with intermittent positive pressure ventilation.

The mechanical work of breathing has been experimentally estimated in dogs by Shimizu and Lewis[25] and in patients undergoing thoracic and abdominal surgery, by a number of authors, starting as long ago as 1955.[26-34] Karlson et al.[35] analysed the work of breathing in 22 thoracic patients as part of their study of pulmonary mechanics. They found that patients who had increased work of breathing pre-operatively were much more likely to develop post-operative pulmonary complications, following a decrease in pulmonary compliance and an increase in non-elastic resistance during the course of the operation. Lewis and Welch[36] have made similar observations, and they applied an on-line digital computer technique to the evaluation of their results;[37] in a study of 56 patients post-operatively, they found a regular trend of a decreasing compliance, a falling arterial oxygen saturation, and the development of a metabolic acidosis. By contrast, Norlander et al.,[38] from analogue computer measurements of respiratory mechanics, did not demonstrate any changes in compliance and resistance.

Austen et al.[39,40] have pointed out the frequent occurrence post-operatively of such problems as congestive cardiac failure and pulmonary complications, which are hard to distinguish between in their clinical presentations. Iribarren and Ekeström[41] demonstrated respiratory insufficiency as the cause of death in 15 out of 119 fatal cases in a series of 507 open-heart operations during the years 1957 to 1962. Provan, Austen, and Scannell[42] demonstrated an incidence of 19.8% severe respiratory complications after open-heart surgery.

Osborn,[43] when describing the phenomenon of respiratory insufficiency following open-heart surgery, noted that patients in whom this was seen during the post-operative period had normal cardiac outputs but greatly increased ventilation, increased alveolar-arterial gradients, and cyanosis. One possible explanation for these findings may be a reduction in the diffusion capacity of the alveolar membrane. Several authors have described a diminished pulmonary diffusion capacity following artificial perfusion.[44-46] Another possible explanation which has been put forward is that arterio-venous shunting takes place past atelectatic alveoli. If part of the pulmonary blood is shunted past an atelectatic alveolus, that part of the blood receives no oxygen and when a significant fraction of all alveoli is atelectatic in this way, then even hyperventi-

lation or administration of an increased oxygen percentage will not prevent hypoxaemia.

In this connection, Gardner et al.[47] have described an increase in surface tension of alveolar lining material following anoxia or artificial lung perfusion with a fall in the concentration of specific surface-active agent. They have been able to associate this with pathological function studies suggesting diffuse atelectasis. In these situations, therapy must be directed towards positive pressure ventilation with continuous positive airway pressure, so as to maintain the patency of as many alveoli as possible throughout the respiratory cycle.

As was pointed out in the introduction to chapter 3, the object of this study was to develop a reliable monitoring system which would permit identification and post-operative treatment of these patients at risk. Before and during cardiac surgery, all patients had their pulmonary functions closely monitored, using the framework of the Methodological Platform, and any deterioration was quantified in such a way as to categorize the patient as being very likely, less likely or unlikely to require post-operative ventilatory support.

In the immediate post-operative period, and at frequent intervals thereafter, the patient's respiratory and circulatory performance was reassessed with reference to a series of criteria; depending on which criteria were fulfilled, and what the patient's pre- and intra-operative pulmonary performance had been, decisions were made regarding discontinuation or recommencement of ventilation, and extubation or re-intubation. Based on this concept, a paper with summary of the results and conclusions of this investigation will now be presented.

Anesth Analg
56:703-708, 1977

CHAPTER 5.3.

Criteria for Early Extubation After Intracardiac Surgery in Adults

OMAR PRAKASH, MD*
BJORN JONSON, MD†
SIMON MEIJ, MSc‡
EGBERT BOS, MD§
PAUL G. HUGENHOLTZ, MD‖
JAN NAUTA, MD§
WILLEM HEKMAN, MD*
Rotterdam, The Netherlands**

Of 142 adult patients undergoing open-heart surgery, 123 were extubated either in the operating room or within 3 hours after admission to the recovery room, to avoid the discomfort and risks of prolonged mechanical ventilation. The remaining 19 patients, who had impaired cardiac function, were mechanically ventilated for 1 to 7 days postoperatively. The most important criteria for cardiopulmonary malfunction indicating the need for continued mechanical ventilation were a low mixed venous O_2 saturation ($S\bar{v}o_2$) of <60% and a high left atrial pressure (>20 torr). Of the 123 patients, 118 had an uneventful postoperative recovery and 5 needed reintubation, 2 because of low $S\bar{v}o_2$ and 3 because of complications unrelated to respiratory management.

Most adult patients can spontaneously breathe adequately immediately after or within 3 hours of completed open-heart surgery, but a thorough physiologic and clinical evaluation should precede extubation, to identify those who need prolonged mechanical ventilation in the postoperative phase. Criteria for selection of patients for early extubation are presented.

BENEFICIAL effects of prolonged mechanical ventilation after cardiac surgery have been well documented.[1-9] The undesirable effects of mechanical ventilation are risks of pulmonary infection, life-threatening airway obstruction, discomfort, and the need for heavy sedation. Recent progress in surgery and anesthesia merits a reevaluation of the need for postoperative mechanical ventilation.

The purpose of the present study was to test whether a set of physiologic data describing postoperative heart and lung function allows proper identification of patients in need of continued mechanical ventilation. The goal was to extubate as many patients as feasible in the operating room or within 3 hours after chest closure. This was defined as early extubation. The criteria for or against early extubation were established on

*Senior Anaesthetist, Department of Anesthesiology.
†Senior Clinical Physiologist, Department of Clinical Physiology, University of Lund, Lund, Sweden.
‡Computer Engineer.
§Professor of Cardiac Surgery.
‖Professor of Cardiology.
**Thorax Center, University Hospital and Erasmus University, Rotterdam, The Netherlands.

This study was supported by the Dutch Foundation for Pure Medical Research and by the Swedish National Association against Heart and Chest Diseases.
Paper received: March 24, 1976
Accepted for publication: January 24, 1977

TABLE 1
Operations Performed

	Total	Successful early extubation
Aortic valve replacement	21	20
Mitral valve replacement	26	18
Aortic and mitral valve replacement	3	2
Mitral valve replacement and saphenous vein coronary bypass	3	2
Saphenous vein coronary bypass, on average 2.2 grafts per patient	62	56
Resection of ventricular aneurysm	5	4
Acute infarction—closure of septum perforation. In 3 cases also resection of ventricular aneurysm	6	3
Closure of atrial septum defect of secundum type	10	9
Total correction of tetralogy of Fallot	3	1
Outflow patch for pulmonary stenosis	1	1
Resection of idiopathic hypertrophic subvalvular aortic stenosis	1	1
Resection of myxoma in left atrium	1	1
Total	142	118

the basis of prior experience and tested in 142 consecutive adult patients.

MATERIAL AND METHODS

Patients studied—104 men and 38 women—averaged 48 years (range 14 to 68) in age. The operations performed are listed in table 1.

Anesthetic Technic.—Night sedation was with 100 mg of butobarbital and 5 mg of nitrazepam.* Premedication included papaverine (10 to 15 mg), haloperidol (2 to 5 mg), and atropine (0.25 mg) IM. Prior to induction, arterial, venous, and pulmonary artery catheters (Swan-Ganz 6 F or "Grandjean" 4 F) were introduced. Orotracheal intubation (9 mm ID for males and 8.5 mm for females) was performed after induction with fentanyl (0.2 to 0.4 mg), pancuronium bromide (6 to 8 mg), and thiopentone (50 to 150 mg) IV.

Anesthesia was maintained with fentanyl, pancuronium bromide, and 60 percent N_2O in O_2. No other inhalational agent was used. When arterial systolic pressure (Pa_{syst}) was over 180 torr, 1 to 2 mg chlorpromazine was given IV. The perfusate was whole blood and Haemaccel* (Hoechst) given at a temperature of 25 to 37° C by bubble oxygenator* in a proportion resulting in a hematocrit of 30 percent, during extracorporeal circulation. The flow was 1.8 to 2.6 L/m², depending on body temperature, $S\bar{v}o_2$, and arterial pressure. Blood loss was estimated by swab weight, from suction bottles, and the residual volume left in the heart-lung machine. Blood was administered via a Swank transfusion filter. A chest x-ray film was obtained before leaving the operating room.

METHODS

The Servoventilator† has transducers for airway pressure and flow, and monitors airway pressure and expired minute ventilation. It can be set to allow the patient to breathe spontaneously through the ventilator, which then supplies gas at atmospheric pressure. As the transducers within the ventilator are working, the apparatus can still be used as a diagnostic tool.

A calculating unit[11] receives signals for flow, pressure, timing, and power from the Servoventilator 900B. It monitors 12 variables, simultaneously displaying 2 at a time, such as respiratory resistance and compli-

*Mogadon®, a benzodiazepine derivative not commercially available in the U.S.A.—Ed.

*Optiflow, Galen Laboratories, Inc., Denver, Colorado.

†Model 900B (Siemens Elema).[10]

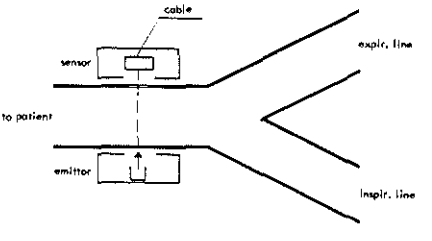


FIGURE. Sensor of the CO_2 unit. Windows in the Y-piece connecting the patient to the ventilator transmit impulses of narrow-band infrared light. Light-absorption difference between inspired and expired gas gives a signal proportional to CO_2 concentration; signaling the CO_2 unit to allow automatic calculation of $\dot{V}co_2$.

ance. A CO_2 unit in a prototype configuration measures the instantaneous CO_2 content of the gas at the airway opening (figure). The 100 percent response time is 6 msec. Measurement is not influenced by humidity or anesthetic gases. The CO_2 unit displays 6 parameters, including end-tidal CO_2 concentration and CO_2 production ($\dot{V}CO_2$). A paramagnetic O_2 analyzer* or a mass-spectrometer† continuously measures the O_2 difference between inspired and mixed expired gas, from which O_2 consumption ($\dot{V}O_2$) is calculated.

Pressure was measured in an artery, left atrium (P_{LA}), right atrium (P_{RA}), and in the pulmonary artery via fluid-filled catheters, also used for blood sampling. Arterial O_2 saturation (Sao_2) and $S\bar{v}o_2$ were intermittently determined with a Hemoreflector‡. Arterial data for pH, Pao_2, and $Paco_2$ were measured at 37° C with a Radiometer ABL 1. Cardiac output ($\dot{Q}t$) was calculated by the Fick principle, dead space from the Bohr equation, and alveolar ventilation ($\dot{V}_A$) from the $\dot{V}CO_2$ and alveolar fraction of CO_2. The pulmonary venous admixture ($\dot{Q}s/\dot{Q}t$) was calculated from the O_2 content of arterial and mixed venous blood. The temperature on the skin of the big toe (T_t) was measured by thermocouples§ covered by loose gauze wrappings. In the postoperative care unit a previously described intensive-care computer monitoring (ICPM) system[12] allowed record-keeping over 24 hours of cardiac rhythm, various intravascular pressures, and the signals from the calculating and CO_2 units.

Selection of Patients for Early Extubation.—Patients were maintained on mechanical ventilation for reasons given in table 2. Clinical indications included factors such as severe arrhythmia, poor lung mechanics (low compliance or high resistance), bleeding, hypovolemia, obesity, and preexisting lung disease. If none of the reasons for continued mechanical ventilation was present, the ventilator mode was switched to spontaneous breathing. If the patient maintained adequate ventilation with a stable end-tidal CO_2 of less than 5.5 percent and still did not meet any criterion of table 2, he was extubated. This is called the spontaneous ventilation test, SVT.

*Taylor Servomex, Crowborough, Sussex, England.

†Perkin Elemer, Pomona, California.

‡American Optical Company, Bedford, Massachusetts.

§Ellab, Copenhagen, Denmark.

TABLE 2
Criteria for Continued Mechanical Ventilation

Criteria 1-7 were first checked during mechanical ventilation with 40% O_2 in N_2. If no indication for continued ventilation was observed, a second check was made during the spontaneous ventilation test (criterion 8).

1. Pa_{syst} < 80 torr
2. P_{LA} > 20 torr
3. $S\bar{v}o_2$ < 60%
4. Sao_2 < 90%
5. $Paco_2$ > 55 torr
6. T_t < 30° C
7. Clinical evaluation indicating continued artificial ventilation
8. Inadequate spontaneous ventilation (unstable ventilation or end-tidal CO_2 > 5.5%)

RESULTS

Nineteen patients could not be extubated early (table 3). In most patients, several reasons coexisted for continued mechanical ventilation; of these, the most frequent were a low $S\bar{v}o_2$ (14 cases) and a high P_{LA} (8 cases). Sixteen were extubated the next morning, and 2 after 36 hours, when they met the criteria in table 2 and passed the SVT. One Fallot patient died of hemorrhage after 7 days on mechanical ventilation. All others in this high-risk group recovered, although in a few cases after a stormy course.

Early extubation was considered feasible in 123 patients, most of these in the operating room within 1 hour after operation. Of these, 5 had to be reintubated. Two of those 5 had an $S\bar{v}o_2$ of only about 50 percent before and during the SVT. Because of laboratory delay, this was not known and these 2 patients were extubated contrary to our

TABLE 3
Condition of Patients Not Amenable to Early Extubation
(n = 19)

Pathology or procedure	Number
Coronary artery disease (graft)	8
Mitral valve replacement	6
Fallot's tetralogy	3
Repair of ASD	1
Aortic valve replacement	1

protocol. One patient with mitral valve replacement was reintubated within 1 hour, as he was in obvious distress. After a further 14 hours on the ventilator, he had a smooth recovery. The other, a 63-year-old man with interventricular septum perforation after myocardial infarction, was brought to the operating room after 25 days of circulatory assistance by intra-aortic balloon pumping. Four days later he died in arrhythmia. In the remaining 3 "failures" there was no indication for continued ventilation at the time of extubation. All 3 had mitral valve replacements. Serious problems included bleeding in 2 patients and myocardial infarction in 1 patient. Drastic action had to be taken consisting of reintubation, reoperation, defibrillation, intra-aortic balloon pumping, and treatment of allergic shock. These 3 patients recovered.

The respiratory and circulatory status of all patients was carefully followed, especially for the first 36 postoperative hours. There were no problems in maintaining Pa_{O_2} at sufficient levels. Pa_{CO_2} was generally adequate (table 4). However, 17 of 118 extubated patients had a Pa_{CO_2} of 50 to 60 torr after 1 hour in the postoperative unit. After 36 hours, only 1 patient still had a Pa_{CO_2} >50 torr. Changes in arterial pH generally reflected changes in Pa_{CO_2}. The circulatory status of successfully extubated and ventilated patients reflected by such parameters as $S\bar{v}o_2$ and P_{LA} were in general satisfactory (table 4). The peripheral circulation judged from T_t rapidly improved during the first few hours. In the "failures," the $S\bar{v}o_2$ was insufficient, as was the peripheral circulation. As P_{LA} was high (table 4), left ventricular failure was the most likely mechanism in these cases.

Extensive physiologic studies were performed in 27 patients. They were studied on mechanical ventilation, first after induction of anesthesia prior to surgery, then 1 to 3 hours after chest closure while still under anesthesia. A third study was performed after 30 minutes of spontaneous breathing when the patients were awake and responsive. All measurements were done with the patients breathing 40 percent O_2 in N_2.

During postoperative mechanical ventilation, $\dot{V}o_2$ was increased by 29 percent compared to preoperatively, and during SVT it increased further by 19 percent. It is not known how much of this increase in metabolism is caused by the work of breathing. Part of the increase must be due to the withdrawal of anesthesia and increasing

TABLE 4
Hemodynamic and Blood-Gas Data During First 36 Hours in Recovery Unit

		Ventilated subjects (n = 19)		Early extubation: successful cases (n = 118)		Early extubation: failures (n = 5)	
	Period	Mean	SD	Mean	SD	Mean	SD
Pa_{CO_2}, torr	A	35	± 5	44	± 6	43	± 7
	B	34	± 4	42	± 5	33	± 3
	C	39	± 6	42	± 5	35	± 7
	D	41	± 5	41	± 5	39	± 4
$S\bar{v}o_2$, %	A	65	± 10	70	± 7	61	± 8
	B	67	± 8	73	± 7	59	± 9
	C	69	± 7	68	± 6	60	± 9
	D	64	± 9	66	± 7	60	± 6
P_{LA}, torr	A	11	± 3	11	± 5	17	± 8
	B	9	± 2	9	± 4	12	± 2
	C	11	± 5	9	± 4	15	± 1
	D	9	± 3	9	± 4	14	± 4
T_t, °C	A	27	± 4	26	± 3	24	± 2
	B	32	± 4	34	± 4	29	± 7
	C	35	± 3	35	± 3	24	± 1

Periods: A: 1 hour after transfer to recovery unit; B: operative day evening; C: morning of postoperative day 1; D: evening of postoperative day 1.

stress. That there was no postoperative reduction in $S\bar{v}O_2$ reflects an increase in cardiac index in proportion to $\dot{V}O_2$. Cardiac function therefore appeared adequate for postoperative requirements, a conclusion supported by the smooth postoperative course.

Variables related to the efficiency of the pulmonary gas exchange (V_D/V_T, $\dot{Q}s/\dot{Q}t$, $\dot{V}_A/\dot{Q}t$) were either unchanged or showed only small differences. PaO_2 was thus adequate. The total compliance of the respiratory system fell by about 26 percent. The peak pressure in the airway increased partly because of the lower compliance and partly because of the higher ventilation needed at the higher $\dot{V}CO_2$. A slight increase in expiratory resistance was also observed. These changes of lung function with respect to mechanics and gas exchange occurring during the surgical procedure thus appear quite moderate.

The data from the extensive studies in 2 "failures" differed from those of successfully managed patients only in postoperative indices related to cardiac output. Thus, $S\bar{v}O_2$ was only about 50 percent and postoperative cardiac index was below 2.7 $L/min^{-1}/m^2$ in those cases. The poor cardiac function also showed up in terms of high ventilation:perfusion ratios. Nevertheless, these patients had adequate values for respiratory parameters such as V_D/V_T, compliance, and resistance.

DISCUSSION

Routine use of prolonged mechanical ventilation after open-heart surgery is based on the concept that the work of breathing should be eliminated.[1-9] A trend to cut the period of mechanical ventilation short has, however, been observed during the last few years.[13] Sykes and coworkers[14] have shown that spontaneous ventilation may be resumed as soon as the patient is conscious and can maintain adequate blood gases. We found that 123/142 adult patients could breathe unassisted within 3 hours after intracardiac surgery.

Most patients in the present study were extubated after the spontaneous ventilation test immediately after skin closure. On the average, the successfully extubated patients stayed only 1.5 days in the postoperative unit, and none had infections or pulmonary complications. Oxygenation was adequate with 40 percent O_2 administration. Several patients developed some CO_2 retention during the first 24 postoperative hours; however, transient values of $PaCO_2$ up to 60 torr were in no case associated with clinical complications and should not require such drastic action as reintubation.

The circulatory status reflected by parameters such as P_{LA}, Pa_{syst}, and $S\bar{v}O_2$ could generally be controlled by routine measures, in particular the maintenance of an adequate blood volume, and sometimes the use of cardiotropic drugs such as isoproterenol. Provided the levels of hemoglobin concentration and SaO_2 are adequate, a decreased $S\bar{v}O_2$ reflects a cardiac output that is low in relation to O_2 demand.[15]

Pa_{syst}, P_{LA}, and $S\bar{v}O_2$ together give a picture of circulation that has prognostic value for survival after myocardial infarction.[16] Our study indicates that these variables are of similar value also after open-heart surgery. In fact, a low $S\bar{v}O_2$ and a high P_{LA} were the most frequent reasons for continued mechanical ventilation in our series of patients.

Abnormal PaO_2 and $PaCO_2$ were included as indications for prolonged mechanical ventilation as a safeguard against the danger of impaired gas exchange. The patients in this series had few problems concerning gas exchange, despite considerable preoperative lung pathology in many cases. Inadequate lung mechanics can be analyzed in terms of compliance and resistance.[11]

On the basis of the present experience, it is not believed possible to establish fixed criteria for resistance values that would provide an indication for continued ventilation. However, peak airway pressure >25 cm H_2O does suggest caution. This value must be judged with regard to the ventilatory pattern (square inspiratory flow, 14 to 16 breaths/min, minute ventilation adjusted to yield an end-tidal CO_2 of about 5%). SVT is of course also important as a guide to when a patient in good general condition can be extubated.

The value of physiologic measurements is further emphasized by the important role of $S\bar{v}O_2$, which should have led to continued ventilation in 2 "failures." There was no clinical or physiologic reasons to expect complications in the other 3 "failures." There was no obvious causal relationship between early extubation and postoperative bleeding and infarction. In those 3 patients,

careful monitoring of cardiac function and prompt intervention undoubtedly prevented a catastrophe.

The data from our studies allow evaluations of heart and lung functions that may be of value in many ways. However, more easily available and less specific indices of defective function, such as low $S\bar{v}o_2$, appear adequate indices for continued mechanical ventilation. Postoperative toe temperatures were similar in all groups (table 4). A T_t which did not increase to above 32° C within a few hours after operation was always associated with a low $S\bar{v}o_2$, as illustrated by the outcome in the "failures" (table 4). Simple means of judging the circulatory status, as by peripheral skin temperature, merit closer studies.

Hilberman's study[17] statistically analyzed many physiologic and clinical observations to find factors that coexisted with successful early weaning. Their results suggest that forced expiratory tests might be used to predict the outcome of extubation. Such a hypothesis should be tested on a second group of patients, before it can be recommended for clinical application. The present study and that of Beach and colleagues[18] indicate that measures describing the status of the heart are important selection criteria for early extubation, whereas Hilberman's report[17] suggests that data describing the patient's ability to perform forced ventilatory maneuvers are more important. These different approaches may explain the difference in results.

Our extensive physiologic data show that heart and lung function are remarkably well preserved in open-heart surgery patients, suggesting that, in light of today's advanced cardiac-surgery and anesthesiologic technics, the great majority of such patients can safely be extubated promptly.

ACKNOWLEDGMENT

The excellent cooperation of postoperative care nurses, the laboratory, and the secretarial help of Mrs. M. Roks-Wester are gratefully acknowledged.

REFERENCES

1. Damman JF, Thung N, Christlieb JJ, et al: The management of the severely ill patients after open heart surgery. J Thorac Surg 45:80-90, 1963

2. Lefemine AA, Harken DE: Post-operative care following open heart operation: routine use of controlled ventilation. J Thorac Surg 52:207-216, 1966

3. Thung N, Herzog P, Christlieb JJ, et al: The cost of respiratory effort in post-operative cardiac patients. Circulation 28:552-559, 1963

4. Cooperman LH, Man EG: Post-operative respiratory care. A review of 65 cases of open heart surgery on the mitral valve. J Thorac Cardiovasc Surg 53:504-507, 1967

5. Starr A, McCord CW, Wood J, et al: Surgery for multiple valvular disease. Ann Surg 160: 596-613, 1964

6. Starr A, Herr RH, Wood J: Mitral valve replacement: a review of 6 years experience. J Thorac Cardiovasc Surg 54:333-358, 1967

7. Robertson DS: Tracheostomy and open heart surgery. Proc Roy Soc Med 57:855-864, 1964

8. Macrae WR, Masson AB: Assisted ventilation in post-bypass period. Br J Anaesth 36:711-717, 1964

9. Zeitlin GL: Artificial respiration after cardiac surgery; some physiological considerations. Anaesthesia 20:145-156, 1963

10. Ingelstedt S, Jonson B, Nordström L, et al: On automatic ventilation. Acta Anaesthesiol Scand 47:5-27, 1972

11. Jonson B, Nordström L, Olsson SG, et al: Monitoring of ventilation and lung mechanics during automatic ventilation. A new device. Bull Physiopathol Respir 11:729-743, 1975

12. Hugenholtz PG, Miller AC, Krauss XH, et al: Automation in the management of data in the intensive care. Proc Eight Pfizer Internat Symp, Edinburgh, 1973

13. Midell AI, Skinner DB, DeBoer A, et al: A review of pulmonary problems following valve replacement in 100 consecutive patients. The case against routine use of assisted ventilation. Ann Thorac Surg 18:219-227, 1974

14. Sykes MK, Adams AP, McCormick PW, et al: The effect of mechanical ventilation after open heart surgery. Anaesthesia 25:525-540, 1970

15. Krauss XH, Verdouw PD, Hugenholtz PG, et al: On-line monitoring of mixed venous oxygen saturation after cardiothoracic surgery. Thorax 30: 636-643, 1975

16. Verdouw PD, Hagemeijer F, Van Dorp WG, et al: Short-term survival after acute myocardial infarction predicted by hemodynamic parameters. Circulation 52:413-419, 1975

17. Hilberman M, Kamm B, Lamy M, et al: An analysis of potential physiological predictors of respiratory adequacy following cardiac surgery. J Thorac Cardiovasc Surg 71:711-720, 1976

18. Beach T, Miller F, Grenvik A: Hemodynamic response to discontinuance of mechanical ventilation. Crit Care Med 1:85-90, 1973

5.4. Discussion

Hilberman et al.[48] statistically analysed a wide range of physiological and clinical observations to try to find factors which pointed to a successful outcome of early weaning from mechanical ventilation in his cardiac surgery patients. They compared the values of pre-operative and post-operative cardiopulmonary function tests, and found that the parameters "Vital Capacity versus Weight", "Maximum Expiratory Force", and "Maximum Voluntary Ventilation versus Minute Volume", most accurately predicted the outcome of weaning. In particular, the patient's performance in the "Maximum Expiratory Force" test was thought to be very useful in predicting the outcome of extubation. Based on this work, they devised a protocol similar to the one described in the present study for weaning cardiac surgery patients from controlled ventilation; a similar paper by Peters et al.[49] also laid down criteria and a protocol for weaning these patients.

A difference between the studies of the two authors just mentioned, and of Beach et al.[50] and the one undertaken at the Thorax Centre, is that in their studies, apart from pre-operative assessment, the monitoring of lung and heart function commenced at the *end* of the surgical procedure, i.e. after the patient had returned to the intensive care unit. In addition, their data emphasize much more the patient's ability to perform certain ventilatory manoeuvres. By contrast, our approach and that of Beach et al. is to initiate intensive care and monitoring at the very beginning of anaesthesia, prior to surgical intervention, and then to continue throughout the surgical procedure and straight on into the immediate post-operative phase.

Hilberman and Peters also differ from us in that they leave their patients for the first 24 post-operative hours on full ventilatory support. After this, they use their criteria to decide on the correct timing for the replacement of controlled ventilation by spontaneous breathing and for extubation.

In a more recent paper, Peters et al.[49] reported a further study on 49 adult cardiac surgery patients, where they showed that a combination of the parameters "Maximum Mid-Expiratory Flow" and "Maximum Expiratory Pressure" predicted correctly success or failure to wean within 24 hours in 90% of the instances. On the basis of these tests, these workers suggested that patients predicted to succeed should be weaned from ventilator support immediately on recovery from anaesthesia.

5.5. Summary

It is a widespread assumption that long-term tracheal intubation and ventilation of cardiac patients after surgery is in part responsible for the improved post-operative care achieved during the past 10 years.

However, this approach also carries some negative aspects, which have

often been ignored. Large doses of depressant drugs may be necessary to alleviate patient discomfort and to facilitate ventilatory control. Furthermore, prolonged intubation predisposes to pulmonary infection through contamination of equipment as well as via the attending staff, and may interfere with normal tracheal clearance mechanisms by disturbing ciliary movements and the cough mechanism. In fact, obstruction of the endotracheal tube or bronchi may become life-threatening, a complication particularly feared in infants and children. Thus the clinician, caught between the Scylla and Charybdis of this dilemma, is often perplexed as to when the appropriate time has come for discontinuing controlled ventilation and extubating the patient.

The feasibility of early extubation in adults is proven by the rate of successful extubation, which in our series is higher than in that previously mentioned.[49] This can also be concluded from our extensive physiological data which show that the cardiac function after surgery in these successfully extubated patients was adequate and the pulmonary function sufficiently well preserved. Indeed, at the time of writing, over 2000 adult open-heart surgery patients have been subjected to the spontaneous ventilation test while connected to the Servo 900 B ventilator in the spontaneous respiration mode. Using this facility, together with more conventional data for the appraisal of ventilation and circulation, we continue to see a rate of between 83% and 85% of patients who require no ventilatory support at all and who can be extubated uneventfully on the operating table. These results illustrate the progress that has taken place in thoracic surgery both with respect to the surgical procedure itself and the accompanying anaesthesia and intensive care.

In conclusion, it is recommended that early extubation be carried out in most patients, provided a thorough physiological analysis of cardiopulmonary function, a clinical evaluation, and the results of spontaneous ventilation testing, are consistent with this course of action.

5.6. References

1. Dammann JF, Thung N, Christlieb II et al: The management of the severely ill patient after open-heart surgery. J Thorac Cardiovasc Surg 45: 80, 1963.
2. Lefemine AA, Harken DE: Postoperative care following open-heart operations: Routine use of controlled ventilation. J Thorac Cardiovasc Surg 52: 207, 1966.
3. Thung N, Herzog P, Christlieb II et al: The cost of respiratory effort in postoperative cardiac patients. Circulation 28: 552, 1963.
4. Cooperman LH, Mann PEG: Postoperative respiratory care. A review of 65 consecutive cases of open-heart surgery on the mitral valve. J Thorac Cardiovasc Surg 53: 504, 1967.

5. Starr A, McCord CW, Wood J et al: Surgery for multiple valve disease. Ann Surg 160: 596, 1964.
6. Starr A, Herr RH, Wood JA: Mitral replacement; Review of six years' experience. J Thorac Cardiovasc Surg 54: 333, 1967.
7. Robertson DS: Tracheostomy and open heart surgery. Proc Roy Soc Med 57: 855, 1964.
8. MacRae WR, Masson AHB: Assisted ventilation in the post-bypass period. Br J Anaesth 36: 711, 1964.
9. Zeitlin GL: Artificial respiration after cardiac surgery (Some physiological considerations). Anaesthesia 20: 145, 1965.
10. Midell AI, Skinner DB, DeBoer A et al: A review of pulmonary problems following valve replacement in 100 consecutive patients: the case against routine use of assisted ventilation. Ann Thorac Surg 18: 219, 1974.
11. Prakash O, Jonson B, Meij S et al: Criteria for early extubation after intracardiac surgery in adults. Anesth Analg 56: 703, 1977.
12. Liljestrand G: Untersuchungen über die Atmungsarbeit. Skandinav Arch für Physiol 35: 199, 1918.
13. Cherniack RM: The oxygen consumption and efficiency of the respiratory muscles in health and emphysema. J Clin Invest 38: 494, 1959.
14. Otis WO: The work of breathing. In: Handbook of Physiology: Respiration, Vol. 1 (p. 463). Washington, Am Physiol Soc, 1964.
15. Gerbode F, Norlander O, Herzog P et al: Oxygen uptake during anesthesia in patients before and after total body perfusion. Ann Surg 159: 481, 1964.
16. Norlander OP, Nordén I: Intensive care of the surgical thoracic patient. Postgrad Med J 43: 268, 1967.
17. Cournand A, Richards DW Jr. et al: The oxygen cost of breathing. Trans Ass Am Phys 67: 162, 1954.
18. Sykes MK, Adams, AP, McCormick PW et al: The effect of mechanical ventilation after open-heart surgery. Anaesthesia 25: 525, 1970.
19. Holmdahl MH:son: The respiratory care unit. Anesthesiology 23: 559, 1962.
20. Björk VO, Grenvik Å, Holmdahl MH:son et al: Cardiac output and oxygen consumption during respirator treatment. Acta Anaesthesiol Scand Suppl 15: 158, 1964.
21. Clowes GHA Jr, Cook WA, Vujovic V et al: Patterns of circulatory response to the use of respirators. Circulation 31, Suppl I: 157, 1965.
22. Grenvik Å: Respiratory, circulatory and metabolic effects of respirator treatment. A clinical study in postoperative thoracic surgical patients. Acta Anaesthesiol Scand Suppl 19: 1, 1966.
23. Ellison LT, Duke III JF, Strickland GW Jr et al: Oxygen requirements in the early postoperative period (48 hours): Ventilation and respiratory exchange. Ann Surg 163: 559, 1966.
24. Thung NS, Norlander OP: Cardio-respiratory changes during anesthesia for open-heart surgery. Acta Anaesthesiol Scand 10: 79, 1966.

25. Shimizu T, Lewis FJ: An experimental study of respiratory mechanics following chest surgery. J Thorac Cardiovasc Surg 52: 68, 1966.
26. Holmdahl MH:son, Westerholm C-J: Postoperative respirator treatment. Symp. Anaesthesiologiae Internationale. Abstracta Prague, CSSR, 54, 1965.
27. Holaday DA, Israel J: Alterations of the work of respiration during anesthesia. Fed Proc 14: 74, 1955.
28. Brownlee WE, Allbritten FF Jr: The work of breathing during surgical operations. AMA Arch Surg 74: 846, 1957.
29. Gliedman ML, Siebens AA, Timmes JJ et al: Unilateral lung compliance during thoracotomy. Ann Surg 147: 494, 1958.
30. Gliedman ML, Siebens AA, Vestal BL et al: Effect of manual versus automatic ventilation on the elastic recoil of the lung. Ann Surg 148: 899, 1958.
31. Lynch S, Brand L, Levy A: Changes in lung thorax compliance during orthopedic surgery. Anesthesiology 20: 278, 1959.
32. Karlson KE, Fleischaker RJ, Pollard HS et al: The effect of volume-cycled automatic ventilation on the elastic recoil of the lung. J Thorac Cardiovasc Surg 44: 189, 1962.
33. Gold MI, Helrich M: Pulmonary compliance during anesthesia. Anesthesiology 26: 281, 1965.
34. Okinaka AJ: The pattern of breathing after operation. Surg Gynecol Obstet 125: 785, 1967.
35. Karlson KE, Seltzer B, Lee S et al: Influence of thoracotomy on pulmonary mechanics: association of increased work of breathing during anaesthesia and post operative pulmonary complications. Ann Surg 162: 973, 1965.
36. Lewis FJ, Welch JA: Respiratory mechanics in postoperative patients. Surg Gynecol Obstet 120: 305, 1965.
37. Lewis FJ, Shimizu T, Scofield AL et al: Analysis of respiration by an on-line digital computer system: Clinical data following thoracoabdominal surgery. Ann Surg 164: 547, 1966.
38. Norlander O, Herzog P, Nordén I et al: Compliance and airway resistance during anaesthesia with controlled ventilation. Acta Anaesthesiol Scand 12: 135, 1968.
39. Austen WG, Corning HB, Moran JM et al: Cardiac hemodynamics immediately following aortic valve surgery. J Thorac Cardiovasc Surg 51: 461, 1966.
40. Austen WG, Corning HB, Moran JM et al: Cardiac hemodynamics immediately following mitral valve surgery. J Thorac Cardiovasc Surg 51: 468, 1966.
41. Iribarren COS, Ekeström S: The causes of death after open-heart surgery. J Thorac Cardiovasc Surg 47: 725, 1964.
42. Provan JL, Austen WG, Scannell JG: Respiratory complications after open-heart surgery. J Thorac Cardiovasc Surg 51: 626, 1966.

43. Osborn JJ, Popper RW, Kerth WJ et al: Respiratory insufficiency following open heart surgery. Ann Surg 156: 638, 1962.
44. Ellison LT, Nix AR, Ellison RG: Pulmonary membrane injury during surgery. Surg Forum 12: 50, 1961.
45. Kontaxis A, Tomin R, Wittles B et al: Pulmonary changes secondary to prolonged perfusion. Surg Forum 12: 52, 1961.
46. Schramel RJ, Cameron R, Ziskind MM et al: Studies of pulmonary diffusion after open heart surgery. J Thorac Cardiovasc Surg 38: 281, 1959.
47. Gardner RE, Tooley W, Findlay TA: Abstract presented at Int Cardiovasc Soc, Dublin Sept 1961.
48. Hilberman M, Kamm B, Lamy M et al: An analysis of potential physiological predictors of respiratory adequacy following cardiac surgery. J Thorac Cardiovasc Surg 71: 711, 1976.
49. Peters RM, Hilberman M: Respiratory insufficiency; diagnosis and control of therapy. Surgery 70: 280, 1971.
50. Beach T, Miller F, Grenvik Å: Hemodynamic response to discontinuance of mechanical ventilation. Crit Care Med 1: 85, 1973.

CHAPTER 6

Ventilation, metabolism, and acid-base balance in profound hypothermia

6.1. Introduction and background

The concept of hypothermia as a means of reducing the metabolic rate has been known for many years. As long ago as 1798, Currie of Liverpool described the treatment of a patient with a high fever by immersion in cold water,[1] while the loss of activity of peripheral nerves at very low temperatures was made use of in the Napoleonic Wars in order to perform painless amputations of refrigerated limbs. This latter approach has been more recently revived by Allen in 1938.[2]

In 1950, Bigelow et al.,[3] and in 1951, Boerema et al.,[4] presented brilliant pioneering papers on the use of hypothermia for intrathoracic surgery. They realized that if body metabolism – especially cerebral and cardiac metabolism – could be sufficiently diminished by lowering the body temperature, the circulation could be arrested for a considerable period of time without producing any permanent damaging sequelae. The reason for this is that if the metabolism is decreased to, e.g., 10% of normal, then the oxygen demand of that organ is also reduced to around 10% of normal; it will therefore take much more time than in the normal state to become hypoxic following circulatory arrest.

Since then, profound hypothermia has increasingly been applied in surgery, especially in the repair of congenital cardiac defects in infants. In the techniques generally used nowadays, the body temperature is lowered to around 16°C, and the circulation is then arrested in order to allow up to 90 minutes of intracardiac surgery in a quiet bloodless surgical field.

However, it is not properly understood how the body utilizes oxygen and maintains the interior milieu during profound hypothermia. Because of this, there is much controversy regarding the optimal ventilation and pH control in these patients during the cooling and re-warming phases. With the availability of comprehensive monitoring equipment such as that contained in the Methodological Platform, it became feasible to study in detail some physiological features (metabolic, respiratory and circulatory) which are occurring throughout the period of disturbed body temperature produced for intracardiac surgery.

6.2. Acid-base balance during hypothermia

In 1934, Sir Joseph Barcroft[5] wrote that in all vertebrates there appears to be a direct relationship between the acid-base balance and body temperature.

Thus, despite the fact that cellular life processes might be expected to produce large unpredictable swings in hydrogen ion concentration, in fact this parameter remains remarkably constant "within narrow limits in man and other mammals". It is generally accepted that the pH in man approximates a value of 7.4.

But what is the significance of a pH value at different temperatures? Is it, in fact, the primary acid-base parameter which must be considered, or is there some more fundamental concept at work governing the cellular constancy of Claude Bernard's "milieu intérieur"? It has been recognized for some years that intracellular metabolism occurs in an acid-base environment which is not equal to electro-chemical neutrality. The latter is achieved when the relative concentrations of hydrogen and hydroxide ions are equal, and this state occurs in water at a pH of 6.8 at 37°C. It becomes apparent that at normothermic temperature at least, the acid-base state of the extracellular fluid regarded by the cells as being optimal, is some 0.6 pH units alkaline from electro-chemical neutrality.

The whole process of acid-base changes has been studied in great detail by Professor Rahn, who in 1974 wrote a comprehensive review article.[6] Rahn started by considering the pH changes occurring in blood in different parts of the body. Arterial blood leaving the heart at 37°C with a pH of 7.4 and a pCO_2 of 40 will not change its chemical composition before it arrives at the capillaries; it will thus behave up to this point in an identical fashion to blood in vitro as it is cooled or warmed.

In the skin of the hand in a cool, windy environment, the temperature may well be 25°C; at this temperature, the same blood will have a pH of 7.6 and a pCO_2 of 24. By contrast, in exercising muscles, the temperature may be 40-41°C, with a blood pH of 7.35 and a pCO_2 of 48. However, despite these profound *apparent* changes in blood acid-base balance, the total carbon dioxide content is the same and the plasma bicarbonate concentration is virtually unaltered. How can these results be compatible with an acid-base milieu that is adequate for proper cellular functioning?

A fundamental idea is to examine what happens to the pH of an electro-chemically neutral solution in water at different temperatures, since it is water in which the various electrolytes and cellular constituents are dissolved. When this is done, a surprising fact emerges:

When the pH of water is equal to pOH, water is electro-chemically neutral. It can be seen from Fig. 6.1 that pH at neutrality, i.e. pN, varies with temperature. If blood is cooled or warmed its pH will change parallel with the change in pN.[7,8] Thus, the difference of 0.6 pH units alkaline mentioned above holds equally at temperatures of 25°C and 41°C; in other words at 25°C, 37°C and 41°C, the hydrogen ion/hydroxide ion ratio in the blood is exactly the

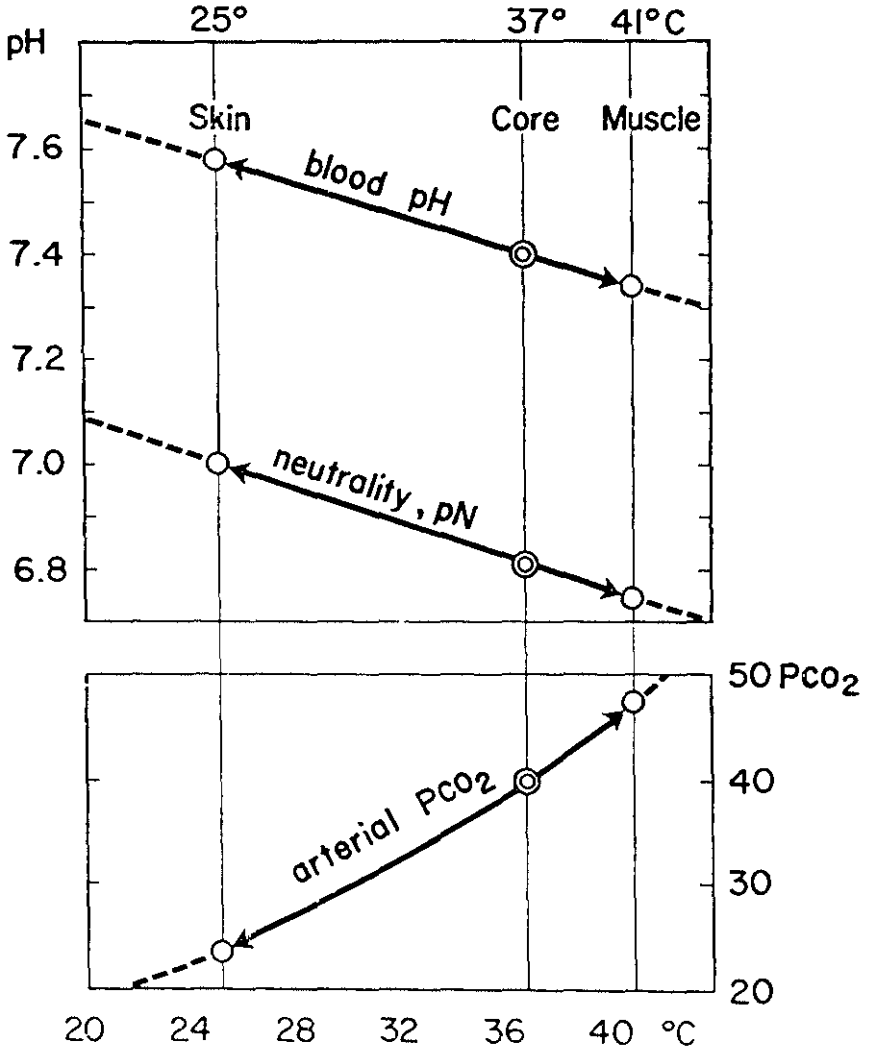


Fig. 6.1. Changes in arterial pH and P_{CO_2} as 37°C blood arrives at the skin or exercising muscle at temperatures of 25 and 41°C, respectively. Neutrality of water, pN, changes in parallel with the changes in blood pH. Thus the relative alkalinity of the blood or the ration between (OH^-) and (H^+) ion remains constant. Reproduced, with permission, from Rahn.[6]

same, namely 1:16, even though the actual pH and pCO_2 values are vastly different. All these values have been derived from the in vitro temperature effects on blood described by Kelman and Nunn[9] and Severinghaus.[10]

Thus, it might be postulated that a pH of 7.4 will only apply to an animal

whose body temperature is around 37°C, and will not be appropriate (in order to maintain the same relative alkalinity, and therefore the same net buffer dissociation charge) at different temperatures. Many of the cold-blooded animals remain subject to wide variations in body temperature. If blood samples are taken from these animals and the pH levels are plotted against temperature, then this curve is also found to run parallel to the pN curve, over a very much wider temperature range and throughout many different species maintaining the constant 0.6-0.7 pH units of alkalinity relative to pN (Fig. 6.2). Measurements of bicarbonate concentrations showed a remarkable constancy with changing temperatures, though the actual values varied from species to species. By contrast, the pCO_2 of blood is affected by temperature, in almost exactly the same way, whether in vitro or in vivo. The conclusion is that there are clearly underlying principles of acid-base regulation which have not been adequately understood in the past because they were only relevant at normothermia.

It has already been observed that the remarkable consistency of in vivo blood pH-pN difference with a concurrent stability in blood bicarbonate concentration must be achieved by an effective buffer system in the blood. Reeves,[11] in 1972, performed an elegant experiment in which he compared the pK changes of two buffer solutions with those of a solution of 20 mmol of

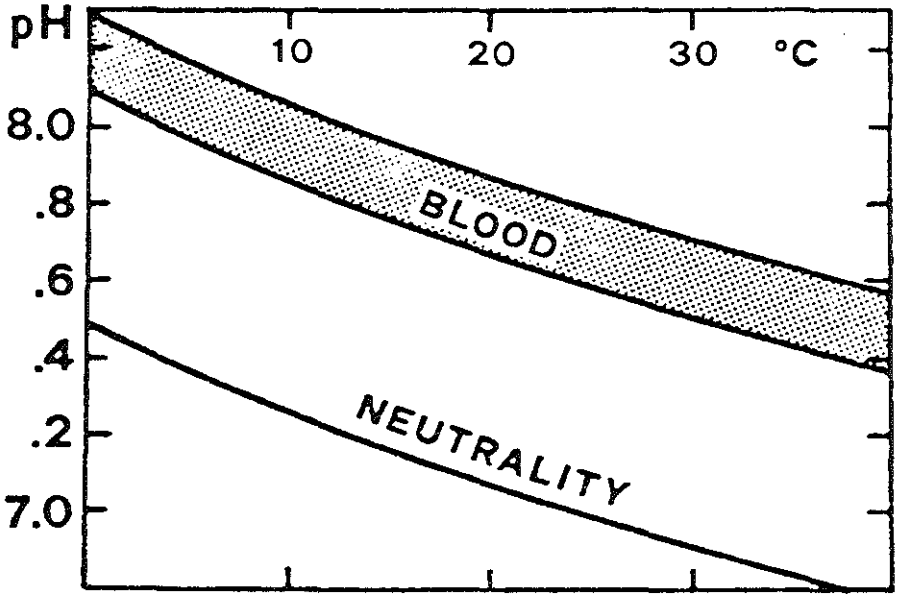


Fig. 6.2. Blood pH of ectotherms, homeotherms and the pH of neutral water as a function of body temperature.
Reproduced, with permission, from Rahn.[6]

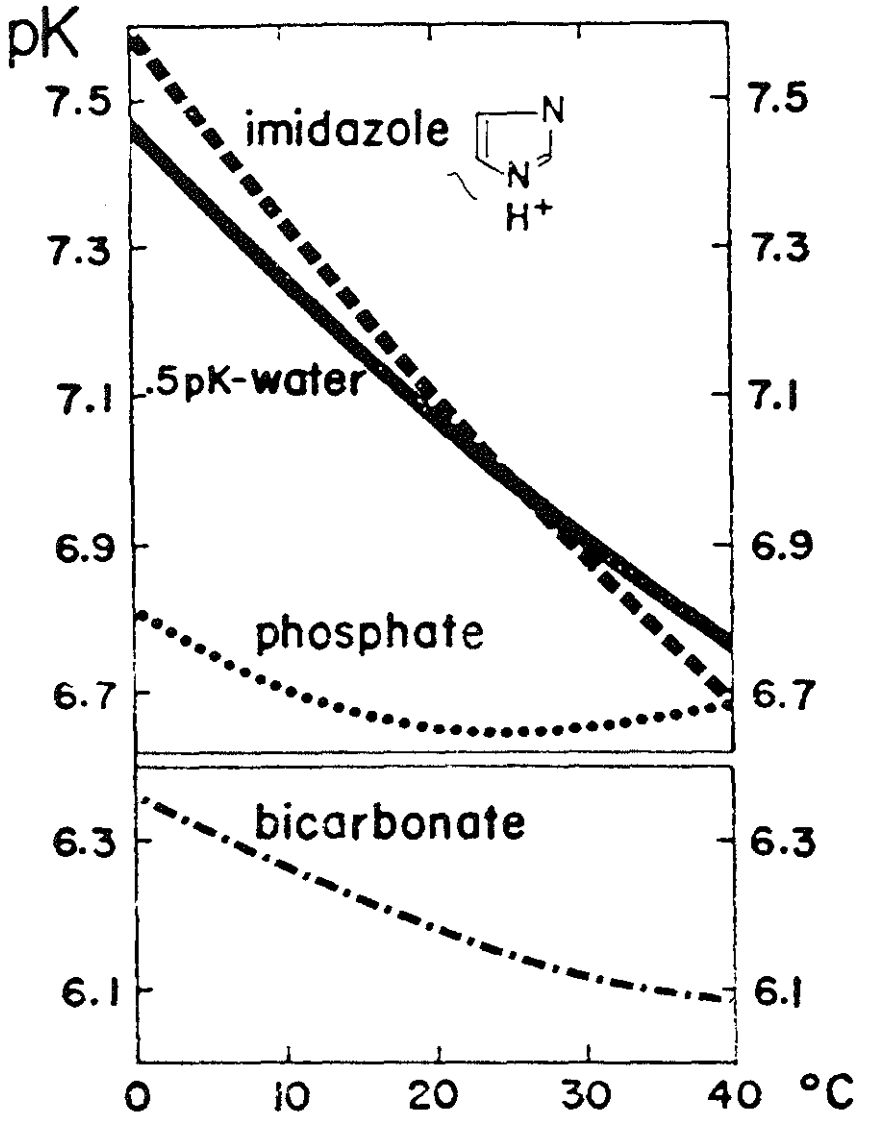


Fig. 6.3. Changes in the dissociation constants, pK' of CO_2-bicarbonate, phosphate and imidazole with temperature. The 0.5 pK of water, or neutrality, is also shown.
Reproduced, with permission, from Rahn.[6]

imidazole in water at different temperatures. He found that imidazole produced a temperature curve remarkably parallel to neutrality. This led him to propound his "imidazole alphastat hypothesis", which simply stated that the most important buffer in the extracellular fluid is the imidazole group of

peptide histidine residues, the dissociation or net charge of which remains constant at all temperatures.

In Fig. 6.3 we see that the dissociation curves of bicarbonate and phosphate alone do not run parallel to the pN curve, which is considered as being 0.5pK in this figure.

In the blood there is no other suitable buffer present in sufficient quantities. Thus, Fig. 6.3 strongly suggests that in the course of evolution a protein was selected which was able to maintain a constant net charge within the blood, and allowed the solvent to maintain a constant hydrogen/hydroxide ion ratio over a wide range of body temperatures. The intracellular pH will follow suit, since similar buffers are present within the cells and so the intracellular environment for metabolic activities is maintained very consistently at a stable acid-base balance, over a large temperature range. Further support for this concept is given by Peters and Van Slyke[12] who stated that "for a state compatible with life, the reaction of the minor fluids must be slightly to the alkaline side of the neutral point".

In the light of what has been discussed above, it is important to consider how cold-blooded animals adjust their ventilation at different temperatures in order to maintain this constant ratio between pH and pN. Reeves[11] suggested that in some way respiration was not controlled simply by brainstem pH but by a brainstem sensitive to the fractional dissociation of imidazole buffer and maintains this parameter constant at any temperature by variations in pulmonary ventilation. What happens is that, as temperature falls, there is a *relative increase* in ventilation·($\dot{V}_A/\dot{V}_{O_2}$), which causes the pH to become electrochemically more alkaline, and also counteracts the increasing solubility of carbon dioxide in the blood, whereas the volume of carbon dioxide in the blood and tissues, the Donnan ratio, and the pH-pN, all remain constant. If the ventilation fell in proportion to the fall in temperature, the observed changes would not occur, since pCO_2 would fall much less, pH would remain near 7.4, and the tissues would actually become physiologically acidotic because of the fall in pH-pN value.

What actually happens in the turtle was shown by Jackson in 1971.[13] As the animal's temperature was lowered from 30°C to 10°C, the ventilation remained almost unaltered, causing a steep fall in pCO_2 and a rise in pH. But closer examination of the blood revealed that the carbon dioxide volume store, the net charge of the imidazole buffer and the relative alkalinity (pH-pN) all remained constant. Thus, whilst by conventional concepts these animals became profoundly alkalotic at low temperatures, which is clearly paradoxical in a cold-blooded animal, once the concept of relative extracellular alkalinity is introduced, their tissues are actually seen to have maintained a normal acid-base balance.

Although at present there is not sufficient evidence to allow us to state categorically that lessons learned from cold-blooded "ancestors", and the behaviour of human blood in vitro, may be applied to man undergoing hypothermic surgery, it is nevertheless very suggestive and would seem to be an attractive and worthwhile concept to investigate.

In order to maintain a constant blood carbon dioxide content, a constant relative alkalinity and a constant charge of imidazole buffer, it would be necessary to monitor the arterial pH and/or pCO_2 and have them conform to the changes shown in Fig. 6.1. This is much easier than is at first apparent because Fig. 6.1 actually applies to the behaviour of blood in vitro. It was pointed out much earlier that if blood in an isolated environment is cooled or warmed, its actual electrochemical composition remains constant in spite of apparent changes in pH. Thus, if an arterial blood sample is taken from a patient at 25°C, the *actual* acid-base status of the blood (as appreciated by the cells) will be the same at any temperature; if the blood sample is therefore warmed to 37°C and acid-base analysis performed *without* temperature correction, the results obtained may be interpreted as though the patient's cells were also at 37°C (Rosenthal formula[14]). For example, an arterial blood sample withdrawn at 25°C, with a pH of 7.6 and pCO_2 of 24 at that temperature will after immediate re-warming to 37°C give an uncorrected pH of 7.4 and a pCO_2 of 40 mmHg; thus, the relative alkalinity of the blood in this case is *normal,* despite the fact that the actual blood pH might appear grossly *alkalotic.*

Thus, it would appear that during cooling, maintenance of a normal minute volume ventilation established at 37°C will allow the pH to rise, the pCO_2 to fall (as the metabolic rate of carbon dioxide production declines) and the all-important relative alkalinity to remain fairly constant. Additional small adjustments to ventilation will allow the correct pH for that particular temperature to be achieved, and hence the plasma bicarbonate and imidazole buffer dissociation to remain constant. In 1975, Rahn and his colleague[15] gave further support to this concept of the maintenance of pulmonary ventilation at or near normothermic levels during hypothermia in order to maintain a constant relative alkalinity.

They compared the in vivo pH and pCO_2 changes in other cold-blooded animals with the in vitro behaviour of human blood, and deduced a striking parallel in the behaviour of the two. They found that at any body temperature, the animals adjusted their ventilation so as to preserve a constant relative alkalinity, a constant tissue and blood carbon dioxide, a normal red cell to plasma Donnan ratio and, last but not least, a constant net charge of dissociation of imidazole of histidine protein buffer. This almost exactly paralleled the in vitro changes seen in human blood, as illustrated in Fig. 6.1.

In summary, we see that the problem for the cells is how to defend their

"physiological neutrality", whilst also eliminating acid metabolites and carbon dioxide. They must be provided with an aqueous environment which is relatively alkaline, pH-pN being around 0.6 pH units, and this gradient must be maintained at lower body temperatures. These requirements demand a radically different approach to artificial acid-base balancing by ventilation during induced hypothermia during cardiac surgery.

In the light of the foregoing discussion, it is now becoming possible to see the principles upon which the control of ventilation must be based in these circumstances. Accepting that the concept of relative alkalinity, and the maintenance of a constant imidazole buffer dissociation regardless of temperature, is correct, criteria for the control of ventilation by monitoring *blood* can be formulated relatively easily. This is because we are concerned primarily with the elimination of carbon dioxide from the blood and the maintenance of a constant blood and tissue carbon dioxide content. As was pointed out in earlier discussions, blood gas analysis can be performed very simply by warming the blood sample to 37°C and then interpreting the uncorrected data as if the patient's own temperature was also 37°C. It is clearly important to check this from time to time during the surgical procedure.

But for routine monitoring, use can be made of the end-tidal pCO_2, since this accurately reflects the arterial pCO_2 in normal lungs. The values obtained from these measurements at any particular temperature are then compared with those on a graph of the type shown in Fig. 6.1, which enables the relative alkalinity of the blood to be deduced immediately. The objective of the study performed at the Thorax Çentre, Rotterdam[16] was to assess the effectiveness of maintaining tissue relative alkalosis constant, simply by ventilating the patient throughout the cooling/re-warming process at the same minute volume ventilation as that producing normocapnia at 37°C. Variables reflecting total body metabolism, pulmonary function, cardiac function and acid-base balance were studied in depth in 29 infants. A paper with summary of the results and conclusions of this investigation forms the following part of this chapter.

0090-3493/78/0605-0340$02.00/0
CRITICAL CARE MEDICINE

CHAPTER 6.3

Vol. 6, No. 5
Printed in U.S.A.

Cardiorespiratory and metabolic effects of profound hypothermia

OMAR PRAKASH, MD; BJÖRN JONSON, MD; EGBERT BOS, MD; SIMON MEIJ, Msc; PAUL G. HUGENHOLTZ, MD; WILLEM HEKMAN, MD

At operation the body temperature of mechanically ventilated infants was initially decreased to 25–22°C with surface cooling and further lowered to 16°C by total body perfusion. During circulatory arrest, averaging 40 min, repair of complex intracardiac deformities was carried out. Rewarming to 36°C was achieved by 35–65 min of total body perfusion. Of 29 infants, 23 under 10 kg survived their correction: normothermic ventilation without added CO_2 was given throughout the cooling period. The following measurements were made: gas exchange, lung mechanics, heart rate, arterial pressure, right atrial pressure, cardiac output (Qt), ECG, core and nasopharyngeal temperature, as well as biochemical determinations. During surface cooling O_2 consumption (V_{O_2}), CO_2 production (V_{CO_2}), endtidal CO_2 ($P_{ET_{CO_2}}$) and $PaCO_2$ decreased proportionally and linearly with body temperature. Inspiratory resistance, total compliance, physiological dead space (V_D/V_T), and the single breath CO_2 curve did not reveal disturbed lung function. Mean arterial pressure was 98, 90, and 70 mm Hg and heart rate was 141, 107, and 76 beat/min, at temperature 35, 30, and 25°C, respectively. Cardiac index was 2.2 ± 0.2 liter/min/m² (mean ± SEM, n = 25) 2 hours after surgery. Arterial lactate reached peak values of 4.1 ± 0.3 mM/liter (n = 17), during rewarming but returned to normal. Respiratory alkalosis caused by hyperventilation during cooling caused no apparent harm. No neurological damage was observed. It is concluded that surface cooling performed with normothermic ventilation under guidance of core temperature, V_{O_2}, $P_{ET_{CO_2}}$, and V_{CO_2}, is a safe method.

During cardiac surgery, the circulation may be temporarily arrested provided metabolism is sufficiently diminished by lowering body temperature. Profound hypothermia is increasingly used by several methods, particularly in infants. However, the optimal ventilation during cooling and rewarming these infants is controversial and reflects lack of knowledge of the detailed physiological events. With the introduction of modern monitoring equipment in the operating room, it is feasible to study metabolism, respiration, and circulation throughout the time of temperature change and open heart surgery for congenital heart disease.

The present paper describes the induction of profound hypothermia together with variables reflecting total body metabolism, pulmonary function, and cardiac function in 29 infants.

MATERIALS AND METHODS

Clinical Material

The operations on 29 infants which were aimed at total correction of the defects, included: 15 ventricular septal defects, eight transpositions of the great vessels, and six tetralogies of Fallot. Details are given in Table 1.

Physiological Measurements

The Servo ventilator 900 B[1] containing transducers for airway flow and pressure was connected to the Lung Mechanics unit 940[2] and the CO_2 Analyzer 930 (all from Siemens-Elema). This system was used for ventilation and lung function studies. The lung mechanics unit gives data on compliance and inspiratory resistance of the respiratory system. The CO_2 analyzer displays six derived variables, such as endtidal CO_2 concentration ($C_{ET_{CO_2}}$ in %) and $\dot{V}_{CO_2}$. Single breath CO_2 curves are displayed on an X-Y oscilloscope (Fig. 1). $C_{ET_{CO_2}}$ was recalculated to the corresponding par-

From the Thoraxcenter, University Hospital and Erasmus University, Rotterdam, The Netherlands.
This study was supported by the Dutch Foundation for Pure Medical Research and by the Swedish National Association against Heart and Chest Diseases.
Dr. Prakash is Senior Anesthetist.
Dr. Bos is Professor of Cardiac Surgery.
Mr. Meij is Computer Engineer.
Dr. Hugenholtz is Professor of Cardiology.
Dr. Hekman is Senior Anesthetist.
Dr. Jonson is Senior Clinical Physiologist, Department of Clinical Physiology, University of Lund, Lund, Sweden.

TABLE 1. Summary of clinical data (average and range)

Diagnosis	No.	Age (mo)		Weight (kg)		Survivors
		Mean	(Range)	Mean	(Range)	
Ventricular septal defect[a]	15	8.5	(1–24)	5.7	(3.1–11)	13
Transposition of the great vessels[b]	8	7.9	(2–24)	5.7	(2.9–10.5)	6
Tetralogy of Fallot	6	13.5	(6–24)	8	(5.5–11.5)	4
Total	29	9.4 ± 7.1		6.2 ± 2.5		

[a] In three cases combined with other major defects.
[b] In three cases combined with other major defects.

tial pressure $P_{ET_{CO_2}}$ for comparisons with arterial blood gases.

The difference between O_2 in inspired and expired gas was measured by mass spectrometer (Perkin Elmer). $\dot{V}_{O_2}$ was calculated from these data and from expired volume measured with the ventilator. Airway flow and pressure, arterial and central venous pressures, and ECG were continuously recorded on a multichannel recorder (Hewlett-Packard).

Blood gas and pH in arterial blood (Pa_{O_2}, Pa_{CO_2}, and pHa) were measured intermittently at 37°C on the ABL 1 (Radiometer). The data were corrected to the temperature of the body core. Temperature was continuously measured in the nasopharynx, esophagus, and rectum. Oxygen saturation in arterial and mixed venous blood (Sa_{O_2} and $S\bar{v}_{O_2}$) was determined intermittently with hemoreflector (American Optical). Cardiac output ($\dot{Q}t$) was calculated from the Fick principle, dead space from the Bohr equation, and alveolar ventilation from the $\dot{V}_{CO_2}$ and the alveolar fraction of CO_2.

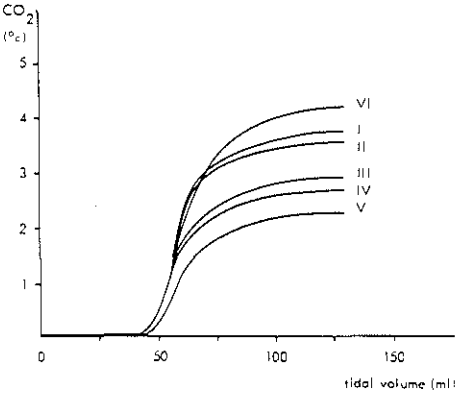


FIG. 1. CO_2 single breath curves recorded before and after surgery in an infant. I: before cooling, temp. 35.2, II, III, IV and V: during surface cooling at temp. 34.5, 32.4, 30.2 and 28.3°C, respectively. VI: after closure of the chest, temp. 37.0°C.

Anesthesia Technique

No premedication was given. Anesthesia was induced by cyclopropane in oxygen, and continued by iv injection of fentanyl (5 μg/kg) and pancuronium (0.2 mg/kg). Controlled ventilation was established with 40% oxygen and 60% nitrogen. Volume was adjusted to yield a $C_{ET_{CO_2}}$ of 4.5% at a frequency of 20 breath/min. The square wave inspiratory flow pattern was used. Thus, the ventilation adjusted at a core temperature of 36–37°C was not changed during cooling or rewarming, nor was CO_2 added to the respiratory circuit. To prevent lung collapse, 2–3 cm of H_2O of positive end expiratory pressure (PEEP) were applied after opening of the chest. No fluids were given to the patient before cardiopulmonary bypass was initiated.

Surface cooling was performed by placing the child on a cooling blanket and covering the entire body surface with plastic bags of crushed ice. During surface cooling, arterial and venous samples were taken for blood gas analysis every half hour. When the core temperature reached 30°C, the CO_2 production and $C_{ET_{CO_2}}$ were carefully observed. When these values reached 45% of initial value, i.e., at a $C_{ET_{CO_2}}$ of 2% or when the temperature was about 25°C, the chest was opened and cannulations for extracorporeal circulation performed. Heparin, 3 mg/kg, was given. The patient was then further cooled on cardiopulmonary bypass.

Extracorporeal Circulation

The extracorporeal circulation was maintained by a Sarns roller pump, a Temptrol Q 130 oxygenator and a Pall millipore blood filter in the arterial line. The circuit was primed with 1000 ml of a mixture of Haemaccel (Behring Pharma) and fresh heparinized blood. The amount of Haemaccel was adjusted to provide a perfusion hematocrit of about 30%. K^+ and HCO_3^- were added in sufficient amount to give 2 to 3 mEq/liter and HCO_3^- 20–40 mEq/liter, respectively, to the perfusate, depending on preperfusion levels. The short-term perfusion for the core cooling was continued until the rectal, esophageal and nasopharyngeal temperatures were below 16°C.

The period of total circulatory arrest averaged 40 min (range 25–90). After intracardiac repair, cardio-

pulmonary bypass was reinstituted. Perfusion for rewarming was continued until esophageal and nasopharyngeal temperatures reached 36°C. The gradient between blood and rectal temperature was maintained less than 10°C.

Physiological Observations

$\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ were strongly correlated to one another before and during surface cooling (Fig. 2). During surface cooling, $\dot{V}_{CO_2}$ fell in proportion to $\dot{V}_{O_2}$, the RQ was largely unchanged. Some of the scatter observed in Figure 2 is explained in the oscillations observed during continuous recording of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ (Fig. 3). $\dot{V}_{O_2}$ had small fluctuations with a cycle time

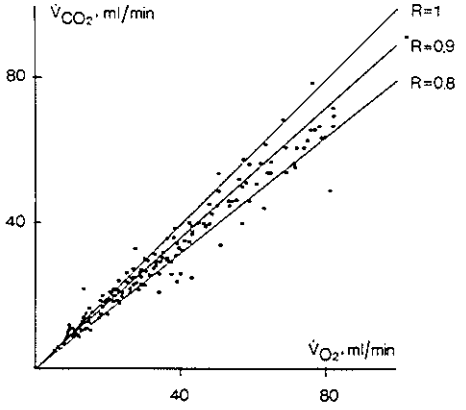


FIG. 2. O_2 uptake ($\dot{V}_{O_2}$) and CO_2 elimination ($\dot{V}_{CO_2}$) were closely related. The respiratory quotient (R) was between 0.8 and 1 in the majority of measurements.

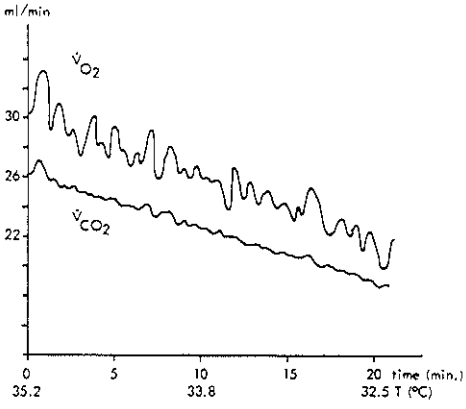


FIG. 3. This shows a continuous record of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ of an infant during surface cooling. $\dot{V}_{CO_2}$ demonstrates much less prominent oscillations than the $\dot{V}_{O_2}$ tracing.

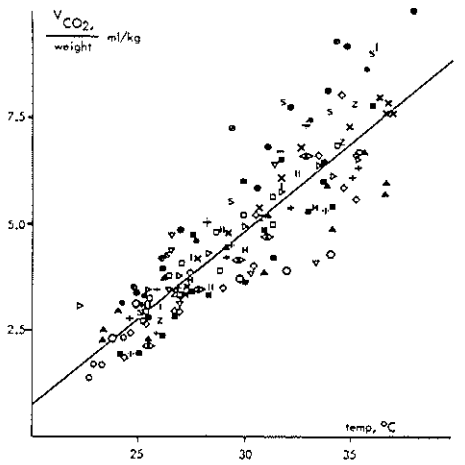


FIG. 4. CO_2 elimination/kilogram body weight plotted against the corresponding body core temperature during surface cooling. The regression line is: $\dot{V}_{CO_2}/W = 0.416 \times T - 7.573$. $\dot{V}_{CO_2}$ is given in ml/min.

of about 1 min and large fluctuations about every 5 min; $\dot{V}_{CO_2}$ fluctuated synchronously but to lesser degrees. This pattern was consistently observed. A possible explanation is that cyclical variations in aerobic metabolism were reflected in O_2 uptake but are dampened in the CO_2 curves because the larger CO_2 stores in blood act as a buffer between the sites of production and the lungs. In individual infants, $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ decreased linearly with temperature. Thus, the coefficient of correlation between $\dot{V}_{CO_2}$ and T was on the average 0.98 in 28 infants with about six sets of observation in each of them.

The $\dot{V}_{CO_2}$ and its temperature dependence can for the total material be described by the formula: $\dot{V}_{CO_2}/Wt = 0.416 \times T - 7.573$ (Fig. 4). From this equation, $\dot{V}_{CO_2}$ was calculated at 7.82 ml/kg at 37°C. The decrease of $\dot{V}_{CO_2}$ with temperature was 5.3% per °C. After chest closure at a core temperature of 35 to 36°C, the $\dot{V}_{CO_2}$ returned on the average to 41.6 ml/min as compared to 41.7 ml/min before cooling. Both measurements were made during anesthesia and at the same temperature. Before extubation, at an average of 29 hours after surgery, when the infants were awake but ventilated, the mean $\dot{V}_{CO_2}$ was 57.4 ml/min.

As a result of unchanged ventilation and a falling metabolic rate, $Paco_2$ also fell during cooling (Fig. 5); the average $Paco_2$ reduction was 1.48 ± 0.55 (SD) torr/°C. At the same time, pHa decreased linearly with temperature; this decrease averaged 0.014 ± 0.06/°C (Fig. 6). In general, $Paco_2$ values were about 3 torr higher than the corresponding $P_{ET_{CO_2}}$

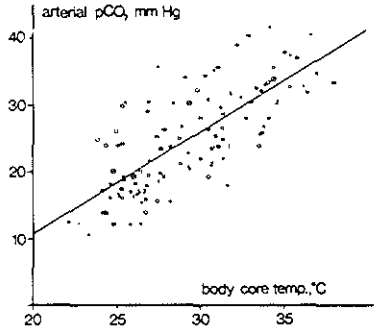


FIG. 5. Arterial P_{CO_2} data plotted against the corresponding body core temperature during surface cooling. The regression line is: $Pa_{CO_2} = 1.526 \times T - 19.86$.

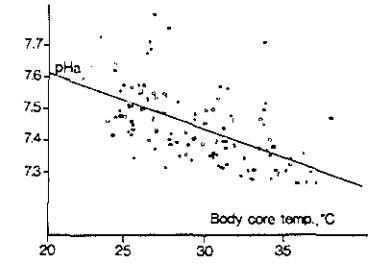


FIG. 6. Arterial pH data plotted against the corresponding body core temperature during surface cooling. The regression line is: $pHa = 7.955 - 0.017 \times T$.

values (Fig. 7). In most of the infants the difference between the two values did not change during cooling and rewarming. High arterial-endtidal CO_2 differences were associated with low arterial oxygen saturation (SaO_2) and a sizeable right to left pumonary shunt (Fig. 8).

In most cases SaO_2 values did not deviate during cooling from the initial value that was 98–99% in 12 cases, 90–98% in four and 50–90% in five. In five other cases, all transpositions, the SaO_2 increased steadily during the cooling period, i.e., from an average of 75 to 87%. In four cases, the SaO_2 fell by more than 8% during cooling (Fig. 8). Three of them had Fallot's tetralogy and one had a ventricular septal defect with pulmonary artery stenosis. The fall was sudden and pronounced at temperatures between 29 and 25°C. The fall of SaO_2 paralleled an increasing arterial-endtidal pCO_2 difference (Fig. 8). The changes in gas exchange were not associated with changes in lung mechanics or in the available hemodynamic data. In one case in which cardiac output was measured, no important change was observed. The changes in SaO_2 were attributable to varying degrees of right to left shunt. The surgery was successful in three of the children; in the two who had severe arterial desaturation, no sign of cerebral damage was observed. Lactate levels were similar to those of other infants.

In 17 of the infants lactate was measured in arterial blood every half an hour during cooling, immediately after bypass, and repeatedly during rewarming. The concentration reached a peak of 4.1 ± 1.45 (SD) mmole/liter during rewarming.

The arterial-end tidal P_{CO_2} differences did not change appreciably during cooling; this suggests that ventilation-perfusion disturbances during cooling were not severe. Single breath CO_2 curves were recorded in seven infants (Fig. 1). Apart from the falling expired P_{CO_2} amplitude, the shape of the curves did not change; their amplitudes and shapes after surgery were similar to those observed preoperatively. Physiological dead space ratios (V_D/V_T) increased slightly during surface cooling (Table 2). After surgery and

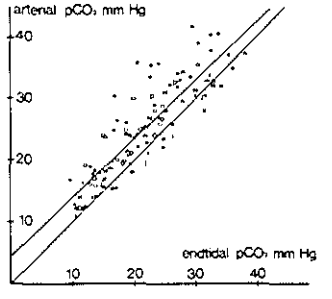


FIG. 7. Pa_{CO_2} plotted against the corresponding endtidal CO_2 concentration. Pa_{CO_2} was about 3 mm Hg higher than endtidal P_{CO_2}. Line of identity and the regression line: $Pa_{CO_2} = 4.58 + 0.939 \times P_{ET_{CO_2}}$ are drawn.

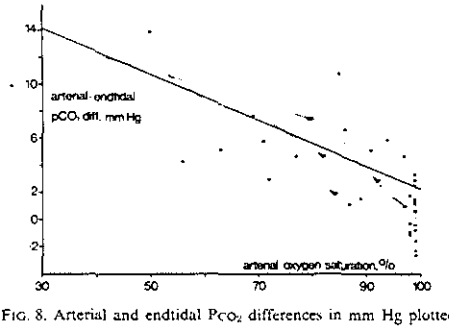


FIG. 8. Arterial and endtidal P_{CO_2} differences in mm Hg plotted against corresponding SaO_2. Open symbols—after induction of anesthesia at about 36°C. Closed symbols at about 25°C. The drawn line is the regression line of all data: $y = 19.24 - 0.17X$, $r = 0.93$. The dotted lines illustrate the fall of arterial oxygen saturation that occurred in three patients with tetrology and one with VSD at temperatures between 29 and 25°C. The fall of SaO_2 paralleled an increasing arterial—endtidal P_{CO_2} difference.

TABLE 2. Compliance and resistance of the respiratory system and dead space ratio during the period of artificial ventilation[a]

	Compliance (ml/cm H_2O)	Resistance (cm H_2O/liter/sec)	V_D/V_T (%)
After induction of anesthesia	7.6 ± 5.6	51 ± 18	51 ± 11
	$n = 29$	$n = 29$	$n = 29$
Before opening of the chest	7.1 ± 4.6	50 ± 15	58 ± 11
	$n = 28$	$n = 28$	$n = 28$
After closure of the chest	6.8 ± 3.9	47 ± 17	54 ± 10
	$n = 26$	$n = 28$	$n = 29$
Next morning	6.0 ± 2.1	41 ± 15	52 ± 10
	$n = 14$	$n = 14$	$n = 18$

[a] Significant changes were looked for with Student's *t*-test (paired comparisons). The only significant change was the V_D/V_T which increased during cooling and returned to preoperative values after surgery ($p < 0.01$).

just before extubation, V_D/V_T returned to initial values. The single breath curves and the V_D/V_T data further support the conclusion that the infants did not have further ventilation-perfusion abnormalities during the cooling and operative procedure.

Data on lung mechanics before and during cooling and after surgery are shown in Table 2. Resistance did not change, compliance fell from 7.6 ml/cm H_2O to 7.1 during surface cooling and was 6.8 after surgery; these differences were not significant. Resistance and compliance of 13 infants examined just before extubation were not significantly different from data after induction of anesthesia.

Heart rate fell in proportion to temperature, i.e., 6.5 beat/min/°C. Mean arterial pressure averaged 98 mm Hg at 35°C, 90 mm Hg at 30°C, and 70 mm Hg at 25°C. The fall in arterial pressure was more rapid in the lower temperature range.

In one patient with Fallot's tetralogy, there was a gradual decrease of $S\bar{v}O_2$ from 72 to 63% and then a sudden drop to 40%; the latter value was associated with a corresponding fall in SaO_2, probably due to an increased right to left shunt. In one patient with an ASD and VSD, $S\bar{v}O_2$ fell from 58% at 31°C to 24% at 24.8°C. The latter value was associated with a fall in cardiac index to 0.36 liter/min/m^2 during a transient circulatory disturbance at preparations for cardiopulmonary bypass.

Most infants developed a supraventricular arrhythmia at temperatures between 30 and 25°C. It is difficult to say whether these arrhythmias were associated with marked hemodynamic changes. In one case, ventricular fibrillation occurred during opening of the chest.

Six patients died in the postoperative period. In four of these patients the measurements made immediately after surgery revealed high right to left shunt with low cardiac output.

DISCUSSION

There are few reported studies of the effect of deep hypothermia on ventilation and gas exchange in infants. Yet, deep hypothermia is increasingly used in major surgical centers during the correction of congenital cardiac defects. The switch towards earlier operation in the sick child suggests that the procedure also may be increasingly utilized in newborns. Therefore, it is of interest to study cardiopulmonary physiology during deep hypothermia. The results of the present study indicate that aerobic metabolism diminished linearly with temperature in each individual infant. The decrease/°C averaged 5.3% of the value at 37°C, but the slope varied in different children. Similar degrees of reduction in aerobic metabolism have previously been reported from studies on the rat brain[1] and in dogs.[4–6] Barratt-Boyes[7] measured in children up to 1 year of age $\dot{V}O_2$ of 1.26 ml · kg^{-1} min^{-1} at 22.9°C during cold perfusion, a finding which closely agrees with the present study. It is likely that size and age of the child may be important determinants in the degree of metabolic depression. In the present series, the larger, older infants tended to have more pronounced depressions with low temperatures, but these differences were not statistically significant.

Assuming that metabolic depression with further cooling continues at the rate observed in the present cases, metabolism should arrest between 21–15°C. This temperature range was sometimes reached during the final period of cooling just before beginning extracorporeal circulation. However, clinical experience has shown that metabolism does not arrest at this level. Presumably, regulatory systems of some kind must play a role in body metabolism and permit other pathways to be utilized at low temperatures. Cellular damage during slow rewarming has been reported in dog studies.[8] Therefore, it would seem prudent to proceed to the very low temperature zones as fast as possible. This can only be achieved by means of the extracorporeal circulatory cooling system. On the other hand, the period of extracorporeal circulation should be kept as brief as possible in order to prevent hemolysis and other hematologic disorders. Surface cooling, which produces a much more uni-

form temperature depression over the entire body, is too slow a procedure to be useful for the entire operation. As a result of these conflicting considerations, both methods of cooling have been chosen in sequence, first surface cooling to 25 to 22°C, then by the pump's heat exchanger to 16°C. The experience with the present series has demonstrated that untoward events, such as long periods of hypotension, excessive pH changes or serious arrhythmias, can be avoided.

Although there is a good overall relation between temperature and $\dot{V}_{CO_2}$, the depression of the metabolic processes in a given infant could not be adequately predicted from temperature alone. It was necessary to make measurements to determine the level of metabolic depression. The metabolic rate at 25°C calculated from the individual regression lines between the temperatures and $\dot{V}_{CO_2}$ values varied between 24 and 65% of the value at 35°C. If surface cooling would have been continued to about 25°C in all infants, some might have proceeded to a dangerous metabolic depression. It has become our practice to start surgery when $\dot{V}_{CO_2}$ is 40% of the value at 35°C, independent of the temperature at that time. Since endtidal CO_2 concentrations are proportional to $\dot{V}_{CO_2}$ in the individual child, a concentration of 2% CO_2 provides the indication to begin the thoracotomy. Extracorporeal circulation should be started before the endtidal CO_2 reaches 1.5%. In cases, not in the present series, when cannulation for perfusion has been delayed, because of technical difficulties, severe arrhythmia and hypotension were observed at $P_{ET_{CO_2}}$ and $\dot{V}_{CO_2}$ of about one-third of initial values.

Transient drops of $\dot{V}_{CO_2}$ were observed with sudden circulatory disturbances. Such occurrences also indicate the need for rapid initiation of extracorporeal circulation and add to the practical value of continuous monitoring of the gas exchange. In infants without a right to left shunt, $P_{ET_{CO_2}}$ reflects closely $PaCO_2$ and can be used to adjust ventilation properly. In cases with right to left shunts, $P_{ET_{CO_2}}$ must be used with caution, as it can be misleading.

During cooling in patients with the tetralogy of Fallot and transpositions of the great vessels, the right to left shunt appears to change in opposite directions. In the latter cases SaO_2 often goes up, while in tetralogy it declines. The clinical significance of the drop of SaO_2 at the time of opening the chest in some cases with Fallot's tetralogy is not clear. In two cases it was very pronounced but occurred at temperatures at which the need for O_2 was greatly reduced. One of the two cases had a very low cardiac output after surgery and died; the other child recovered after surgery. Monitoring of SaO_2 appears to be indicated until more is known about the circulatory disturbances.

The maintenance of normothermic ventilation, i.e., a ventilation adjusted to maintain $P_{ET_{CO_2}}$ and $PaCO_2$ values at about 35 torr at 35°C produces respiratory alkalosis at lower temperatures as CO_2 was not added to the inspired gas. Potential hazards of such an alkalosis have been debated. The shift of the hemoglobin dissociation curve to the left could be disadvantageous[9] but the practical importance of this has been argued.[11]

Respiratory alkalosis causes a cerebral vascular constriction[10] and a reduction in cerebral blood flow.[11] However, metabolic studies on hypothermic rats did not indicate any change toward cerebral metabolism of hypoxic nature when blood flow decreased.[12]

The clinical experience from the present series and that of others[10, 13] does not support the view that there is a need for added CO_2 in the inhaled gas to avoid cerebral damage.

Alkalosis has been said to increase the risk for ventricular fibrillation.[9] Others[14-16] have come to the conclusion that ventricular fibrillation is prevented rather than provoked by respiratory alkalosis, and this view is supported by our experiences. A recent report has shown that coronary blood flow, left ventricular performance and aerobic metabolism of the left heart were much enhanced when arterial pH was 7.7 compared to 7.4 at a temperature of 28°C.[17] This was attributed to changes in the neutrality point towards higher values at low temperatures. Therefore, pH of 7.4 during hypothermia may be regarded as "acidosis." Circulatory data during cooling, the absence of brain, kidney and liver damage, and the low levels of lactate indicate that the alkalosis did not cause anaerobiasis or other harm in our subjects. Normothermic ventilation without added CO_2 is simple to carry out and apparently safe.

The data during surface cooling and after surgery showed that the entire procedure has little deleterious effect on lung function. Compliance just before extubation was found to be not much lower than after induction of anesthesia. V_D/V_T and the CO_2 single breath test are sensitive indices of disturbances of the ventilation perfusion ratios, but did not change much. These findings agree largely with our previously reported results in adults[18] and indicate that the so-called "ventilator lungs" or "postperfusion lungs" largely can be avoided. The remarkable preservation of the lung function is probably due to several factors besides optimal ventilation, e.g., correct volume replacement, light anesthesia, careful extracorporeal circulation, and well controlled induction of hypothermia. It is remarkable that lung function can for all practical purposes be preserved adequately even after anesthesia, hypothermia, extracorporeal circulation, exsanguination, intracardiac surgery, rewarming, and postoperative artificial ventilation.

CONCLUSIONS

Profound hypothermia by surface cooling appears to have gained a place in the treatment of infants requiring corrective cardiac surgery under one year of age and under 10 kg.

This study describes the status of metabolism, circulation and lung function down to low temperatures (25°C). It appears that valuable information can be obtained by monitoring of CO_2 concentration of expired gas. It also emphasizes the need for combining surface cooling with extracorporeal circulation to provide a uniform and nondeleterious cooling and to avoid prolonged periods of hypotension, excessive pH changes and ventricular arrhythmias at very low temperature.

In infants undergoing correction for Fallot's tetralogy, surface cooling should be performed with special caution as profound arterial hypoxia can be caused by an increasing right to left shunt at temperatures below 30°C.

Normothermic ventilation without CO_2 added to inspired gas did not cause any apparent harm and is suggested as a simple and safe method for ventilation during cooling. Lung function with respect to mechanics and gas exchange is for practical purposes fully preserved during the whole process until extubation.

ACKNOWLEDGMENTS

The excellent postoperative care by our nurses, the laboratory support and the secretarial help of Mrs. M. Roks-Wester are gratefully appreciated. Also acknowledged is the outstanding technical help of Mr. S. G. van der Borden and Mr. J. van de Kolk, our respiratory laboratory technicians.

REFERENCES

1. Ingelsted S, Jonson B, Nordström L, et al: On automatic ventilation. *Acta Anesth Scand Suppl* 47, 1972
2. Jonson B, Nordström L, Olsson SG, et al: Monitoring of ventilation and lung mechanics during automatic ventilation: A new device. *Bull Physiopathol Resp* 11:729, 1975
3. Hagerdal M, Harp J, Nilsson L, et al: The effect of induced hypothermia upon oxygen consumption in the rat brain. *J Neurochem* 24:311, 1975
4. Ishitoya T, Sato S, Dibenedetto G, et al: Oxygen consumption during surface-induced deep hypothermia under halothane anesthesia. *Ann Thor Surg* 23:52, 1977
5. Mohri H, Martin WE, Sato S, et al: Oxygen utilization during surface-induced deep hypothermia. *Ann Thor Surg* 18:494, 1974
6. Bigelow WG, Callaghan JC, Hopps JA: General hypothermia for experimental intracardiac surgery. *Ann Surg* 132:531, 1950
7. Barratt-Boyes BG, Neutze JM, et al: Complete correction of cardiovascular malformations in the first year of life. *Prog Cardiovasc Dis* 15:229, 1972
8. Niazi SA, Lewis FJ: Profound hypothermia in the dog. *Surg Gynecol Obstet* 122:98, 1956
9. Penrod KE: Cardiac oxygenation during severe hypothermia in dog. *Am J Physiol* 164:79, 1951
10. Mohri H, Dillard DH, Alvin Merendino K: Hypothermia: Halothane anesthesia and the safe period of total circulatory arrest. *Surgery* 72:345, 1972
11. Hagerdal M, Harp J, Siesjo BK: Influence of changes in arterial pCO_2 on cerebral blood flow and cerebral energy state during hypothermia in the rat. *Acta Anesth Scand Suppl* 57:25, 1975
12. Carlsson C, Hagerdal M, Siesjo BK: The effect of hypothermia upon oxygen consumption and upon organic phosphates, glycolytic metabolites, citric acid cycly intermediate and associated amino acids in rat cerebral cortex. *J Neurochem* 26:1001, 1976
13. Sato S, Vanini V, Mohri H, et al: A comparative study of the effects of carbon dioxide and perfusion rewarming on limited circulatory occlusion during surface hypothermia, under halothane and ether anesthesia. *Ann Surg* 180:192, 1974
14. Dillard DH, Mohri H, Alvin Merendino K, et al: Total surgical correction of transposition of the great arteries in children less than six months of age. *Surg Gynecol Obstet* 129:1258, 1969
15. Baum D, Dillard DH, Mohri H, et al: Metabolic aspects of deep surgical hypothermia in infancy. *Pediatrics* 42:93, 1968
16. Mohri H, Hessel EA, Nelson RJ, et al: Use of rheomacrodex and hyperventilation in prolonged circulatory arrest under deep hypothermia induced by surface cooling. *Am J Surg* 112:241, 1966
17. McConnell DH, White F, Nelson RL, et al: Importance of alkalosis in maintenance of "ideal" blood pH during hypothermia. *Surg Forum* 26:263, 1975
18. Prakash O, Jonson B, Meij S, et al: Early extubation after intracardiac surgery in adults. *Anes Analg* 56:703, 1977

6.4. Discussion

The results of this study indicate that aerobic metabolism diminishes linearly with temperature in any given individual infant. The best way to monitor this depression is not by temperature alone, but also by following the reduction in carbon dioxide production which ensues from it. This is very easily done when the principle of maintaining normothermic ventilation levels during the cooling phase is applied.

During mechanical (or spontaneous) ventilation, the blood carbon dioxide concentration that is achieved is a reflection of the balance between the volume of carbon dioxide production and alveolar ventilation. During artificial cooling the body's carbon dioxide production falls. If ventilation remains fixed at normothermic level, end-tidal carbon dioxide and $PaCO_2$ fall proportionately with the decline in carbon dioxide production.

However, the situation is complicated by the change in solubility of carbon dioxide in blood at lower temperatures. As the temperature falls, the solubility rises almost linearly; hence, for any given carbon dioxide tension, the volume of carbon dioxide dissolved rises linearly with falling temperature.

The net result of these two opposing factors is that at lower temperatures, the carbon dioxide production and elimination rates fall, as does the $PaCO_2$, but at this new lower tension, the volume of carbon dioxide dissolved in the blood is approximately the same as at normothermic temperatures and a higher $PaCO_2$. Thus, the body's carbon dioxide stores remain largely unchanged in volume at low body temperatures, provided that normothermic ventilation levels are maintained.

6.5. Summary

Profound hypothermia by surface cooling appears to have gained a place in the treatment of infants requiring corrective cardiac surgery, who are under one year of age and under 10 kg body weight.

This study describes the performance of the circulation, pulmonary function and metabolic activity during and following cooling to low temperatures (25°C and below). It appears that valuable information can be obtained by monitoring the carbon dioxide concentration in the blood. Continuous monitoring of this was found to be desirable, not only for direct control of progressive hypothermia, but also that the correct timing to begin surgery might be chosen precisely; this time was taken as the point at which the carbon dioxide production per minute or end-tidal carbon dioxide had reached 45% of its value at 35°C. It is difficult to obtain blood samples so frequently; therefore, the end-tidal carbon dioxide was monitored continuously, and this was found to be a good reflection of the arterial pCO_2, so reducing the necessity for reliance upon frequent blood-gas analysis. Thus, after induction of anaes-

thesia, ventilation was controlled so as to produce an end-tidal carbon dioxide of about 4.5 – 5.0% at normothermia.

It was found that the "end-point" of a $\dot{V}_{CO_2}$ of 45% of its value at 35°C was generally equivalent to an end-tidal carbon dioxide of about 2% absolute; this value was therefore taken as the metabolic "end-point" at which opening of the chest and cannulation of the great vessels should start.

Normothermic ventilation without the addition of carbon dioxide to the inspired gases did not cause any apparent harm at low body temperatures, and is therefore suggested as a simple and safe method of ventilatory control during cooling. Mechanical lung function and gas exchange appears for practical purposes to be fully preserved during the whole operative process until extubation; and the post-operative phase is apparently significantly improved.

The study also emphasizes that combining surface cooling with extracorporeal circulatory cooling appears to be a non-deleterious process, during which prolonged periods of hypotension are avoided, as are non-physiological pH changes and ventricular dysrhythmias.

In infants undergoing correction of Fallot's tetralogy, surface cooling should be performed with special caution, since the abrupt rise in right-to-left shunt which was seen in two patients at temperatures below 30°C could easily produce profound arterial hypoxia. This severe cardiovascular disturbance can only readily be detected by regular arterial blood-gas estimations, which should therefore be performed regularly in those patients. One should also carefully observe any sign of non-stable circulation.

6.6. References

1. Currie J: Medical reports on effects of water, cold and warm, as a remedy in fever and other febrile diseases. Liverpool, J M'Creery, 1798.
2. Allen FM: Responses to hypothermia in several species of infant mammals. Am J Physiol 166: 75, 1938.
3. Bigelow WG, Callaghan JC, Hopps JA: General hypothermia for experimental intracardiac surgery. The use of electrophrenic respirators, an artificial pacemaker for cardiac standstill, and radio-frequency rewarming in general hypothermia. Ann Surg 132: 531, 1950.
4. Boerema I, Wildschut A, Schmidt WJH et al: Experimental researches into hypothermia as an aid in the surgery of the heart. Preliminary communication. Arch Chir Neerl 3: 25, 1951.
5. Barcroft J: Features in the architecture of physiological function. Cambridge, U.K., Cambridge University Press, 1934.
6. Rahn H: Body temperature and acid-base regulation. Pneumonologie 151: 87, 1974.
7. Howell BJ, Baumgardner FW, Bondi K et al: Acid-base balance in cold-

blooded vertebrates as a function of body temperature. Am J Physiol 218: 600, 1970.
8. Rahn H: Acid-base regulation and temperature in the evolution of vertebrates. Proc Int Union Physiol Sci 8: 91, 1971.
9. Kelman GR, Nunn JF: Nomograms for correction of blood P_{O_2}, P_{CO_2}, pH, and base excess for time and temperature. J Appl Physiol 21: 1484, 1966.
10. Severinghaus JW: Blood gas calculator. J Appl Physiol 21: 1108, 1966.
11. Reeves RB: An imidazole alphastat hypothesis for vertebrate acid-base regulation: tissue carbon dioxide content and body temperature in bullfrogs. Respir Physiol 14: 219, 1972.
12. Peters JP, Van Slyke DD: Quantitative clinical chemistry; interpretations. Vol. 1, 2nd Edition. Baltimore, Williams & Wilkins, 1946.
13. Jackson DC: The effect of temperature on ventilation in the turtle, Pseudemys scripta elegans. Respir Physiol 12, 131, 1971.
14. Rosenthal TB: The effect of temperature on the pH of blood and plasma in vitro. J Biol Chem 173: 25, 1948.
15. Rahn H, Baumgardner FW: Temperature and acid-base regulation in fish. Respir Physiol 14: 171, 1972.
16. Prakash O, Jonson B, Bos E et al: Cardiorespiratory and metabolic effects of profound hypothermia. Crit Care Med 6: 340, 1978.

CHAPTER 7

The application of the Methodological Platform in a study of an anaesthetic regimen

7.1. Introduction and background

Induction of anaesthesia may lead to a depression of myocardial function, and if this causes the diastolic pressure to fall sufficiently, a critical impairment in myocardial oxygen delivery can result. This is particularly a problem in patients who already have their myocardial performance compromised by ischaemic heart disease. On the other hand, induction of anaesthesia by most of the "traditional" methods (intravenous barbiturates or gaseous inhalation techniques) generally causes an outpouring of catecholamines from the adrenal cortex, which in turn will lead to a large increase in cardiac work and hence myocardial oxygen demand; this increased demand may also not be met in a patient with ischaemic heart disease. These problems are particularly seen in patients who present for coronary artery bypass graft surgery, since by definition their myocardial blood flow is critically reduced by the pathological process at which the surgery is aimed.

An investigation was therefore instituted to examine the cardiac, vascular, and perceptive performance of the short-acting narcotic drug fentanyl when it was used as the sole agent, or in conjunction with nitrous oxide in oxygen, for the institution and maintenance of anaesthesia for coronary artery surgery. Use was made of most of the different monitoring tools which form the framework of the Methodological Platform; in particular, use was made of blood gas analysis equipment, a mass spectrometer to determine accurately inspired and mean expired gas concentrations, a reflection oximeter to measure arterial and mixed venous oxygen saturations, and a colorimeter to determine haemoglobin concentrations. Cardiovascular measurements included the systematic arterial pressure, the pulmonary artery pressure, using a trans-venous pulmonary artery catheter, and the electrocardiogram. In about 25% of cases, a pulmonary artery thermodilution catheter was also inserted in order to measure cardiac outputs and cardiac index.

CHAPTER 7.2

HAEMODYNAMIC AND BIOCHEMICAL VARIABLES AFTER INDUCTION OF ANAESTHESIA WITH FENTANYL AND NITROUS OXIDE IN PATIENTS UNDERGOING CORONARY ARTERY BY-PASS SURGERY

O. PRAKASH, P.D. VERDOUW, J.W. DE JONG, S.H. MEIJ, S.G. VAN DER BORDEN, K.M. DHASMANA AND P.R. SAXENA

ABSTRACT

The effects on the haemodynamic and biochemical parameters of three different anaesthetic induction regimes, namely fentanyl (4.1 $\mu g \cdot kg^{-1}$ or 15 $\mu g \cdot kg^{-1}$) plus 60 per cent nitrous oxide with oxygen and fentanyl 15 $\mu g \cdot kg^{-1}$ plus 60 per cent nitrogen with oxygen, were studied in patients undergoing coronary artery surgery. Fentanyl 15 $\mu g \cdot kg^{-1}$ with nitrous oxide and oxygen produced simultaneous reductions in oxygen uptake, cardiac index and left ventricular stroke work with an unaltered oxygen extraction. Diastolic blood pressure (an index of coronary artery perfusion) was only slightly reduced, and there were no changes in arterial lactate, glucose and free fatty acids. The lower dose of fentanyl (4.1 $\mu g \cdot kg^{-1}$) with nitrous oxide produced no haemodynamic changes but decreased the oxygen uptake and extraction. The patients receiving fentanyl 15 $\mu g \cdot kg^{-1}$ with nitrogen and oxygen showed increases in heart rate, blood pressure, cardiac index and left ventricular stroke work, together with a significant fall in oxygen extraction. Moreover, in the patients who received fentanyl 4.1 $\mu g \cdot kg^{-1}$ with nitrous oxide and oxygen and fentanyl 15 $\mu g \cdot kg^{-1}$ with nitrogen and oxygen there were significant increases in blood lactate, glucose and free fatty acids, indicating increased sympathetic activity. We conclude that fentanyl 15 $\mu g \cdot kg^{-1}$, together with 60 per cent nitrous oxide with oxygen provides a satisfactory haemodynamic and biochemical state during induction of anaesthesia in patients with myocardial function prejudiced by coronary artery insufficiency.

FENTANYL IS WIDELY USED as a narcotic analgesic for cardiovascular anaesthesia. The drug is usually given in combination with other anaesthetic agents since, when given alone, fentanyl can enhance the activity of the adrenergic nervous system.[1] However, recent studies have shown that high doses of fentanyl, up to 160 $\mu g \cdot kg^{-1}$, neither depress myocardial performance nor increase whole body oxygen consumption in dogs[2] and produce adequate anaesthesia in man.[3,4] On the other hand, Verdouw, de Jong, Merin and Schamhardt[5] have reported elevated arterial free fatty acid (FFA) levels in swine given fentanyl 50 $\mu g \cdot kg^{-1}$; this might be considered undesirable in view of the evidence that free fatty acid utilization by the heart may be harmful during ischaemia, especially when accompanied by elevated sympathetic activity.[6]

O. Prakash, M.D., P.D. Verdouw, Ph.D., J.W. de Jong, Ph.D., S.H. Meij, M.Sc., S.G. van der Borden, B.Sc., K.M. Dhasmana, M.D., P.R. Saxena, M.D. Department of Anaesthesia and Cardiovascular Research, Thoraxcentrum, University Hospital and Department of Pharmacology, Erasmus University Rotterdam, P.O. Box 1738, Rotterdam, The Netherlands.

Correspondence: O. Prakash, Consultant Anaesthetist, Thoraxcentrum, Erasmus University, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands.

In the present study, we have examined the haemodynamic and metabolic variables in patients during routine induction of anaesthesia for coronary artery by-pass surgery. The effect on these variables of fentanyl in combination with nitrous oxide or nitrogen and oxygen has been studied against a background of neuromuscular blockade with pancuronium, to evaluate the cardiovascular suitability of the drug in patients with coronary artery disease.

METHODS

Seventy-four patients were studied during induction of anaesthesia for coronary artery by-pass surgery (Table I). Twenty-five patients (Group I) received fentanyl 4.1 $\mu g \cdot kg^{-1}$ and were ventilated with a mixture of 60 per cent nitrous oxide and 40 per cent oxygen. The remaining 49 patients received fentanyl 15 $\mu g \cdot kg^{-1}$. Twenty-seven of these patients (Group II) were ventilated with 60 per cent nitrous oxide with oxygen, whereas 22 patients received a mixture of 60 per cent nitrogen with oxygen (Group III). All patients were premedicated 1–2 hours before operation with Opial (10–15 mg) and atropine sulphate 0.25 mg and received an intravenous infusion of NaCl 0.9 per cent (200 ml) during the period of the

TABLE I

Patient Data

	Group I	Group II	Group III
Gas mixture Fentanyl	N_2O 60%/O_2 40% 4.1 $\mu g \cdot kg^{-1}$	N_2O 60%/O_2 40% 15 $\mu g \cdot kg^{-1}$	N_2 60%/O_2 40% 15 $\mu g \cdot kg^{-1}$
Number of patients	25	27	22
Age (years)			
range	39–67	37–66	33–59
median	49	50	52
Weight (kg)	75 ± 2	75 ± 2	76 ± 2
Number of coronary by-passes per patient	2.6 ± 0.3	2.5 ± 0.2	2.9 ± 0.2

study. Digitalis, diuretics and β-adrenergic blockers were withheld for at least 48 hours before operation.

General Preparation

Before the induction of anaesthesia, a 17 gauge Sorensen catheter was inserted percutaneously into the radial or brachial artery in all patients, under local anaesthesia. This catheter was used for the determination of blood pressure and for the withdrawal of arterial blood samples for determination of blood gases (ABL-2, Radiometer, Copenhagen), lactate, glucose, free fatty acid (FFA) and potassium. Another catheter was inserted in a forearm vein for the administration of drugs. Electrodes were connected for the recording of the electrocardiogram (Lead V5) and the heart rate was derived from electrocardiograph signals. In addition, a 7F Swan Ganz thermodilution catheter was guided into the pulmonary artery through the right internal jugular vein in 21 of the 74 patients (seven in each group), for cardiac output measurements and for the collection of mixed venous blood samples. Arterial and mixed venous oxygen saturations (So_2) were determined with a reflector oximeter (American Optical Co., Bedford, Mass., U.S.A.). The haemoglobin concentration of arterial blood was measured with a Vitatron Colorimeter (Meyvis & Co., Bergen op Zoom, The Netherlands), and oxygen content (Co_2) of the blood was calculated by the formula: Co_2 (vol %) = $(So_2(\%)/100) \cdot Hb$ $(g\%) \cdot 1.39 + 0.0031 \cdot Po_2$ (mmHg).

For each cardiac output value (converted into cardiac index: CI, $l \cdot min^{-1} \cdot m^{-2}$), an average of three separate measurements were made. Cardiac output in these patients was also calculated after the induction of anaesthesia by Fick's principle from oxygen uptake measured with a mass spectrometer (Perkin Elmer MGA 1100, Pomona, Calif., U.S.A.) during anaesthesia. These values correlated well with the cardiac output measured simultaneously using the thermodilution technique (Spearman rank correlation coefficient of 0.81; $P < 0.001$; $n = 23$).

Biochemical Analysis

Standards and arterial blood samples were prepared for assays as previously described.[7,8] Plasma glucose and potassium were assayed with an Auto-Analyser (Technicon Instruments Corporation, Tarrytown, N.Y., U.S.A.). Lactate was determined enzymatically in deproteinized samples.[9] Serum free fatty acids were measured[10,11] with a Titrigraph (Radiometer, Copenhagen, Denmark).

Experimental Protocol

Baseline (control) measurements of haemodynamic and biochemical variables were obtained 15–20 minutes after the insertion of the cannulae, during the awake period. After all the baseline data had been obtained, induction of anaesthesia with fentanyl was initiated. The appropriate dose of fentanyl was administered slowly into the peripheral venous line over a period of three minutes. In addition, pancuronium bromide (Pavulon®) 90 $\mu g \cdot kg^{-1}$ was given to facilitate tracheal intubation and subsequent artificial ventilation with nitrous oxide (or nitrogen) with oxygen, using a servoventilator (model 900 B, Siemens-Elema, Solna, Sweden). In the 21 patients in whom a Swan Ganz catheter was inserted, heart rate and arterial (systemic and pulmonary) pressures were measured at 5, 10 and 25 minutes after administration of fentanyl. Finally, in all patients, the haemodynamic measurements were made and arterial blood was withdrawn for

TABLE II

HEART RATE AND ARTERIAL PRESSURES DURING BASELINE (CONTROL) PERIOD AND 35 MINUTES AFTER INDUCTION OF ANAESTHESIA

Haemodynamic variable	Baseline value† n = 74	% Change from baseline after induction of anaesthesia: Fentanyl 4.1 μg·kg⁻¹ + N_2O/O_2 Group I n = 25	Fentanyl 15 μg·kg⁻¹ + N_2O/O_2 Group II n = 27	Fentanyl 15 μg·kg⁻¹ + N_2/O_2 Group III n = 22
Heart rate (beats/min)	71 ± 3	4 ± 3	−2 ± 5	30 ± 5*
Arterial pressure (kPa)				
systolic	19.2 ± 0.4	−7 ± 4	−18 ± 2*	4 ± 4
diastolic	10.6 ± 0.2	−5 ± 5	−8 ± 3*	12 ± 4*
mean	13.8 ± 0.3	−6 ± 4	−12 ± 2*	7 ± 3*
pulse	8.6 ± 0.3	−9 ± 6	−30 ± 2*	−3 ± 6

†Baseline data of three groups have been combined.
*Significant ($P < 0.05$, paired t-test) change from the baseline value in the corresponding patients.

biochemical analyses 35 minutes after administration of fentanyl. During this 35-minute period no surgical stimuli were given to the patients.

Presentation of Data and Statistical Analysis

All data are presented in the text as means ± standard error of the mean (S.E.M.). The effects of fentanyl with nitrous oxide or nitrogen with oxygen have been expressed separately in the three groups as percentage changes from the baseline value in each individual patient. However, for the sake of clarity, the baseline values of haemodynamic and biochemical variables in the three groups have been combined. The effects of the anaesthetic schedules were evaluated statistically using the two-tailed paired t-test.[12] P-values of 0.05 or less were considered significant.

RESULTS

Clinical Assessment

During the 35-minute experimental period, electrocardiographic abnormalities (ST segment depression) were observed mainly in Group III patients. All patients underwent uneventful surgical procedures and regained consciousness within one hour after termination of anaesthesia. The use of a narcotic reversal agent or postoperative mechanical ventilation was not required in any of these patients.

Arterial Blood Gas Tensions

During ventilation, shortly after induction had been completed, there was a slight increase in Pa_{O_2} and a slight decrease in Pa_{CO_2} in all three groups. This resulted in a slight decrease in cH^+ (increase in pH). However, all blood gas values remained within the normal range during the entire experimental period: cH^+ 44.67–35.48 nmol/l (pH 7.35–7.45); P_{CO_2} 4.7–6.0 kPa (35–45 mmHg); P_{O_2} 12–20 kPa (90–150 mmHg).

Haemodynamic Changes

The effect of induction of anaesthesia by fentanyl (with or without nitrous oxide) on the heart rate and blood pressure is shown in Table II. While the heart rate remained unchanged in Groups I and II, fentanyl 4.1 and 15 μg·kg⁻¹ with nitrous oxide and oxygen, it was increased in the patients belonging to Group III, fentanyl 15 μg·kg⁻¹ with nitrogen and oxygen. The mean arterial pressure decreased from its baseline value in Group II (12 per cent), mainly due to a fall in systolic pressure (18 per cent), since the diastolic pressure dropped by only 8 per cent. In Group III, mean (7 per cent) and diastolic (12 per cent) pressures increased significantly, while no changes were observed in Group I patients.

A more extensive examination of the haemodynamic variables was carried out in 21 patients (seven in each group). Apart from the measurements of ventricular haemodynamic data and heart rate, systemic and pulmonary arterial pressures were also recorded at intervals of 5, 10 and 25 minutes after administration of fentanyl. While no major changes were observed in the patients of Group II, heart rate did increase in Groups I and III. The rate returned to control (baseline) values after 10–25 minutes in Group I, but remained at a higher level in Group III pa-

TABLE III

HAEMODYNAMIC AND RESPIRATORY DATA BEFORE AND AFTER INDUCTION OF ANAESTHESIA IN 21 PATIENTS (7 in each group)

		% change from baseline after induction of anaesthesia		
	Baseline value† n = 21	Fentanyl 4.1 $\mu g \cdot kg^{-1}$ + N_2O/O_2 Group I n = 7	Fentanyl 15 $\mu g \cdot kg^{-1}$ + N_2O/O_2 Group II n = 7	Fentanyl 15$\mu g \cdot kg^{-1}$ + N_2/O_2 Group III n = 7
Heart rate (beats/min)	65 ± 3	12 ± 8	5 ± 7	41 ± 9*
Mean arterial pressure (kPa)	14 ± 0.5	15 ± 9	−10 ± 3*	23 ± 8*
Cardiac index ($l \cdot min^{-1} \cdot m^{-2}$)	3.6 ± 0.2	3 ± 16	−14 ± 8	30 ± 17
Stroke volume index ($cm^3 \cdot m^{-2}$)	56 ± 4	−11 ± 9	−15 ± 9	−13 ± 8
Systemic vascular resistance ($kPa \cdot s \cdot m^{-3}$)	13 ± 1	8 ± 6	6 ± 13	−1 ± 18
Left ventricular stroke work (J)[1]	1.5 ± 0.1	−1 ± 17	−23 ± 8*	15 ± 8
Left ventricular O_2 demand (Pa/min)[2]	1.3 ± 0.1	28 ± 16	−11 ± 7	72 ± 20*
O_2 uptake ($cm^3 \cdot min^{-1} \cdot m^{-2}$)[3]	139 ± 7	−24 ± 6*	−21 ± 9*	−16 ± 9
O_2 extraction[4]	0.21 ± 0.01	−29 ± 5*	−6 ± 7	−40 ± 4*

1, Calculated as: stroke volume (cm^3) × Mean arterial pressure (mmHg) × 0.00014. 2, Calculated as the double product: systolic artery pressure × heart rate. 3, Total body O_2 uptake = cardiac index × (C_{O_2} art − C_{O_2}) mixed venous). 4, Defined as (C_{O_2} art − C_{O_2} mixed venous)/C_{O_2} art.

†Baseline data of the three groups have been combined.

*Significant ($P < 0.05$, paired t-test) change from the baseline value in the corresponding patients.

tients. In each group the systemic arterial pressure increased slightly immediately after the tracheal intubation (t = 5 min) and then returned to baseline values in Group I, decreased below the baseline value in Group II and increased further in Group III patients. The pulmonary arterial pressure changed little in the first two groups but was slightly elevated at all measurement periods in the last group. Table III shows a number of haemodynamic and respiratory variables before and 35 minutes after induction of anaesthesia. Opposite effects on cardiovascular function were observed in the patients who received fentanyl 15 $\mu g \cdot kg^{-1}$ when nitrous oxide was replaced by nitrogen (compare Group II and III). This was most pronounced in the mean arterial blood pressure and cardiac index, which showed a decrease of 10–14 per cent in Group II and an increase of 23–30 per cent in Group III. The decrease in cardiac index and left ventricular stroke work in Group II did not result in impaired oxygen supply, since total body oxygen extraction did not change (Table III). On the other hand, oxygen extraction decreased by 40 per cent ($P < 0.001$) compared to the awake value in Group III. In addition, there was a marked increase in myocardial oxygen demand calculated as double product systolic arterial pressure × heart rate. When the lower dose of fentanyl (Group I) was administered in combination with nitrous oxide no significant haemodynamic changes were seen (Table II). However, there was a remarkable decrease in total body oxygen uptake and extraction.

Biochemical Changes

The effects of the different anaesthetic schedules on the biochemical variables are shown in Table IV. It is to be noted that the glucose values in the control period are relatively high but are comparable to those reported by others in patients with coronary heart disease.[8,13,14] Several factors may have contributed to the increased level of glucose in our patients. For example, total opium alkaloid (Opial), given in the pre-anaesthetic phase, contains 66 per cent

TABLE IV

BIOCHEMICAL VARIABLES BEFORE AND AFTER ANAESTHESIA WITH FENTANYL

Biochemical variables	Baseline value† $mol \cdot m^{-3}$ n = 52	% change from baseline after induction of anaesthesia: Fentanyl 4.1 $\mu g \cdot kg^{-1}$ + N_2O/O_2 Group I n = 18	Fentanyl 15 $\mu g \cdot kg^{-1}$ + N_2O/O_2 Group II n = 19	Fentanyl 15 $\mu g \cdot kg^{-1}$ + N_2/O_2 Group III n = 15
Lactate	0.41 ± 0.02	45 ± 11*	−4 ± 5	118 ± 34*
FFA	1.06 ± 0.05	20 ± 11	−1 ± 4	40 ± 8*
Glucose	6.7 ± 0.2	22 ± 7*	1 ± 2	23 ± 6*
Potassium	4.3 ± 0.1	−3 ± 2	−5 ± 1*	−9 ± 2*

†Baseline data of the three groups have been combined.
*Significant ($P < 0.05$, paired t-test) change from baseline value in the corresponding patients.

morphine, which raises the blood glucose level.[15,16] Similarly, withdrawal of beta-blockers[17] and stress[18,19] before operation may also increase blood glucose levels.

Increases in arterial lactate (118 per cent), free fatty acids (40 per cent) and glucose (23 per cent) were found in the patients of Group III (the group without nitrous oxide), whereas no such changes could be detected in patients of Group II (Table IV). However, with the low dose of fentanyl in combination with oxygen and nitrous oxide (Group I) a significant increase in lactate and glucose was again seen, without significant changes in the free fatty acid level. A small decrease in arterial serum potassium concentration was found in Groups II and III (Table IV).

DISCUSSION

Anaesthetic agents may have diverse effects on metabolic and hormonal activity. One group of drugs (e.g. halothane) may increase the blood levels of glucose, cortisol and lactate[20] while decreasing levels of catecholamines.[21] Other agents, such as fentanyl, may increase the activity of the adrenergic system, thereby causing enhanced excretion of catecholamines in urine[22] and, presumably, increased concentration in the blood as well. Since an increase in sympathetic activity potentially could lead to serious complications during anaesthesia in patients undergoing surgery for ischaemic heart disease, a knowledge of the haemodynamic and biochemical effects of the anaesthetic regimes used is particularly essential.

When fentanyl 15 $\mu g \cdot kg^{-1}$ was administered to patients without nitrous oxide (Group III), both haemodynamic and biochemical effects, consisting of tachycardia, hypertension, enhanced left ventricular oxygen demand and elevated blood levels of lactate, free fatty acids and glucose, indicate an increase in sympathetic nervous system activity probably due to "unbalanced" anaesthesia. A lower dose of fentanyl (4.1 $\mu g \cdot kg^{-1}$) given with nitrous oxide (Group I) had no haemodynamic effects but produced biochemical changes similar to those in Group III. However, when the patients were given fentanyl 15 $\mu g \cdot kg^{-1}$ together with nitrous oxide (Group II), no changes in the blood levels of lactate, free fatty acids and glucose occurred and the blood pressure fell only moderately. The slight decrease in cardiac index in Group II appears to have been due to the addition of nitrous oxide, since the cardiac index tended to increase in Group III in which the same dose of fentanyl was given without nitrous oxide. The changes in the left ventricular work paralleled those in the cardiac index and, despite the slight decrease in cardiac index in Group II, overall oxygen supply was adequate because total body extraction remained unchanged after the administration of fentanyl 15 $\mu g \cdot kg^{-1}$ in combination with the inhaled nitrous oxide and oxygen mixture.

The decrease in the total body oxygen uptake in all three groups of patients was apparently secondary to a diminution of the metabolic rate during the anaesthetic state resulting from fentanyl and nitrous oxide.[23,24] Group III patients, in whom the myocardial oxygen demand increased (as suggested by the changes in the heart rate, cardiac output and blood pressure) exhibited a reduction in total oxygen uptake probably for two reasons. First, in the patients with coronary artery disease, increased myocardial oxygen demand may not have been accompanied by an adequate increase in oxygen supply, thus leading to myocardial ischaemia. A retrospective examination of the available electrocardiographic

records confirmed that 9 out of 11 patients in Group III exhibited ischaemic electrocardiogram changes (ST depression) in the 35-minute observation period. One out of three in Group I and only two of 17 patients in Group II showed these changes in the corresponding period. The second and perhaps more important reason for the decrease in total body oxygen uptake in the presence of a possible increase in myocardial oxygen consumption (MVO_2) is that the latter (MVO_2 changes) would be dissipated by the former (total body oxygen uptake changes) since, normally, the heart consumes only 8–10 per cent (20–25 ml/min^{-1})[26] of the amount of oxygen used by the body. The marked decrease (40 per cent) in oxygen extraction in Group III patients was apparently due to reduced total body oxygen uptake coupled with a high cardiac output.

The data reported in the present investigation suggest that, from both haemodynamic and biochemical viewpoints, a combination of fentanyl 15 $\mu g \cdot kg^{-1}$ and nitrous oxide with oxygen provides adequate and "balanced" anaesthesia, while, at the same time, this anaesthetic regimen significantly reduces any tendency to increased left ventricular work. This combination also maintains an adequate oxygen supply and provides a satisfactory coronary artery perfusion pressure. These cardiovascular effects may well be beneficial for the patients undergoing coronary artery surgery during which a stress-free induction of anaesthesia is so essential. Moreover, the lack of a rise in free fatty acids indicates the absence of a further potential hazard for these patients.

Recently, Stanley and coworkers[3,4] have demonstrated that large doses of fentanyl (50–100 $\mu g \cdot kg^{-1}$) can be used as the sole anaesthetic without deleterious cardiovascular changes in patients with coronary artery disease. When such doses were used in combination with nitrous oxide in female patients undergoing tubal surgery, no abnormal metabolic and hormonal responses were seen but apnoea requiring urgent ventilation and administration of naloxone was encountered in a few cases.[20] It seems that larger doses of fentanyl (50–100 $\mu g \cdot kg^{-1}$) could also be used safely in cardiac surgery, but one has to be on the lookout for potential respiratory hazards, particularly when these doses are used in conjunction with another anaesthetic agent.

Finally, we ought to focus attention on some limitations of our study, which was carried out during routine surgery. All patients received premedication about 1.5 hours before transportation to the surgical theatre and the patients had tracheal intubation and received pancuronium to facilitate intubation. Although pancuronium may have interfered with the changes in heart rate[27,28] and blood K^+ levels,[29] our study does provide adequate information for a clinical setting.

ACKNOWLEDGEMENTS

The authors are grateful to Marlys Stewart, Wout Breeman, Jaap Deckers, M.Sc. for expert technical assistance. We also thank all nurses in the anaesthetic and post-operative unit for their cooperation and Louise van Solkema for her assistance in the preparation of the manuscript.

J.W. de Jong is an established investigator for the Dutch Heart Foundation, which supported part of this study.

REFERENCES

1. DE CASTRO, J. Neuroleptanalgésie et système adrenergique. Ars Med. *1*: 69 (1970).
2. FREYE, E. Cardiovascular effects of high dosages of fentanyl, meperidine and naxolone in dogs. Anaesth. Analg. Curr. Res. *53*: 40 (1974).
3. LUNN, J.K., WEBSTER, L., STANLEY, T.H., EISELE, J. & WOODWARD, A. Fentanyl blood levels during high dose fentanyl anesthesia in man: Correlation with cardiovascular effects. Abstract Amer. Soc. Anesth. Ann. Meeting. p. 583 (1978).
4. STANLEY, T.H., PHILBIN, D.M. & COGGINS, C.H. Fentanyl oxygen anaesthesia for coronary artery surgery: cardiovascular and antidiuretic hormone response. Canad. Anaesth. Soc. J. *26*: 168 (1978).
5. VERDOUW, P.D., DE JONG, J.W., MERIN, R.G. & SCHAMHARDT, H.C. Influence of different anesthetics on myocardial performance and metabolism. J. Mol. Cell. Cardiol. Supp. *9*: 60 (1977).
6. SIMONSON, S. & KJEKSHUS, J.K. The effect of free fatty acids on myocardial oxygen consumption during atrial pacing and catecholamine infusion in man. Circulation *58*: 484 (1978).
7. DE JONG, J.W., VERDOUW, P.D. & REMME, W.J. Myocardial nucleoside and carbohydrate metabolism and hemodynamics during partial occlusion and reperfusion of pig coronary artery. J. Mol. Cell. Cardiol. *9*: 297 (1977).
8. REMME, W.J., DE JONG, J.W. & VERDOUW, P.D. Effects of pacing-induced myocardial ischemia on hypoxanthine efflux from the human heart. Am. J. Cardiol. *40*: 55 (1977).
9. APSTEIN, C.S., PUCHNER, E. & BRACHFIELD, N. Improved automated lactate determination. Anal. Biochem. *38*: 20 (1970).
10. DOLE, V.P. & MEINERTZ, H. Microdetermination of long-chain fatty acids in plasma and tissues. J. Biol. Chem. *235*: 2595 (1960).
11. TROUT, D.L., ESTES, E.H. JR. & FRIEDBERG, S.J. Titration of free fatty acids in plasma. A study of current methods and a new modification. J. Lipid Res. *1*: 199 (1960).

12. COLTON, T.H. Statistics in Medicine. Boston: Little, Brown Co. (1974).
13. MOST, A.S., GORLIN, R. & SOELDNER, J.S. Glucose extraction by the human myocardium during pacing stress. Circulation *45*: 92 (1972).
14. INOUE, S., OHTA, M., IIZUKA, T. & MURA, S. Glucose tolerance, serum insulin and lipid abnormalities in patients with coronary heart disease. Jap. Heart J. *16*: 670 (1975).
15. VASSALE, M. Role of catecholamine release in morphine hyperglycemia. Amer. J. Physiol. *200*: 530 (1961).
16. BORISON, H.L., FISHBURN, B.R., BHIDE, N.K. & MCCARTHY, L.E. Morphine-induced hyperglycaemia in the cat. J. Pharmacol. Exp. Ther. *138*: 229 (1962).
17. ABRAMSON, E.A. & WOEBER, K.A. Effects of propranolol on the hormonal and metabolic responses to insulin-induced hypoglycaemia. Lancet *2*: 1386 (1966).
18. TAGGART, P. & CARRUTHERS, M. Suppression by oxprenolol of adrenergic response to stress. Lancet *2*: 256 (1972).
19. TAGGART, P., CARRUTHERS, M. & SOMERVILLE, W. Electrocardiogram, plasma catecholamines and lipids, and their modification by oxprenolol when speaking before an audience. Lancet *2*: 341 (1973).
20. HALL, G.M., YOUNG, C., HOLDCROFT, A. & ALAGHBAND-ZADEH, J. Substrate mobilisation during surgery. A comparison between halothane and fentanyl anaesthesia. Anaesthesia *33*: 606 (1978).
21. ROIZEN, M.F., MOSS, J., HENRY, D.P. & KOPIN, I.J. Effects of halothane on plasma catecholamines. Anesthesiology *41*: 432 (1974).
22. LIU, W.S., BIDWAI, A.V., LUNN, J.K. & STANLEY, T.H. Urine catecholamine excretion after large doses of fentanyl, fentanyl and diazepam and fentanyl, diazepam and pancuronium. Canad. Anaesth. Soc. J. *24*:371 (1977).
23. WESTENSKOW, D.R. & JORDAN, W.S. Changes in oxygen consumption induced by fentanyl and thiopentone during balanced anaesthesia. Canad. Anaesth. Soc. J. *25*: 18 (1978).
24. BRISMAR, B., BERGENWALD, L., CRONESTRAND, R., JORFELDT, L. & JUHLIN-DANNFELDT, A. The cardiovascular effects of neuroleptanaesthesia. Acta Anaesth. Scand. *21*: 100 (1977).
25. SCHMIDT, D.H., WEIS, M.B., CASARELLA, W.J., FOWLER, D.L., SCIACCA, R.R. & CANNON, P.J. Regional myocardial perfusion during atrial pacing in patients with coronary artery disease. Circulation *53*: 807 (1976).
26. GIBBS, C.L. & CHAPMAN, J.B. Cardiac energetics. *In*: The Handbook of Physiology, section 2. The cardiovascular system, vol. I. The Heart (eds. R.M. Berne, N. Sperdakis & S.R. Geiger) American Physiological Society, Bethesda, p. 775 (1979).
27. SAXENA, P.R. & BONTA, I.L. Mechanism of selective cardiac vagolytic action of pancuronium bromide. Specific blockade of cardiac muscarinic receptors. Europ. J. Pharmacol. *11*: 332 (1970).
28. SAXENA, P.R. & BONTA, I.L. Specific blockade of cardiac muscarinic receptors by pancuronium bromide. Arch. Int. Pharmacodyn. *189*: 410 (1971).
29. KONCHIGERI, H.N. & TAY, C.H. Influence of pancuronium on potassium efflux produced by succinylcholine. Anesth. Analg. Curr. Res. *55*: 474 (1976).

RÉSUMÉ

Les auteurs ont comparé les modifications de paramètres hémodynamiques et biologiques amenées par trois techniques d'induction d'anesthésie dans des cas de pontages aorto-coronariens. Les patients d'un premier groupe ont reçu une dose de 4.1 $\mu g \cdot kg^{-1}$ de fentanyl et ont été ventilés avec un mélange de protoxyde d'azote et d'oxygène dans des proportions de 60 et de 40 pour cent; ceux d'un second groupe recevaient 15 $\mu g \cdot kg^{-1}$ de fentanyl avec le même mélange de protoxyde; enfin, dans un troisième cas, une dose de 15 $\mu g \cdot kg^{-1}$ était administrée et les patients étaient ventilés avec un mélange d'azote et d'oxygène dans un rapport 60/40. Le fentanyl à la dose de 15 $\mu g \cdot kg^{-1}$ avec une ventilation au protoxyde d'azote amenait une diminution simultanée de la consommation d'oxygène, de l'index cardiaque, du travail d'éjection ventriculaire gauche avec extraction d'oxygène diminuée. La pression diastolique (témoin de la perfusion coronarienne) n'était que peu diminuée et l'on n'a pas observé de modification des lactates, du glucose et des acides gras libres artériels. Les doses inférieures de fentanyl avec le protoxyde n'amenaient pas de modifications hémodynamiques mais diminuaient la consommation et l'extraction d'oxygène.

D'autre part, les patients qui ont reçu les doses de 15 $\mu g \cdot kg^{-1}$ de fentanyl avec une ventilation à l'azote-oxygène, ont présenté des élévations de la fréquence cardiaque, de la pression artérielle, de l'index cardiaque et du travail d'éjection ventriculaire gauche en même temps qu'une diminution significative de l'extraction d'oxygène.

Chez les malades ayant reçu 4.1 $\mu g \cdot kg^{-1}$ de fentanyl avec protoxyde, ainsi que chez ceux ayant reçu 15 $\mu g \cdot kg^{-1}$ avec le mélange azote-oxygène, on a trouvé des augmentations significatives des lactates, du glucose et des acides gras libres, témoin d'une augmentation de l'activité sympathique.

Nous concluons que le fentanyl à la dose de 15 $\mu g \cdot kg^{-1}$ associé à une ventilation avec un mélange de 60 pour cent de protoxyde d'azote et d'oxygène, produit une induction satisfaisante au point de vue hémodynamique et biochimique chez les coronariens.

CHAPTER 8

Computerized monitoring of lung and heart function in the operating room Part II: Clinical application

8.1. Introduction

It has already been shown in previous work from the Thorax Centre, Rotterdam, how comprehensive pulmonary and cardiac monitoring can be used in specific studies, e.g. on respiratory gas exchange and the effects of drugs during and after surgery. But it should also be pointed out that the routine use of pulmonary and haemodynamic monitoring at the Thorax Centre has shown the usefulness of this technique particularly under routine circumstances. As a result of observations made during constant use of the Methodological Platform a few problems which sometimes come up during cardiac surgery and anaesthesia have become easier to detect, analyse, and treat.

In this chapter data are presented of a consecutive series of 33 patients without complications as well as a number of short case reports. Both illustrate some of the observations which have come to light as a result of the routine use of the Platform. Each case will be discussed briefly and compared to the ordinary experience in order to show how the data from this type of monitoring can be employed in the early diagnosis and treatment of pathological problems or in the modification of planned programmes of patient care.

CHAPTER 8.2.
SECTION A

Cardiorespiratory monitoring during open-heart surgery

O. PRAKASH, M.D.*, senior anaesthetist
N. JEFFS, M.B., B.S., F.F.A.R.C.S.*, anaesthetist
S.H. MEIJ, M. Sc.*, computer engineer
S.G. VAN DER BORDEN, B.Sc.*, research assistent
P.G. HUGENHOLTZ, M.D.*, professor of cardiology

8.2.1. Introduction

Advances in monitoring techniques have made it possible for us to obtain detailed information of cardiopulmonary status during and after cardiac surgery. Variables measured included minute volume, end-tidal carbon dioxide, cardiac index, oxygen consumption, and blood gases, from which it was possible to derive much useful information (e.g. dead space, ventilation/perfusion ratio, ventricular stroke work).

Continuous monitoring of such a large number of variables enables quick diagnosis and treatment of unfavourable trends in the condition of the patient. This leads to an improved survival rate, early extubation, and a shorter duration of time spent in intensive care. In the last two decades, the improvement in surgical and perfusion techniques has been paralleled by an improvement in the measuring of body function. The present report details the routine measurements performed within the framework of the Methodological Platform of the Thorax Centre in Rotterdam.[1]

8.2.2. Clinical material and methods

Of a total of 33 patients studied, 24 patients had coronary artery disease; eight of these had angina at rest, and the remainder had angina following mild exercise, i.e. walking 100 meters or climbing up one flight of stairs. All of these 24 patients had been treated with propranolol pre-operatively, which was discontinued one day prior to coronary artery bypass grafting. Four patients had a combination of coronary artery bypass grafting and valve replacement (three aortic and one mitral valve), and five patients underwent valve replacement only (three mitral and two aortic valves). No patient had chronic lung disease.

---

* From the Thorax Centre, Erasmus University and University Hospital, Rotterdam, The Netherlands.

Anaesthesia consisted of fentanyl 15 μgm/kgm for induction; nitrous oxide and oxygen (40%) for maintenance, and pancuronium for muscle relaxation. Supplementary doses of fentanyl and pancuronium were used as necessary during anaesthesia. Pharmacological reversal of muscle relaxation was not employed at the end of the procedure.

Before induction of anaesthesia, a 17 gauge Sorenson catheter was inserted percutaneously under local anaesthesia into the radial or brachial artery in all patients. This catheter was used for the determination of blood pressure and for the withdrawal of arterial blood samples for the determination of blood gases (ABL-2 Radiometer, Copenhagen). Another catheter was inserted into a forearm vein for the administration of drugs. Electrodes were connected for the recordings of ECG (lead V 5), and heart rate was derived from the ECG signals. In addition, a 7F Swan-Ganz thermodilution catheter was guided into the pulmonary artery via the right internal jugular vein for the intermittent measurement of cardiac output (CO), and for the collection of mixed venous blood samples.

The extracorporeal circulation was maintained by a Sarns roller pump, an Optiflo II Bubble oxygenator or a T.M.O. membrane oxygenator, and a Swank Hf 6000 filter in the arterial line. The circuit was primed with 2000 ml of a mixture of Haemaccel (Behring Pharma), 2500 ml with the T.M.O. membrane oxygenator, also, Mannitol 20% 100 ml, albumin 20% 125 ml, 50 ml Na

Table 8.1

Data on age, number of bypasses received, perfusion time, and aorta clamping time

	coronary artery bypasses* (24 patients)	coronary artery bypasses with valvular lesions (4 patients)	valvular lesions (5 patients)
age (in years)	52 ± 2	51 ± 4	48 ± 5
number of bypasses	3.2 ± 0.3	2.8 ± 0.8	
perfusion time (in minutes)	89 ± 5	115 ± 16	129 ± 5
total aorta clamping time (in minutes)	28 ± 2	65‡ ± 18	87‡ ± 6

Mean values ± the standard error of the mean.

* Of the 24 patients, 4 had 1 bypass, 4 had 2, another 4 had 3, and 12 patients had 4 or more bypasses.

‡ With cardioplegia.

Table 8.2

Catheterization data recorded at rest

	coronary artery bypasses (24 patients)	coronary artery bypasses with valvular lesions (4 patients)	valvular lesions (5 patients)
heart rate (beats/minute)	72 ± 2	80 ± 1	78 ± 4
cardiac index ($l/min/m^2$)	3.3 ± 0.2	3.4 ± 0.7	3.7 ± 0.4
left ventricular pressure (mmHg)			
systolic	144 ± 4	203 ± 42	151 ± 16
diastolic	6 ± 1	6 ± 2	5 ± 2
end diastolic volume (ml/m^2)	84 ± 7	101 ± 22	164 ± 31
left ventricular (dp/dt) max (mmHg/sec)	1940 ± 170		
left ventricular Vmax (sec^{-1})	54 ± 4		
ejection fraction[1]	0.57 ± 0.03	0.52 ± 0.09	0.58 ± 0.07

Mean values ± the standard error of the mean.

[1] Following the methods described in: Meester GT, Bernard N, Zeelenberg C et al: A computer system for real time analysis of cardiac catheterization data. Catheterization and cardiovascular diagnosis 1: 113, 1975.

HCO_3 8.4%, and 10 ml KCl 10%. Only when the perfusion hematocrit dropped below 20% during cardiac bypass surgery was blood added.

Table 8.1 contains data on age, number of bypasses, perfusion time, and aorta clamping time, and in table 8.2 catheterization data are given. All data are presented in the text as mean ± the standard error of the mean. "Student's" two-tailed paired t-test was used;[1] p-values of less than 0.05 were considered significant.

8.2.3. Experimental Protocol

Phase I and Phase II measurements were taken in the operating room, and those for Phases III, IV, and V in the post-operative intensive care unit.

Phase I: Pre-operative; patient ventilated with 40% oxygen and 60% nitrous oxide

Control measurements of haemodynamic variables, cardiac output, and blood gas values were obtained 30 min after induction of anaesthesia, prior to surgery, when stabilization was considered adequate.

Phase II: Post-operative; patient ventilated with 40% oxygen and 60% nitrous oxide

After surgery was completed and the chest closed, sufficient time was allowed for stabilization of the patient's condition, at which time Phase II studies were carried out. A patient was considered stable when all of the following were present: i) systolic arterial pressure >13.3 kPa; ii) right atrial pressure <1.3 kPa; iii) left atrial pressure <2 kPa; iv) absence of dysrhythmias; v) no need for cardio-active drugs; and vi) bleeding through the chest drains less than 100 ml per hour.

Phase III: Post-operative; patient ventilated with 40% oxygen and 60% air

Phase III took place 60 to 90 min after transfer to the post-operative intensive care unit, when the mean expired nitrous oxide was less than 0.5% as measured by a mass spectrometer. Blood and plasma were given to compensate for operative and post-operative losses. Cardiorespiratory measurements were then carried out. No cardio-active drugs were given to the patients in this series. No analgesic agents were administered during this phase.

Phase IV: Post-operative; spontaneous ventilation test

Studies for Phase IV were begun when the following criteria were met: i) return to adequate consciousness; ii) recovery from muscle relaxation as judged by the ability to obey verbal commands to raise the head or an arm; iii) maintenance of haemodynamic variables such as described for Phase II; iv) blood gas analysis showing partial pressure of arterial oxygen (Pa O_2) >10.7 kPa, on a fraction of inspired oxygen concentration of 40% (FiO_2 0.4), mixed venous oxygen ($S\bar{v}O_2$) >65%, and partial pressure of arterial carbon dioxide ($PaCO_2$) <6.7 kPa; and v) a rectal temperature of at least 36.5°C.

After all these criteria were met, the patient was subjected to a spontaneous breathing test for a period of 30 to 60 min. The ventilator (Siemens Elema Servo 900 B) was set at F/O, a setting at which the patient is able to breathe spontaneously through the ventilator, but without assistance from it. This was done to introduce some stress while breathing through an endotracheal tube and through the ventilator circuit. During this testing, expired minute volume, end-tidal carbon dioxide, and all the variables shown in Figs. 8.1 to 8.6 were watched and carefully recorded. A satisfactory spontaneous breathing test was

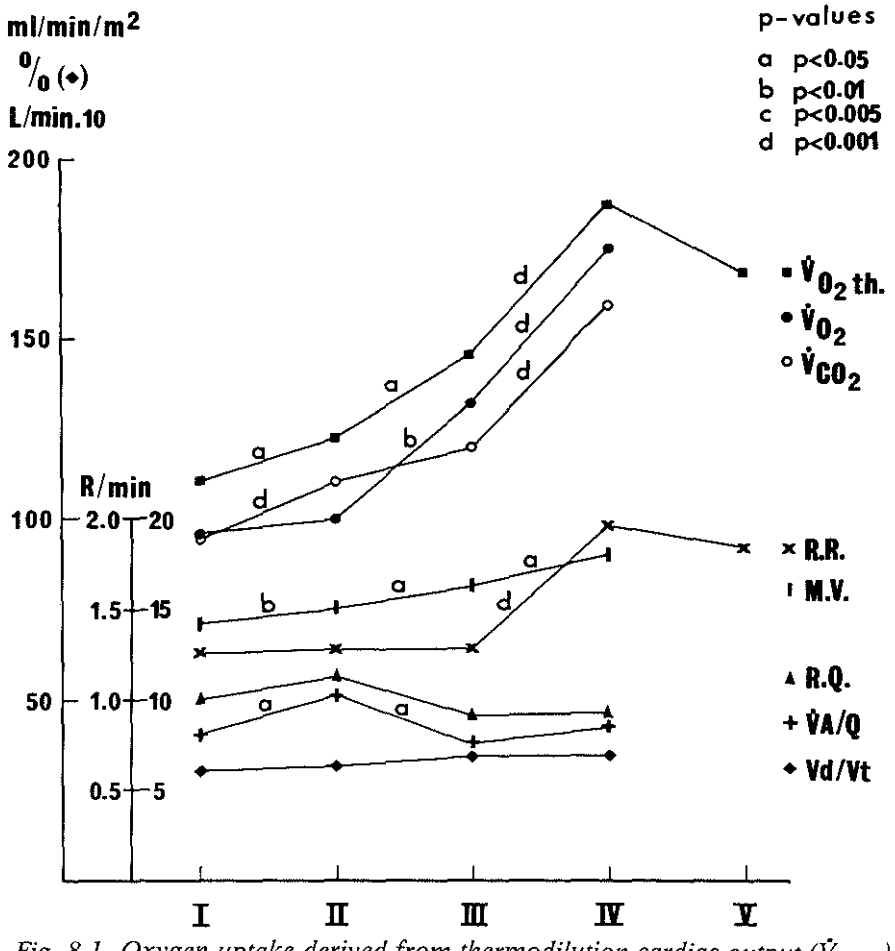


Fig. 8.1. Oxygen uptake derived from thermodilution cardiac output ($\dot{V}_{O_2th.}$), oxygen uptake derived from mass spectrometer ($\dot{V}_{O_2}$), carbon dioxide output ($\dot{V}_{CO_2}$), rate of respiration (R.R.), minute volume (M.V.), respiratory quotient (R.Q.), alveolar ventilation/perfusion ratio (VA/Q), and physiological dead space to tidal volume (Vd/Vt), from Phase I to Phase V.

defined as a rate of respiration not exceeding 26 breaths/minute for adults, expired minute volume not less than 10 ml/kg body weight, and end-tidal carbon dioxide not more than 6.5%. If the patient passed the spontaneous breathing test, he was extubated.

Phase V: Patient extubated, breathing oxygen/air

Studies for Phase V were obtained 2 hours after extubation of the trachea. The patients were settled comfortably and were breathing oxygen-enriched air

given by mask or by nasal catheter. Oxygen consumption values were then derived from cardiac output measured by thermodilution and arterial venous oxygen content difference.

8.2.4. Results

The results are summarized in diagrammatic form in Figs. 8.1. to 8.6. Patients received FiO_2 0.4, except in Phase V when oxygen was given by mask or catheter and FiO_2 was not measured. From Phase I to Phase III, there was a marked upward trend in oxygen consumption and carbon dioxide production (Fig. 8.1). There was an increase of heart rate and mean arterial pressure, and only a slight increase in cardiac index (Fig. 8.2). There was some decrease in PaO_2, but as PaO_2 did not fall below 13.3 kPa, the arterial oxygen saturation (SaO_2) did not change. There was a downward trend of the pulmonary artery oxygen saturation, and therefore, an increasing oxygen extraction coefficient (Fig. 8.3). There was a rise in arterial pCO_2 notwithstanding attempts to counterbalance the rise of carbon dioxide production and end-tidal carbon dioxide by increasing the minute ventilation. The rise of $PaCO_2$ was reflected by a fall in the pH of arterial blood (pHa). Base excess was taken as the

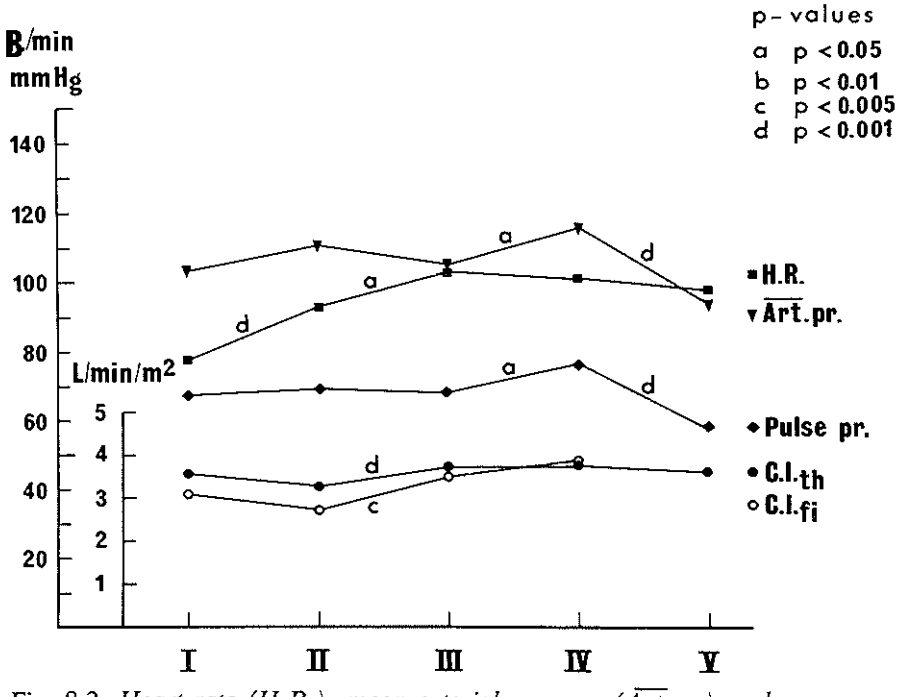


Fig. 8.2. Heart rate (H.R.), mean arterial pressure ($\overline{Art.pr.}$), pulse pressure (Pulse pr.), Cardiac Index, thermodilution ($C.I._{th}$), and Cardiac Index, Fick ($C.I._{fi}$), from Phase I to Phase V.

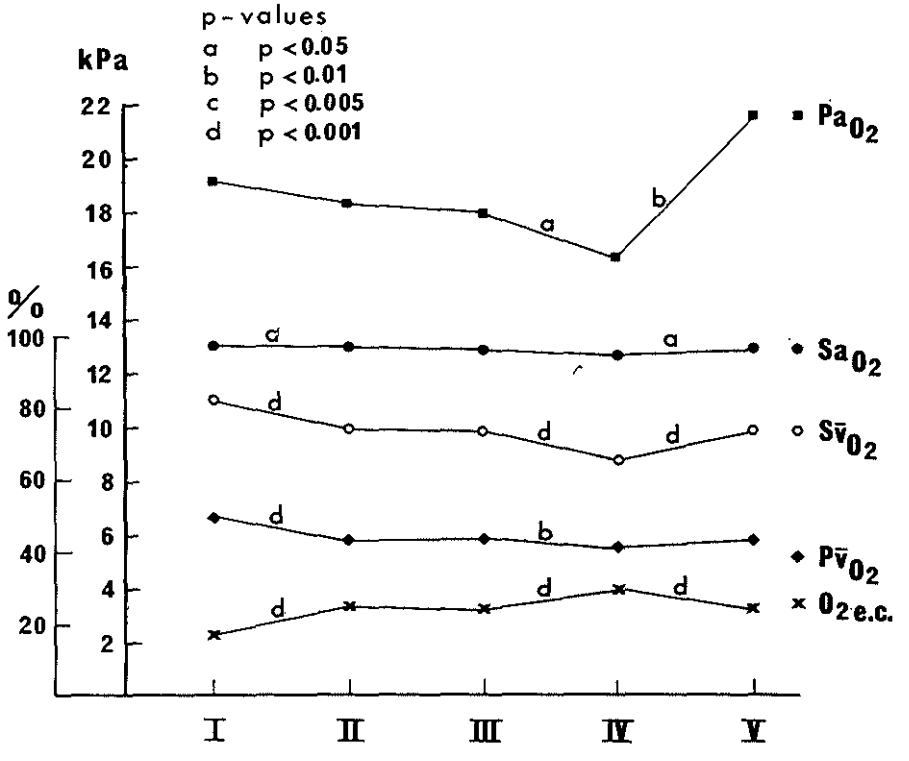


Fig. 8.3. Arterial oxygen (Pa_{O_2}), arterial oxygen saturation (Sa_{O_2}), mixed venous oxygen saturation ($S\bar{v}_{O_2}$), pulmonary venous oxygen ($P\bar{v}_{O_2}$), and oxygen extraction coefficient ($O_{2e.c.}$), from Phase I to Phase V.

indicator of the non-respiratory component of the acid-base balance. A slight progressive metabolic acidosis was seen which corrected itself after extubation (Fig. 8.4). The changes observed from Phase I to Phase III became very pronounced during Phase IV, when the patients were subjected to the spontaneous ventilation test. At that time, the highest values were measured for oxygen consumption, carbon dioxide production, minute volume and frequency of respiration, $PaCO_2$, end-tidal carbon dioxide, and the oxygen extraction coefficient. The lowest values were reached for pulmonary artery oxygen saturation and for pHa. Phase V is marked by a fall of oxygen consumption, a higher pulmonary artery oxygen saturation, and lower vascular pressures without a fall in cardiac index. The rise in pHa from Phase IV to Phase V is a sign of an improved acid-base state, as $PaCO_2$ did not change much. $PaCO_2$ remained high, probably as an effect of some respiratory depression, caused by residual fentanyl. Carbon dioxide elimination could not be measured after removal of the tracheal tube. The significant rise of PaO_2

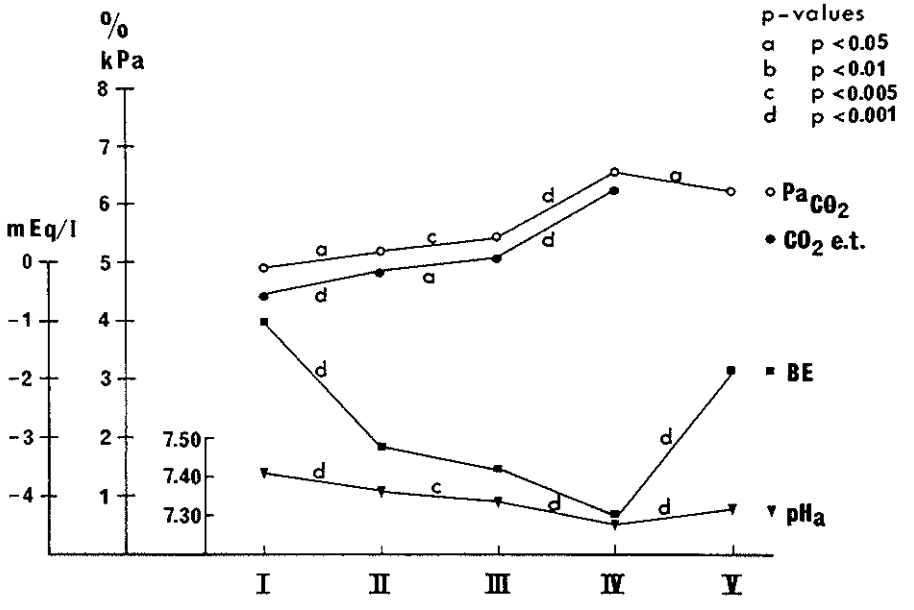


Fig. 8.4. Arterial carbon dioxide (Pa_{CO_2}), end-tidal carbon dioxide (CO_2e.t.), excess of the base (BE), and arterial pH (pH_a), from Phase I to Phase V.

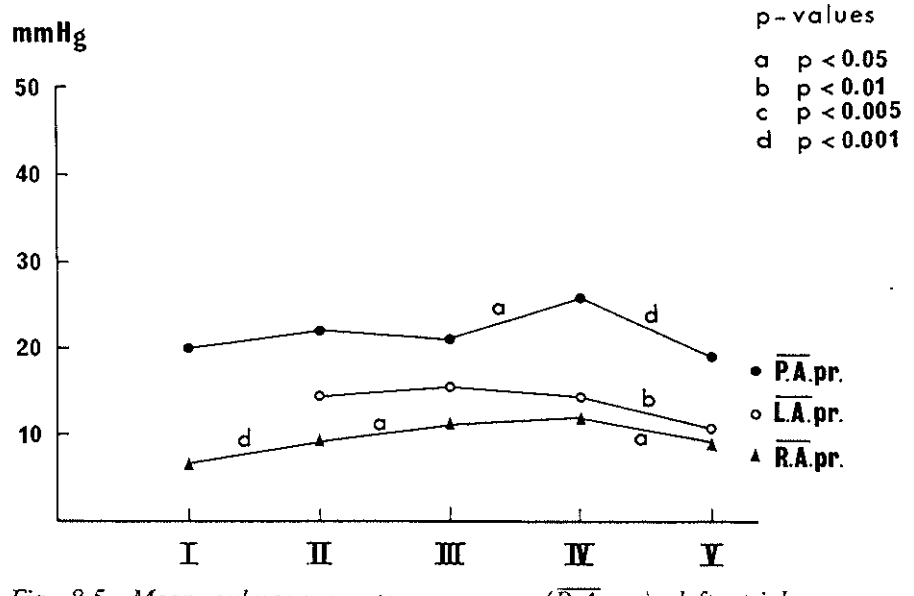


Fig. 8.5. Mean pulmonary artery pressure ($\overline{P.A.pr.}$), left atrial pressure ($\overline{L.A.pr.}$), and right atrial pressure ($\overline{R.A.pr.}$), from Phase I to Phase V.

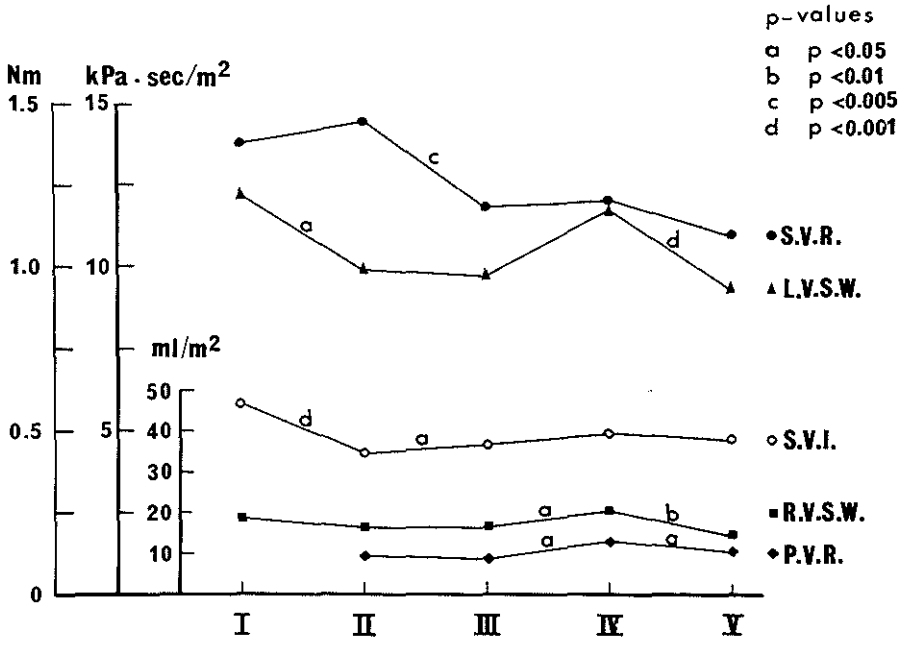


Fig. 8.6. Systemic vascular resistance (S.V.R.), left ventricular stroke work (L.V.S.W.), stroke volume index (S.V.I.), right ventricular stroke work (R.V.S.W.), and pulmonary vascular resistance (P.V.R.), from Phase I to Phase V.

after extubation can not be compared with earlier values, because the percentage of oxygen inhaled was not measured after extubation. But this rise still indicates some improvement in the respiratory system.

The rate of respiration and the minute volume increased significantly during spontaneous breathing. The dead space to tidal volume ventilation ratio did not change throughout the period of observation.

The pre-operative respiratory data collected were compared to post-operative data (table 8.3). The compliance fell by 23%, which was synchronous with the rises in peak pressure of 38%; the expired resistance increased by 26%, and the inspired resistance by 16%. Similar findings were reported in a previous publication.[2]

The mean arterial blood pressure remained remarkably constant while the patients underwent ventilation (Phases I, II and III); see Fig. 8.5. There was a slight rise in pressure during Phase IV, but a sharp fall was seen 2 hours after extubation. Similar changes were seen in the pulse rate (Fig. 8.4).

The left and right ventricular stroke work remained fairly constant throughout Phases I to IV, but fell sharply after extubation (Fig. 8.6). This may reflect

the fall in mean systemic arterial pressure, mean pulmonary arterial and mean right and left atrial pressures that occurred during this phase. Systemic vascular resistance showed similar changes, but pulmonary vascular resistance remained constant.

8.2.5. Discussion

There were two major aims in this study: first, to provide background data on a number of physiological variables on patients undergoing cardiac surgery during the intra-operative and post-operative periods, and second, to use this data to predict the post-operative course of the patients, with a view to early extubation. Clearly, if a range of normal responses could be established, deviations from this pattern can be detected and attributed an appropriate clinical relevance.

Clinically, Phase I represents a state of anaesthesia undisturbed by surgical interference. At Phase II, immediately after surgery, anaesthesia has become very light, and the patient may attempt to move, and to resist manipulation. At Phase III he is awake, responding to his environment, yet quiet and tolerating artificial ventilation. At Phase IV, circumstances are altered. He must then breathe for himself through the endotracheal tube and the open ventilator circuit. At Phase V, after extubation, he is breathing free from external

Table 8.3

Pulmonary mechanics data

	pre-operative	post-operative	p-value
peak pressure ($cm\ H_2O$)	16.7 ± 0.6	23.1 ± 1.1	<0.001
pause pressure ($cm\ H_2O$)	9.2 ± 0.5	14.3 ± 0.8	<0.001
end expiratory lung pressure ($cm\ H_2O$)	0.1 ± 0.1	0.7 ± 0.2	<0.05
inspired resistance ($cm\ H_2O/(l/sec)$)	17.6 ± 0.5	20.5 ± 0.9	<0.001
expired resistance ($cm\ H_2O/(l/sec)$)	23.2 ± 1.1	29.2 ± 2.3	<0.005
compliance ($ml/cm\ H_2O$)	56 ± 3	44 ± 2	<0.001

Mean values ± the standard error of the mean.

impediments, and resting. The successive Phases are clearly reflected by the measurements.

The study shows that, on the whole, heart and lung function are remarkably well preserved in patients undergoing cardiac surgery. The exception to this is Phase IV, when patients were allowed to breathe spontaneously through an endotracheal tube, still connected to the ventilator. This was shown to cause a statistically significant increase in cardiac and somatic work with rises in mean pulmonary artery pressure and left ventricular stroke work and falls in PaO_2 and mixed venous oxygen saturation ($S\bar{v}O_2$) due to an increase in total oxygen consumption. These data indicate that spontaneous breathing with a tube in situ must be considered to be a form of involuntary exercise leading to higher pulmonary pressures, and increased left ventricular stroke work with a reduction of PaO_2 and $S\bar{v}O_2$ saturation due to an increase in oxygen consumption.

As has been shown,[2] a test which imposes such a load may be used to test whether a patient will tolerate extubation (the spontaneous ventilation test). Obviously, such a test should not be prolonged as this will cause an undesirable stress to patients with poor cardiac performance. The test should either lead to a continuation of mechanical ventilation if the patient totally fails to achieve adequate ventilation, or to early extubation if the patient can perform reasonably during the test.

As stated in an earlier publication from this centre, the estimation of $S\bar{v}O_2$ is a useful guide for the prediction of the adequacy of tissue perfusion during the post-operative period.[3-5] Normally, the arteriovenous oxygen saturation difference is 25%. Any widening of this difference indicates an increase in oxygen consumption and/or a decrease in cardiac output. It can be seen from this series that while the cardiac output remained relatively stable, there was an increase in the oxygen utilization coefficient, compared to pre-operative values. This increase, associated with a fall in PaO_2 and $S\bar{v}O_2$, has been shown to occur during exercise.[6] In patients who have undergone cardiac surgery, it has been observed that the cardiac index remains constant during the immediate post-operative period. When there is an increase in somatic work, such as the effort of breathing, as the cardiac output is fixed, the arterio-venous oxygen difference must increase. This provides a useful indicator of the amount of effort needed to maintain PaO_2 and $PaCO_2$ values and of the adequacy of cardiac output. The lowest $S\bar{v}O_2$ was observed during Phase IV when patients breathed spontaneously while still intubated and connected to the ventilator (67% ± 2% compared to 83% ± 3% pre-operatively). As soon as the patient was disconnected from the ventilator and extubated, there was a distinct improvement in $S\bar{v}O_2$, indicating a greater cardiopulmonary reserve.

This suggests that the overall resistance to breathing through an endotracheal tube was too high, leading to an increase in the work of breathing.

However, the ability of the patient to maintain a stable cardiopulmonary system in the face of an increased workload is a useful test of his ventilatory capability. As such it could be compared with tests for the prediction of successful ventilator weaning described by other workers, such as vital capacity per kg and maximum inspiratory force[7] and maximum mid-expiratory flow and maximum expiratory pressure.[8]

The main difference between the spontaneous ventilation test and the above measurements is that our test continually monitors response to a small stress over several minutes, and is thus able to detect trends. We think that this compares favourably with isolated tests of post-operative respiratory function. Although the fibre optic measurement system[3,4] provides information on $S\bar{v}O_2$ continuously from an indwelling catheter in the pulmonary artery, its cost and, until recently, complexity, have regrettably not made it a very widely-employed technique. Hopefully, further technical improvements will make this approach more generally employed.

8.2.6. Summary

Thirty-three patients underwent extensive cardiorespiratory monitoring during cardiac surgery. Recordings of measurements, with derived variables, were made pre-operatively, post-operatively, and after extubation approximately three hours after operation. The data provide a reference that allows decisions on whether the condition of a patient after cardiac surgery deviates from the ordinary course. Details are given of the spontaneous ventilation test, which, taken together with monitored data, provided criteria for successful early extubation in uncomplicated cases.

8.2.7. Acknowledgements

The authors wish to extend their sincere thanks to the surgical staff, anaesthetic technicians, and theatre and post-operative intensive care unit nurses of the Thorax Centre for their cooperation in this project. Special thanks are due to Dr. W. Hekman for his invaluable criticism and suggestions, and also to Miss Carla L. Vermeulen for revising and typing the manuscript.

8.2.8. References

1. Colton TH: Statistics in Medicine. Boston, Little, Brown & Co, 1974
2. Prakash O, Jonson B, Meij S et al: Criteria for early extubation after intracardiac surgery in adults. Anesth Analg 56: 703, 1977.
3. Hugenholtz PG, Krauss XH, Verdouw PD et al: Clinical experience with on-line fibre-optic oximetry. In: Payne JP, Hill DW (Eds.): Oxygen measurements in biology and medicine (p. 383). London, Butterworths, 1975

4. Krauss XH, Verdouw PD, Hugenholtz PG et al: On-line monitoring of mixed venous oxygen saturation after cardiothoracic surgery. Thorax 30: 636, 1975.
5. Prakash O, Meij S, Hugenholtz PG et al: Predictive value of core-toe temperature and mixed venous oxygen saturation after cardiac surgery. In: Tavares BM, Frey R (Eds.): Anaesthesiologie und Intensivmedizin, Band 116. Acute Care (p. 274). Berlin, Springer-Verlag, 1979.
6. Ashley WW, Bhaduri U, Pietras RJ et al: Pulmonary arterial oxygen saturation during treadmill exercise. A discriminative index of functional class. Am Heart J 90: 463, 1975.
7. Hilberman M, Kamm B, Lamy M et al: An analysis of potential physiological predictors of respiratory adequacy following cardiac surgery. J Thor Card Surg 71: 711, 1976.
8. Peters RM, Brimm JE, Utley JR: Predicting the need for prolonged ventilatory support in adult cardiac patients. J Thor Card Surg 77: 175, 1979.

8.3 SECTION B

8.3.1. Introduction

In this section is presented a number of short case reports which illustrate some of the observations which have come to light as a result of the routine use of the Platform. Each case will be discussed briefly, in order to show how the data from the monitoring have been used in the early diagnosis and treatment of pathological problems, or in the modification of planned programmes of patient care.

The reports are of two types: those in which continuous monitoring of expired carbon dioxide concentrations brought problems to light, and those in which continuous monitoring of pulmonary mechanics was found to be useful. In some of the cases discussed below the explanation of the pattern observed offers no difficulty. In others the explanations discussed are to be regarded with some caution. From clinical experience, pattern interpretation has proven valuable in choosing suitable therapy. The exact nature of such patterns deserve further detailed studies in which the Platform certainly has a role to play.

8.3.2. The value of monitoring lung compliance and resistance

Case reports

Case 1: Early changes in lung compliance with intrathoracic bleeding

This report concerns a patient who underwent cardiac surgery for mitral and aortic valve replacement. On return to the post-operative unit his general condition demanded a continuation of controlled ventilation (table 8.4).

Table 8.4

Data obtained at the conclusion of surgery in Case 1

mixed venous oxygen saturation ($S\bar{v}O_2$)	50%
left atrial pressure	28 mmHg
systemic arterial pressure, systolic	80 mmHg
rectal temperature	30°C
arterial oxygen saturation (SaO_2)	89%
blood loss	200 ml/hr
heart rhythm	unstable

Because of this, parameters of pulmonary mechanics such as compliance, expiratory and inspiratory resistance were monitored with the Lung Mechanics Calculator type 940 from the Servo 900 ventilator system. A 24-hour plot of the pulmonary mechanics parameters obtained from the patient is shown in Fig. 8.7. It can be seen that over an 8-hour period following return to the post-operative unit there was a marked reduction in lung compliance.

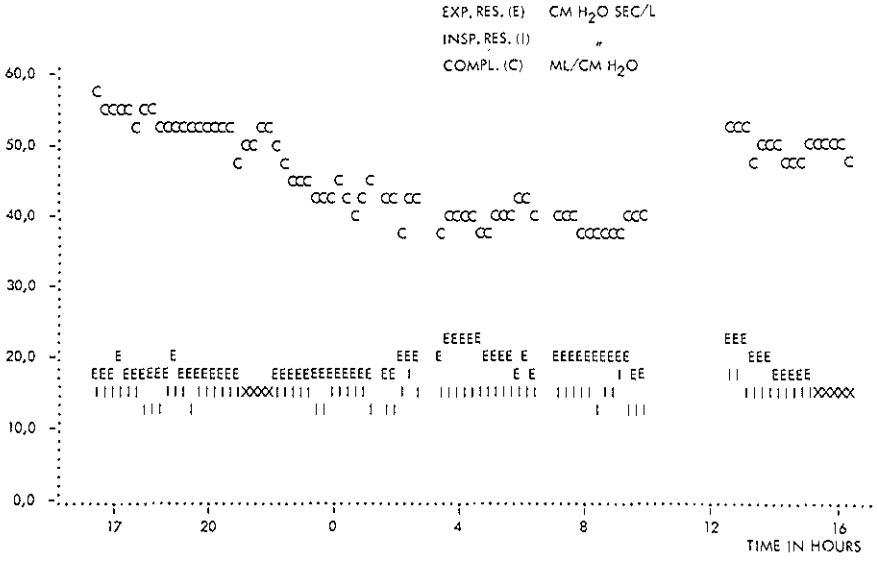


Fig. 8.7. Computer print-out shows compliance (C), inspiratory resistance (I), and expiratory resistance (E) in a patient with intrathoracic bleeding. The blank space (from 10-12 hours) represents re-operation, followed by further monitoring with compliance returning to control levels.
Reproduced from Prakash O et al: Lung mechanics in patients undergoing mitral valve replacement. The value of monitoring of compliance and resistance. Critical Care Medicine 6: 370-372, 1978.

Chest X-rays dit not show any gross abnormalities. Towards the end of this time there was also a slight rise in expiratory resistance and at the same time the patient became oliguric and his systemic arterial pressure fell to 80/50 mmHg.

At this stage, some 8 hours after the fall in compliance had first been noted, the diagnosis of intrathoracic bleeding was decided upon, and the patient returned to the operating theatre for re-exploration of the chest. At thoracotomy a large blood clot was evacuated from the right pleural space. Subsequently, the lung compliance was substantially improved, although it did not return to its orginal level as the bleeding process had clearly affected the lung itself.

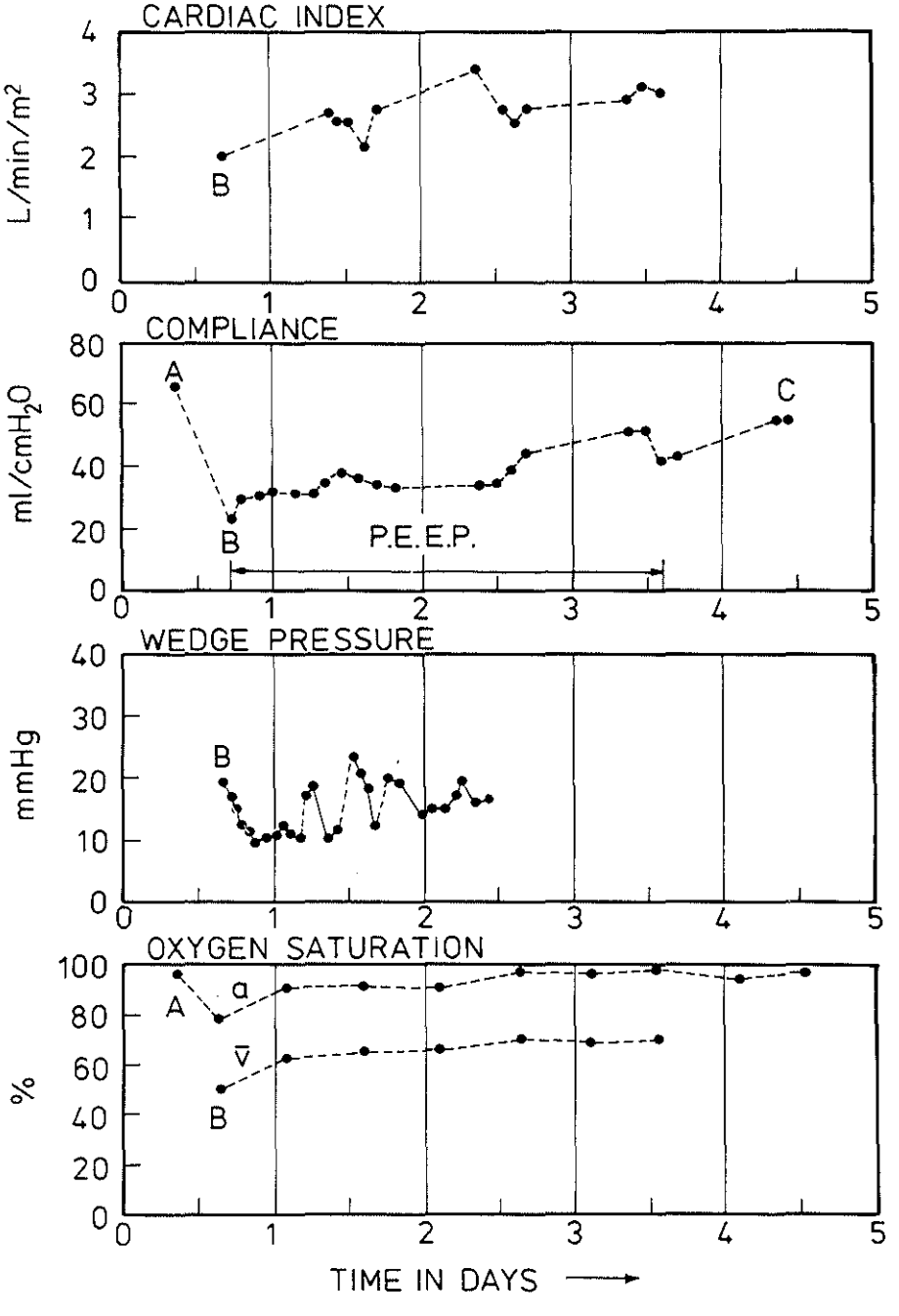
This is an example where the significance of the falling compliance had been incompletely understood for 8 hours, as a result of which the correct diagnosis was delayed. Since this experience much more reliance is now put on compliance monitoring when an intratracheal tube is left in place.

Case 2: The use of compliance monitoring to assess the progress of treatment of pulmonary oedema using PEEP

This was a 50 year old man who underwent coronary artery bypass surgery. After coming off cardiopulmonary bypass and when ventilation was reinstituted, compliance was found to be very low, 220 ml/kPa. Arterial blood gas analysis showed severe cardiopulmonary function failure with arterial desaturation, low mixed venous oxygen saturation, and a low cardiac index (Fig. 8.8).

The analysis of its cause in this case was incomplete because chest X-rays could not be taken during surgery. Even so, a number of possible diagnoses must be entertained when lung mechanics and gas exchange are severely disturbed. These include obstruction of the endothracheal tube, ventilator hose kinking or obstruction of the trachea or of a major bronchus by sputum or blood clot. There is also the possibility of interstitial pulmonary oedema due to heart failure or fluid overload, and atelectasis. The two latter conditions should be suspected when compliance is low, especially when the chest is open.

Fig. 8.8. Data on cardiac index and compliance during initiation of positive end-expiratory pressure ventilation (P.E.E.P.) and subsequent improvement during treatment. Point A indicates the pre-operative value of compliance, and point B the compliance and cardiac index values after termination of extra-corporeal circulation. The decision to apply P.E.E.P. was made at point B. Point C denotes recovery of compliance values.
Arterial and mixed venous oxygen saturations at point B before initiation of P.E.E.P. and subsequent recovery in blood gas values during the next four days. ▶


CARDIAC INDEX
L/min/m²
B
COMPLIANCE
ml/cmH₂O
A
B
C
P.E.E.P.
WEDGE PRESSURE
mmHg
B
OXYGEN SATURATION
%
A
a
v̄
B
TIME IN DAYS

In this case, after ensuring that no gross airway obstruction was present, the remaining likely diagnoses were pulmonary oedema or atelectasis. It was therefore considered rational to apply a positive end-expiratory pressure of 0.6 kPa. Immediately after the conclusion of the operation, a chest radiograph was taken which showed fulminating pulmonary oedema, confirming the appropriateness of the diagnosis while the patient was still in the operating room.

Some improvement in compliance was observed when PEEP had taken effect. During the succeeding 5 days the patient continued to be ventilated with PEEP (Fig. 8.8). The data on compliance and cardiac index showed a gradual improvement toward normal values, as did the blood gas data shown in Fig. 8.8.

In this case the availability of continuous monitoring of pulmonary mechanics within the operating room permitted timely intervention in what is otherwise a very difficult-to-manage situation. In patients who have been subjected to extracorporeal circulation with total haemodilution, a low compliance is often seen. This probably reflects a pulmonary oedema of a lower degree than in the present case. Monitoring of compliance has been found useful as a guideline for ventilation with PEEP in the immediate post-perfusion period.

Case 3: Diagnosis of hypovolaemia at the conclusion of the cardiopulmonary bypass procedure.

A 46 year old male patient underwent coronary artery bypass surgery. It is known that most patients on coming off total heart/lung bypass are hypovolaemic and peripherally "shut down" so that it is difficult to assess the degree of fluid deficit requiring correction. Although during the operative procedure the amount of fluid lost is determined by the blood losses measured from suction bottles, perfusion equipment, swabs, and drapes, this procedure remains rather inaccurate such that significant discrepancies may not always be detected. A real problem is that even an ever-so-accurate estimate of the losses does not help; unknown quantities of fluid may drain into the extravascular spaces while some of the vessels (mainly venules) may change the capacity and content of the vascular space.

The end-tidal carbon dioxide and expired oxygen curves, in this case derived with a mass spectrometer, demonstrate a pronounced slope of "the alveolar plateau" during expiration immediately following surgery rather than the more horizontal pattern normally observed. This indicates uneven composition of alveolar air due perhaps to uneven ventilation perfusion relationships in the lungs. If uneven ventilation secondary to bronchial obstruction is excluded, hypovolaemia should be considered, especially when the left atrial pressure is low, as it was in this particular patient. During artificial ventilation,

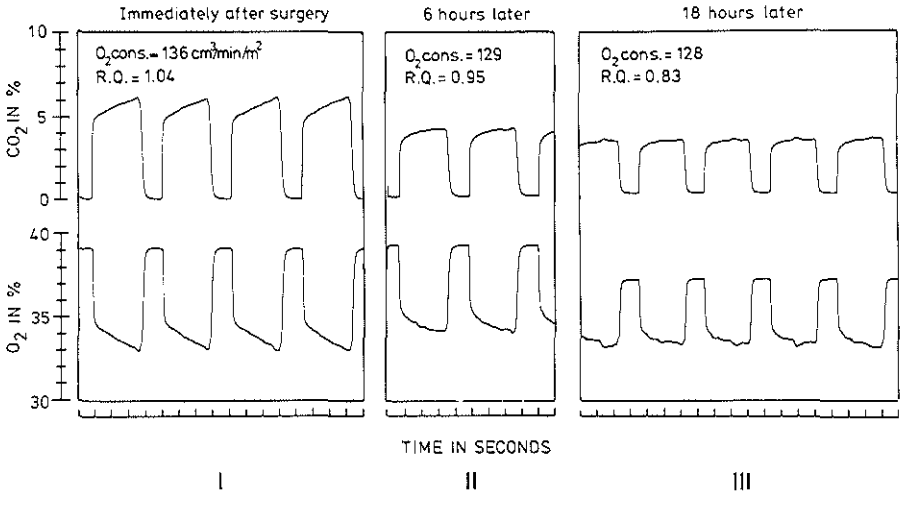


Fig. 8.9. In 8.9.I, the carbon dioxide and oxygen tracings show the plateau part of the curve distorted due to hypovolaemia, which was restored to near normality after 6 and 18 hours. 8.9.II and 8.9.III indicate the change after the administration of 2800 ml of fluids.

especially during surgery with the thorax open and the patient in supine position, the anterior areas of the lungs are better ventilated, while the posterior areas of the lungs are better perfused due to gravity. During expiration the better-ventilated less-perfused lung areas empty first and therefore there is always some upward slope of the carbon dioxide curve.

We have repeatedly observed this steep upward slope in hypovolaemic subjects, and this is thus probably analogous to the increased dead space during hypotension.[1] As explained, it probably reflects a ventilation perfusion mismatch. In the present case, the carbon dioxide and oxygen curves regained their normal configurations following blood volume expansion. At the Thorax Centre Rotterdam the shape of the carbon dioxide tracing has been found to be of great help in everyday management of immediate post-perfusion transfusion. See Fig. 8.9.

Case 4: Accidental clamping of the left pulmonary artery during right-sided pneumonectomy

A 68 year old man was admitted for right-sided pneumonectomy. After induction of anaesthesia, the patient was intubated with a 39 Carlens tube. Deliberate collapse of the right lung was produced after right-sided thoracotomy while the left lung was ventilated separately. Carbon dioxide

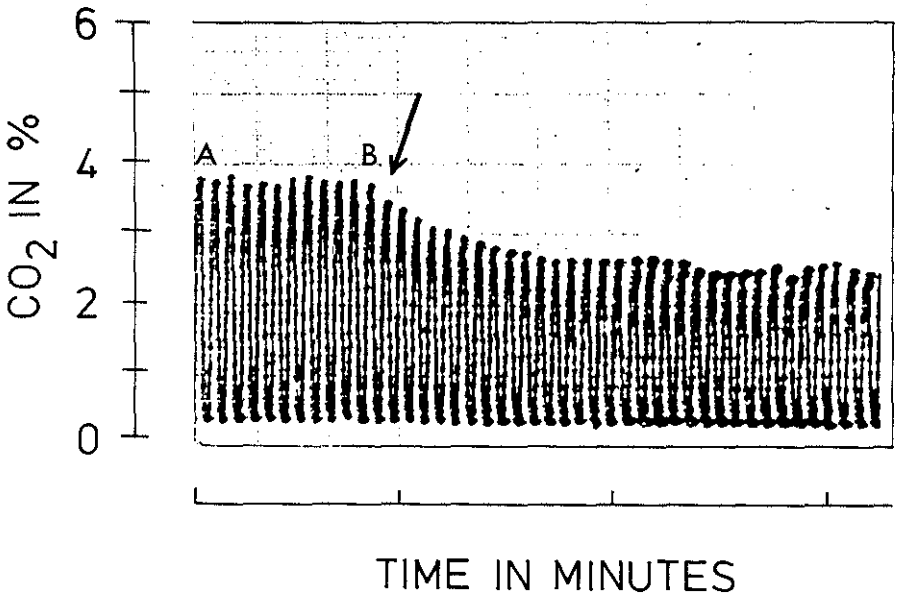


Fig. 8.10. Continuous monitoring of end-tidal carbon dioxide during lung surgery. Arrow indicates time of faulty clamp application.

monitoring after collapse of the lung is reflected in Fig. 8.10 (A to B). During the actual resection, the right pulmonary artery was clamped as intended. Even so, an immediate decline of end-tidal carbon dioxide representing the left lung occurred (arrow). This was found to be the result of partial obstruction of the left pulmonary artery by the clamp, which had been misplaced to include not just the right pulmonary artery, but also part of the left. Readjustment of the clamp restored the end-tidal carbon dioxide to normal (not indicated in the Fig.). In this instance, end-tidal carbon dioxide monitoring led to the early recognition of a complication which, if not recognized promptly, may have had serious consequences.

Case 5: Early detection of the return of spontaneous muscle activity

During controlled ventilation it is sometimes difficult to assess the exact degree of the neuromuscular blockade, particularly when patients are lightly anaesthetized. This is especially true when the head and body are entirely covered by surgical drapes, so that the anaesthetist fails to appreciate minor muscular movements. Muscular tone interferes with the efficiency of pulmonary ventilation, increases the inspiratory pressure, and may interfere with surgery.

Carbon dioxide monitoring provides early warning of the return to muscle

activity, since during the latter part of expiration diaphragmatic contractions cause a drawing of gas, which is partly mixed with fresh gas, from the inspiratory line into the analyser, which then results in dips in the expiratory plateau of the carbon dioxide tracing. A typical example of this is shown in Fig. 8.11.I. At this instant, the administration of pancuronium to the patient restored a state of complete muscular paralysis and, as shown in fig. 8.11.II, the carbon dioxide trace resumed its normal appearance.

In the Thorax Centre the minimum necessary amount of drug is given, so that possible adverse drug effects are reduced. Although this approach is generally accepted, it is not always practicable as there is no means of determining precisely the minimum effective dose. The pattern shown in Fig. 8.11.I is regularly observed when muscular relaxation is insufficient. Hence,

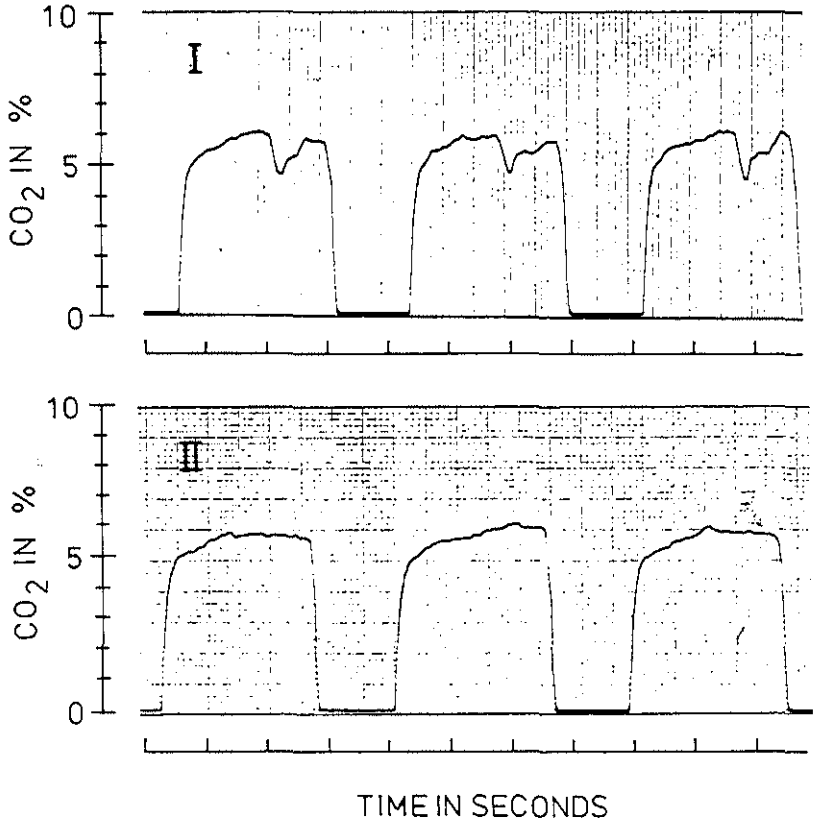


Fig. 8.11. 8.11.I shows trigger waves or "dips" on the plateau part of the end-tidal carbon dioxide curve due to inspiratory movements during expiration. 8.11.II illustrates resumption of the normal end-tidal carbon dioxide curve after the administration of pancuronium.

such monitoring is a valuable guideline in efforts to reduce the administration of drugs, especially with infants and children. Airway pressure tracing can also give an indication about attempts at spontaneous ventilation, however, we find the carbon dioxide tracing to be even more sensitive.

Case 6: Detection of leaks in the sampling line

A 3 year old male child underwent surgical correction of tetralogy of Fallot. It was observed in the traces of oxygen and carbon dioxide concentration (measured by mass spectrometer) that there were repeated dips to very low levels (Fig. 8.12.I). The oxygen fell to about 21%, which represents room air, and carbon dioxide dropped to zero during expiration. A check of the ventilator hoses and sampling line showed there was a leak.

Even minor leaks may be of serious consequence to a small infant or neonate, since, although small, they represent a significant fraction of the alveolar ventilation volume. Thus, with volume-preset ventilation, alveolar ventilation will fall by a corresponding amount, which in turn may rapidly lead to inadequate ventilation. Ultimately, atelectasis and serious arterial oxygen desaturation may supervene. For example, a leak of 200-300 ml/min, not large in itself, represents a substantial fraction to an infant whose alveolar minute volume ventilation is only 800-900 ml, and is certainly sufficient to interfere with gas exchange. This example is given to demonstrate that continuous monitoring of the airway concentration of carbon dioxide and oxygen by noticing a change in the shape of the curves allows the physician to spot a potentially serious air leak very rapidly. This leak actually occurred within the

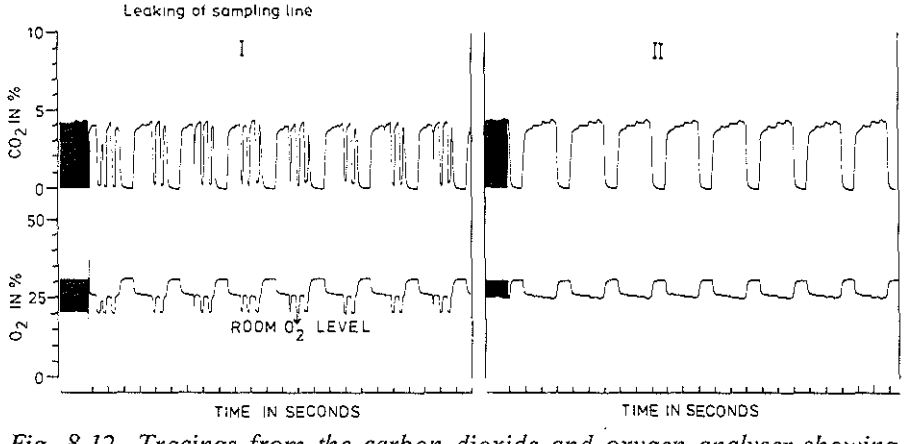


Fig. 8.12. Tracings from the carbon dioxide and oxygen analyser showing repeated dips to very low levels (8.12.I). The lower diagram shows the % oxygen falling to 21%, the level of room air, and the upper diagram shows the % carbon dioxide falling to zero. Return to normal tracings after correction of leaks in the sampling line of the system is shown in 8.12.II.

monitoring system, but was fortunately detected via the same system. Leaks are not rare between the ventilator and the patient. They may produce a variable pattern in the tracings, depending upon the site of leakage. However, a significant leak can hardly go undetected as long as the carbon dioxide elimination remains undisturbed.

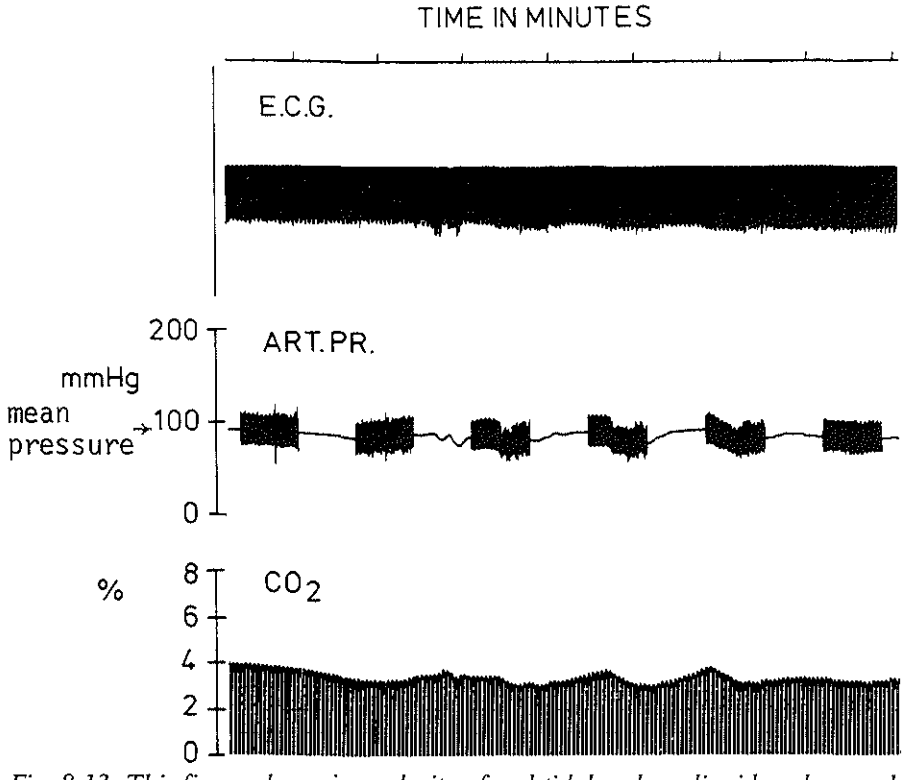


Fig. 8.13. This figure shows irregularity of end-tidal carbon dioxide values and arterial pressure curves at 28°C, revealing instability of cardiac performance. Close observation should reveal that the mean arterial pressure follows closely fluctuations in the carbon dioxide curve.

Case 7: Unstable circulation in infants with Fallot's tetralogy under cooling

A 7.5 kg male child was anaesthetized for total correction of tetralogy of Fallot. Because of the complexity of the surgical correction, this patient was subjected to deep hypothermia. When the patient's temperature had reached 28°C during surface cooling, carbon dioxide elimination started to fluctuate in an abnormal manner and this was reflected in the tracing of expired carbon dioxide. Rapid changes of carbon dioxide elimination (at stable ventilation) correspond to changes in pulmonary perfusion. In this case the arterial

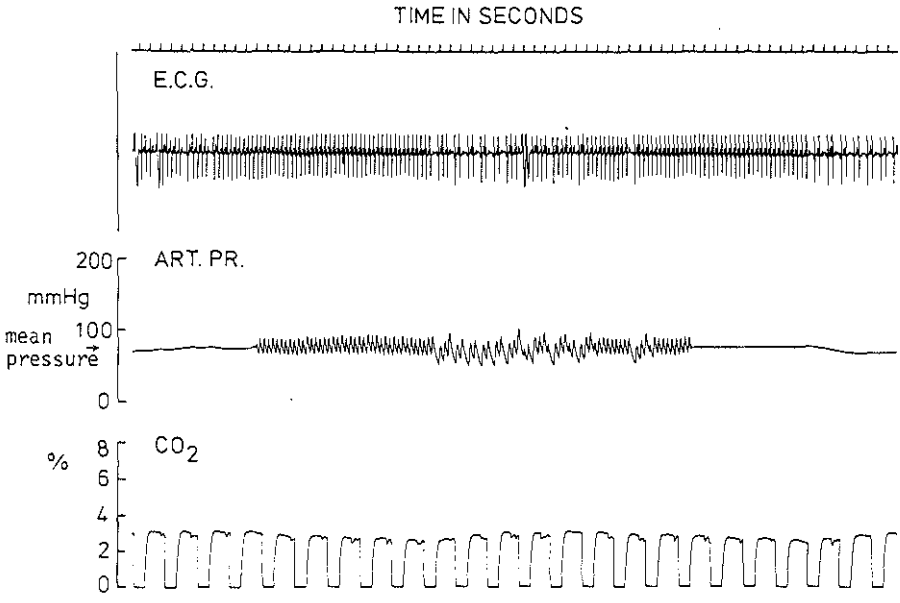


Fig. 8.14. Electrocardiogram (ECG), arterial pressure (Art. Pr.), and carbon dioxide end-tidal tracings showing irregularity of heart beat and its effect on carbon dioxide and arterial pressure tracings. During arrhythmias, the rise in carbon dioxide output is very clearly demonstrated.

pressure varied in parallel with carbon dioxide elimination. Obviously, perfusion of the lungs and the body varied synchronously (Fig. 8.13 and Fig. 8.14).

As found in a previous study,[2] patients with Fallot's tetralogy or similar vitiae may during cooling develop severe increases of right-to-left shunting. We regard any sign of unstable circulation as a warning. An arterial sample drawn at that time showed that a pronounced arterial desaturation had developed. Periods of stable rhythm alternated with arrhythmia. Remarkably, it appears that the periods with arrhythmia were associated with increased carbon dioxide elimination. The reason for this is obscure. Extracorporeal circulation was started immediately and the child recovered. He could be extubated within one hour after his arrival in the intensive care unit. See Fig. 8.14.

Case 8: Diagnosis of collection of water in the ventilator hoses

It is commonly observed that water condenses out and collects in ventilator hoses. Water in the inspiratory line may be driven into the patient's lungs, especially in infants. In the expiratory line it hinders expiration such that expiration occurs as a series of discontinuous gas pulsations. An undue PEEP effect may also develop.

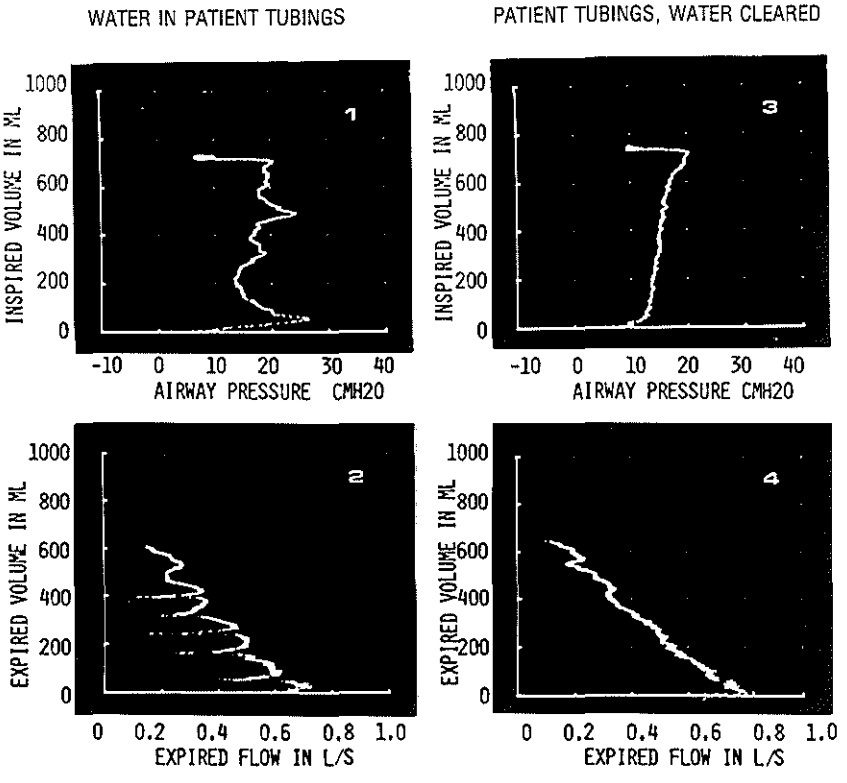


Fig. 8.15. 8.15.1 shows an irregular shape of the loop by plotting airway pressure versus inspired volume, and a similar pattern in 8.15.2 was seen in expired flow versus expired volume loops. 8.15.3 and 8.15.4 represent "normal" tracings in the same patient after water was cleared.

Fig. 8.15 shows abnormalities of the plots of inspired volume against airway pressure and expired volume against flow. Water had collected in both expiratory and inspiratory lines. This is an example where visual monitoring of flow/pressure and flow/volume curves can aid in avoiding difficulties in actual patient care. Osborn[3] has described several important circumstances which are easily recognized from patterns of flow/volume and pressure/volume diagrams, once they have been observed, analysed, and understood.

It is our belief that "pattern recognition", aided by efficient displays, may sometimes be more effective in drawing the attention of a busy anaesthetist to impending problems than numerical data would. For this "pattern recognition", a device was developed which consists of a microprocessor and a display unit. The microprocessor system converts the analogue signals from the ventilator to digital signals and feeds this digital information to the display unit, such that a continuous display of the pattern, flow/volume or pressure/

volume is present on the screen of the display unit. The microprocessor system also has the capability of freezing a particular pattern for making photographs such as that shown in Fig. 8.15.

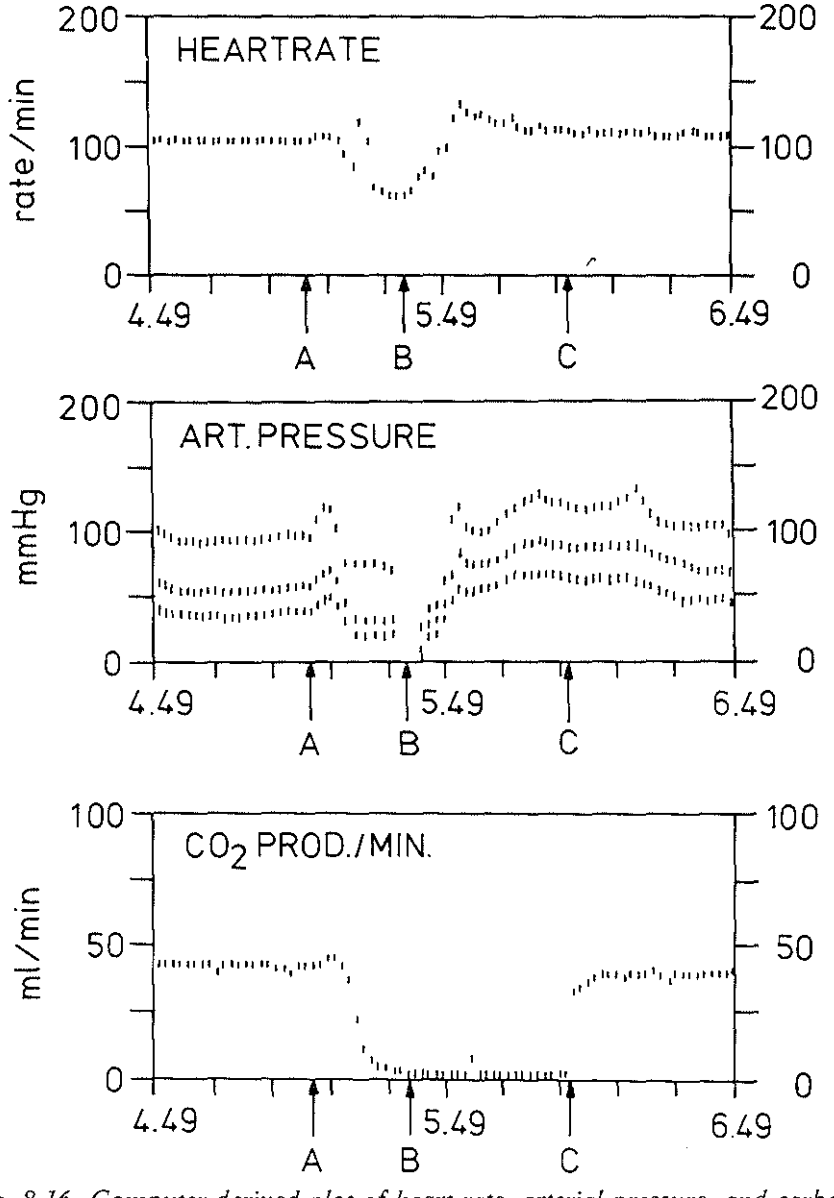


Fig. 8.16. Computer-derived plot of heart rate, arterial pressure, and carbon dioxide production per minute in a baby after open-heart surgery. Between points B and C the patient was hand-ventilated. The units are hours.

Case 9: Carbon dioxide production tracings in sudden blood loss

A 4.4 kg female infant underwent operative correction of a muscular V.S.D. under deep hypothermia. Cooling and surgery were uneventful. The patient was mechanically ventilated during the post-operative period. Twenty-four hours after admission to the intensive care unit the radial arterial monitoring line became partially disconnected, which led to profuse bleeding. Sudden changes were observed in arterial pressure and heart rate (Fig. 8.16), although these changes did not immediately indicate the severity and extent of the bleeding. However, when it was seen that the carbon dioxide production tracing had fallen to near zero, a severe drop in pulmonary perfusion was virtually certain, and hypovolaemic shock appeared imminent. The severity of the haemodynamic change was instantly reflected by a change in carbon dioxide elimination (Fig. 8.16).

This observation has a general application. Sudden changes of lung perfusion are always accompanied by changes of carbon dioxide elimination. This has been used to detect such phenomena as pulmonary embolization.[4] The following two cases provide other examples.

Case 10: Carbon dioxide tracings in an infant with pulmonary edema

A 2 kg prematurely born infant aged 2 months was admitted to Sophia Children's Hospital Rotterdam with symptoms of respiratory distress. On blood gas analysis, it was found that the child had a $PaCO_2$ of 8.7 kPa and an arterial oxygen saturation of 90%. A chest X-ray revealed both the lung areas were severely congested. On cardiac catheterization, a ventricular septal defect with pulmonary hypertension was diagnosed.

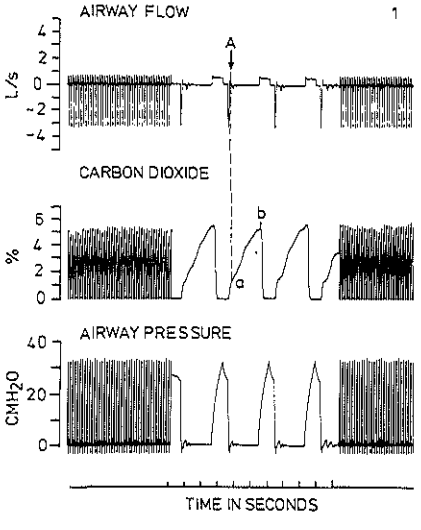


Fig. 8.17. 8 hr. 15 min. The carbon dioxide curve does not show an alveolar plateau. This signifies that the alveolar fraction of expired air did not pass the infra-red carbon dioxide sensor. Therefore, peak values of 5.4% carbon dioxide do not represent the real alveolar carbon dioxide and could be misleading if used for carbon dioxide control of mechanical ventilation. Airway flow stops very early (point A), at a time when the carbon dioxide of expired gas is very low. During the rest of expiration, carbon dioxide in the Y-piece slowly increases due to diffusion, cardiac oscillations, and very low flow (points a to b). This ventilation pattern represents largely dead space ventilation. It can only be understood from the recordings if expired flow and carbon dioxide are regarded together.

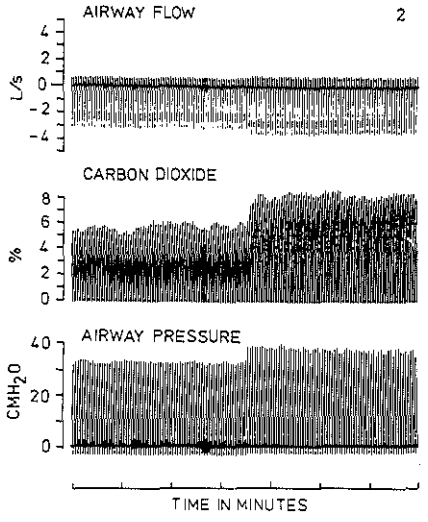


Fig. 8.18. 8 hr. 46 min. The minute volume of ventilation increased from 2.0 l to 2.5 l, and the peak inspiratory pressure rose from 33 to 38 cmH_2O. Frequency of ventilation remained the same at 20 breaths per minute. The tidal volume changed from 100 to 125 ml. Due to this increase in tidal volume, peak values of carbon dioxide rose from 5.4 to 8%. This signifies that before this change the real alveolar carbon dioxide content was at least 8%. A greater tidal volume reaches the alveoli, and end-tidal gas then represents more closely alveolar pCO_2.

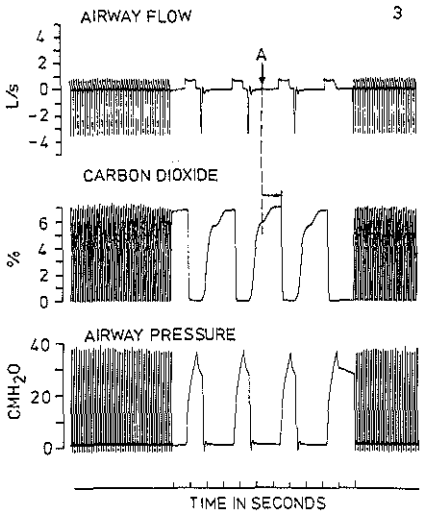


Fig. 8.19. 8 hr. 55 min. Carbon dioxide and expired flow curves are essential in order to analyse ventilation. The difference from Fig. 8.17 is clearly seen. Flow continues until point A when carbon dioxide is much higher than in Fig. 8.17. The carbon dioxide increases from that point because of reasons similar to those given previously (arrow). Thus, improved gas exchange has occurred, but gas exchange is still severely compromised. At 8 hr. 56 min. the value of Pa_{CO_2} was 10.3 kPa, and Pa_{O_2} was 11.0 kPa.

The child was anaesthetized for emergency surgery for the correction of V.S.D. After induction of anaesthesia, the infant's temperature was lowered to 26°C by surface cooling and then to 16°C by extracorporeal circulation. During the period of total circulatory arrest an open ductus Botalli and an atrial septal defect with abnormal inflow of the right pulmonary veins in the right atrium were identified and repaired. The ventricular septum was intact. The patient was ventilated for three weeks after the operation and is now thriving and well.

In this infant the main impediment to adequately controlled ventilation was a low compliance and an increased airway resistance due to oedematous lungs, secondary to heart failure. The patient needed a larger minute volume and a higher inflation pressure than under normal conditions. Pressure, flow, and % carbon dioxide tracings during anaesthesia and positive pressure ventilation are shown and explained in Figs. 8.17 to 8.21. For comparison, similar tracings without any pulmonary pathology are shown in Fig. 8.22.

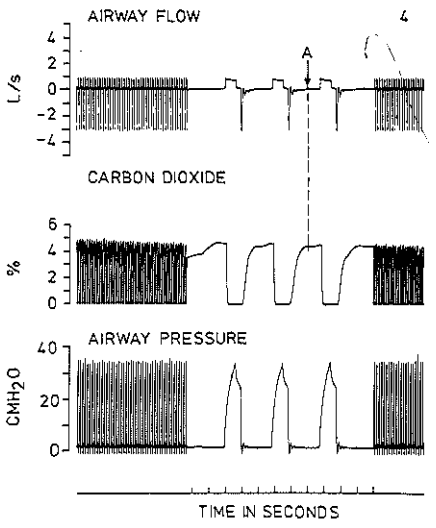


Fig. 8.20. Tracings at nasopharangeal temperature of 28°C. Ventilation remained the same. The end-tidal carbon dioxide was 4.9%, and the single breath carbon dioxide trace shows a broader plateau. The value of Pa_{O_2} was 20.1 kPa, with Pa_{CO_2} at 5.4 kPa. Here we see that at a lower temperature the gas exchange improved tremendously, which we find difficult to explain. Analysis of pressure and flow curves revealed that compliance improved with the entry of more gases into the alveoli. Slower expiration can also be seen in the tracings when the gas flow stops at point A; the carbon dioxide tracing has then nearly reached a stable plateau.

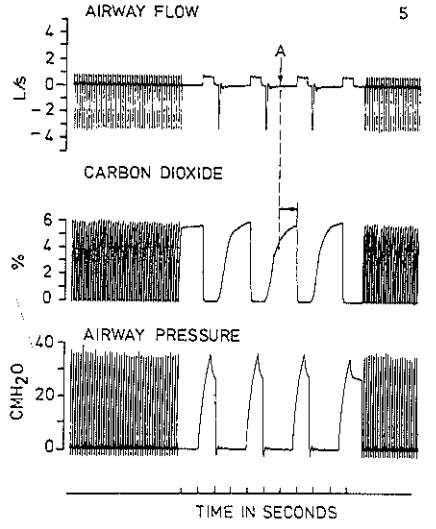


Fig. 8.21. 13 hr. 15 min. Tracings after closure of the thorax. There was no change in ventilation. The end-tidal alveolar plateau is again missing. When flow ceases (point A), carbon dioxide continues to rise, as during cooling (arrow), although the pattern is not that severe. The peak value of 6 vol % carbon dioxide (about 6 kPa) only roughly indicates alveolar carbon dioxide content. The arterial blood gas values were Pa_{CO_2} 6.7 kPa and Pa_{O_2} 9.8 kPa. Compared with the previous tracings, compliance fell again. A large dead space reappears. The explanation for this occurrence is difficult to ascertain.

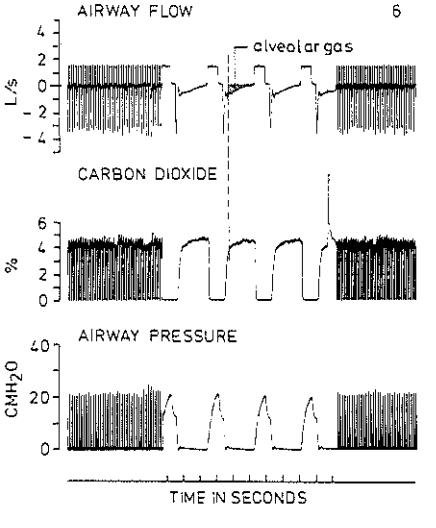


Fig. 8.22. Single-breath tracings of end-tidal carbon dioxide from a child undergoing deep hypothermia without lung congestion, showing adequate carbon dioxide exchange from a large part of expired volume (shaded area). Inspiratory peak pressure is normal.

The main conclusion derived from the tracings is that carbon dioxide curves are indispensable for accurate analysis of alveolar ventilation. Also, visualization or recording of flow curves along with carbon dioxide is indispensable for the determination of whether alveolar space or dead space "only" is ventilated. This example further demonstrates the value of non-invasive flow-pressure and carbon dioxide monitoring. The ventilator should not just push gases into the lungs, but also should be able to monitor patterns electronically.

Case 11: Short-term variations in cardiac output revealed by end-tidal carbon dioxide monitoring

A 6½ week old, 2.3 kg male infant underwent surgery for Truncus Arteriosis type I with V.S.D. This was an emergency operation. After induction of anaesthesia, the patient's temperature was lowered to 25°C by surface cooling and then to 16°C by extracorporeal circulation.

During the post-correction, post-perfusion period, a sudden severe fall in end-tidal carbon dioxide occurred, although ventilation and lung mechanics were unchanged. Within 6 minutes end-tidal carbon dioxide diminished to 0.7% (Fig. 8.23). This change occurred simultaneously with acute blood loss and a fall in arterial pressure.

A fall in end-tidal carbon dioxide during steady lung ventilation signifies a diminished delivery of carbon dioxide to the alveolar space, due to decreased pulmonary blood flow. Appropriate transfusion in this infant improved the circulation, and this was reflected by the increase to normal of end-tidal carbon dioxide.

8.3.3. Conclusion

The basic feature of our monitoring system which sets it apart from more conventional systems is the use of respiratory signals, i.e. airway pressure, flow, and gas composition. This makes it possible to detect and diagnose respiratory problems such as airway obstruction, tube disconnection, the efficiency of gas exchange, etc. The automated calculation performed by the

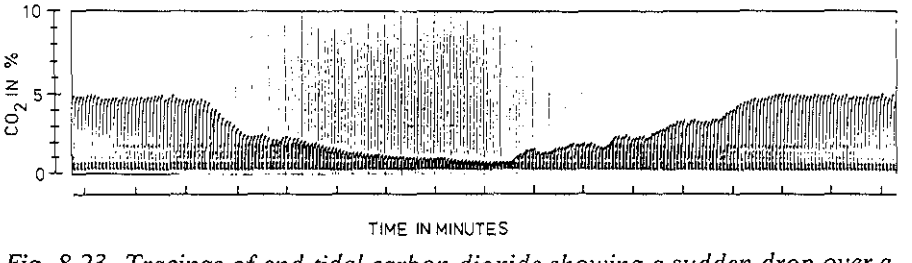


Fig. 8.23. Tracings of end-tidal carbon dioxide showing a sudden drop over a period of 5 minutes due to acute bleeding.

lung mechanics unit 930 and the carbon dioxide analyser 940 of several parameters relating to lung mechanics and gas exchange facilitates such a use of the system.

Respiratory monitoring in this context is very important in order to promote adequate ventilation and patient safety. In combination with conventional monitoring of circulation (e.g. ECG, arterial pressure), or even without it, the measurement of primarily respiratory signals offers new possibilities of detecting and analysing impending circulatory disasters.

In this context, the relationship between expired carbon dioxide and circulation is of great importance. As is well known, end-tidal carbon dioxide is in most cases readily controlled by a ventilator that is adequate. Once a proper ventilation pattern is established, one expects a stable carbon dioxide elimination via the lungs. If then this stable pattern is broken, the Platform permits a search for causes. As has been shown above, circulatory failure is a common reason for a non-stable gas exchange. A sudden fall in pulmonary perfusion will lead to a decreased delivery of carbon dioxide to the alveoli, which in turn lowers carbon dioxide output, and secondarily, a lower end-tidal carbon dioxide. A slower depression of circulation may constitute another cause for a decreased carbon dioxide output. In such a case one might expect that the increasing venous carbon dioxide content would compensate for the lower pulmonary perfusion and thus maintain carbon dioxide output more or less unchanged. However, this seldom appears to be the case. As is generally recognized, the peripheral circulation is progressively "shut down", leading to a cooling of peripheral tissues; this will lead to a decreasing peripheral metabolic carbon dioxide production and an increased storage of carbon dioxide in peripheral tissues. Carbon dioxide delivery to the central circulation, and hence to the lungs, will decrease.

In the present context it is more rational to watch the carbon dioxide production per minute, available from the carbon dioxide analyser 940, than the end-tidal carbon dioxide. The reason for this is that a more uneven ventilation perfusion relationship, which often accompanies a circulatory depression, will increase the slope of the carbon dioxide concentration curve, and hence give an increased end-tidal carbon dioxide. This is illustrated by one of the cases (Fig. 8.9).

As end-tidal carbon dioxide is useful for other purposes as well, one may choose to use this in spite of what has been said above. A display on an oscilloscope of carbon dioxide single breath curves (carbon dioxide concentration versus expired volume) is a powerful help.[5] Display of carbon dioxide concentration versus expired volume is preferable to the more conventional display of carbon dioxide concentration versus time, since, in most cases, expiratory flow is higher initially, and then rapidly decreases. The conven-

tional presentation may thus create a false impression that a plateau in the curve has been reached. This plateau may only reflect that gas is standing still in the tubings.

As was demonstrated by cases 1 and 2, a fall in compliance may offer the earliest sign of primarily circulatory problems such as intrathoracic bleeding and pulmonary oedema. Again, the sign drawing attention to a problem arising is non-specific. The nature of the problem can only be unravelled after an analysis of the whole situation. This analysis is based on conventional methods and upon those data that are specifically offered by the Platform.

Ventilation and lung mechanics monitoring, carbon dioxide analysis, as well as conventional circulatory monitoring, combine to offer the basis for the detection and diagnosis of a crisis, a circulatory crisis not being the least common.

8.3.4. References

1. Gerst PH, Rattenborg C, Holaday DA: The effects of hemorrhage on pulmonary circulation and respiratory gas exchange. J Clin Invest 38: 524, 1959.
2. Prakash O, Jonson B, Meij S et al: Criteria for early extubation after intracardiac surgery in adults. Anesth Analg 56: 703, 1977.
3. Osborn JJ: Cardiopulmonary monitoring in the respiratory intensive care unit. Med Instrum 11: 278, 1977.
4. Hurter D, Sebel PS: Detection of venous air embolism. A clinical report using end-tidal carbon dioxide monitoring during neurosurgery. Anaesthesia 34: 578, 1979.
5. Jonson B, Nordström L, Olsson SG et al: Monitoring of ventilation and lung mechanics during automatic ventilation. A new device. Bull Physiopath Resp 11: 729, 1975.

CHAPTER 9
Summary and conclusions

Monitoring of heart and lung function today has reached a high standard of technological advancement. This is the result of world-wide contributions to the development and use of highly sophisticated transducers, sensors and minicomputers. The surgical advances made over the last few years have also demanded a corresponding improvement in parameter measurement, so that a knowledge of the varying physiological status of the patient must now be constantly available. The days of casual and often inadequate, or even non-existent, monitoring of patients are at an end; it must now be considered an act of irresponsibility merely to guess at the state of the patient's vital functions. Also, the increasing levels of medico-legal involvement today make it mandatory for the physician to protect his own well-being as well as that of his patient.

This thesis has been written in order to present and emphasize the great value which can be gained from routine monitoring of heart and lung function in the operating theatre. Greater emphasis has been placed on lung rather than on heart function, partly because the former type of monitoring is, generally speaking, inadequately performed or totally ignored, but more especially because abnormalities in lung function often give very early and specific indications of impending problems. These may vary from the early diagnosis of post-operative intrathoracic bleeding to the immediate recognition of the simple but equally dangerous problem of endotracheal tube disconnection during mechanical ventilation.

In patients undergoing major surgery, detailed pulmonary function monitoring is sometimes started only in the post-operative period, once the patient reaches the intensive care unit. This thesis demonstrates that life-threatening situations often begin to develop during the operative period, and may be plainly revealed by the lung function monitors; this is especially true in thoracic surgery or surgery involving the great vessels. If monitoring of the lung functions is not commenced in the operating theatre, the opportunity to anticipate serious complications early on in their development will be missed and they may only be revealed when it is too late to institute effective treatment. Similarly, a lack of baseline monitoring information from the pre-operative period highly reduces the value of observations at the operating table, as the data obtained at this stage cannot be compared with corresponding pre-operative values.

Thus, a comprehensive monitoring system, flexible enough to be tailored to the complexity of the particular operation and anaesthetic involved, must be

attached to the patient on arrival in the anaesthetic induction room. It must then be continued throughout the intra- and post-operative periods.

In this thesis, such a comprehensive monitoring system has been described. At the Thorax Centre Rotterdam, this system has proved to be fully adequate and to allow an accurate study and control of pulmonary physiology during cardiac and pulmonary surgery as well as in the post-operative period. The system has been termed the "Methodological Platform". Some earlier reports of its development have appeared in the literature but in most of the studies considered in this thesis the latest version of the Platform was employed. In addition to allowing the accurate control of respiratory gas exchange and stabilization of desired arterial carbon dioxide tensions, the Methodological Platform has been proved to provide sufficient data for a number of specialized applications.

During progressive hypothermia for cardiac surgery, the need for advanced and comprehensive physiological monitoring systems is even more apparent and vital. A review of the literature on the physiological effects of hypothermia in animals reveals that the "physiological neutrality" intracellularly is achieved at progressively higher pH values as temperature falls, and that this more alkaline acid-base balance is apparently achieved while the total carbon dioxide content of the tissues remains at normothermic (normal body temperature) levels. Based on this, an anaesthetic technique was studied, whereby the ventilation was maintained throughout the cooling/surgery/re-warming cycle at normothermic levels. This allowed a progressively more alkaline acid-base environment to be achieved. This technique is discussed in detail, together with information relating to the circulatory changes and complications seen and the degree of acid-base control obtained. The conclusion is drawn that the addition of carbon dioxide to the ventilation gases, or alternatively, a decrease in ventilation as temperature falls, is not only unnecessary, but perhaps also harmful.

During anaesthesia for coronary artery surgery, the Methodological Platform was used to monitor physiological and biochemical parameters while different regimes of induction and maintenance of anaesthesia, with fentanyl and nitrous oxide, were compared. The results of this investigation demonstrates that only when a high dose of fentanyl (15 μg/kg) is given in conjunction with 60% nitrous oxide in oxygen, does the patient's oxygen consumption and cardiac index fall in the same ratio as blood pressure and respiratory function parameters. In addition, this study reveals a reduction in the circulating free fatty acid levels in these patients. These factors may be of importance to the cardiac patient with severely compromised myocardial function.

Finally, some practical examples of the value of pulmonary and respiratory

function monitoring are briefly described. Attention is drawn to factors such as increased patient safety, early anticipation and diagnosis of surgical and anaesthetic problems, and the easing of decision-making, using this type of monitoring equipment, and each example is briefly discussed with respect to its significance.

The conclusion reached is twofold.

Firstly, the author is convinced that monitoring of pulmonary and respiratory physiology is of fundamental importance in the conduct of anaesthesia for major surgery, especially cardiac and thoracic surgery, and of patient care in the post-operative intensive care unit.

Secondly, the "Methodological Platform" has proved itself to be readily understood by physicians and nurses, and to be flexible and easily used, thus adding significantly to the quality of patient care. It has also given way to a number of important steps forward in the fields of intra- and post-operative patient care.

SAMENVATTING

Het voortdurend gadeslaan van hart- en longfunctie heeft heden ten dage een hoge technische standaard bereikt. Dit is het gevolg van bijdragen uit de gehele wereld tot de ontwikkeling en het gebruik van zeer geavanceerde signaalopnemers, signaalverwerkers en steeds kleinere rekentuigen. De chirurgische vooruitgang van de laatste jaren heeft bovendien op zichzelf geleid tot een verbetering in de metingen van de verschillende parameters, zodat kennis van de steeds veranderende fysiologische toestand van de patiënt voortdurend ter beschikking dient te zijn. De dagen van toevallige, van veelal onvoldoende, of zelfs geheel afwezige, informatie over de toestand van een patiënt zijn voorbij; thans zou het onverantwoord handelen zijn om slechts naar de toestand van de patiënt en zijn vitale functies te gissen. Daarbij komt de toenemende medisch-legale verantwoordelijkheid die de arts haast verplicht om zowel zichzelf als de patiënt te beschermen.

Dit proefschrift is vooral geschreven om de grote waarde van een routinebewaking van hart- en longfunctie in de operatiekamer aan te tonen en het belang daarvan te benadrukken. Vooral op de functie van de long naast hartfunctie wordt de aandacht gevestigd, omdat bewaking van de eerste tot nu toe in het algemeen onvoldoende wordt uitgevoerd of zelfs geheel wordt miskend. Nadruk op de long ook, omdat afwijkingen in longfunctie vaak vroegtijdig en specifieke indicaties geven van dreigende problemen. Deze indicaties kunnen uiteenlopen van de zeer vroege diagnose van een postoperatieve bloeding binnen de borstkas tot aan de onmiddellijke herkenning van het misschien simpele, maar op zichzelf even gevaarlijke probleem van het losraken van de endotracheale buis gedurende mechanische ventilatie.

Bij patiënten die een zware operatie ondergaan, worden de meer gedetailleerde longfunctie-analyses soms pas in de postoperatieve periode aangevangen, nadat de patiënt in de intensieve-bewakingsafdeling is aangekomen. Dit proefschrift toont aan dat levensbedreigende situaties vaak hun begin vinden in de operatieperiode zelf en dat daarvan de tekenen reeds duidelijk kunnen worden waargenomen op de bewakingsapparatuur. Dit is in het bijzonder het geval bij operaties op organen binnen de thorax. Als bewaking van de longfunctie niet reeds in de operatiekamer begint, mist men dé gelegenheid om ernstige problemen tijdig te voorzien of in een vroeg stadium te ontdekken; worden de complicaties later ontdekt, dan kan het te laat zijn voor werkelijk effectieve behandeling.

Op min of meer gelijke wijze is het ontbreken van informatie over de verschillende functies tijdens de pre-operatieve periode een nadeel. Dit

vermindert de waarde van veel observaties aan de operatietafel, aangezien de waarden uit die fase niet kunnen worden vergeleken met de pre-operatieve bevindingen.

Uit het voorgaande volgt, dat een geïntegreerd bewakingssysteem, aanpasbaar aan de vaak gecompliceerde omstandigheden van een specifieke operatie en een bepaald anaestheticum, op de patiënt dient te worden aangesloten, zodra hij arriveert voor de inductie van de anaesthesie. Deze bewaking dient dan te worden voortgezet gedurende de operatiefase zelf en daarna uiteraard voor zover nodig in de postoperatieve periode.

In dit proefschrift wordt een dergelijk geïntegreerd bewakingssysteem beschreven. Ervaringen in het Thoraxcentrum Rotterdam hebben aangetoond, dat het systeem zeer adequaat werkt en een accurate analyse en controle van de longfysiologie gedurende hart- en longchirurgie en in de postoperatieve periode mogelijk maakt. Het systeem is genoemd het "Methodologische Platform". Reeds eerder is over de ontwikkelingsfase gerapporteerd in de wereldliteratuur, maar de meeste ervaringen beschreven in dit proefschrift zijn gebaseerd op de meest recente versie van het Platform. Naast de zorgvuldige controle van de respiratoire gas-uitwisseling en de stabilisatie van de vereiste arteriële CO_2-spanning, bleek het Methodologische Platform ook in staat om voldoende verdere gegevens te leveren, zodat een aantal specifieke berekeningen van afgeleide waarden kon worden uitgevoerd.

Gedurende diepe hypothermie, gebruikt bij hartchirurgie, is de noodzaak van een dergelijke fysiologische bewaking nog duidelijker en van nog meer vitaal belang. Een overzicht van de literatuur over het fysiologische effect van hypothermie bij dieren toont aan, dat "fysiologische neutraliteit" intracellulair wordt bereikt met steeds hogere pH-waarden terwijl de temperatuur zakt. Dit meer alkalische zuur-base-evenwicht wordt blijkbaar bereikt terwijl het totale CO_2-gehalte van de weefsels op normothermisch niveau blijft, d.w.z op normale lichaamstemperatuur. Als gevolg hiervan is een anaesthetische techniek ontwikkeld waarbij de ventilatie op normothermisch niveau werd gehouden gedurende de gehele cyclus van afkoelen→chirurgie→opwarmen. Deze techniek liet een geleidelijk meer alkalisch zuur-base-evenwicht toe. Gedetailleerde informatie wordt ook verstrekt over de veranderingen in de circulatie, de verschillende complicaties die daarbij zijn geobserveerd, en de graad van controle van het zuur-base-evenwicht. De conclusie wordt getrokken, dat het toevoegen van CO_2 aan de gewoonlijk bij de ventilatie gebruikte gassen of als alternatief een vermindering van ventilatie terwijl de temperatuur daalt, niet alleen onnodig is, maar mogelijkerwijs ook schadelijk.

Gedurende de anaesthesie voor coronairvaatchirugie is het Methodologische Platform gebruikt om fysiologische en biochemische parameters te bestuderen en te bewaken terwijl verschillende mengsels van inductie en

onderhoud van anaesthesie met fentanyl en lachgas werden vergeleken. De resultaten van dit onderzoek tonen aan, dat alleen met hoge dosering van fentanyl (15μg/kg) samen met 60% lachgas in zuurstof, het zuurstofverbruik en het hart-minutenvolume van de patiënt in gelijke mate dalen als de verschillende componenten van bloeddruk en ademhalingsfunctie. Deze analyse bracht verder een vermindering in het aantal vrije vetzuren in de circulatie bij deze patiënten aan het licht. Deze factoren kunnen van belang zijn bij de hartpatiënten met pre-operatief ernstig gestoorde hartfunctie.

Tenslotte wordt een aantal praktische voorbeelden gegeven van de waarde van het bewaken van long- en ademhalingsfunctie. Met name wordt de aandacht gevestigd op factoren zoals verhoogde veiligheid van de patiënt, de vroege anticipatie en tijdige diagnose van chirurgische en anaesthetische problemen en het vergemakkelijken van de besluitvorming, wanneer dit soort bewakingsapparatuur wordt gebruikt. Ieder voorbeeld wordt kort toegelicht met betrekking tot zijn klinische belang.

Er zijn in feite twee hoofdconclusies te trekken.

Ten eerste is de auteur overtuigd van het feit, dat continue bewaking van longfunctie en ademhalingsfysiologie van wezenlijk belang is tijdens het uitvoeren van anaesthesie bij de ernstige vormen van chirurgie, met name bij hartoperaties en andere ingrepen binnen de borstkas. Dit is tevens van groot belang tijdens de postoperatieve intensieve-bewakingsfase.

Ten tweede heeft het Methodologische Platform aangetoond dat het gemakkelijk te gebruiken is door artsen zowel als door verpleegkundigen, dat het zeer gemakkelijk onder klinische omstandigheden is aan te passen en dat het derhalve tot de kwaliteit van de patiëntenverzorging bijdraagt. Verder heeft het mogelijkheden geopend om een aantal belangrijke stappen vooruit te doen op het terrein van de intra- en postoperatieve patiëntenverzorging.

CURRICULUM VITAE

The author was born July 7, 1936 in Gorakhpur (India). He completed high school at D.B. Intermediate College, Gorakhpur, and obtained his Bachelor of Science degree from Agra University. The author then obtained medical education (M.B., B.S.) at King George's Medical College, Lucknow, India. From 1961 to 1966, training in general medicine, general surgery, and anaesthesia was acquired in National Health Services Hospitals in the United Kingdom. Further training in anaesthesia and intensive care management was obtained in Denmark and Norway.

For a short period commencing in 1970 the author was an anaesthetist at Sint Franciscus Gasthuis, Rotterdam, and subsequently took a position as anaesthetist at the Thorax Centre, Academic Hospital, Erasmus University, Rotterdam. His Dutch medical degree was obtained in 1972, and he was registered as a specialist anaesthetist in the same year.