ANAESTHESIA AND HYPERTENSION

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The sympathetic nervous system plays an important role in the regulation of arterial pressure in normal man (Korner, 1979). Figure 1 shows a schema for how perturbation of arterial pressure in everyday arterial pressures well above the normal range, and are therefore deemed to be hypertensive. To what extent does failure of pressure regulation play a role in the development of hypertension, and to what extent is this a primary or a secondary role?

Failure of pressure regulation is a common feature of anaesthesia, even in normal patients (Prys-Roberts, 1980a). In the hypertensive patient its deficiency contributes to the maintenance of undue hypotension caused by anaesthetic agents, and also to the exaggeration of the variations in arterial pressure which occur in response to surgical stimuli.

What is the role of central neurogenic excitation in the development and maintenance of hyperten-
sion? Is enhanced sympathetic activation a feature of hypertension, and do hypertensive patients respond differently, in comparison with normotensive patients, when subjected to stimuli which initiate the defence reaction to normal stimuli? If a minority of humans respond adversely to such environmental perturbations, eventually developing adaptive pathophysiological changes characteristic of all forms of chronic hypertension, regardless of the causal mechanism, why do these patients respond so differently to the effects of drugs during anaesthesia and to the noxious stimuli associated with surgery?

All these, and many other questions, are fundamental to the understanding of the hypertensive patient's responses to anaesthesia and surgery, and the causation of morbidity and mortality in this group of patients. As there have been a number of reviews of this subject in recent years (Foëx and Prys-Roberts, 1975; Prys-Roberts, 1980b, 1981, 1982a, 1983), the present review will concentrate on special topics related to the sympatho-adrenal system and its relevance to anaesthesia for the hypertensive patient, and on new developments in the management of the hypertensive patient.

ADRENERGIC AND OTHER PATHOPHYSIOLOGICAL MECHANISMS IN HYPERTENSION

Haemodynamic patterns in human hypertension

It has long been known that resting cardiac output is increased, by about 15% above that of a normal age-matched cohort, in young patients with "borderline" or "labile" hypertension (Widimsky, Fejfarova and Fejfar, 1957; Eich et al., 1962). It has also been shown that such a state may lead to the development of essential hypertension in which cardiac output is normal but systemic vascular resistance (SVR) is increased. This hypothesis of the development of essential hypertension is now termed the autoregulation theory. While there have been many advocates for this theory (Guyton, 1980), there are also many whose studies are inconsistent with the autoregulation theory (Korner, 1982). The theory alone fails to explain why cardiac output decreases below normal in longstanding hypertension (Frohlich and Pfeffer, 1975; Lund-Johansen, 1981), or why the time for transformation from high cardiac output to high SVR is between 1 and 2 weeks in experimental salt and fluid overloading. The latter interval is far greater than that for short-term (1-15 min) autoregulation of cardiac output (Korner, 1982). Autoregulation of cardiac output does not appear to be effective during anaesthesia.

Hypothesis for dominance of SVR in long-standing hypertension

The concept proposed and later developed by Folkow (Folkow, Grimby and Thulesius, 1958; Folkow, 1971, 1978) remains the outstanding contribution to our understanding of the haemodynamic state of all types of hypertension. Folkow and his colleagues proposed that adaptive hypertrophy of smooth muscle in the walls of arterioles, and later hypertrophy of left ventricular muscle, played an important role in amplifying both pressor and inotropic stimuli respectively. The importance of this relationship, to the haemodynamic responses of hypertensive patients to constrictor (drugs or noxious stimuli) or dilator (drugs) influences during anaesthesia, has been stressed (Prys-Roberts, Meloche and Foëx, 1971; Prys-Roberts, 1980b). Figure 2 demonstrates two aspects of this adaptive hypertrophy: first the relationship between SVR and arteriolar smooth muscle tone (Folkow, 1978), and second that between left ventricular inotropic state (LV dP/dt) in response to infusion of noradrenaline in normal dogs, and dogs with experimental renovascular hypertension. The abcissa of each graph could be regarded as interchangeable, or substituted by "sympathetic nervous activity".

Various pressor substances (noradrenaline, angiotensin II and vasopressin) cause a greater increase (1.6 to 1.9 times) of hind-limb or whole body vascular resistance in hypertensive animals compared with normotensive controls (Folkow, 1971, 1978; West, Angus and Korner, 1975). The influence of inotropic agents (noradrenaline) on left ventricular performance has also been shown to be greater in hypertensive compared with normotensive dogs (Broughton and Korner, 1983). The increased inotropic performance was proportional to increased left ventricular mass and indicated that the hypertrophied heart can maintain a given cardiac output at a higher pressure, that is against a greater output impedance, than can the normal heart. While this is clearly true for Korner and Broughton's experimental preparation, it may not be so in the hypertensive patient with associated coronary artery disease in whom the increased myocardial work may precipitate myocardial ischaemia and consequent impaired contractile function (Hollander, 1973). Myocardial ischaemia remains the single most important cause of morbidity during anaesthesia for the elderly hypertensive patient.

In the hypertensive patient the hypertrophic arterioles and the hypertrophied left ventricle exert
different amplifying characteristics, which eventually lead to the dominance of the role of SVR irrespective of the initial cause of the hypertension (fig. 1). During the early stages of hypertension, increased SVR or cardiac output, or both, can maintain high arterial pressures independently through their individual amplifying effects. Continuing hypertrophy of the arteriolar muscle has a positive feedback effect in further increasing SVR and therefore the load of the left ventricle. By contrast, increasing left ventricular hypertrophy severely limits diastolic compliance and thus ventricular filling, so that stroke volume and cardiac output eventually decrease, and fail to increase in response to either transient or sustained increases in SVR. This aspect of the pathophysiology of hypertension deserves special attention in relation to the enormous variations of SVR which may occur during anaesthesia and surgery.

Total blood volume in hypertensive patients is normal or only slightly reduced, but there is a central redistribution of this volume probably as a result of increased tone in capacitance vessels (Lund-Johansen, 1980). This redistribution is essential for the maintenance of cardiac output as the hypertrophied left ventricle of the hypertensive patient is more dependent on the Frank-Starling mechanism to maintain its performance (Folkow, 1978; Tarazi, 1982, Tarazi and Levy, 1982). The hypertensive patient is then more vulnerable to the dilatation of capacitance vessels with a concurrent decrease in venous return and possibly the loss of the central redistribution of blood volume. Antihypertensive treatment may also lead to regression of left
ventricular hypertrophy (Folkow, 1978; Tarazi, 1982).

Endocrine hypertension such as primary hyperaldosteronism (Tarazi et al., 1973) or Cushing's syndrome (Scoggins et al., 1979; Graham et al., 1980) and “labile” hypertension (Eich et al., 1962) are characterized by increased cardiac output during the early phase, whereas renovascular hypertension is associated with increased SVR secondary to the effects of angiotensin II. In this renin-dependent phase of renovascular hypertension, both plasma renin and angiotensin II concentrations are high, and the use of specific angiotensin antagonists (Saralasin) or angiotensin-converting enzyme inhibitors (captopril) restores pressures to normal (Ayers et al., 1974), or prevents the development of hypertension (Miller et al., 1975). Patients with hypertension of renovascular origin present special problems during anaesthesia (Prys-Roberts, 1982a). Postoperative renal dysfunction has been identified as a problem even in well controlled or mild hypertensive patients (Goldman and Caldera, 1979), but in patients who have pre-existing renal dysfunction associated with renovascular hypertension, the regulation of arterial pressure and the maintenance of adequate glomerular filtration becomes even more important.

Adrenergic overactivity in the genesis of hypertension

Traditionally, overactivity of the sympathetic nervous system and increased sensitivity to salt have both been linked to the causation of human hypertension. Until Folkow’s recognition of the adaptive hypertrophic mechanisms and their amplifying effects on arterial pressure, many authorities described increased sympathetic nervous activity or increased arteriolar sensitivity to circulating catecholamines as important factors in the development and maintenance of hypertension.

Phaeochromocytoma is the only indisputable cause of hypertension in which increased circulating catecholamines are consistently found (Manger and Gifford, 1977). However, recent developments in the radio-enzymatic (Engleman and Portnoy, 1970; Passon and Peuler, 1973) and high pressure liquid chromatography (Hallman et al., 1978) assay of catecholamines, have led to an increased interest in the role of these neuronal and hormonal transmitters in the genesis of hypertension (Louis et al., 1974; De Quattro et al., 1979; de Champlain, Cousineau and Lapointe, 1979). The latter authors found that increased resting catecholamine concentrations resulted mainly from increased adrenaline concentrations in “labile” hypertensives, and from increased noradrenaline concentrations in about 30% of patients with essential hypertension. Although these authors found increased plasma catecholamines in hypertensive patients, Kopin, Goldstein and Feuerstein (1981) have discounted these findings on the basis that age-corrected plasma catecholamine values were not significantly different from normal subjects.

It is clear that approximately 20% of patients with essential hypertension exhibit sympathetic overactivity, based on measurements of increased noradrenaline spillover into the plasma and of the disappearance of $^3$H-noradrenaline (Esler et al., 1981). Spillover of noradrenaline is only a small fraction of the noradrenaline released as adrenergic synapses (Esler, 1982) and is probably only a useful indicator of adrenergic activity under conditions of markedly increased sympathetic activity. The initial exponential decrease of $^3$H-noradrenaline gives an indication of re-uptake of neurotransmitter after adrenergic neuronal release. Esler and colleagues (1981) found that approximately one in five patients with essential hypertension showed impaired re-uptake at adrenergic nerve endings, resulting from a fault in the neural membrane pump, allowing the released noradrenaline to exert a prolonged effect on the postsynaptic cell.

Brown and Macquin (1981) have suggested that increased adrenaline secretion may play an important part in the development of hypertension. They have postulated that adrenaline released intermittently from the adrenal gland is taken up into adrenergic nerve endings where it leads to a prolonged enhancement of noradrenaline release in response to normal sympathetic neuronal activity. The increase of plasma noradrenaline concentrations following exercise (Philipp, Distler and Cordes, 1978) and following postural changes (Sever et al., 1977) also show disturbed patterns in a proportion (15–30%) of patients with essential hypertension.

Whatever the implications for understanding the development of hypertension, these findings are also of considerable importance in relation to the development of postoperative hypertension, both in hypertensive patients, and in patients following coronary artery bypass surgery.

Hypertension and the adrenergic neurone

Most of the work on this aspect has been conducted on animals with genetically determined
hypertension. The spontaneously hypertensive rat (SHR) develops all the characteristics of human essential hypertension, and is particularly useful as a means of studying the early phases in the development of the structural adaptation. Early in the development of genetic hypertension in SHR, the ability of the arteriolar wall to synthesize noradrenaline (assessed by tyrosine hydroxylase activity) is increased (Tarver, Berkowitz and Spector, 1971). Tyrosine hydroxylase activity is also increased in the vas deferens of men with increased arterial pressure (De Quattro et al., 1975).

Neuronal re-uptake of released noradrenaline is enhanced in the adult SHR (Vanhoutte, Webb and Collis, 1980), unlike the findings described above for man. By contrast, neuronal re-uptake of noradrenaline in the hypertensive heart is universally depressed. In the arterioles these adrenergic neuroeffector interactions tend to diminish the efficiency of sympathetic nervous control, whereas in the heart the efficiency is enhanced (Vanhoutte, Webb and Collis, 1980).

ANAESTHESIA, SURGERY AND HYPERTENSION

Adrenergic neuronal activation and adrenal release of catecholamines occur in response to a wide variety of stimuli before, during and after anaesthesia and surgery. To what extent hypertensive patients behave differently from normal patients has only been partially clarified as a result of observations of the haemodynamic responses of hypertensive patients to various forms of anaesthesia and surgery. To what extent hypertensive patients behave differently from normal patients has only been partially clarified as a result of observations of the haemodynamic responses of hypertensive patients to various forms of anaesthesia and surgery. Certain-ly there is evidence that patients with severe untreated hypertension (arbitrarily defined as diastolic pressures > 120 mm Hg, whatever the cause or classification) show exaggerated hypotensive responses to induction and maintenance of anaesthesia, and exaggerated hypertensive responses to noxious stimuli such as laryngoscopy and endotracheal intuba-tion (Prys-Roberts, Meloche and Foëx, 1971; Prys-Roberts et al., 1971). These events were also associated with secondary morbidity events such as subendocardial ischaemia. Patients with lesser degrees of untreated hypertension (diastolic pressures > 90 mm Hg but < 110 mm Hg), or those whose high arterial pressure was well controlled by antihypertensive drugs, showed no increase of postoperative morbidity compared with their normoten-sive counterparts (Goldman and Caldera, 1979). In specific areas of surgery, notably carotid endarterectomy (Asiddao et al., 1982), the pre-existence of inadequately controlled hypertension has been clearly shown to be associated with an increased frequency of both transient and permanent neurological deficit. Pre-existing hypertension has been shown to increase the occurrence of postoperative myocardial re-infarction in patients who had a history of previous myocardial infarction (Steen, Tinker and Tarhan, 1978). An improvement in the frequency of postoperative myocardial re-infarction has been attributed to aggressive intraoperative monitoring and aggressive management of hypertension during the perioperative period (Rao and El-Etr, 1981).

Drug therapy of hypertension

Table I indicates the broad pharmacological groups of drugs used in the treatment of hypertension. Current attitudes to drug therapy have changed little over the past 25 years, in that the treatment of most patients who present with hypertension is based on a purely empirical approach. The present style of empiricism may have altered with the development of new anti-hypertensive drugs, but the general pattern remains to achieve a decrease of arterial pressure towards the "normal" range by a combination of drugs which has the least probability of inducing undesirable side-effects.

This is achieved by treating all patients who present with hypertension in the outpatient clinic according to the schema in table II. Initially, patients are treated with either a diuretic or a beta-adrenoceptor antagonist, or if this does not achieve adequate control, a combination of the two. Long acting beta-adrenoceptor antagonists such as atenolol or nadolol, or slow-release preparations of blockers which have a short elimination half-life (propranolol, oxprenolol, metoprolol), are preferable as the once-a-day tablet increases compliance in therapy. The majority of patients are adequately controlled with few side-effects on such therapy, and only a small percentage require addition of a third drug, or a change to more aggressive therapy with drugs which have a high frequency of side-effects (Barritt, 1980). A more detailed account of anti-hypertensive therapy in relation to anaesthesia can be found in Prys-Roberts (1983).

Most forms of anti-hypertensive drug therapy are compatible with the subsequent management of anaesthesia. The normal daily morning doses of the relevant drugs should be administered by mouth on the morning of the projected surgery. This may require special prescribing, as many hospitals have a nursing policy which omits all oral medications on
the day of surgery. Most of the common anti-hypertensive drugs are sufficiently long-acting that, after a morning preoperative dose, a satisfactory anti-hypertensive effect can be maintained until the following day.

Calcium-channel blockers

The duration of action potentials, and thus the duration and strength of contraction, in both cardiac and vascular smooth muscle, is largely regulated by the influx of calcium ions across the sarcolemma and across the boundaries of the sarcoplasmic reticulum. Verapamil and nifedipine represent two types of calcium-channel blockers, each having a different spectrum of activity.

Verapamil, a derivative of papaverine, is a racemic mixture of the D and L optical isomers. The D isomer has no effect on calcium channels, but exerts a quinidine-like effect on the fast inward influx of sodium. The L isomer inhibits calcium influx by prolonging the inactivation phase of the slow chan-
Verapamil is used for the treatment of angina pectoris by virtue of its coronary arterial dilating action, combined with a mild systemic arteriolar dilatation which leads to a decrease of left ventricular afterload (Ferlinz and Turbow, 1980). Its main clinical application is in the management of supraventricular tachycardias (Reves et al., 1983). Although verapamil increases the arrhythmogenic dose of adrenaline in halothane-anaesthetized dogs (Kapur and Flacke, 1981), it does not appear to prevent tachycardia in response to the stimulus of laryngoscopy and endotracheal intubation in man (Gorven, Cooper and Prys-Roberts, unpublished observations).

Nifedipine has an effect on calcium influx different from that of verapamil, in that it blocks the slow channels on the cell surface (Henry, 1980), while it does not affect slow-channel kinetics. It produces profound dilator effects on both coronary and systemic arterioles, and it has become a popular drug for the treatment of hypertension, especially in those patients with coincidental coronary arterial disease. Nifedipine 10–30 mg orally three times daily can maintain excellent control of chronic hypertension, although in a number of patients heart rate and plasma renin concentrations are increased (Stone et al., 1980). Nifedipine is frequently combined with beta-adrenoceptor antagonists in this context, as reduced dosages of both drugs can be achieved. A typical dose regimen would combine nifedipine 10 mg three times daily with atenolol 50 mg daily. While this regimen is clearly effective in the everyday management of hypertension, it may cause problems in the anaesthetic management of such a patient (see below).

**Lidoflazine** is a drug similar to nifedipine, in that it exerts coronary and systemic vasodilator effects without a significant chronotropic effect. The vasodilator effects of lidoflazine become maximal about 3–4 months after starting therapy.

**Problems in the management of patients treated with calcium-channel blockers**

While verapamil may be a very effective drug for the treatment of supraventricular arrhythmia before or during anaesthesia, some caution is necessary in the management of hypertensive patients receiving verapamil. First, because of its marked effects on A–V conduction, halothane and other anaesthetics which depress A–V conduction should be administered with care in order to avoid the development of heart block. Figure 3 shows the development of first degree heart block (prolonged P–R interval) in a patient who had received verapamil 80 mg by mouth 4 h before anaesthesia for parotid surgery. In order to avoid muscle relaxants, 1% halothane was added to the inspired gas mixture of nitrous oxide and oxygen, precipitating a profound degree of hypotension and evidence of subendocardial ischaemia. Withdrawal of halothane and the institution of a continuous infusion of Althesin resulted in a resolution of the first degree heart block, while maintaining an acceptable degree of hypotension and minimal evidence of myocardial ischaemia.

Another example of a similar problem was a 57-yr-old male treated with nifedipine 20 mg three times daily for hypertension, together with verapamil 40 mg twice daily to slow the ventricular rate in response to his atrial fibrillation and to prevent

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**TABLE II. Plan of treatment for hypertensive patients**

<table>
<thead>
<tr>
<th>Decision to treat: Objectives</th>
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<tr>
<td>(1) Decrease arterial pressure</td>
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<tr>
<td>(2) Minimize side-effects</td>
</tr>
<tr>
<td>Avoid non-selective beta-adrenoceptor antagonists in patients with:</td>
</tr>
<tr>
<td>asthma, anaemia, peripheral arterial disease, cardiac failure</td>
</tr>
<tr>
<td>Avoid diuretics in patients with: gout</td>
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<table>
<thead>
<tr>
<th>Choice of drug</th>
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<tr>
<td>Step 1 Either beta-adrenoceptor antagonist or thiazide diuretic</td>
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<tr>
<td>Step 2 Beta-adrenoceptor antagonist + diuretic</td>
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<tr>
<td>Step 3 Beta-adrenoceptor antagonist + diuretic + centrally acting agent (methylodopa) or vasodilator (hydrallazine, prazosin)</td>
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<tr>
<td>Step 4 Resistant hypertension</td>
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<tr>
<td>Consider: (1) adrenergic neurone blocker (2) minoxidil</td>
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<tr>
<td>or Renin dependent hypertension</td>
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<tr>
<td>Consider: (1) captopril</td>
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Remember: If the treatment is not effective, the patient may not be taking drugs.
FIG. 3. Interaction of halothane in a hypertensive patient receiving verapamil 80 mg 4 h before anaesthesia for parotid surgery. A: awake before anaesthesia; B: following induction of anaesthesia with fentanyl and thiopentone. When the lungs were ventilated with 1% halothane in 50% N₂O with oxygen during surgery (c), first degree heart block, marked arterial hypotension and subendocardial ischaemia led to the discontinuation of halothane anaesthesia. D: the reversion to normal sinus rhythm following substitution of Althesin infusion instead of halothane.

episodes of paroxysmal atrial tachycardia. The patient was given his normal drug doses on the morning of surgery. Following laryngoscopy and endotracheal intubation the heart rate accelerated to more than 150 beat min⁻¹ in atrial fibrillation, although no hypertension ensued. During recovery from anaesthesia, his arterial pressure, which had been stable during surgery, increased to 240/130 mm Hg during transfer from the operating theatre to the intensive care unit (Gorven, Cooper and Prys-Roberts, unpublished observations).

These two cases serve to emphasize the potential problems of anaesthesia for patients receiving calcium-channel blockers, either alone or in combination with low doses of beta-adrenoceptor antagonists:

1. Pre-existing therapy with verapamil does not preclude either tachycardia or hypertension in response to laryngoscopy or other noxious stimuli.
2. Pre-existing therapy with verapamil may predispose the patient to heart block if other drugs which impair A-V conduction are administered during or after anaesthesia.
3. Pre-existing therapy with nifedipine, while adequate to maintain everyday control of hypertension, does not preclude the tachycardia or hypertensive responses associated with adrenergic stimulation during or after anaesthesia. The low doses of beta-adrenoceptor antagonists often used in combination with nifedipine, may be quite inadequate to block these same adrenergic responses.

Given these provisos, the anaesthetist faced with the management of a patient receiving calcium antagonists is clearly faced with a number of dilemmas. These are accentuated if the surgery is major and especially when it involves the manipulation of intra-abdominal contents. There is abundant evidence, from both haemodynamic studies and measurements of plasma catecholamine responses (Pflug, Halter and Tolas, 1982), that intra-abdominal surgery is a potent cause of sympathetic nervous activation despite halothane or opioid supplementation of nitrous oxide anaesthesia. Spinal or extradural local anaesthesia may effectively suppress the afferent transmission of the noxious stimuli which initiate the sympatho-adrenal response (Pflug, Halter and Tolas, 1982). However, one must also bear in mind the potential for depression of A-V conduction by local anaesthetics (Covino, 1983). Following extradural blockade in the lumbar region, plasma concentrations of lignocaine (2.9 - 4.5 µg ml⁻¹) or bupivacaine may exceed the values required to enhance A-V conduction block in patients receiving verapamil (Dagnino and Prys-Roberts, unpublished observations). Although one might predict that the lower volumes of local anaesthetic required for thoracic segmental extradural block would produce lower plasma concentrations of the local anaesthetic,
the values observed by Dagnino and Prys-Roberts were greater than those following lumbar block in hypertensive patients.

**Beta-adrenoceptor antagonists**

These drugs form the mainstay of anti-hypertensive therapy for patients with mild to moderate essential hypertension. A continuing series of studies by the author has identified no serious problems in the anaesthetic management of such patients related to drug interactions between the adrenergic blockers and anaesthetics. Most of the problems encountered have been related directly to the background pathological state of the patient, most commonly the associated atheromatous vascular disease of the coronary or cerebral arteries (Prys-Roberts, 1980b, 1982b).

Pre-existing therapy with beta-adrenoceptor antagonists, maintained up to and including the morning of surgery, has been shown to be effective in suppressing the haemodynamic response to laryngoscopy and intubation and the subsequent responses to surgical stimulation. In 20 hypertensive patients receiving propranolol 120–480 mg per day (or other drugs having an equivalent effect), laryngoscopy and endotracheal intubation caused a negligible increase in heart rate and a mean increase in arterial pressure of 15 mm Hg, compared with a mean increase of 60 mm Hg in hypertensive patients treated with drugs other than adrenoceptor antagonists (Prys-Roberts, 1980c). In these patients, intra-abdominal surgical manipulations caused a 24% increase of systolic arterial pressure (SAP), but only a minor increase in cardiac output (4%) and no change in heart rate.

Patients receiving very large doses of propranolol (mean 21.6 mg kg$$^{-1}$$ day$$^{-1}$$), or equivalent doses of oxprenolol or labetalol, for the preoperative management of severe renovascular hypertension (before the introduction of captopril) were studied during the perioperative period (Prys-Roberts, 1982b). Although the arterial pressures of these patients during anaesthesia were high before laryngoscopy (SAP 156±8 SEM), the increase in response to laryngoscopy and intubation was small (3%), and no significant change in heart rate was observed. By contrast, the response to intra-abdominal manipulations comprised a 33% increase in SAP, but no significant changes in cardiac output, heart rate or pulmonary artery (PA) wedge pressure. By the appropriate use of arterial, central venous or PA wedge pressure monitoring, no difficulty was found, in any of the patients described above, in recognizing and replacing blood and fluid losses, thus maintaining adequate arterial pressures throughout surgery and the period after operation.

**Maintenance of adequate beta-adrenoceptor blockade following surgery**

For most surgical patients, the administration of a beta-adrenoceptor antagonist by mouth on the morning of surgery provides adequate blood concentrations to maintain a therapeutic effect for 12–24 perioperative hours. This is especially true for patients taking the long-acting blockers atenolol, nadolol, sotalol or the newer sustained-release preparations of the shorter-acting drugs propranolol, oxprenolol or metoprolol. Patients who have undergone intra-abdominal surgery frequently develop postoperative ileus and are unable to absorb drugs taken by mouth for a number of days. For patients with severe hypertension or ischaemic heart disease, or both, dependent on their beta-adrenoceptor antagonists for control of either arterial pressure or angina pectoris, or both, such a period must be covered by parenteral administration of their appropriate drugs. Depending on the bioavailability of the relevant blocker (approximately 10% for alprenolol, to 100% for sotalol) the calculation of the required dose for i.v. infusion is by no means reliable. The approach that the author has adopted (Prys-Roberts, 1984) is based on the use of two drugs, labetalol or atenolol. For the hypertensive patient, labetalol, a combined alpha- and beta-adrenoceptor antagonist, infused at a rate of 2.5–10 mg h$$^{-1}$$ provides good control of arterial pressure, with adequate renal output. At 6-hourly intervals, an isoprenaline dose–response curve may be easily performed (Dagnino and Prys-Roberts, 1983) allowing precise control of the infusion rate necessary to maintain the same degree of beta-adrenoceptor blockade as that achieved by the patient's normal oral therapeutic dose. In practice, once a single four-point isoprenaline dose–response curve has been performed, the subsequent 6-hourly information can be achieved by observing the response to a single dose of isoprenaline, usually 10 µg. For the patient with ischaemic heart disease without hypertension, or the hypertensive patient whose arterial pressure or urinary output is too sensitive to the effects of labetalol, atenolol infused at 2–6 mg h$$^{-1}$$ provides the same degree of blockade and myocardial protection.
Angiotensin-converting enzyme inhibitors

The conversion of angiotensin I to angiotensin II occurs as blood passes the pulmonary vascular endothelium, where the reaction is catalysed by the angiotensin-converting enzyme (ACE). This enzyme removes the histidyl-leucine dipeptide from the end of the angiotensin I molecule. This enzyme is also effective in deactivating the nonapeptide, bradykinin. The venom of the pit viper Bothrops jararaca was found to inhibit ACE, and this led to the development of several peptides which had a similar effect. Captopril (SQ 14 225) has been widely used for the treatment of both essential and renin-dependent hypertension, and congestive heart failure (Vidt, Bravo and Fouad, 1982). Captopril decreases arterial pressure by decreasing SVR with little effect on cardiac output or plasma volume. Plasma renin activity (PRA) increases rapidly as its feedback inhibition by angiotensin II is removed. No changes in plasma catecholamines have been detected during acute therapy with captopril (Morganti et al., 1980). No major withdrawal phenomena have been observed after abrupt cessation of captopril therapy (Maslowski et al., 1981). In a personal series of eight hypertensive patients receiving captopril, no untoward problems were associated with their anaesthetic management (Prys-Roberts, unpublished observations).

CHOICE AND MANAGEMENT OF ANAESTHESIA

For the principles of preoperative evaluation of the hypertensive patient, the reader is referred to the reviews by Foex (1980), Prys-Roberts (1982a; 1983) and Prys-Roberts and Meloche (1980). These discuss the problems of decision making in relation to the adequacy of antihypertensive therapy at the time of the preoperative visit. The decision to postpone surgery should be made only if the anaesthetist can convince himself, and his medical and surgical colleagues, that by doing so the risk of operative or postoperative morbidity may be significantly decreased. Briefly, patients with severe untreated hypertension (diastolic pressure > 120 mm Hg), with or without coronary arterial, renal or cerebrovascular dysfunction, should not be considered suitable for elective surgery, and should be referred for a cardiological or medical opinion regarding the establishment of adequate therapy before further surgery is scheduled. Patients with mild or poorly controlled hypertension (diastolic pressure 105–120 mm Hg) should be discussed carefully with a cardiologist or physician, and with the surgeon, to determine the wisest course of action. Patients with well controlled hypertension, maintained on their normal therapy up to and including the morning of surgery, rarely present problems of anaesthetic management. Exceptions have been discussed in the earlier section on calcium-channel blockers.

No particular anaesthetic techniques, or specific drug combinations have been shown to be better than others for the hypertensive patient. The choice of general or regional anaesthesia, or a combination of both, must depend primarily on the skill and experience of the anaesthetist rather than on the apparent suitability of any technique in the hands of others.

General anaesthesia

Premedication. Because the hypertensive patient demonstrates exaggerated arterial pressure responses to those events or stimuli which would cause an increase of pressure in the normal patient, there is considerable advantage in selecting premedicant drugs which will decrease apprehension in the period before anaesthesia. Because of their anxiolytic actions, benzodiazepines are very effective in this respect. The author's present choice is to give lorazepam 2–4 mg orally at least 2 h before the anticipated starting time of anaesthesia. Because of its propensity to cause tachycardia in the elderly patient, atropine should be avoided. Small doses of hyoscine (0.2 mg) are equally effective if an anticholinergic effect is specifically indicated.

Monitoring. All monitoring methods should be established before the induction of anaesthesia. Electrocardiographic lead placement should be selected to allow the highest probability of detecting inferior or lateral wall (or both) myocardial ischaemia. For this purpose the CM5 configuration is preferable to other single lead systems. Arterial pressure may be monitored non-invasively in those patients undergoing minor surgical procedures, and the newer automatic systems provide more consistent and repeatable measurements than manual techniques (Hutton, Dye and Prys-Roberts, 1984). For major surgery, the advantages of direct arterial pressure monitoring far outweigh any minor disadvantages, and the method provides beat-by-beat information on the cardiovascular system. Central venous pressure is neither more nor less useful in the hypertensive patient than in his normotensive counterpart. Pulmonary artery pressure monitoring is specifically indicated in those patients with evidence of left ventricular hypertrophy, a history of left
ventricular failure, or signs of poor left ventricular function. For a more complete review of monitoring for the patient with cardiovascular disease, the reader is referred to a previous postgraduate education issue of this journal (Prys-Roberts, 1981).

**Induction.** Choice of induction agents is not critical in the hypertensive patient, although the method of administration is. Two factors combine to decrease arterial pressure during induction of anaesthesia: (1) inhibition of sympathetic nervous activity and loss of baroreflex control resulting from the suppression of arousal (Bristow et al., 1969; Prys-Roberts, Meloche and Foex, 1971), and (2) the direct pharmacological effects of the anaesthetic agents. Where it is appropriate in relation to the projected surgery and its duration, the use of an i.v. opioid such as fentanyl or alfentanil (the latter for short procedures) reduces the dose of hypnotic induction agent required subsequently (Prys-Roberts et al., 1971; Prys-Roberts, 1980c, 1982b).

**Laryngoscopy and endotracheal intubation.** Before the advent of muscle relaxants, endotracheal intubation was achieved usually under deep anaesthesia, and the physiological disturbances which have been reported recently were not much in evidence. During light general anaesthesia, facilitated by muscle relaxants, laryngoscopy and endotracheal intubation provokes activation of the sympathetic nervous system as indicated by characteristic haemodynamic responses, and by increased plasma catecholamine concentrations (Russell et al., 1981; Derbyshire et al., 1983). In untreated hypertensive patients, and those treated with agents other than beta-adrenoceptor antagonists, this noxious stimulus provokes exaggerated haemodynamic responses. These responses, of hypertension and tachycardia, can be partially suppressed by beta-adrenoceptor antagonists (Prys-Roberts et al., 1973; Prys-Roberts, 1982b). Recent studies have shown that plasma catecholamine concentrations start at increased values in untreated hypertensive patients, and increase to a greater degree in response to laryngoscopy, than the values of normotensive patients (Low, Harvey, Dagnino and Prys-Roberts; unpublished observations). By contrast, hypertensive patients treated with beta-adrenoceptor antagonists show increased plasma catecholamine concentrations comparable to normotensive patients, even though the effector organ response is suppressed by the adrenoceptor blocker. Similar findings have been reported by Magnusson and colleagues (1983) who studied the responses to microlaryngoscopy in patients treated with metoprolol.

Topical anaesthesia can ameliorate the response, but it is rarely totally effective. As it is the laryngoscopy rather than the endotracheal intubation which generates the stimulus, it is of little value to use topical anaesthesia after placement of the laryngoscope blade.

Moderate doses of fentanyl (5–10 μg kg⁻¹) have been shown to minimize the hypertensive response to intubation, in both normal and hypertensive patients (Prys-Roberts, 1982b). Provided that controlled ventilation is planned, and where such doses are appropriate for the planned duration of surgery, they may be used as a component of the induction of anaesthesia. Much larger doses of fentanyl (80–100 μg kg⁻¹), sufentanil or alfentanil are necessary to suppress the noxious stimuli of sternotomy in patients undergoing cardiac surgery (de Lange, 1982).

**Maintenance anaesthesia.** The choice of drugs for maintenance of general anaesthesia can be decided only on the basis of each individual patient’s requirement. The early studies carried out by the author and his colleagues (Prys-Roberts, Meloche and Foëx, 1971) were based on the spontaneous breathing of 1% halothane in 67% nitrous oxide. Junctional rhythm, associated with arterial hypotension, occurred in both treated and untreated hypertensive patients, occasionally causing episodes of myocardial ischaemia.

While one may predict that inhalation anaesthetics such as enflurane or isoflurane, which are known to decrease SVR, would have a greater hypotensive effect in hypertensive patients than in normotensive patients, there are no definitive studies which either confirm or disprove such a prediction. There is no convincing evidence that i.v. anaesthetics cause more or less hypotension than inhalation anaesthetics, despite ample evidence of their effects during induction of anaesthesia.

**Artificial ventilation.** Artificial ventilation associated with either increased airway pressure or acutely decreased PaCO₂ may compromise cardiac output in normal man. Both treated and untreated hypertensive patients show a similar response to IPPV, with marked arterial hypotension when hypocapnic hyperventilation is utilized (Prys-Roberts et al., 1972). Hyperventilation to the extent
that $P_{\text{aCO}_2}$ is decreased to less than 4.0 kPa (30 mmHg), can cause acute hypokalaemia in hypertensive patients receiving thiazide diuretics before operation, especially in those whose serum K$^+$ concentrations are at the lower end of the normal range. Such acute hypokalaemia may be associated with supraventricular arrhythmia and consequent arterial hypotension.

**Laryngeal extubation, and recovery from anaesthesia.** Provided that the tracheal tube is removed during anaesthesia, and the patients are not allowed to wake to the point of coughing on the tube, the process of extubation does not cause significant haemodynamic responses (Prys-Roberts, Meloche and Foëx, 1971). Following the withdrawal of inhalation anaesthetic agents, arterial pressure and heart rate remain at the values established during anaesthesia, and only increase at the time of arousal. At this time, systolic and diastolic arterial pressures increase dramatically, returning to pre-anaesthetic values, and sometimes exceeding them. The increase of diastolic pressure reflects the increase of SVR as the patient vasoconstricts, and the increase of systolic arterial pressure reflects the increase of cardiac output associated with an increase of heart rate. In patients who have received neostigmine for the reversal of neuromuscular blockade, these changes are attenuated, and only a modest increase of arterial pressure occurs.

The recovery phase may be associated with rebound hypertension in a small percentage of patients. Most exaggerated increases of arterial pressure at this time are related to sympathetic nervous activation, commonly resulting from inadequately suppressed pain, or bladder distension.

**Regional anaesthesia**

**Spinal and extradural blockade.** Although countless hypertensive patients must have received spinal and extradural blocks in the past, there have been few scientific studies of the responses of such patients. Spinal anaesthesia has been shown to produce unpredictable and more profound arterial hypotension in hypertensive patients than in their normotensive counterparts (Kety et al., 1950; Pugh and Wyndham, 1950; Kleinerman, Sancetta and Hackel, 1958). It must be noted, however, that the patients in these series were largely untreated hypertensives, and that the segmental spread of the spinal anaesthesia was designed to produce "high spinal" conditions. No recent studies have defined the response of well controlled hypertensive patients on modern drugs, to the effects of a spinal anaesthetic covering segments up to but no higher than T8, or of the effects of combined light general anaesthesia.

Patients with well controlled hypertension, predominantly treated with beta-adrenergic antagonists, tolerate either lumbar or thoracic segmental extradural blockade without unpredictable or profound decreases of arterial pressure (Dagnino and Prys-Roberts, 1984). These patients showed a moderate (24%), statistically significant decrease in both systolic and diastolic arterial pressures in response to 1.5% lignocaine injected by catheter in the lumbar region. The decrease in arterial pressures resulted from a decrease in SVR, and was not associated with adverse effects in any patient. Another group of treated hypertensive patients showed only a 19% decrease in systolic pressure and a 17% decrease in diastolic pressure in response to a segmental block extending from T4 to L1 after mid-thoracic injection of 1.5% lignocaine 8 ml.

By contrast, a small group ($n = 5$) of patients with untreated hypertension (diastolic arterial pressure $> 100$ mmHg but $< 120$ mmHg) showed an average decrease of 44% in systolic arterial pressures, and three of the five required active intervention in the form of head-down tilt, atropine 0.6 mg for bradycardia, or methoxamine 2–6 mg for arterial hypotension.

The combination of extradural block with light general anaesthesia was not associated with serious arterial hypotension in the treated hypertensive patients (both lumbar and thoracic extradural groups), and this form of anaesthesia can be recommended for intra-abdominal, hip and lower limb vascular surgery. The main proviso, as always, is that the patients should be monitored carefully.

No serious sequelae have been observed in any of these hypertensive patients (treated or untreated) managed with extradural block combined with light general anaesthesia. Indeed it has been the author's experience that these patients showed minimal cardiovascular disturbances in response to intra-abdominal surgical manipulations, and that their postoperative conditions were excellent. Most of these patients were given extradural diamorphine 2.5–5 mg for pain control after operation.

**REFERENCES**


