SOME RECENT DEVELOPMENTS IN ANAESTHESIA*

D. J. C. NICHOLSON, M.B., CH.B., D.A., R.C.P. AND S.

Chief Anaesthetist, Johannesburg Hospital

The student of anaesthesia is now faced with a vast literature and, without guidance, it is easy to stray far from sound physiological principles. Much of the research on which current advances in anaesthesia are based is the work of chemists and pharmacologists, but the final assessment of any new drug or technique must always be clinical and a large proportion of the literature which the modern anaesthetist reads consists of this type of review. In the bulk of these papers there is nothing fundamentally new. The agents and methods discussed differ only in detail from those in common use and the advantages claimed for them often lie mainly in the imagination of the writer. Such investigations form part of a general process of trial and elimination but, for the most part, they have little influence on general trends. From time to time, however, there are more important advances which are based on new concepts and these are the developments which, if they survive exhaustive trial, lead to real progress.

Any new and interesting development in anaesthesia is likely to attract a good deal of attention, and the present fiercely competitive spirit which pervades the whole of medicine will ensure that there is no lack of clinical investigators. With the best of intentions, the earlier papers, especially those where impression rather than scientific observation has been relied on, are likely to have a leaning towards positive findings and the advantages of the innovation tend to be over-emphasized. Unfortunately these advantages may be taken too seriously by enthusiasts having little time for reflection but a deep horror of being considered unprogressive.

The two main factors which determine whether an innovation is to be of lasting importance or whether it is destined to early oblivion are (1) its clinical utility, and (2) the extent to which it can be reconciled with physiological principles. The second factor is the crux of the matter, for it is much easier to produce dramatic results than to produce them safely. It is intended to pursue this theme in relation to 3 important developments in anaesthesia during the last decade, viz. (1) muscular relaxants, (2) controlled hypotension, and (3) hypothermia and autonomic block.

MUSCULAR RELAXANTS

The use of curare in anaesthesia by Griffiths and Johnson,[1] whose work was published in 1942, was probably one of the most important advances in anaesthetic technique since the application of the narcotic properties of nitrous oxide and ether for the relief of pain in surgical operations. Profound muscular relaxation, especially for abdominal work, has alwyas been a much sought-after ideal but the problem was to achieve it without submitting the patient to the effects of prolonged 4th-plane ether anaesthesia. Attempts to get relaxation by combining regional (or spinal) analgesia with light general narcosis have met with considerable success but, besides being somewhat cumbersome and time consuming, these methods often lack sufficient flexibility to meet modern surgical requirements.

The state termed 'surgical anaesthesia' has a much wider significance than the progressive depression of the central nervous system which is often described in text-books. The whole neuromuscular mechanism is involved and the quality of the anaesthesia depends on the selective action of the agent employed at numerous points on that vast complex. Though perhaps oversimplified, this concept has been admirably expressed by Nosworthy[2] in a discussion of the central and peripheral effects of different anaesthetics. The patient's main concern is to be put comforably to sleep and this aspect of anaesthesia is a matter of central depression. The peripheral effect is, however, largely responsible for good muscular relaxation and absence of undesirable reflexes at a reasonable level of narcosis, and this factor is only appreciated by the surgeon and anaesthetist. Ether has retained its position as the most important anaesthetic agent for more than a century because in it is to be found a better balance of central and peripheral action than in any other single drug, and it was not until the idea of 'balanced anaesthesia', by the use of multiple drugs, came into being that much improvement was possible.

By combining neuromuscular block with light general anaesthesia it is possible to obtain both muscular relaxation and a supression of reflex response to surgical stimuli without undue central depression, which is an important factor in a well-balanced anaesthetic. The effect on the respiratory muscles, although in some respects a disadvantage, is of great value in solving the anaesthetic problems of the open pneumothorax. Experience with prolonged intrathoracic procedures has also shown that mechanical ventilation of the lungs, if properly carried out, can be made to fulfil essential physiological requirements extremely well. Provided the administration is controlled so as to avoid *post-operative* respiratory depression, the muscular relaxants now in common use have few drawbacks and are singularly free from toxic side-effects.

In short, the use of neuromuscular block has clearly shown that the most satisfactory balance in surgical anaesthesia is attained with a greater degree of peripheral depression (relative to central depression) than can be realized by the use of any known narcotic agent. Apart from the great improvement in operating conditions, it is therefore possible to get much closer to the physiological ideal, and this is reflected in the universal acceptance of muscular relaxants in anaesthetic practice.

CONTROLLED HYPOTENSION

Rightly or wrongly, the anaesthetist has always been blamed for causing excessive haemorrhage during

* A paper presented at the South African Medical Congress, Pretoria, October 1955.

operations and, in the past, the anaesthetist who was an accomplished chloroformist was usually popular with his surgical colleagues. It is well known that many anaesthetic agents cause peripheral vasodilatation and that some are directly responsible for a considerable increase in the cardiac output. Faulty technique involving such factors as inadequate depth of anaesthesia, respiratory disturbances, or excessive re-breathing, may also increase the haemorrhage from the operation site. Care in administration, and in the choice of agent, can do much to mitigate this nuisance, but much more is required to satisfy the modern conception of 'bloodless surgery' and the realization of this end by direct assault on the haemodynamics is a more recent development.

Gardner and Hale[3] recommended arteriotomy to minimize bleeding in surgical operations, and Gillies[4] used high spinal block to secure haemostasis in cases of thoracolumbar sympathectomy. These methods have never become widely popular, but Paton and Zaimis[5] investigated the ganglion-blocking properties of certain methonium compounds (pentamethonium iodide and hexamethonium bromide), and the arteriolar dilatation produced by the intravenous injection of these agents has been used clinically[6] in the technique generally referred to as 'controlled hypotension'. The methonium compounds were followed by Arfonad (a thiophanium derivative), which has a much shorter action making for greater flexibility.[7,8] The intravenous methods of producing hypotension, because of their greater simplicity, have attracted much more attention.

The degree of haemostasis which can be secured by such means is very striking, and it is not surprising that controlled hypotension should be popular with surgeons, especially those interested in procedures where excessive bleeding may prejudice the result of the operation. The term hypotension does not, however, give the whole story. In the absence of other important changes in the haemodynamics, lowering the blood pressure by reducing the peripheral resistance would not provide an avascular operation field—in fact quite the reverse. The mechanism by which this is attained is a pooling of the blood in the dependent parts of the body accompanied by a decreased flow in those which are uppermost. Posture thus plays an important part and, if the operation is within the area from which blood is returned to the heart *via* the superior vena cava, an anti-Tredelenburg position must be employed. In such a case, it is clear that the blood supply to the brain must be affected in a similar manner. To a certain extent human tissues will tolerate a subnormal blood-supply and may compensate by an increase in their oxygen-utilization coefficient. Hughes[9] has shown that in hexamethonium bromide hypotension, with a head-up position, the blood supply to the brain is diminished but oxygen utilization increased as demonstrated by an increased arterio-venous oxygen difference. This means that the safety margin is necessarily reduced.

Although there is a widely prevalent idea that a bloodless operation-field can be obtained without affecting the blood supply to the various important organs, the condition of the circulation differs from that in true shock only in so far as the arterioles are dilated instead of contracted so that, within limits, the effect is reversible. While it is maintained it is associated with the same anoxic hazards and, if too protracted, there is always a risk that real shock may supervene. Controlled hypotension may produce dramatic improvement in operating conditions but it is far from realizing the happy union of clinical utility and physiological ideal which is found in neuromuscular block. The administrator is often achieving his end in conflict, rather than in conformity, with vital principles and must depend on his judgment and experience to avoid going too far. The weight of responsible opinion is very reserved[10,11] and may be summed up in the verdict that hypotension is probably justified for an essential operation which cannot be undertaken without it but is certainly not to be used as a convenience.[12] A relatively short time has revealed an alarming number of serious complications which are attributable to the technique.[13]

HYPOTHERMIA AND AUTONOMIC BLOCK

Further interesting developments have arisen from attempts to lower the oxygen requirements of the body in order to make possible procedures which may require the temporary suspension of the circulation. This involves the production of a state similar to that of a hibernating animal and, up to the present, the only way of getting the metabolic rate down to the levels aimed at is by lowering the body temperature. This process is beset by some formidable problems, the most serious being the liability to ventricular fibrillation below 28° C. There is also evidence that the techniques normally employed may cause damage to tissues.[14]

Laborit and Huguenard[15] have investigated drugs of the phenathiazone group as a means of reducing shock and potentiating anaesthesia by blocking the autonomic nervous system, thus preventing excessive response to stress. These drugs, the most important of which is chlorpromazine, have also been used as an adjunct to hypothermia where it is necessary to control the shivering reaction[16], and the association seems to have led to the idea that chlorpromazine itself has an important influence on the metabolic rate. Dobkin, Gilbert and Lamoureux[17] have, however, shown that this is not the case, so that the application of the term 'hibernation' to the use of chlorpromazine (otherwise than in association with hypothermia) is misleading.

The scope of hypothermia in anaesthesia is still very restricted, but chlorpromazine, as an autonomic blocking agent, has become very popular. Its employment appears to be particularly applicable where an operation of exceptional severity has to be performed on a poor-risk subject but *where there are full facilities for control of shock and haemorrhage by fluid replacement.* Unfortunately, the acceptance of the unqualified platitude that 'hibernation' is good for shock has frequently led to this vital principle being lost sight of; and it is not uncommon to find references to the use of chlorpromazine in cases of uncontrolled circulatory failure (due to both trauma and toxaemia) on the reports submitted for inquests on deaths in association with anaesthesia. The pre-operative condition of most of these cases has been sufficiently grave to make it impossible to draw the conclusion that the drug had significantly influenced

the outcome but, at the same time, there did not seem to be any valid reason for imagining that it would do any good.

If used in large doses, chlorpromazine considerably prolongs the period of post-operative unconsciousness, though reflexes are usually active and the patient able to respond to stimuli. Such an effect may be of value in certain cases for combating post-operative pain and shock but, if the principle that early movement is an important factor in reducing the incidence of embolism and pulmonary complications still holds good, its wholesale use in anything but minimal dosage is to be deprecated.

In conclusion, it may be of interest to return to the subject of hypothermia proper and to indulge in a little speculation. It must be remembered that, in hibernating mammals, the lowering and re-establishment of the normal metabolic rate are relatively gradual processes while, in the operating theatre, an attempt is made to achieve in less than an hour a change which takes nature a very much longer time. While as yet there is no satisfactory solution to the problem, the finding of such a solution would mean an advance of the utmost importance. The pieces in the puzzle with which surgeons and anaesthetists are now groping would then fit into a common pattern, for an adequate reduction in the oxygen requirements of the body, besides facilitating the performance of operations requiring a suspension of the circulation, would bring the bloodless field fully into conformity with physiological principles. One might even go further and suggest that such a control of metabolism would go a long way towards eliminating the need for narcotics; for anaesthesia itself is intimately associated with a reduction in cellular oxygen-consumption. The nature of the problem should not, however, be under-estimated and it would probably be unwise to imagine that medicine is on the brink of its solution.

REFERENCES

1. Griffiths, H. R. and Johnson, G. E. (1942): Anesthesiology, **3,** 418.
2. Nosworthy, M. D. (1953): Anaesthesia, **8,** 247.
3. Gardner, W. J. and Hale, D. G. (1946): J. Amer. Med. Assoc., **132,** 572.
4. Griffiths, H. W. C. and Gillies, J. (1948): Anaesthesia, **3,** 134.
5. Paton, W. D. M. and Zaimis E. J. (1949): J. Physiol., **108,** 55.
6. Enderby, G. E. H. (1951): Proc. Roy. Soc. Med. **44,** 829.
7. Sarnoff, S. J., Goodale, M. T. and Sarnoff, L. C. (1953): Circulation **6,** 63.
8. Sadove, M. C., Wynant, G. M. and Gleave, M. D. (1953): Anaesthesia, **8,** 175.
9. Hughes, G. (1955): Brit. J. Anaesth., **27,** 229.
10. Shackman, R., Graber, I. G., Melrose, D. G. and Smith, J. (1952): Anaesthesia, **7,** 217.
11. Davison M. H. A. (1953): *Ibid.*, **8,** 255.
12. Editorial (1952): *Ibid.*, **7,** 65.
13. Anaesthesia (1953): '*Report of Association of Anaesthetists' Committee upon deaths associated with anaesthesia*', *Ibid.*, **8,** 263.
14. Knocker, P. In press.
15. Laborit, H. and Huguenard, P. (1952): Presse méd., **59,** 1329.
16. Dundee, J. W., Gray, T. C., Mesham, P. R. and Scott, W. E. B. (1953): Brit. Med. J. **2,** 1237.
17. Dobkin, A. B., Gilbert, R. R. B. and Lamoureux, L. (1954): Anaesthesia, **9,** 157.