

Hypertension

— clinical features and investigations

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Hypertension is one of the most common diseases in the world and is an important risk factor for coronary events. This article, the first in a special feature, will describe the current classification of hypertension, its clinical features and the role of lifestyle modifications in treating the disease



Hypertension is one of the most common diseases in the world, affecting an estimated 20 per cent of the adult population.¹ It is associated with marked morbidity and mortality and places a high burden on health care systems. Hypertension is the most important single, modifiable risk factor for coronary artery disease, stroke and end-stage renal disease. However, early recognition and implementation of effective pharmacological and non-pharmacological therapies allows for early modification of cardiovascular risk.

— Definition

A precise definition of hypertension is difficult to establish because blood pressure is a continuous variable and has a skewed normal distribution within the population. An arbitrary value for hypertension is one where a certain blood pressure is associated with a significant increase in the risk of cardiovascular disease compared with the population as a whole. This defines a population at risk and allows for screening and initiation of treatment. The International Society of Hypertension and World Health Organization define hypertension as a sustained blood pressure of $\geq 140/90$ mmHg.²

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However, most people will have a blood pressure of $< 140/90$ mmHg but may still experience hypertension-related disease. The risk to an individual may correlate with the severity of the hypertension. Panel 1 (p112) describes factors affecting the risk posed by hypertension.

The seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure proposed categories of hypertension depending on severity³ (see Panel 2, p112). Again, these are arbitrary figures that do not address the presence of co-morbidities such as diabetes, hypercholesterolaemia and smoking, which might enhance the risk of cardiovascular disease for any given blood pressure reading.

Hypertension may be classified by aetiology into two groups: essential (or primary) hypertension and secondary hypertension. Essential hypertension is diagnosed when no identifiable cause can be found and accounts for 95 per cent of all cases of hypertension. Secondary hypertension, where a cause can be identified, accounts for less than 5 per cent of cases (see Panel 3, p114). Essential hypertension is now recognised as a heterogeneous condition. In classical essential hypertension both the systolic and diastolic blood pressures are high, but isolated systolic and isolated diastolic hypertension are also seen.

Malignant or accelerated hypertension is associated with a rapid rise in arterial pressure and, if untreated, results in rapid end-organ damage and death.

The term “benign” essential hypertension has been used to describe a less aggressive form of hypertension but this term is not widely accepted because the condition is not benign. It is associated with significant morbidity and mortality.

Resistant hypertension is used to describe cases of hypertension that are refractory to standard medical therapy (three different classes of anti-hypertensive drugs).

“White coat” hypertension refers to individuals that have elevated blood pressure readings when taken in a clinical setting such as an outpatient clinic, but have normal readings when taken in other environments. It was initially thought to be a benign condition but 75 per cent of patients with white coat hypertension will go on to develop sustained hypertension within five years and some studies suggest that it is an independent risk factor for cardiovascular disease.⁴

— Epidemiology

Age The prevalence of hypertension increases with age. The Health Survey for England¹ reported the prevalence of hypertension to be 3.3 per cent in those aged under 40 years, 27.9 per cent in those aged 40–79 years and 49.9 per cent in those aged over 80 years. However, these figures probably underestimate the true prevalence of hypertension in the population due to poor identification of cases.

Similar figures are seen throughout the developed world and, overall, 20 per cent of the world's adult population are estimated to have hypertension (with a blood pressure of $\geq 140/90$ mmHg).

Age-related hypertension is predominantly systolic. Systolic blood pressures continue to rise throughout life, whereas diastolic blood pressures remain constant or begin to decline after the fourth decade.

Ethnic group Black people have a higher prevalence and incidence of hypertension than white people. In the US, the prevalence of hypertension in African Americans is 50 per cent greater than in white Americans. Mortality rates from hypertension in Afro-Caribbean populations are 3.5 per cent higher than the national rate. Similar figures are seen in the UK. Ethnic differences also exist in the pathogenesis of hypertension, with black populations developing hypertension at an earlier age and having lower renin activity. Black people also have poor response to treatment with angiotensin-converting enzyme (ACE) inhibitors and beta-blockers (see p125).

Sex Women are less likely than men to develop hypertension at an early age. The third national health and nutrition examination survey⁵ found the prevalence of hypertension to be 12 per cent for white men and 5 per cent for white women aged 18–49 years. However, the age-related increase in blood pressure is greater in women. The survey found that, by the age of 70, the prevalence of hypertension in white women was 55 per cent compared with 50 per cent in white men.

The progressive rise in the incidence of hypertension is clearly documented in all sex and race groups. In general there is a 5 per cent increase in the incidence of hypertension per decade.⁶

— Aetiology

Pathophysiology Arterial blood pressure is a product of cardiac output and total

Category	Systolic BP (mmHg)		Diastolic BP (mmHg)
Normal	<130	and	<85
High-normal	130–139	or	85–89
Hypertension			
Stage I	140–159	or	90–99
Stage II	160–179	or	100–109
Stage III	≥ 180	or	≥ 110

peripheral vascular resistance. Therefore, blood pressure is determined by factors that influence cardiac output and arteriolar physiology, which are controlled by integrated physiological mechanisms. Sympathetic nervous system activity increases cardiac output and increases vascular resistance, resulting in increased blood pressure. Stimulation of the renin-angiotensin system results in the release of angiotensin II that acts as a direct vasoconstrictor on the peripheral vasculature and also promotes aldosterone release from the adrenal cortex, promoting salt and water retention. These actions are counterbalanced by the action of the parasympathetic nervous system.

The vascular endothelium plays an essential role in the maintenance of normal blood pressure. It produces various hormonal, humoral and growth factors, including angiotensin II, bradykinin, endothelin, nitric oxide and platelet-derived growth factor. Interaction of these factors results in vessel wall remodelling, vasodilatation, vasoconstriction and regulation of blood pressure.

The baroreflex also contributes to short-term regulation of blood pressure. Baroreceptors in the aortic arch and carotid arteries detect arterial pressure and fire signals to the central blood pressure regulatory centre in the brain at a rate proportional to the blood pressure. This determines the degree of sympathetic and parasympathetic output and maintains tight control of blood pressure.

Regulation of blood pressure is a complex interplay of the autonomic nervous system together with the neuro-hormonal cascade

and vasculature autoregulation to produce a balance of vasoconstriction, vasodilation and intravascular volumes.

Pathogenesis The pathogenesis of essential hypertension is multifactorial, complex and not clearly defined. There is a clear interplay between genetic and environmental factors. An increase in sympathetic tone and a decrease in parasympathetic tone plays a substantial role in the development of hypertension.

Essential hypertension is associated with an increase in both systolic and diastolic pressures and a rise in total peripheral resistance. The medial layer of the arterial wall becomes thickened due to smooth muscle proliferation, resulting in a further rise in peripheral resistance. It is not clear whether these changes are a primary factor in the development of hypertension or whether they are secondary changes.

Baroreceptors become less sensitive in hypertensive patients, which may be due to medial hyperplasia. The impaired baroreflex and increased systemic vascular resistance further increase the blood pressure.

Isolated systolic hypertension results from the stiffening of the large arteries. Unlike essential hypertension, it is not associated with a rise in peripheral resistance. The pathogenesis is unclear but may be due to disruption of collagen and elastin fibres within the arterial wall, resulting in dilation and stiffening of the artery. It was originally thought to be the end-stage of diastolic hypertension but less than 20 per cent patients with isolated systolic hypertension have records of previous diastolic hypertension.⁷ Isolated systolic hypertension is treated with traditional antihypertensive drugs, which are effective because a reduction in mean arterial pressure reduces arterial wall stiffness and pulse pressure.

Diet Epidemiological studies have shown a clear association between obesity, salt and alcohol intake and the development of hypertension. The prevalence of hypertension in obese people is at least 50 per cent greater than in the lean population⁸ and a recent Cochrane review suggested that 40 per cent of people with hypertension are obese.⁹ The association between salt intake and hypertension is more pronounced in the older population. There is a significant

Panel 1: Predicting risk

Hypertension confers a significant contribution to an individual's risk of cardiovascular disease but must be considered in the context of other cardiovascular risk factors. Various analyses have been used to determine the contribution of hypertension alone to overall risk. Hypertension confers a 3–19 per cent increase in the risk of stroke, a 3 per cent increase in the risk of developing heart failure and accounts for 25 per cent of deaths from coronary artery disease. Hypertension is one of the most significant, single, modifiable risk factors in cardiovascular disease and appropriate treatment has the potential to reduce cardiovascular morbidity and mortality significantly.

Data from the Framingham Heart Study suggest that diastolic blood pressure is the best predictor for coronary artery disease in people aged under 50 years. Both diastolic and systolic pressures predict the risk in those aged 50–60 years, and systolic pressure is the best predictor in those aged over 60 years. In people aged over 50 years, for any given systolic pressure, the lower the diastolic pressure, the higher the risk of coronary artery disease.

relationship between drinking more than three units of alcohol per day and the development of hypertension, independent of weight and salt intake.¹⁰

— End organ damage

End organ damage is a term used to describe the abnormalities that occur to organs due to exposure to persistently high blood pressure. Increased wall stress in small arterioles, known as resistance arterioles, results in smooth muscle hypertrophy and collagen deposition in the sub-endothelial space. This results in hyaline arteriosclerosis (thickening of the resistance arterioles). Many organs are protected from this effect by autoregulation, which maintains normal tissue blood flow. Continuous exposure ultimately results in organ damage and the most critical sites are the kidney, heart and brain.

Hypertensive nephrosclerosis (hardening of the blood vessels in the kidney) is

Panel 3: Secondary hypertension

In the vast majority of cases, no underlying cause can be found for hypertension. In 5–10 per cent of cases an underlying cause is found — this is known as secondary hypertension and its causes are listed below.

Renal (50 per cent of cases)

- Renal parenchymal disease
 - Glomerular nephritis
 - Polycystic disease
- Renovascular disease

Endocrine (20 per cent of cases)

- Hyperaldosteronism: Conn's syndrome and adrenal hyperplasia
- Cushing's syndrome
- Pheochromocytoma
- Hyperthyroidism and hypothyroidism
- Hyperparathyroidism
- Acromegaly

Vascular

- Coarctation of the aorta
- Vasculitis

Other

- Pregnancy-induced hypertension
- Polycythaemia rubra vera (a primary blood disorder resulting in too many red blood cells)
- Paget's disease
- Drugs (alcohol, oral contraceptives, steroids, cocaine, ciclosporin)

Secondary hypertension is more frequently found in younger patients and in those who are resistant to medical therapy. Patients may exhibit other symptoms that suggest an underlying cause.

associated with a gradual decline in creatinine clearance but there is clear evidence that early detection and treatment can prevent progression to end-stage renal disease.

Left ventricular hypertrophy (LVH) is the principal cardiac end organ damage and results from a persistently raised afterload (the force against which the heart muscle must work to overcome resistance to blood flow in the aorta and peripheral arteries). Diastolic filling and stroke volume are reduced, which, together with the increased myocardial mass, predisposes to myocardial ischaemia. LVH is also associated with atrial and ventricular arrhythmias, heart failure and an increased risk of sudden death.

Alteration of normal cerebral blood flow results in progressive cortical loss and dementia. There is a clear association between raised blood pressure and the development of acute haemorrhagic strokes. In malignant hypertension the rapid rise in blood pressure overwhelms cerebral autoregulation resulting in cerebral oedema and microhaemorrhages. This is known as hypertensive encephalopathy.

— Clinical features

History Most patients with essential hypertension will be asymptomatic. Initial diagnosis will depend on the routine measurement of blood pressure and confirmation of elevated pressures on three separate occasions. Patients may have a history of headache but this is more common in secondary and malignant hypertension.

A detailed history should include assessment of overall cardiovascular risk including any history of hypercholesterolaemia, diabetes mellitus and smoking. Aggravating factors for hypertension should be looked for, including alcohol and salt intake and level of physical activity. Symptoms suggestive of a secondary cause should also be sought.

Because essential hypertension is asymptomatic and may have been present for many years it is important to take a history for any end organ damage. This may include a history of stroke or worsening memory and symptoms suggestive of LVH, such as chest pain, breathlessness or palpitations.

Examination A full physical examination is required in addition to measurement of blood pressure. Height and weight should be measured and body mass index (BMI) calculated. Throughout, signs of secondary causes of hypertension should be looked for.

Cardiovascular examination should concentrate on heart rhythm, evidence of heart failure, LVH and peripheral arterial disease. Abdominal examination should check for renal masses and bruits (an unusual sound that blood makes when it rushes past an obstruction in an artery). Neurological examination should include assessment of memory, evidence of neurological deficit

Panel 4: Investigations

Following are the routine and additional investigations carried out in patients with essential hypertension:

Routine investigations

- Serum urea, creatinine and electrolyte levels
- Blood glucose levels
- Lipid profile
- Urinalysis for proteinuria and haematuria
- Echocardiogram

Additional investigations

- Chest X-ray
- Echocardiogram

and the appearance of both retinas, to look for signs of hypertensive retinopathy. Hypertensive retinopathy is another example of end organ damage. Features include the appearance of "cotton wool" spots, flame-shaped haemorrhages, macular oedema, exudates and eventually papilloedema. The severity of hypertensive retinopathy is divided into four grades with Grade IV being the most severe and associated with malignant hypertension.

Investigations Unless a secondary cause of hypertension is suspected, routine investigations for essential hypertension are carried out, as listed in Panel 4. These are used to assess the overall level of cardiovascular risk and to look for any evidence of end organ damage.

Urinalysis is important because proteinuria is a sensitive marker of early hypertensive renal damage and may be associated with an increase in plasma urea and creatinine levels. Established microalbuminuria is a predictor of progression of renal disease in hypertensive patients and early recognition and commencement of ACE inhibitor therapy has been shown to slow the progression of worsening renal function. Microscopic haematuria can be seen in hypertensive renal disease but is not as good an indicator of the disease as the presence of proteinuria. Haematuria may be seen in some forms of glomerulonephritis and this would suggest an underlying cause for hypertension.

An electrocardiogram is used to screen for LVH and may show evidence of underlying ischaemia, previous myocardial infarction and the presence of arrhythmias. Echocardiography is indicated if there is suspicion of LVH or any other evidence of end organ damage. Chest X-ray is not routinely indicated in the hypertensive patient unless there is evidence of underlying respiratory disease, heart failure or the suspicion of a secondary cause, such as coarctation of the aorta.

Panel 5: Features suggestive of secondary hypertension

Cause	Suggestive features	Investigations
Renal artery stenosis	Elderly male Atherosclerosis Flash pulmonary oedema Renal bruits Rise in creatinine with ACE inhibitor therapy	Renal artery magnetic resonance image scan or angiography
Phaeochromocytoma	Headache Sweating Palpitations Anxiety	Plasma catecholamine levels 24-hour urinary catecholamine levels Nuclear scan
Hypothyroidism	Bradycardia Cold intolerance Lethargy	Thyroid function tests
Cushing's syndrome	Cushingoid appearance Muscle weakness Hirsutism	Cortisol levels Dexamethasone suppression test Abdominal computed tomography scan

If a secondary cause is suspected then further investigations may be warranted (see Panel 5).

— Lifestyle management

The mainstay of treatment of hypertension is pharmacological intervention, which will be described in the second part of this feature (p119–125). However, there is a clear association between obesity, salt and alcohol intake and the development of hypertension. Lifestyle modifications to influence these factors can play an important part in the overall management of the hypertensive patient. Smoking cessation is the most important life style modification for reducing overall cardiovascular risk.

Weight Obesity is clearly associated with the development of hypertension but is also related to other mechanisms, such as insulin resistance, dyslipidaemia and sympathetic nervous system upregulation, which further increase the risk of developing cardiovascular disease. Several trials have demonstrated that losing weight reduces both systolic and diastolic blood pressure. A 10 per cent weight loss can reduce total blood pressure by 7/5mmHg. In addition, there is an improvement in lipid profile, reduction in insulin resistance and improved vascular tone, further reducing cardiovascular risk. The effects of weight loss are additive to pharmacological treatment.

Any patient with a BMI of over 25kg/m² should be encouraged to lose weight. This

requires a multidisciplinary approach and the establishment of a tailored weight loss programme. Dietary advice must be combined with a physical activity plan to achieve optimal results. The use of anti-obesity drugs may be considered as part of a programme in well motivated patients in a specialist clinic.

Diet A reduction in salt intake of 100mmol/day can reduce systolic blood pressure by 6mmHg and diastolic pressure by 2mmHg.¹¹ Some patients are particularly sensitive to salt reduction and can achieve systolic pressure reductions of over 10mmHg. The benefits of pharmacological management are also enhanced by salt restriction. Salt restriction, in combination with a thiazide diuretic, can result in an additional reduction in systolic pressures of 3mmHg. Patients should be encouraged to reduce their daily salt intake and avoid processed foods with high salt levels. Potassium chloride can be used as a substitute for sodium chloride in the diet. Initial studies suggested that an increase in potassium intake may actually help reduce blood pressure, but this has not been confirmed in larger placebo-controlled studies.¹² Reassuringly, no adverse outcomes were seen with increased potassium and potassium chloride can be considered as a safe alternative to sodium chloride.

Alcohol Observational data show a linear association between alcohol intake and blood pressure in both sexes, although a causal relationship has not been confirmed. Indeed, there is evidence of a J-shaped curve, with low levels of alcohol consumption actually providing cardiovascular protection.¹³ Binge drinking is associated with a greater risk compared to the overall level of alcohol consumption and is associated with higher rises in blood pressure overall. Abstinence from alcohol in hypertensive patients can reduce systolic blood

pressure by 5–8mmHg and diastolic pressure by 2–3mmHg. Patients should be encouraged to reduce their alcohol consumption to no more than the recommended safety levels and to abstain where possible.

Exercise Regular aerobic exercise can reduce blood pressures by 8/4mmHg and reduce left ventricular mass. This effect is most pronounced in those patients who previously took no or little exercise. The effects of exercise are independent of weight loss. Patients should be encouraged to perform dynamic exercise, such as walking, cycling and swimming, of moderate intensity, for 45–60 minutes three to four times per week. Shorter episodes of exercise have less effect on blood pressure reduction, even if they are more frequent.

— Conclusion

Hypertension is one of the most common diseases in the world. Recognition of hypertension is often difficult because most patients have no symptoms and diagnosis relies on routine blood pressure measurements. Physical examination may be entirely normal. The goal of therapy is to prevent end organ damage and reduce overall cardiovascular risk in the population. Searching for a secondary cause of hypertension is impor-

tant because treating the underlying cause may alleviate the hypertension and avoid the need for long-term antihypertensive medicines. Lifestyle modifications are effective in reducing blood pressure and they enhance pharmacological therapy, which will be discussed in the next section of this article (p119).

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