INVESTIGATION

Because secondary hypertension is rare in patients with raised arterial pressures, routine screening to detect renovascular and endocrine hypertension shows a poor return. A policy of selection is therefore necessary.

Detailed investigation may be confined to those patients who:
(a) have malignant hypertension (bilateral retinal haemorrhages),
(b) have poorly controlled blood pressure with adequate doses of the commonly used antihypertensive drugs (not due to non-compliance),
(c) are aged under 30 years,
(d) have an unusual clinical history—for example, sweating attacks, as occur in phaeochromocytoma,
(e) have abnormal plasma concentrations of urea, creatinine, or potassium,
(f) have positive urine tests for protein, blood, or sugar,
(g) have a rapid rise in blood pressure or an abdominal bruit.

Investigations for all patients

Does the average middle-aged patient with mild to moderately raised arterial pressure need any tests? Many patients in Britain are treated by their family doctors without initial biochemical or radiological investigations, but a limited number of tests are justified. Apart from a full history these should include an examination of the optic fundi, an electrocardiogram, a plain chest radiograph, and simple blood and urine tests.

Apart from excluding secondary hypertension these tests are useful for identifying other correctable risk factors for vascular disease. It is also valuable to look for evidence of damage to “target” organs, though treatment must not be left until damage occurs. Many patients with high blood pressure have no symptoms or signs until a lethal cardiovascular catastrophe occurs.
History

Specific inquiry about the use of oral contraceptives is necessary when taking a history in women with raised blood pressure. In most women the oestrogen-containing pill causes a small rise in arterial pressure and in some the rise may be pronounced; in rare cases malignant hypertension may supervene. The effect is smaller but still present with the lower-dose oestrogen preparations. The progestagen mini-pill, a less effective contraceptive, probably has no effect on blood pressure. The effect is smaller but still present with the lower-dose oestrogen preparations.

The progestagen mini-pill, a less effective contraceptive, probably has no effect on blood pressure. The history may be useful in the very small percentage of patients with endocrine hypertension. In phaeochromocytoma there may be attacks of sweating, throbbing headache, or palpitations; in primary aldosteronism attacks of muscular weakness, polyuria, or paraesthesia; and in Cushing's syndrome rapid weight gain or ready bruising.

Clinical examination

Delayed femoral pulses are present in the rare, usually young, patient with coarctation of the aorta. Patients with acromegaly or Cushing's syndrome have a distinctive appearance. Polycystic kidneys may be palpable on abdominal examination, and a unilateral renal artery stenosis is usually present if a systolic-diastolic bruit is audible lateral to the midline.

It is useful to seek clinical evidence of cardiac enlargement and to examine the optic fundi in all patients.

Using the ophthalmoscope

In the past too much emphasis has been placed on arteriolar appearances in the retina, and confusion may result from using the conventional Keith-Wagener-Barker classification.

Hyaline degeneration of the arterial wall (indicated by increased light reflex) occurs with aging and with high blood pressure.

Retinal haemorrhages should be carefully looked for. Bilateral flame-shaped haemorrhages occur in patients with malignant hypertension and their presence indicates the need for prompt treatment with hypotensive drugs. The appearance of these haemorrhages correlates with the development of fibrinoid necrosis in the arterioles of the kidney, the pathological hallmark of malignant hypertension.

Cotton-wool spots, due to infarction of the nerve fibre layer of the retina, are an ominous sign, as is papilloedema. Hard exudates, which often cluster round the macula, are slightly less important and result from leakage of plasma from damaged vessels.
X rays and ECGs

A plain radiograph of the chest should be taken and an ECG recorded in all patients. Radiology occasionally shows cardiac enlargement and, very rarely, the characteristic notching on the underside of the ribs caused by collateral vessels in patients with coarctation of the aorta.

The ECG is considerably more sensitive in detecting left ventricular enlargement than x-ray studies. Hypertensive patients who develop evidence of left ventricular hypertrophy on ECG, particularly if accompanied by ST and T-wave changes in the leads overlying the left ventricle, are in great jeopardy. The Framingham study showed that 30% of patients with definite left ventricular hypertrophy on ECG die within five years. All patients with such changes should be treated, although high-voltage changes alone can sometimes be explained by other factors, such as a thin chest wall in a young subject.

Urine tests

Tests using reagent strips ("Stix" tests) of urine for blood, protein, and sugar are easy to perform but all too often omitted. The test for blood becomes more sensitive if red cells in urine are lysed with a drop of detergent—for example, saponin.

Proteinuria or haematuria in the absence of malignant hypertension suggests underlying renal disease—for example, glomerulonephritis. Urine microscopy is necessary in patients with positive strip test results, but the value of routine urine culture in the absence of either a positive strip test result or a history suggesting urinary tract infection is doubtful: it is unlikely to be of value in men but may be useful in women.

Routine screening for phaeochromocytoma by measuring the urinary excretion of normetanephrine is not worth while. If a patient has blood pressures that fluctuate widely, increase with drug treatment, or show a pronounced postural fall then measurements of urinary catecholamine metabolites of plasma noradrenaline concentrations, or both, are necessary. Sweating attacks and weight loss are other indications for these tests.

Maturity-onset diabetes and raised arterial pressure are common conditions, and both often occur together in patients who are overweight. Blood pressure must be carefully controlled in diabetics since high pressure accelerates the development of retinopathy. Only rarely are diabetes and high blood pressure caused by endocrine diseases such as phaeochromocytoma, Cushing’s syndrome, and acromegaly. Mild impairment of glucose tolerance is common in patients with primary aldosteronism but is corrected by effective treatment of the underlying condition. Thiazide diuretics may precipitate or worsen diabetes mellitus.

Blood tests

<table>
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<tr>
<th>RESULTS</th>
<th>CRITERIA FOR NORMAL VALUE</th>
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<tbody>
<tr>
<td>145</td>
<td>HIGH</td>
<td>SODIUM</td>
<td>130-144 (m mol/l)</td>
</tr>
<tr>
<td>2.8</td>
<td>LOW</td>
<td>POTASSIUM</td>
<td>3.4-4.9 (m mol/l)</td>
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<tr>
<td>105</td>
<td>LOW</td>
<td>CHLORIDE</td>
<td>95-105 (m mol/l)</td>
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<tr>
<td>29</td>
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<td>CO₂</td>
<td>21-28 (m mol/l)</td>
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<tr>
<td>3.8</td>
<td></td>
<td>UREA</td>
<td>2.5-7.0 (m mol/l)</td>
</tr>
<tr>
<td>71</td>
<td></td>
<td>CREATININE</td>
<td>35-115 (μ mol/l)</td>
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Renovascular hypertension

In primary aldosteronism (or in other rare forms of mineralocorticoid hypertension such as 11-β-hydroxylation deficiency, 17-α-hydroxylation deficiency, and carbeneoxolone or liquorice ingestion) the typical electrolyte picture includes hypokalaemia, increased serum concentrations of bicarbonate, and slightly increased plasma sodium concentrations. In contrast, patients with aldosterone excess due to depletion of sodium or malignant hypertension usually have low normal or low plasma sodium concentrations: the high aldosterone concentrations are then accompanied by and caused by high concentrations of circulating renin and angiotensin II.

Thiazide diuretics cause a fall in the serum concentration of potassium that is related to dose: severe hypokalaemia with muscle paralysis may result from the administration of diuretics to patients with primary aldosteronism. Serum potassium concentrations should preferably be measured before the start of drug treatment on venous samples taken without exercise of the forearm.

Raised plasma concentrations of urea and creatinine occur in patients with impaired renal function owing either to primary renal disease or to renal damage from severe hypertension. Retention of sodium is often a factor in the pathogenesis of the high blood pressure that accompanies renal impairment; thiazide diuretics are relatively ineffective in this condition, and loop diuretics, such as frusemide administered twice a day, are usually necessary.

This simple scheme of investigation will fail to detect the cause in most patients with renovascular hypertension. Narrowing of a renal artery may result from atheroma, usually in older patients, or from fibromuscular hyperplasia, which occurs in young women. An intravenous urogram is usually necessary to detect this narrowing, but the routine use of this test in all patients with hypertension is expensive and unrewarding. It is worth investigating only those patients who (a) are young; (b) have poorly controlled blood pressure with drug treatment; (c) have bilateral retinal haemorrhages; or (d) have a rapid rise in blood pressure or an abdominal bruit.

Other screening procedures such as isotope renography or measurements of plasma renin activity have been used. Renography is a sensitive test, but false-positive results are common. With renin estimation both false-positive and false-negative results are common, and similar problems may occur with the saralasin test (saralasin is a competitive antagonist of angiotensin II).

Surgery in patients with renal ischaemia does not always cure hypertension, even with careful selection of patients. Indeed, it is not certain that the overall outcome after surgery is better than with drug treatment. Intravenous urography may show a non-functioning kidney, which can result from occlusion of the main renal artery, a potent cause of high blood pressure. Such changes may be wrongly attributed to pyelonephritis or hypoplasia unless renal arteriography is carried out.

Since up to 15% of the middle-aged population of this country have raised blood pressures investigations should be kept to a minimum in most patients. Investigation and treatment are best carried out in general practice, though detailed study and hospital referral may be necessary in a small proportion of patients.

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