

THE HISTORY OF CONTROLLED HYPOTENSION

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Controlled hypotension has been changing continuously and evolving not only as the result of the discovery of new agents and techniques, but also from an improved understanding of the underlying physiological changes which accompany its practice.

Almost without exception, the techniques and agents used for controlled hypotension have arisen from an "accidental" finding. Examples of the former are the haemorrhagic hypotension described by Gardner (1946), or the hypotension of high spinal block described by Griffiths and Gillies (1948), both of which are of historic interest only. The prime examples of the latter are the ganglionic blocking agents themselves, which were discovered by accident during systematic research (see later). The only technique which was deliberately applied was that described by Small and Campkin (Brown and Horton, 1966) in which a cardiac pacemaker electrode was used to pace the heart so rapidly that stroke volume was extremely curtailed. However, this has limited application in some neurosurgical centres. Neurosurgical practice has an obvious requirement for a technique of extreme evanescence, and it was for this reason that sodium nitroprusside was introduced into clinical practice (Moraca et al., 1962).

Historical aspects

Interest in induced hypotension was extremely limited until the advent of the ganglionic blocking agents, although bleeding had undoubtedly been a problem since surgery began. This was clearly in the mind of Humphry Davy when he penned perhaps the most enigmatic statement in the history of anaesthesia, ". . . it (nitrous oxide) may probably be used with advantage during surgical operations in which no great effusion of blood takes place" (Davy, 1800). Once the practice of anaesthesia became established, although the surgeon still caused the bleeding, the anaesthetist took the blame. This had some justification, since conscious patients certainly bleed less during surgery than those who are anaesthetized with volatile anaesthetic agents, although this could be considered a

small price to pay in exchange for freedom from pain. However, in addition, anaesthesia was not always conducted in a manner which was associated with gaseous homeostasis nor freedom from some degree of respiratory obstruction and straining—factors which promote bleeding.

In a few short years, following the Second World War, anaesthesia took a second leap forward after a century of relative quiescence.

1846–53 had seen the birth of anaesthesia and had taken the specialty from September 30, 1846—William Thomas Green Morton and Eben Frost's aching tooth—to April 7, 1853, when "Dr Snow gave the blessed chloroform and the effect was soothing, quieting and delightful beyond measure" (Queen Victoria, after the birth of her eighth child).

A century later similar dates, 1946–53, saw the rapid blossoming of modern anaesthesia. Political events produced the war-experienced anaesthetist, and the National Health Service ensured the permanency of the professional anaesthetist with consultant status, ready to apply instantly any new techniques and drugs at a speed which today would not be possible. Death from anaesthesia passed its zenith in spite of an increase in the number of administrations (Scurr, 1971). Intravenous induction of anaesthesia came into its own. The use of muscle relaxants and deliberate paralysis with artificial ventilation via an endotracheal tube—the triad approach of narcosis, relaxation and reflex suppression (Gray and Rees, 1952) and its concomitant of gaseous homeostasis—became firmly established.

Although methods for causing deliberate hypotension were already known to some anaesthetists, it was during this same period that controlled hypotension by means of pharmacological blocking agents swept into popular use. It is interesting that research into muscle relaxant drugs gave birth to the hypotensive agents but, paradoxically, it was the clinical acceptance of the muscle relaxants which obviated persistence of the initial panacea of the latter agents.

Anaesthesia in 1944

It is important to have an idea of the anaesthetic practice of the era into which induced hypotension

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was ushered. Perusal of a contemporary textbook of anaesthesia by Minnitt and Gillies (1944) shows that anaesthesia was maintained with either chloroform, ether, cyclopropane or sometimes trichloroethylene together with nitrous oxide and oxygen. Abdominal relaxation could only be achieved by deep anaesthesia, or sometimes by the use of a local anaesthetic technique (abdominal field block or spinal block), with light anaesthesia. Although endotracheal intubation was well established, this procedure of itself necessitated deep anaesthesia, and controlled ventilation was used only when inadequate respiration (judged by movements of the reservoir bag) necessitated some assistance. This was the case, even during lung surgery. It was routine that a large proportion of surgical patients were ill for some time after surgery, caused entirely by the "soaking of the tissues" with high concentrations of volatile anaesthetic agents.

Furthermore, there is little doubt that the spectrum of general health of the population was different. Wyman (1953) gave details of the starting systolic pressures in his 1000 cases of induced hypotension. Out of this number, 114 had an initial arterial pressure of over 200 mm Hg, while in a further 200 patients the figure was between 160 and 200 mm Hg. A 1975 anaesthetist might consider it unusual to meet arterial pressures of over 160 mm Hg in more than 1% of patients.

Thus, the population had a higher average arterial pressure, and anaesthetic techniques which had little regard to gaseous homeostasis were the rule rather than the exception, so that bleeding could often be a troublesome problem during surgery at this time when agents for reducing arterial pressure and thence bleeding became available.

Research into neuro-humoral blockers

The introduction of ganglionic blocking agents was inextricably involved with interest in neuromuscular blocking agents, with the result that the first ganglionic blockers were introduced as decamethonium antagonists.

Systematic research into the activity of certain compounds arose from the discovery of the quaternary nitrogen atoms in the structure of tubocurarine (King, 1935). In the May 1948 edition of *Nature* there are two juxtaposed letters to the Editor of the identical date—March 16, 1948—and under an identical heading, but from Oxford and Hampstead respectively. These detailed work by Barlow and Ing (1948), and Paton and Zaimis

(1948a), who set out to explore the tubocurarine-like action of polymethylene bis-quaternary ammonium salts. The former noted increasing activity with increasing length of CH₂ groups, while the latter also noted antagonism between tubocurarine followed by C10 (decamethonium) but not when C10 preceded tubocurarine. Six months later, in another letter despatched on August 17, Paton and Zaimis (1948b) wrote on the clinical potentialities of two members of the series of compounds, namely C6 (hexamethonium) and C10, and reported that C6 was a ganglionic blocking drug "offering possibilities of clinical usefulness in such fields as hypertension and vascular disease", whereas C10 was a useful neuromuscular junction blocker not antagonized by prostigmine (and therefore unlike tubocurarine; note that suxamethonium was introduced into clinical practice 3 years later—Scurr, 1951), but by the C5 member of the series, pentamethonium. And, recruiting an anaesthetist, Sir Geoffrey Organe (Organe, Paton and Zaimis, 1949), they each took C10 and produced postural hypotension in themselves with C5, and a severe syncopal attack in a further anaesthetist. This was reported on January 1, 1949, and clinical trials were then commenced under the auspices of the Medical Research Council. However, the release on to the market of C10 as "decamethonium" necessitated early publication on May 7, 1949 (Organe, 1949). Pentamethonium was the recommended antidote, although Hunter (1950) considered hexamethonium to be more effective.

It was immediately realized by some clinical anaesthetists that the "side-effect" of postural hypotension could be employed usefully during surgery to limit bleeding. By April, 1950, Enderby was sufficiently experienced to demonstrate the technique at a meeting of the South West Metropolitan Society of Anaesthetists (1950). Simultaneously, the definitive scientific paper reporting studies of this series of drugs appeared (Paton and Zaimis, 1949). At the same time both Davison (1950) from Newcastle and anaesthetists at Westminster Hospital (Organe, 1950) were deliberately lowering arterial pressure during anaesthesia.

Enderby's 1950 title was extremely apposite, since he wrote on "Controlled circulation with hypotensive drugs and posture to reduce bleeding in surgery" (Enderby, 1950) which embraces a precise description of the objective, the methods and the aim of the technique as practised clinically. Indeed, this title contains the credo of the modern

practitioner of controlled hypotension; that is, circulation in the surgical field is controlled to improve operating conditions without necessarily producing significant hypotension—a state of affairs for which Pallister (1973) has coined the term “rheostasis”.

1953 was a watershed year for induced hypotension. In the first place, Wyman became the first anaesthetist to deliver a Hunterian Oration, his subject being “The use of pentamethonium and hexamethonium salts in major surgery”. Although this was not published, Wyman led a discussion at The Royal Society of Medicine on February 4, 1953, based on a series of 1000 major surgical cases in which controlled hypotension had been used (Wyman, 1953). In the second place, it was clear from the discussion that the indications for induced hypotension were shrinking as the series of cases progressed. Not only that, the practice was on the wane, for Davison (1950, see earlier) reported that he had given up the technique, and Gray—of the triad approach—was opposed to its use unless it was restricted to certain cerebral, plastic, and otolaryngological operations. This was the last of the very enthusiastic clinical-type presentations on the subject. As Gillies himself has said (Gillies and Holmes, 1965), with reference to the tenets of the modern anaesthesia which emerged from the triad approach: “the venous congestion associated with respiratory obstruction, and the cardiovascular effects of carbon dioxide retention, are the commonest causes of abnormal oozing; prevention of these factors may obviate the need for special hypotensive measures”. It is of more than passing interest that the next edition of the book in which this statement was published did not include a chapter on the clinical aspects of deliberate hypotension. Although other ganglionic blocking agents have been introduced into clinical practice, such as trimetaphan (Magill, Scurr and Wyman, 1953), pentolinium (Enderby, 1954) and phenactropinium (Robertson, Gillies and Spencer, 1957) only the former has changed clinical practice, being sufficiently short-acting to be given by infusion and thus permitting a new dimension in controllability which has been surpassed only by sodium nitroprusside.

Changing concepts in the treatment of shock

The history of induced hypotension embraces the development of important new concepts in the pathophysiology of shock. An important lesson

which was learned in those few frantic years of deliberate hypotension was that a low arterial pressure with vasodilatation is a very much safer condition than a low pressure in the presence of vasoconstriction. At the Royal Society of Medicine meeting, mentioned earlier, Cox noted the potentially bad effects of compensatory vasoconstriction in shock, and Wyman emphasized the effects of ganglionic blocking agents in providing an apparent protection, both from shock caused by haemorrhage, and from trauma. In addition, the effects of ganglionic blockade in preventing established shock from becoming irreversible were discussed. Wyman commented adversely on the use of vasopressor drugs in shock and, based on the treatment of two cases of irreversible shock, he advocated that vasodilatation would be efficacious where “our present means of resuscitation fails”. Although, nowadays, ganglionic blocking agents themselves are not used for this purpose, other vasodilator substances are employed with success.

The influence of research

The last 15 years or so has seen an increase in the application of careful monitoring techniques during deliberate hypotension. In addition, deeper investigation into the physiological changes associated with the various techniques of deliberate hypotension have been carried out, and is dealt with elsewhere. Broadly speaking, the dissimilarity between haemorrhagic shock and induced hypotension has been confirmed biochemically. On the other hand, the decrease in cardiac output associated with most techniques except nitroprusside administration was not originally predicted. Nor was the severe depressant effect of high doses of halothane on the myocardium appreciated originally (Prys-Roberts et al., 1972, 1974) while the role of posture and an increased airway pressure in relation to pharmacological blockade is better understood (Blackburn et al., 1973).

These physiological investigations have led to an evolution of ideas in relation to the practice of artificial ventilation during deliberate hypotension. As has been said, the technique of controlled ventilation was not common when induced hypotension was first introduced into practice, and so induced hypotension was applied to spontaneously breathing subjects. There are those who still advocate this technique, since regular respiration is theoretically a good monitor of the adequacy of medullary perfusion. The maintained arterial carbon dioxide con-

centration which results will, in addition, ensure cerebral vasodilatation and an adequate cerebral perfusion. On the other hand, if ventilation is controlled and hyperventilation exists, a lowered P_{CO_2} would have an adverse effect on cerebral perfusion. However, since the work of Eckenhoff and colleagues (1963), which demonstrated enormous deadspaces during induced hypotension, most authorities advocate controlled ventilation to ensure adequate alveolar ventilation, but without hyperventilation (Eckenhoff and Leigh, 1974).

Changing concepts—morbidity and mortality

Since controlled hypotension and shock have in common a low arterial pressure, and since the latter may prove fatal, an instinctive reaction has always been that deliberate hypotension must of itself increase morbidity and mortality over non-hypotensive techniques for the same surgical procedure. With the exception of very occasional errors or abuses, this remains difficult to quantitate and is considered elsewhere in this issue (Lindop, 1975).

SUMMARY

As the physiology of deliberate hypotension has been unravelled, and as each new pharmacological agent has become available which either depresses or blocks peripheral vascular tone, depresses myocardial performance, or interferes with the conducting tissues within the myocardium, its possible incorporation into the armamentarium of the anaesthetist who offers induced hypotension has been considered. The result has been a sequence of variations in technique of characteristically recognizable vintage.

No matter how the condition of induced hypotension is produced, there is usually vasodilatation, and the characteristic disturbance in physiology is of a loss of postural reactivity in the cardiovascular system.

Important lessons have been learned concerning the management of shock states. Though it is difficult to evaluate the morbidity of deliberate induced hypotension, and terms such as "physiological trespass" have been used by its antagonists, it would appear that a well-considered and skilfully managed controlled hypotension is no more of a physiological trespass than anaesthesia, nor indeed than the trespass of the surgeon's knife itself.

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