CONTROLLED HYPOTENSION IN THEORY
AND PRACTICE*

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It has been said, with an element of truth, that progress in surgery is dependent upon advances in the field of anaesthesia.

The development of induced hypotension as an adjuvant to surgery is an excellent example of this interdependence. Fundamentally unrelated to anaesthesia, the techniques have been evolved almost exclusively by anaesthetists, who must be prepared to accept responsibility for the management of such cases. This, however, is but one example of the extension of the anaesthetist’s duties in recent years. Today, he is expected to modify, disturb or otherwise alter basic physiological functions to meet the increasing demands of modern surgery. It behoves him therefore to be not only willing to accept these new responsibilities but also to be capable of undertaking them. Such capability presupposes a knowledge of basic physiological principles together with an understanding of the modifications produced by clinical intervention.

This paper is an attempt to correlate these factors as applied to induced hypotension and to discuss, within a limited experience, their practical application.

Under normal physiological conditions, the blood pressure is maintained by a finely adjusted balance between two

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fundamentally different mechanisms, the volume of circulating blood on the one hand, and the capacity of the vascular bed on the other.

The production of induced hypotension is based on the disruption of one or other of these mechanisms. Before going on to discuss the physiology of this state of induced hypotension, it may be convenient to review briefly the classical conceptions of blood pressure control.

In its simplest sense, blood pressure is the product of cardiac output and peripheral resistance. A fall in blood pressure, then, may be produced by a reduction in cardiac output or by a diminished peripheral resistance, or by a combination of both.

Cardiac output is influenced by a number of factors including the force and rate of the heart. In the presence of a normal myocardium, however, the most important factor is the volume of blood returning to the right auricle. But, in the absence of an adequate venous return, an increase in the force and rate of the heart will not maintain output.

Normally, a positive pressure exists between the peripheral veins and the right heart. This pressure is the principal driving force by which blood is returned to the right auricle. In addition the venous return is assisted by a number of subsidiary forces. Both the contractions of the heart and the expansion of the lungs act to draw blood into the chest, and the normal tonic contractions of muscle squeeze blood centrally towards the great veins, while the veins themselves are under vasomotor control, so limiting their capacity.

Peripheral resistance can be defined as the resistance offered to the blood flow by the minute vessels. The degree of resistance is dependent primarily on active changes in the calibre of the vessels. These changes are under the control
of nervous, chemical and physical influences acting centrally, reflexly and directly on the vessels themselves.

Normally, the tone of the vessels is maintained through vasoconstrictor fibres relayed from the vasomotor centre. However, a degree of autonomy is superimposed on this neurogenic control, for the minute vessels may alter their calibre in response to the direct effects of metabolite accumulation.

Induced hypotension may be either hypovolaemic or normovolaemic, depending upon whether the volume of circulating blood is reduced or whether the capacity of the vascular bed is increased.

Hypovolaemic hypotension is obtained by deliberate arterial bleeding in order to reduce the circulating blood volume. Control of bleeding by this method was first described by Gardner in 1946. Three years previously Kohlstaedt and Page (1943) published a method for producing hemorrhagic shock in dogs by arterial bleeding. These workers demonstrated that recovery was both more rapid and more certain if the blood was returned by the arterial route, and suggested that intra-arterial transfusion had a clinical application in the treatment of shock. They described three such cases treated by intra-arterial plasma. In 1951, Bilsland reviewed a series of 63 cases of induced hypotension by arteriotomy. His results on patients undergoing craniotomy are encouraging.

The technique has a limited application, being confined almost entirely to neurosurgery, where the control of bleeding is a major problem. A large number of patients about to undergo craniotomy suffer from increased intra-cranial tension. The oedematous brain limits accessibility and oozing of blood obscures the operating field. Adequate haemostasis is time-consuming and often difficult to obtain. Finally, the volume of blood lost hinders recovery and,
indeed, in some cases endangers life. Arteriotomy by lowering the systemic blood pressure reduces not only the brain volume but also the venous ooze. Haemostasis is obtained easily and the volume of blood lost is considerably diminished.

The effect of haemorrhage on the body is dependent on the volume of blood lost and the rate at which this loss occurs. The immediate effect of a moderate loss of blood is a fall in blood pressure. McMichael and Sharpey-Schafer (1944) have demonstrated the sequence of events by which this fall is produced. The lowering of the blood volume diminishes the pressure in the great veins. This is followed by a reduction in the volume of blood reaching the right auricle, cardiac output is consequently diminished and the blood pressure falls. With the fall in blood pressure, afferent stimulation through the sino-aortic nerves is reduced, with the result that their inhibiting influence on the cardiac sympathetic is relieved and the heart rate is correspondingly increased.

The compensatory response of the body to haemorrhage is well known. Initially, the peripheral vascular bed adjusts its capacity to the reduced blood volume by vasoconstriction. Consequently, the pressure rises, tending to stabilize, usually at a pressure lower than normal, but occasionally a hypertensive response is obtained. The balance, however, is a precarious one and any additional loss will precipitate a further fall. Indeed, this phase may occur without additional blood loss if the compensatory stage has been prolonged without adequate therapy. With the development of this decompensatory period, the peripheral bed loses its ability to restrict the circulation effectively; the venous return is reduced still further and the cardiac output falls. Such a state may rapidly become irreversible.

Control of bleeding in induced hypovolaemic hypotension
may therefore be said to be dependent on the limitation imposed on a reduced circulating blood volume by a marked vasoconstriction of the peripheral vascular bed. On the other hand, in normovolaemic hypotension control of bleeding is dependent on a great increase in the capacity of the vascular bed relative to the circulating blood volume.

The fall in blood pressure subsequent to spinal analgesia has been recognized since the introduction of the technique. Until recently this fall in blood pressure has always been regarded as a complication of the method and every precaution taken to guard against it. In 1948, Griffiths and Gillies, working in Edinburgh, demonstrated that the dangers had been exaggerated. They used spinal analgesia with the deliberate intention of reducing blood pressure, and showed that, subject to certain requirements being fulfilled, such hypotension was not to be regarded as dangerous but, indeed, as a most desirable state for surgery in many fields.

The total spinal technique of induced hypotension necessitates the successful depositing of an anaesthetic drug in the sub-arachnoid space in sufficient quantity to obtain paralysis of the entire sympathetic outflow. Such a drug has a selective action on the nerve fibres exposed to its influence. Depression of function appears to be related to two factors, the diameter of the individual fibre and the degree of myelination. Fine fibres have been shown to be more rapidly anaesthetized than thick ones, while un-medullated fibres are depressed more quickly than the medullated type. Clinically, the sympathetic fibres are depressed more rapidly and by a lower concentration of anaesthetic drug than any other type of fibre. Sensory fibre depression is intermediate between that of sympathetic and motor depression.

As a result of inactivation of the sympathetic outflow,
the vasoconstrictor fibres are paralysed. The arterioles
dilate and the peripheral resistance falls. Under normal
physiological conditions, collapse of the blood pressure is
prevented by an increased cardiac output. Under spinal
analgesia this mechanism is inhibited by the reduction in
venous return and by the depression of the sympathetic
cardio-accelerator fibres.

A number of factors combine to reduce the venous return.
The veins in the body are subject to the same vasomotor
control as the arterioles, consequently, the depression of
vasoconstrictor impulses results in veno-dilatation. The
extent of this veno-dilatation has yet to be determined but
there is little doubt that it adds considerably to the capacity
of the vascular bed. The venous return is further handi-
capped by the paralysis of the abdominal and intercostal
muscles. Respiratory excursion is diminished, thereby re-
ducing the negative pressure in the thorax. The suction
pump action of the thorax is dependent on the extent of this
negative pressure. At the same time, the general voluntary
muscle paralysis reduces the pumping action on the venous
circulation.

Depression of the sympathetic outflow implies a conse-
quent preponderance of the parasympathetic system.
Following total spinal analgesia this preponderance is to all
intents and purposes vagal, for the sacral parasympathetic
outflow is depressed together with the sympathetic. The
vagus exerts a continuous restraining action on the rate
of the heart and, following depression of the sympathetic,
this action is unopposed. The heart rate is slow, the
force of cardiac contraction is lessened and the cardiac
output falls.

Total spinal analgesia therefore produces hypotension by
reducing both the cardiac output and the peripheral resis-
tance.
A later development in the production of normovolaemic hypotension has been the introduction of the group of drugs described as ganglion blocking agents. Following the suggestion by Paton and Zaimis (1948) that hexamethonium had an obvious clinical application in the treatment of hypertension and other vascular diseases, Arnold and Rosenheim (1949) described its use in the treatment of the hypertensive patient. In February 1950, Armstrong Davison published a paper drawing attention to the use of pentamethonium in the production of a bloodless operating field. This was followed in June 1950 by Enderby's description of hypotension in anaesthesia induced by means of the ganglion blocking agents.

The drugs used are closely related synthetic compounds belonging to the methonium series, of which hexamethonium bromide is probably the most popular. This drug produces its effect by competition block of autonomic ganglia without initial excitation. The compounds have a selective action on the ganglia and the selection seems to vary with the agent used.

To reiterate, normovolaemic hypotension is produced by greatly increasing the capacity of the vascular bed relative to the volume of circulating blood. The capacity of the vascular bed depends upon the degree of dilatation of the arterioles, capillaries and veins, all of which are directly affected by the action of the methonium compounds. The failure of the vasoconstriction is manifested clinically by an increase in skin temperature, an increase in limb volume and the presence of visibly distended peripheral veins.

The fall in blood pressure differs from that obtained as a result of spinal block in so far as when recovery appears to be complete in the recumbent patient, the adoption of the upright position is accompanied by an immediate fall in blood pressure. Paton (1951) suggests that this is due to
pooling of blood in the veins, the tone of which, he postulates, recovers more slowly than arterial tone. The degree of hypertension is less predictable with the ganglion blocking agents than with sub-arachnoid block, and there would appear to be some truth in Paton's contention that ganglia which are abnormally active are more susceptible to the effects of these drugs.

Having discussed the theory of controlled hypotension, we can now examine the problem of its practical application.

In the management of patients undergoing arteriotomy, the blood pressure is generally lowered to a level of 80 mm.

**FIG. 1**

Blood pressure .. systolic \( \Delta \) : diastolic \( \nabla \)

Pulse .....

Respiration .. o--o

Operation: Left Fronto-temporal Craniotomy.
Anesthesia: local infiltration, thiopentone 1.0 g, \( \text{N}_2\text{O} + \text{O}_2 \) + Trilene.
Arteriotomy: blood withdrawn, 900 ml.; replaced 770 ml.
Hg by arterial bleeding. To achieve this, the volume of blood it is necessary to remove varies considerably. In my own cases, the smallest volume was 600 ml., and the largest nearly 2,000 ml. Despite this difference the pattern of the response is very similar in each case.

The immediate reaction is a rise in pulse rate and almost simultaneously a fall in blood pressure occurs. The tachycardia usually persists throughout the operation, increasing when the pressure falls and diminishing when it rises. Figure 1 demonstrates that almost invariably where a spike
occurs in the pulse tracing an inverted spike appears on the blood-pressure record. The respiratory rate in most cases tends to increase, particularly towards the end of the operation and more especially if the procedure has been prolonged. A persistent increase in respiratory rate is regarded as an anoxic manifestation and an indication for blood replacement.

Once the pressure is stabilized at 80 mm. Hg, the occurrence of a further fall in blood pressure can be overcome by the intra-arterial infusion of 50-100 ml. of blood, which usually restores the pressure to its former level within a minute. Figure 2 illustrates the exception. In this case, a brisk hemorrhage occurred from a venous sinus and more than 700 ml. of blood were required before the pressure was stabilized. Such an incident demonstrates the necessity for a careful watch on the operating field; by so doing, the anaesthetist can frequently anticipate blood loss and by taking the necessary action, save himself considerable anxiety.

Hypotension by arteriotomy is accompanied by an intensive vasoconstriction manifested clinically by facial pallor and a cold, clammy skin. This vasoconstriction, though generalized, is not uniform, being more obvious in the face and lower limbs.

Corneille Heymans (Heymans, 1950) explains facial pallor on the basis that the extra-cranial tissues, and particularly the blood vessels of the face, act as a shunt or reservoir for the protection and stability of the cerebral blood flow. Accordingly, when hypotension occurs, it is accompanied by intensive vasoconstriction of the facial blood-vessels in an endeavour to maintain the blood flow to the brain. Conversely, any hypertensive episode will provoke vasodilatation of these vessels.

The lack of uniformity in the vasoconstrictor response is
well demonstrated by the reaction in the limbs. Typically, after the onset of hypotension, percutaneous needling of a vein for intravenous infusion is almost impossible in the lower limbs, yet the same manoeuvre is performed relatively easily in the arms. In one case where a leg vein was exposed, vasoconstriction was so marked that bleeding did not occur when the vein was opened.

Figure 3 demonstrates a case where nearly two litres of blood were removed from the patient before his blood pressure fell to a satisfactory level. It was then maintained at that level for more than five hours before signs of stress developed. At this stage, the pulse rate was suddenly reduced from 130 beats per minute to 65, concurrently the systolic, diastolic and pulse pressures fell and the respiratory rate was slightly depressed. Intra-arterial infusion brought about a slight improvement which, however, was
not maintained and the blood pressure again fell alarmingly to an even lower level, namely 45/30. The rate and volume of the intra-arterial infusion was increased with good effect. After the addition of 500 ml. of blood, the intra-venous injection of Methedrine restored the blood pressure to a more satisfactory level.

The explanation of this sudden decline in blood pressure and pulse rate is difficult. Wiggers (1947) and his colleagues regard the slowing of the heart after an initial acceleration following haemorrhage as a dangerous development and a sign of myocardial asphyxia. If resuscitation is neglected, a significant depression of respiration follows, the blood becomes inadequately oxygenated and the heart slows still further and finally stops, death being due to myocardial failure. Chambers and Zweifach (1944), on the other hand, consider the development of such a circulatory collapse as a manifestation of peripheral circulatory failure. In their opinion, the primary response to blood loss is a period of compensatory activity. During this period, vasoconstriction enables the capillary bed to adjust itself to the diminished blood volume. A subsequent decompensatory period occurs during which time the vascular bed loses its ability to restrict effectively the circulating blood volume. This decompensatory phase is not regarded as due to a failure of neurogenic impulses but rather to interference with the response by the progressive accumulation of vaso-dilator material. In all probability both elements contributed to the onset of the circulatory collapse in this case.

Induced hypotension by the total spinal technique presents a very different clinical picture from hypotension produced by bleeding. The decline in blood pressure is both more abrupt and more profound. The pulse pressure is markedly reduced almost at once but there is no tachycardia. A normal pulse rate or a bradycardia is the rule.
The patient rarely shows facial pallor, more often a healthy pink colour prevails, the skin is hot and dry, and visibly distended peripheral veins are prominent in the dependent parts.

The elderly, slightly arteriosclerotic patient with a high pulse pressure is usually a good subject for this technique,
as can be seen in figure 4. A satisfactory fall in blood pressure was obtained with a 1.5 ml. of heavy cinchocaine (cinchocaine was preferred to procaine, being the longer acting drug). While the biopsy was being obtained a venous sinus was opened in the tumour mass and a moderate but brisk haemorrhage resulted, transforming the benign hypotensive state into a highly dangerous one. 1,200 ml. of blood were given in less than thirty minutes before the patient’s condition was regarded as satisfactory.

It is worth noting that although, in this case, the rapid pulse was accompanied by a fall in blood pressure, frequently the only indication, apart from the obvious bleeding in the operating field, is the alteration in pulse rate.

This account serves to emphasize that blood loss in a patient under total spinal analgesia is much more serious than an equivalent loss in a patient either conscious or under general anaesthesia. Normally when haemorrhage occurs a reflex vasoconstriction ensures an adequate blood supply to the vital centres and the heart. Under total spinal analgesia, this compensatory mechanism is inhibited and peripheral failure results. Blood loss is one of the ever present risks of controlled normovolaemic hypotension and must always be anticipated.

Occasionally paralysis of the sympathetic outflow is incomplete and is manifested by a less profound fall in blood pressure. This is due to a marked vasoconstriction of the blood-vessels of the head and neck and is to be regarded as a compensatory vasoconstriction, the mechanism of which has already been discussed. Accompanying it there is a considerable loss of sweat from the same area. Normally, activation of the sweat glands is by sympathetic nerve impulses (Kuntz, 1934), consequently paralysis of the sympathetic outflow inhibits the secretion of sweat. If, however, the paralysis is incomplete, there is increased
sudomotor activity of the unaffected area of skin, and this also must be regarded as a compensatory mechanism. The secretory output of the sweat glands is determined to some extent by the cutaneous blood flow, but only if the activity of the glands is prolonged (Kuno, 1934). Under normal physiological conditions the cutaneous circulation has little influence on the secretion of sweat, which may continue even in the absence of skin blood flow. Such activity can be demonstrated by the fact that nerve stimulation can elicit sweat secretion in a newly amputated limb (Kuntz, 1934). From the anaesthetic aspect, this sweat secretion is an important potential source of fluid loss which may be overlooked in the assessment of such loss.

Depression of sudomotor activity is a constant feature of the action of ganglion blocking agents. Unfortunately the degree of hypotension is less predictable. Furthermore, with this technique the most satisfactory bloodless field is not necessarily associated with the greatest fall in blood pressure. This is as yet unexplained. Typically the systolic, diastolic and pulse pressures are low and a mild tachycardia is common. The skin is hot and dry and frequently flushed, particularly in dependent areas. Burt and Graham (1950) measured the limb blood flow in patients under the influence of these drugs. They demonstrated that the increase in blood flow was more marked in the legs than in the arms. It is worth recalling at this stage that during hypovolaemic hypotension the degree of venoconstriction was greater in the lower limbs than in the upper limbs. A possible explanation is the fact that owing to the more highly specialized development of the upper limbs the basal blood flow requirements are correspondingly higher.

The following two cases are worthy of mention. Figure 5 demonstrates what appears to be an abnormal response to hexamethonium bromide. Immediately after the intra-
FIG. 5

Blood pressure . . systolic △ : diastolic v
Pulse . . . . . . . .
Respiration . . o--o

Anæsthesia: thiopentone 1.0 g, N₂O + O₂ + Trilene.
venous injection of 50 mg. of the drug the blood pressure rose to 180/110, the pulse pressure increased and a marked tachycardia developed. This reaction was short-lived, however, and the pressure soon dropped to a satisfactory level, moderate tachycardia persisted until the pressure was raised towards the end of the operation by intravenous Methedrine, 10 mg., when the pulse rate dropped to normal. A possible explanation for this response is the release from vagal tone brought about by the action of hexamethonium bromide on hyperactive vagal ganglia. It is known that the action of the methonium compounds is increased in the presence of hyperactivity.

The second case is that of an elderly woman undergoing a pelvic floor repair for vaginal prolapse. Her condition, having been entirely satisfactory throughout the operation, suddenly deteriorated after transfer from the theatre table to the trolley. Two factors probably contributed to her collapse. Firstly, redistribution of blood in the horizontal position after having been lowered from the lithotomy position, and secondly, careless handling from the theatre table to the trolley. Fifteen milligrams of intravenous Methedrine brought an immediate response. Nevertheless, this is but another illustration of the precarious state of the circulation during induced hypotension and serves to emphasize the constant care that is required in the management of such a case.

An outstanding feature of patients with a low blood pressure is the ease with which anaesthesia is maintained. At pressures below 50 mm. Hg it seems probable that patients would remain asleep without any anaesthesia. In pathological states such as surgical shock, Addisonian crises, or sunstroke, the combination of drowsiness associated with hypotension is well recognised. Consideration of the mechanism is handicapped by lack of knowledge of the
nature of consciousness. William James (1904) considers consciousness as such to be of secondary importance. He regards it as entirely dependent on experience and states: “Consciousness is the name of a nonentity and has no right to a place among first principles. Those who still cling to it are clinging to a mere echo, the faint murmur left behind by the disappearing ‘soul’ upon the air of philosophy.”

The idea that consciousness is the outcome of experience is not confined to philosophers. Purdon Martin (1949) has pointed out that consciousness is maintained by an “awareness of the body and of the environment.” He quotes the case of a patient subsequently found to have a pontine haemorrhage involving the medial and spinal fillets. When the bleeding was confined to one side this patient was drowsy, and anaesthetic on the opposite side of the body. When the haemorrhage spread to involve both sides, the sensory loss was bilateral and the drowsiness became extreme, so that when she closed her eyes she became unconscious and could only be roused when the eyes were forcibly opened. He considers that from the point of view of organic neurology, consciousness is dependent upon afferent impulses exerting their influence on a cortex activated by the hypothalamus, the function of which is thought to be purely vegetative.

Recent work in psychiatry (Lovett Doust, 1951) has shown that a depression of consciousness, or a ‘want of awareness’, occurring in schizophrenics is associated with a reduced arterial oxygen saturation level. The same author (Lovett Doust and Schneider, 1952) has drawn attention to the relationship existing between arterial oxygen saturation level and the depth of sleep. Hill (1952), however, stated in criticism—“The anoxia found in deep sleep is not its cause but the result of immobility which slackens the circulation by removing the pumping action of the muscles which in activity reinforces the action of the heart.”
Such views are important to the anaesthetist in assessing the cause of drowsiness or unconsciousness following induced hypotension. In high spinals until recently anoxia has been regarded as the cause. Macintosh (1950), from personal experience, has testified that the higher analgesia spreads, the more the awareness of the body is diminished. The lack of awareness in such cases is undoubtedly due to a direct depression of the spinal roots by the analgesic agent. This explanation, however, cannot be accepted in the case of the methonium compounds. Recently Pask (1952) has thrown some light on this problem. While experimenting on the spinal cord, he was able to show that a fall in blood pressure could inhibit transmission of nerve impulses to the same degree as deep general anaesthesia. It is postulated that as a consequence of the fall in blood pressure, the amount of oxygen available to the tissues is reduced. It has been proved that in the presence of hypoxia the functional cells of such organs as the kidney and liver lose their specificity without detriment to the organ until the hypoxia has been relieved. In a like manner, it is suggested that the individual nerve cells lose their specificity without suffering total suppression of function. Such a hypothesis is in keeping with modern theories on the action of anaesthetic agents. According to Quastel and Wheatley (1932) the action of narcotic drugs is dependent upon an inhibition of carbohydrate metabolism within the nerve cell. This inhibition limits the ability of the cell to obtain the necessary energy for the maintenance of function. They succeeded in demonstrating that in the narcotized cell the only oxidation taking place is that of succinic acid and they believe that although insufficient energy is liberated from this reaction to allow function there is sufficient to maintain life in the cell. In a study of hypoglycaemic coma, Lawrence and his colleagues (Lawrence, Meyer and Nevin, 1942) discovered
a reduction in the oxygen utilization of the brain manifested by a diminished arteriovenous oxygen difference. They explain this by the fact that although oxygen is freely available there is no substrate to be oxidized.

Despite the foregoing concepts of consciousness presented by philosophers, neurologists, physiologists, and biochemists, it must be admitted that our knowledge of the nature of unconsciousness is not much further advanced. The explanation for this failure may be in our approach to the problem. Sinclair (1951), discussing the fundamentals of knowledge, has drawn attention to the fact that our theories of perception are based largely on the theories of vision and touch. He points out that what is typical of the latter need not be true for all perception and therefore assumptions dependent on them may be grossly misleading. These observations certainly seem to apply to the study of consciousness. It may be that we are too circumspect in our approach, certain aspects tending to be neglected entirely, others over-emphasized.

Probably the answer to the problem lies in the development of more comprehensive criteria on which may be based more accurate evaluations of consciousness.

SUMMARY

The classical conceptions of blood pressure control are reviewed.

The mechanisms of induced hypotension are discussed and classified.

Individual case records are presented and discussed.

The relationship between hypotension, tissue oxidation, and the level of consciousness is discussed.

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REFERENCES