THE MANAGEMENT OF HYPERTENSION


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This article is primarily concerned with treatment but it is necessary to make brief reference to the selection of patients who should be treated. The views expressed are based on the experience gained in running a special clinic for hypertensive patients over the past ten years since the introduction of potent hypertensive drugs and are the result of much discussion with those concerned.

None will doubt the magnitude of the problem or the fact that, potentially, high blood pressure is a serious condition. The modern dilemma lies in the fact that much can now be done to relieve symptoms, to prevent or postpone complications and to prolong life, but treatment is beset with difficulties and usually must be continued for life. As yet no really satisfactory drug has been produced. In our experience, few patients with hypertension feel ill. They may be troubled with visual, cerebral or cardiac symptoms, but on the whole they do not suffer from malaise. By contrast, few patients on treatment with hypotensive drugs feel really well. They may be grateful for the relief of symptoms such as those mentioned above but if, for any reason, treatment has to be stopped or should they inadvertently run short of tablets, an unmistakable sensation of relative well being is noticed. Treatment entails frequent medical attention and the daily taking of potent remedies which often have unpleasant side effects. It is our impression that many patients are having treatment which is unwarranted and many others who are in the need of the best that can be offered are receiving treatment which is inadequate.

In most cases it is not considered advisable for treatment to be begun without prior assessment in hospital, and it is believed that a special clinic offers the best means of helping the practitioner to maintain good management thereafter.

Time and facilities are needed to ensure that there is no underlying disease which may require special treatment or which should at least be recognised, to assess the severity of the hypertension itself, the degree of secondary effects in the retinae, brain, heart and kidneys and the degree of disease from associated atheroma, and also to initiate appropriate treatment which then can be continued by the practitioner in association with the clinic.

Multiple readings of the blood pressure are necessary but time-consuming and the medical staff may be inadequate for the purpose. In such cases there is no reason why a technician or nurse should not be trained to take the blood pressure...

What is essential is a standard technique e.g. to record the blood pressure lying and standing at the fourth inflation of the cuff on the right arm and note the systolic pressure and the two diastolic pressures i.e. where the sounds change and where they disappear. The two diastolic readings help to ensure accuracy when the exact point of the change in sound is not easy to determine. In our view this is a better method than relying on single recordings of the blood pressure by the patient as is sometimes recommended. Apart from the introspection engendered and the potential inaccuracy, the advantages of regular attendance at the clinic outweigh the disadvantages. It is necessary for the urine to be tested and renal function to be assessed, for the retina to be examined carefully by an experienced observer and for electrocardiograms to be recorded and interpreted accurately. On occasion special techniques such as pyelography or renal biopsy are required, but in most cases all the necessary information can be obtained if the Physician-in-Charge will make himself thoroughly familiar with these fundamental procedures.

It is not usually our policy to treat those in whom a raised blood pressure is the only abnormal finding i.e. when there is no evidence of hypertensive disease reflected in retinae, brain or heart. Hypertensive symptoms are rarely present without such objective evidence although signs of serious disease may be found in the absence of symptoms. An exception to this rule is made with high, diastolic hypertension particularly in young or middle-aged men. However, whenever there is doubt as to the necessity for treatment, patients are kept under observation for evidence of progression.

Once the decision has been reached as to the
necessity for treatment, the position should be explained to the patient in order to ensure full cooperation.

The aim of treatment should be to achieve optimal control of the blood pressure without undue side effects. In some cases this will mean the maximal control i.e. to bring the blood pressure to as near normal levels as possible and keep it there and in others to achieve moderate control and to avoid severe postural hypertension at all costs because of important associated atheromatous disease or impairment of renal function.

Before discussing treatment certain factors and groups of patients merit special consideration.

Age and Sex

The Elderly

In the elderly hypertension is often mainly systolic or 'benign' in the sense that there is little objective evidence of secondary change except perhaps some left ventricular hypertrophy. Also it can be presumed that primary vascular disease in heart or brain and perhaps nephrosclerosis will be present in greater or less degree. For these reasons the elderly tend to respond badly to lowering the blood pressure and it is easy to make them miserable or actually to shorten life.

The Relatively Young

By contrast with the elderly, hypertension in the relatively young (e.g. under 45 years of age), especially male, should always be taken seriously. In particular it is important to exclude an underlying condition which may be responsible for the raised pressure.

Middle-aged Women

Surprisingly high pressures without evidence of hypertensive disease reflected in retina, brain, heart or kidneys is often found in women of 45 to 60. Usually the resting blood pressure i.e. as recorded in bed before rising is much lower and often quite normal. Any symptoms of which complaint is made are unlikely to be directly related to the hypertension itself and it is not usually advisable to treat such patients with potent hypotensive drugs.

Males

In general the prognosis of hypertension in males is worse than in females.

Atherosclerosis

In particular, we think it very important to recognise the large group of patients in which clinical manifestations are primarily due to atherosclerosis and in whom a raised blood pressure may also be present, but is not the most important condition. There is no doubt that lowering the blood pressure in such patients may have adverse or even catastrophic effects. Caution is also required in those with renal failure or severe impairment of renal function because likewise lowering the blood pressure may have adverse effects.

Systolic Hypertension

A predominant increase in the systolic pressure e.g. 220/100 is most often due to atherosclerosis of the aorta and its main branches. (Cases due to other conditions such as heart block, aortic incompetence or thyrotoxicosis will not be considered here.) In such instances treatment directed to lowering the blood pressure is usually contraindicated but sometimes if symptoms due to hypertension are present or if there is evidence of hypertensive retinopathy or of left ventricular hypertrophy, the blood pressure should be lowered to a moderate degree.

Coronary Artery Disease

Coronary disease will be indicated by a history of cardiac pain, and auricular fibrillation is strong presumptive evidence of its presence. The electrocardiogram may show evidence of past myocardial infarction, of ST-T changes suggesting ischaemic damage or of bundle branch block. Gross cardiac enlargement or failure also usually indicates associated coronary disease. Excessive lowering of the blood pressure may result in further coronary insufficiency or actual myocardial infarction. Caution is therefore required as to the degree to which the blood pressure is lowered by treatment and severe postural falls in pressure must be avoided.

Cerebrovascular Disease

Atherosclerosis tends to be a patchy disease and cerebral thrombosis is not necessarily a contraindication to lowering the blood pressure as discussed above. However, diffuse cerebrovascular disease is suggested by mental changes e.g. impairment of memory and concentration, emotional lability, slurring of speech and transient pareses. Lowering the blood pressure in such cases may have obvious adverse effects.

Peripheral Vascular Disease

Manifestations of defective circulation to the lower limbs may bring patient to doctor and in such cases hypertension may be found. It is important to remember that such patients most often die from coronary artery disease and such should be assumed to be present if lowering the blood pressure is contemplated.
Fundus Oculi

The classification introduced by Keith and Wagener served a useful purpose in drawing attention to the importance of retinal changes in hypertension, but in our opinion has outlived its usefulness. In a large series of patients the classification is an overall guide to prognosis, but for the individual patient too much reliance should not be placed upon it. Paradoxically there is now a tendency to lack of precision in observation and description. Physicians, registrars, housemen and above all perhaps candidates for examination play for safety and having noted a high blood pressure and failing to find evidence of papilloedema, haemorrhages or exudates record 'Fundus grade I-II' regardless of the actual changes or lack of changes present. It is better to record in detail the various changes observed. A hasty glance through undilated pupils should not suffice. What is required is a careful examination of each quadrant in both eyes under favourable conditions. The clinician responsible for deciding on treatment should be familiar with the range of normal and the changes which are no more than physiological accompaniments of advancing years. It must be remembered that a retinal vascular accident may occur, just as may a cerebrovascular accident, in association with normal vessels elsewhere and have no more significance as regards any associated hypertension. In particular changes which are confined to one sector may often be so regarded.

In those under 50 years of age greater significance must be attached than in the elderly to diffuse arteriolar changes such as straightening, narrowing variations in calibre and compression or concealment of veins. Treatment is particularly indicated if in addition there are haemorrhages, exudates or papilloedema. If the fundi are normal or arteriolar changes are slight careful consideration should be given as to whether treatment is really necessary.

Brain

The precise cause of a cerebrovascular accident is often uncertain, but if functional recovery has been reasonably good, if the blood pressure is high and especially if there is evidence of hypertensive disease in the fundi or heart then moderate lowering of the blood pressure is indicated.

Hypertensive encephalopathy is rare and most cases so diagnosed are probably due to a small cerebrovascular accident but if the diagnosis is reasonably certain it constitutes an indication for hypotensive drugs. Caution in treatment is necessary if there is evidence of diffuse cerebral atheroma as discussed below.

Heart

Left ventricular failure or electrocardiographic signs of left ventricular hypertrophy, especially if considerable in degree or progressive, are indications for treatment if other factors are favourable. Caution is necessary if there is evidence for coronary artery disease as discussed below.

The Kidneys

It is important to recognize renal disease and to assess renal function. Hypertension may be secondary to glomerular nephritis, pyelonephritis, or polycystic kidneys or to unilateral renal disease. The latter may be due to an agenetic kidney or there may be renal ischaemia in association with some infection or with vascular obstruction. When hypertension is found in association with bilateral renal disease the prognosis is usually less good than when due to so-called essential hypertension. When due to unilateral renal disease it may be curable by nephrectomy i.e. if changes secondary to the hypertension have not occurred in the other kidney.

Pyelonephritis is often unrecognized and repeated cultures of the urine may be necessary to demonstrate the causative organism. Cultures may be negative and then the diagnosis in life is best proved by renal biopsy. Vigorous and repeated courses of chemotherapy should be given.

By renal failure is meant, for practical purposes, a persistently raised blood urea. By impairment of renal function is meant a reduction below the normal range of special tests of glomerular or tubular function. In either case it is improbable that renal function will be improved by lowering the blood pressure and it may be made worse.

Treatment

There seems to be no doubt that equally good results are being obtained by different observers with varying methods and using different drugs or combination of drugs. In a clinic such as ours it is possible to make comparisons up to a point, but since we are reluctant to change any reasonably satisfactory regime in the individual patient, comparison of different drugs on the same case is rarely justifiable and conclusions must be reached by the comparison of results using different drugs on similar groups of patients.

We have abandoned methonium and veriloid and only use hydralazine as an adjuvant if renal failure is present. Treatment with pentolinium and mepacrine is being maintained in all those who are doing well on either drug, but they are not being used for new patients since neither preparation is ideal and more promising drugs are being offered for trial. However, we do believe at present that there is little to choose between the
various ganglion blocking drugs available and all have undesirable effects from parasympathetic blockade. Serpasil and Rauwiloid are still used, but rarely alone and usually in combination with a ganglion blocking drug. It may be true that in some cases, when used in combination, they ensure slightly smoother control of the blood pressure, that the dose of the ganglion blocking drug can be somewhat lower and side effects somewhat reduced, but recently we have been impressed in most cases by the lack of any significant change on omitting Serpasil or Rauwiloid after a period of good control on the combination. Chlorothiazide is often a very useful adjuvant to treatment with ganglion blocking drugs.

All these factors will now be discussed in more detail.

**Ganglion-Blocking Drugs**

There are now available a number of ganglion blocking drugs of comparable efficacy and as with other drugs e.g. digitalis and anticoagulants except in centres where special facilities exist for making comparisons between different preparations, it is best to master one or two and become thoroughly familiar with their actions and side effects rather than experiment with many.

The ideal drug has not yet been produced and in our experience there is little to choose between pentolinium (Ansolysen), mecamylamine (Inversine), pentacycnum (Presidal), chlorisondamine (Ecolid) and pemipidine (Perolysen, Tenormal). In view of this it would be invidious to recommend one particular drug. In most cases there will be unpleasant side effects in some degree but in a majority these can be overcome by patience and persistence or by combination with some other hypotensive drug or with drugs which counteract side effects from parasympathetic blockade. It is recommended that the drug should normally be given three times in the 24 hours at approximately equal intervals and, if possible, at the same time in relation to meals. The commencing amount for each dose should be:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Tablet strengths</th>
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<tbody>
<tr>
<td>Pentolinium (Ansolysen)</td>
<td>40 mg. 40 and 200 mg.</td>
</tr>
<tr>
<td>Mecamylamine (Inversine)</td>
<td>2½ 2½ and 10 mg.</td>
</tr>
<tr>
<td>Pentacycnum (Presidal)</td>
<td>50 100 mg.</td>
</tr>
<tr>
<td>Chlorisondamine (Ecolid)</td>
<td>25 25 and 50 mg.</td>
</tr>
<tr>
<td>Pemipidine (Perolysen,</td>
<td>2½ 5 and 10 mg.</td>
</tr>
<tr>
<td>Tenormal)</td>
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Each dose should then be raised by small increments every two to three days until a postural effect on the blood pressure is obtained, and thereafter more gradually until the standing diastolic pressure has reached the desired level i.e. according to whether maximal or moderate control is the aim as explained above. Tolerance in greater or less degree will probably develop initially in most cases whichever preparation is used so that a gradual increase in dosage will be indicated until a steady state is achieved. If disabling side effects occur the dose should not be raised for the time being but maintained or slightly reduced and, if necessary, the appropriate antidote given as explained below.

If satisfactory control without undue side effects is still not possible then the dose should be reduced and chlorothiazide added as also explained below.

**Management of Side Effects**

**Postural Hypotension**

Hypotension is not really so much a side effect as evidence of excessive dosage.

If the standing diastolic pressure is lowered excessively, then faintness, giddiness or syncope may develop. Such symptoms are most likely to occur when the patient is standing still e.g. shaving, cooking or queuing and minor manifestations provide a useful warning. Syncope, of course, may be dangerous and must be avoided if possible. At the onset of warning symptoms, syncope may usually be prevented by walking about or bracing the abdominal muscles, but it is best to lie down. If syncope is observed, the patient should be laid flat and the lower limbs or foot of the bed or couch raised.

**Cerebral Circulation**

Apart from cerebral ischaemia from postural hypotension, excessive lowering of the pressure in the presence of atheroma of the cerebral vessels may result in mental disturbances such as confusion, impairment of concentration or memory, emotional lability, slurring of speech, transient pareses or a frank cerebro-vascular accident. Cerebral infarction or softening may occur without actual vascular occlusion. Minor manifestations of cerebral ischaemia constitute a warning either to abandon treatment with hypotensive drugs or to be satisfied with a moderate reduction in pressure.

**Coronary Circulation**

As with the cerebral circulation undue lowering of the blood pressure in the presence of coronary atherosclerosis may result in clinical manifestations from a reduction in blood flow. The appearance or aggravation of angina pectoris is likely to be the first warning, but myocardial infarction may result from an excessive fall in pressure. Treatment with hypotensive drugs should then be abandoned or the dose reduced. The decision as to which is
the best procedure will depend on the overall assessment as to whether hypertension or atherosclerosis is the most important factor in the individual case.

**Difficulty in Accommodation**

Inability to read results from paralysis of the muscles of accommodation. This tends to decrease in time and may be alleviated temporarily by the use of eserine \( \frac{1}{2} \) to 1 per cent. eye drops or a combination of eserine 1 per cent. and pilocarpine 1 per cent. If the trouble continues temporary spectacles or 'slip-over' lenses to existing spectacles can be provided and in the occasional instance when difficulty persists permanent spectacles can be prescribed.

**Dryness of the Mouth**

Dryness of the mouth from diminished salivation is a common complaint but may be counteracted by pilocarpine. Tablets of 1/10 or 1/12 gr. are available and can be taken as required, there being no significant side effects.

**Constipation**

This is the commonest complaint and may be exceedingly troublesome. It may also be serious and if not counteracted lead to paralytic ileus. It is therefore most important that a regular and preferably daily bowel action should be obtained. In our experience the most effective initial step should be to add prostigmine to each dose of the ganglion blocking drug. It is best to begin with half a tablet of \( \frac{7}{2} \) mg. three times daily i.e. with each dose of the ganglion blocking drug and to increase the dose slowly, the morning dose usually being the largest. Should this be insufficient either an evening dose of aloes, cascara or senna according to individual preference or a morning dose of salts should be taken.

**Difficulty with Micturition**

Difficulty or delay in starting micturition is a less frequent complaint and is best counteracted with prostigmine as for constipation.

**Impotence**

Impotence may be a real source of embarrassment and is difficult to counteract. The evening dose of the ganglion blocking drug may be delayed and a dose of prostigmine (15 mg.) taken before retiring, but these measures are not always effective.

**Diarrhoea**

Diarrhoea may be troublesome and in our experience has most frequently occurred with mecamylamine. If associated with distension the treatment is as for constipation, but usually the cause is not obvious and may be a local irritant effect on the bowel. This manifestation can usually be overcome by reducing the dose of the ganglion blocking drug, prescribing an astringent mixture and then increasing the dose again.

**Oedema**

We have noted the appearance of oedema, not attributable to cardiac failure in a number of patients under treatment with ganglion blocking drugs and there have been reports of similar instances in the literature. In our cases the most probable explanation seemed to lie in a retention of sodium from a reduction in renal blood flow. The oedema was eliminated by giving a diuretic and its recurrence prevented by decreasing the dose of the ganglion blocking drug and being satisfied with a lesser degree of reduction in blood pressure. In two patients oedema was considerable in amount and was associated with a demonstrable reduction in the glomerular filtration rate. In each instance impairment of renal function had been noted in the preliminary assessment before commencing treatment.

The appearance of oedema primarily related to treatment and not attributable to any obvious cause should therefore be taken as presumptive evidence of impaired renal blood flow and the warning that not more than a moderate reduction in blood pressure is advisable.

**Rauwolfia**

Rauwolfia and its derivatives have a central inhibitory action particularly on the brain stem and may produce a fall of blood pressure, bradycardia and sedation. Extravagant claims have been made for these drugs particularly by the manufacturers. It has been said that they are suitable for administration to all patients with hypertension and especially for mild cases and that toxic effects are rare. This is contrary to our viewpoint and experience. As explained above it is not recommended that patients with mild hypertension should be treated at all. Benefit is often claimed on account of alleviation of such symptoms as headache, nervousness and tension. In such cases relief of symptoms should not be related to any reduction in blood pressure which may occur and the physician should not be blinded to the fact that the effect is that of any sedative or even a placebo. Side effects of the drug are frequent and include fatigue, lethargy, drowsiness, nasal congestion, anorexia, diarrhoea, paraesthesias, faintness, giddiness, flushing, Parkinsonism, restlessness, agitation and depression. Of these only depression is serious. It cannot be over emphasised that these drugs are potentially
dangerous to some patients. Many cases of severe depression have been reported and more have occurred. Not a few have lost their lives from suicide or been admitted to mental hospitals for convulsion therapy. These effects sometimes happen even with a small dose given over a short period, and also when given in combination with other drugs. They are less likely to occur with rauwolfia than with reserpine (serpasil) and the latter preparation should no longer be prescribed. It is true that side effects tend to decrease in time but not in all patients and many feel better when they stop the drug. It is a particularly undesirable practise to combine rauwolfia and its derivatives with other hypotensive drugs in fixed proportion in the same tablet.

In our experience rauwolfia compounds have no significant effect whatsoever in reducing the blood pressure in more than half the cases and the effect in any case is usually mild. We only find them useful for patients who have considerably raised, labile pressures with associated but probably unrelated symptoms in whom a sedative is indicated and any reduction in blood pressure could only be beneficial but we have not found any close correlation between relief of symptoms and reduction in pressure. The great majority of our patients are under treatment because it is considered essential to maintain a material reduction in pressure and in such cases we consider that ganglion blocking drugs should always be employed. In a few rauwolfia is a useful adjuvant but even in these it is probable that chlorothiazide will prove to be a more useful preparation to enable a lower pressure to be achieved without undue side effects from ganglion blockade.

The object of the above analysis is not to deny the value of rauwolfia in some cases but to emphasise that they should not be prescribed in the blind faith that a useful fall of blood pressure will result, that material fluctuations in blood pressure will be eliminated, that the dose of a concomitant ganglion blocking drug will necessarily be less or side effects from its use will be diminished.

Hydralazine (Apresoline)

Hydralazine has central and peripheral but not ganglion-blocking actions. It is unique amongst hypotensive drugs in increasing cardiac output and at the same time lowering the blood pressure. In our experience the toxic effects of hydralazine were so frequent and so severe that treatment usually had to be abandoned. These effects included headache, nausea, flushing, nasal congestion, angina, oedema, rash, fever, joint pains and general misery. Those who have persisted with large doses have described a syndrome resembling disseminated lupus in about 10 per cent. of cases. When given in combination with a ganglion blocking drug toxic effects are still common but less severe. Some workers have claimed consistently good results if the patient can be persuaded to continue treatment until side effects decrease, but most physicians have found other drugs more satisfactory. In our opinion the only place for hydralazine is in combination with a ganglion-blocking drug for patients in whom renal function is impaired, and one is anxious to try and avoid further depression of renal blood flow.

Veriloid and Protoversatrine

These drugs have a central action and block afferent reflex impulses. The effective therapeutic and toxic doses are close together and with subemetic doses tolerance soon develops. These are of little value in treatment and not recommended for trial.

Hydergine

In recent years Swiss and German workers have made optimistic claims for the hypotensive action of hydergine, which is a mixture of dihydrogenated compounds of ergot and has a central sympathetic inhibitory action. These claims have not been substantiated elsewhere and the general view is that hydergine is too mild to be of appreciable value for the purpose or reducing blood pressure.

Chlorothiazide

Chlorothiazide has largely replaced the need for mercurial diuretics and another very useful action is that of potentiating the hypotensive action of ganglion blocking drugs. By this means the dose of the latter can often be lowered with consequent reduction in side effects. However, caution is necessary or severe postural hypotension may be induced. A good policy is to halve each of the three daily doses of the ganglion blocking drug and at the same time to add to each dose 250 mg. of chlorothiazide. Then, as indicated, the dose of the ganglion-blocking drug can gradually be increased again. With this regime we have had no trouble from electrolyte imbalance but if a larger dose is needed orange juice, which is rich in potassium, may be given or if necessary a potassium supplement in capsule or tablet form (e.g. 1 g. KCl three times daily).

Surgical Treatment

We used to advise bilateral adrenalectomy with lumbo-dorsal sympathectomy as an adjuvant to medical treatment in cases where the blood pressure could not be controlled and renal failure was not present. Surgical treatment has not been necessary in any case during the last three years.
Summary and Conclusions

Modern treatment is effective in that the blood pressure can be controlled and symptoms relieved in most patients. There is good evidence that complications can be prevented or postponed and life prolonged. However, side effects are frequent and few patients on treatment feel really well. The indications for treatment are considered and include objective evidence of hypertensive disease in the form of retinopathy, cerebral haemorrhage, left ventricular hypertrophy or left ventricular failure. Only moderate reduction in pressure should be sought if there is evidence of atherosclerosis in the cerebral or coronary circulation or impairment of renal function. Renal failure is a contraindication to treatment. It is considered that many individuals are receiving unnecessary or inadequate treatment. Drugs in current use are reviewed and the management of side effects discussed. Nowadays surgical treatment is rarely necessary.

I should like to express my gratitude to a succession of assistants who have helped to run our hypertensive clinic, and in particular to my senior registrars, Dr. C. P. Lowther and Dr. A. H. Kitchin who have done so much in recent years.

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