BMJ Best Practice

Assessment of hypertension

The right clinical information, right where it's needed

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Summary

◊ Hypertension is a common disorder that affects a large proportion of the community. It is usually asymptomatic and is detected on routine examination or after the occurrence of a complication such as a heart attack or stroke.[1] It is often referred to as the silent killer.

The definition of hypertension is based on recommendations by the American Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure,[2] the British Society of Hypertension,[3] and the European Society of Hypertension.[4] There are slight differences in the definition of hypertension between guidelines.

- The American guidelines (JNC-7) state that a blood pressure below 120/80 mmHg is normal, 120 to 139/80 to 89 mmHg is pre-hypertension, and anything above this is abnormal. Isolated systolic hypertension is defined as an elevated systolic blood pressure of >140 mmHg with a normal (<80 mmHg) diastolic pressure. It should be noted that the more recent Joint National Commission (JNC-8) guidelines recommended revised treatment thresholds but did not redefine diagnostic categories.[5]
- The European and British guidelines have classified a blood pressure of <120/80 mmHg as optimal. 120 to 129/80 to 84 mmHg is normal, 130 to 139/85 to 89 mmHg is high normal, and anything above that is classified as hypertension and is divided into 3 stages:

1. Stage 1: systolic 140 to 159 and/or diastolic 90 to 99 mmHg
2. Stage 2: systolic 160 to 179 and/or diastolic 100 to 109 mmHg
3. Stage 3: systolic 180 mmHg or higher and/or diastolic 110 mmHg or higher.

Isolated systolic hypertension is also graded according to systolic blood pressure values in the ranges indicated, provided that diastolic values are <90 mmHg.

Although different studies have used a variety of cut-off points for the diagnosis of hypertension in the community, any blood pressure over 120 mmHg systolic is associated with an increased cardiovascular risk. The importance of hypertension is its relation to other cardiovascular risk factors and consequent overall cardiovascular risk.

◊ **Epidemiology :**
In the US, data from the National Health and Nutrition Survey (NHANES) suggest that hypertension has a mean prevalence of 29% in the population >18 years of age, using a cut-off value of 140/90 mmHg. This ranges from around 7% in those aged 18 to 39 years to 66% in those aged >60 years.[6] The prevalence seems to be higher in Western Europe.[7] However, as elevated blood pressure is usually asymptomatic, the exact prevalence of hypertension is difficult to assess, and is expected to rise as the 'cut-off' value for hypertension is re-defined at a lower level.

◊ **Complications and target organ damage :**
Studies have shown that treatment of hypertension can reduce the incidence of future cardiovascular and cerebrovascular events.[8] The aim of early diagnosis and treatment of hypertension is to lower overall cardiovascular risk and prevent cerebrovascular events. The effects of chronic hypertension on organ systems are referred to as target organ damage.

Left ventricular hypertrophy, cardiovascular disease, cerebrovascular disease, hypertensive retinopathy, and nephropathy are the most common manifestations.[9] The presence of left ventricular hypertrophy is a poor prognostic sign, and regression of left ventricular hypertrophy improves prognosis.[10]

◊ **Cardiovascular risk :**
Guidelines on the management of hypertension emphasise the importance of calculating and managing the overall cardiovascular risk of a patient, rather than focusing only on blood pressure readings. For individuals aged 40 to 70 years, each increment of 20 mmHg in systolic blood pressure or 10 mmHg in diastolic blood pressure

across the entire blood pressure range from 115/75 to 185/115 mmHg doubles the risk of cardiovascular disease.[11] Treating associated cardiovascular risk factors such as obesity, diabetes, hypercholesterolaemia, and smoking are as important as managing hypertension in lowering overall cardiovascular risk.

Aetiology

Primary hypertension

This is the most common situation, when no underlying cause can be found to account for raised blood pressure. It is also referred to as essential hypertension. A genetic basis has been suggested. Lifestyle influences such as obesity, sedentary lifestyle, excess alcohol intake, and high sodium intake are all thought to promote the development of essential hypertension.[11] [12] [13]

Secondary hypertension

In a minority of cases, an underlying, often reversible cause can be found. This may be suspected in a younger patient (<40 years of age), when blood pressure is resistant to first-line medication, or if a patient with previously well-controlled hypertension suddenly becomes difficult to manage while remaining compliant with their medication.

Vascular

- One of the most common secondary causes of hypertension is renal artery stenosis. This may be entirely asymptomatic but, if hypertension is difficult to control and the patient is young, renal artery stenosis should be excluded. Stenosis is usually due to fibromuscular dysplasia or atherosclerosis, but other causes include extrinsic compression of the artery by an adjacent tumour or a proximal aneurysm of the renal artery.
- Coarctation of the aorta is a congenital narrowing of the aorta. When presenting in adults with hypertension, this narrowing is usually distal to the ligamentum arteriosum, although coarctation can occur before or at the site of the ligamentous insertion. There is usually hypertension in the upper limbs but weak or absent pulses in the lower limbs. This combination of signs will raise suspicion of a coarctation on clinical examination.
- Pre-eclampsia is a syndrome of hypertension with proteinuria in pregnant women. Its exact cause is unknown, but the placenta is thought to release factors, perhaps in response to hypoxia, that affect the vascular endothelium in susceptible women. It can also occur up to 2 months after birth. Women with pre-existing hypertension, diabetes, or autoimmune disease are thought to be at greater risk of developing pre-eclampsia.

Renal

- Chronic kidney disease: a decrease in the glomerular filtration rate will stimulate the kidneys to up-regulate production of renin to raise the blood pressure and renal perfusion. Fluid overload will also contribute as the kidneys fail to excrete volumes required for homeostasis. Both of these mechanisms can lead to hypertension.
- Nephrotic syndrome: a syndrome of proteinuria, hypoalbuminaemia, and oedema is caused by damage to the filtering capability of the renal glomeruli. Hypertension in this setting is not common but can occur due to salt and water retention and fluid overload. ACE inhibitors are the first-choice agent for blood pressure control with nephrotic syndrome, as they may also reduce proteinuria.
- Glomerulonephritis: a condition characterised by inflammation of the glomeruli. Hypertension is a main feature of this syndrome, via mechanisms similar to those in chronic renal failure.
- Obstructive uropathy: this can produce hydronephrosis, and the back-pressure on the kidneys can result in renal failure and raised blood pressure through similar mechanisms.
- Polycystic kidneys: hypertension is a common presenting symptom, and it is often apparent before renal function abnormalities. Hypertension with polycystic kidney disease can present at a young age (20 to 34 years) and is associated with a high incidence of left ventricular hypertrophy.

Endocrine

- Phaeochromocytoma: this is a neuroendocrine tumour of the adrenal glands, and hypertension results from excessive secretion of epinephrine (adrenaline) and norepinephrine (noradrenaline). It can also occur as part of a

multiple endocrine neoplasia syndrome. Patients may present with malignant hypertension or hypertension that is resistant to usual pharmacological therapy.[14]

- Hyperaldosteronism: excess production of aldosterone by the adrenal glands results in sodium and water retention and potassium excretion. The excess production is usually due to a solitary adrenal adenoma (Conn's syndrome), but hyperaldosteronism and consequent hypertension can also be the result of adrenal hyperplasia.
- Cushing's syndrome: excess production of cortisol by a pituitary or adrenal tumour, or the use of exogenous corticosteroids, can result in Cushing's syndrome. It can be ACTH-dependent or -independent. Hypertension results as cortisol enhances the vasoconstrictor effect of catecholamines.
- Hyperthyroidism: excess thyroxine exacerbates the effect of the sympathetic nervous system. It thereby increases vascular resistance and cardiac output. This can lead to an isolated systolic hypertension. Hypertension should respond to treatment of the underlying cause.
- Hypothyroidism: low levels of circulating thyroid hormone can also result in mild hypertension as the heart rate is slowed and there is an increase in peripheral vascular resistance to compensate. Hypothyroidism can also cause elevation of cholesterol and lipid levels in the blood, thus increasing overall cardiovascular risk if left untreated.
- Hyperparathyroidism: hypertension is often noted in patients with hyperparathyroidism, but a causative relationship has not been confirmed and the mechanism of action is unclear.

Sleep disorders

- Patients with obstructive sleep apnoea are often obese, and the risk for hypertension, MI, and stroke is elevated. The mechanism is unclear but may involve oxidative stress secondary to hypoxia and sympathetic autonomic activation. Such patients often have a number of cardiovascular risk factors that need addressing alongside treatment of their hypertension and sleep apnoea.

Toxic causes

- Chronic alcohol excess: the relationship between alcohol, hypertension, and overall cardiovascular risk is complex and a J-shaped relationship has been suggested, with those who drink a small amount of alcohol having a lower risk than those who abstain completely. However, in various studies, alcoholic people who abstain from alcohol have demonstrated a marked decrease in blood pressure readings after an initial increase during the withdrawal phase. The mechanisms are unclear.[15]
- Medications: use of oral contraceptives and long-term use of NSAIDs have both been implicated in the development of hypertension. The effect of the oral contraceptive pill is thought to be due to the effects of progesterone on small blood vessels. NSAIDs may cause hypertension in susceptible people through effects on the kidney and fluid retention. Hypertension will usually respond to discontinuation of the drugs.
- Illicit drug use such as cocaine and amfetamine abuse can also lead to hypertension due to sympathetic activation. Users of these drugs may also have a compliance issue with antihypertensives that can lead to a persistent high blood pressure even after being initiated on therapy.

Pseudo-hypertension

- 'White-coat hypertension' is an apparent elevation of blood pressure when readings are taken in a clinical environment. The patient may have their own blood pressure monitor at home and report normal readings. This apparent elevation is usually ascribed to anxiety or stress at having their blood pressure measured. It may subside with repeat measurements over time, or persist in the clinical environment. One way to distinguish true hypertension from falsely elevated readings is to record blood pressure over a 24-hour period or arrange measurements at home. This will avoid unnecessary treatment, although overall cardiovascular risk must still be evaluated.

Urgent considerations

(See **Differential diagnosis** for more details)
Severe elevations in blood pressure are classified as either urgencies or emergencies.[16] In hypertensive urgencies, there is no evidence of acute end organ damage, while in hypertensive emergencies there is an immediate threat to the cardiovascular system and the patient. True hypertensive emergencies include hypertensive encephalopathy, hypertensive left ventricular failure, and acute aortic dissection. The management of these conditions includes immediate treatment in an intensive care setting with controlled gradual reduction in blood pressure. Initial laboratory tests should include a full blood profile and urine analysis to search for an underlying cause. Tests such as cardiac enzymes, TFTs, urinary catecholamines, and vanillylmandelic acid may also be required. Elevations in urea and creatinine, raised sodium and phosphate levels, high or low potassium levels (particularly in hyperaldosteronism, as a result of renal potassium wasting), and acidosis are some of the common findings.

Imaging studies such as a chest x-ray and renal ultrasound scan can also help to rule out underlying aetiology. Computerised tomography of the head to assess for intracranial haemorrhage or infarction or space-occupying lesions may also be indicated. A 12-lead ECG is useful to assess for cardiac ischaemia or infarct, presence of left ventricular hypertrophy, and evidence of electrolyte disturbance or effects of drug overdose. If left untreated, these conditions are associated with a high mortality and morbidity. Fortunately, with the widespread use of antihypertensive agents, they are less commonly seen overall.[16] [17] [18]

Hypertensive emergencies

Hypertensive encephalopathy

- This is a symptom complex of severe hypertension with headache, vomiting, visual disturbance, mental status changes, seizure, and papilloedema. Cardiac symptoms such as angina, myocardial infarction, and pulmonary oedema may occasionally be the main presenting symptoms.

Hypertensive left ventricular failure

- Symptoms are those of decompensated cardiac failure with shortness of breath, pulmonary oedema, lethargy, paroxysmal nocturnal dyspnoea, and orthopnoea. A cough productive of frothy pink sputum may be reported. Left heart failure can lead to bi-ventricular failure, and there may be signs of peripheral oedema and hepatomegaly. An echocardiogram will usually be indicated, and imaging of the coronary arteries may be helpful as reversible cardiac ischaemia may improve symptoms and prognosis.

Acute aortic dissection

- Typically presents with acute, severe chest pain with 'ripping' or 'tearing' characteristics. It may radiate to the back or jaw. Syncope, altered cognition, and anxiety are common neurological symptoms. A blood pressure difference of >20 mmHg is suggestive but not diagnostic of an acute aortic dissection. Treatment will depend on the portion of the aorta that is affected and may include surgical repair, endovascular stenting, or medical therapy alone. All patients require close monitoring and intensive treatment of blood pressure and pulse, usually in a high-dependency or intensive care unit with appropriate specialist input.

Malignant or accelerated hypertension

- Malignant hypertension is associated with potentially irreversible target organ damage that occurs over days or weeks, rather than minutes, and is therefore classified as an urgency. It is characterised by very high blood pressure in association with bi-lateral retinal changes, including exudates and haemorrhages, with or without papilloedema. The most common symptoms include headaches (often occipital), visual disturbances, chest pain, dyspnoea, and neurological deficits. Consequences include cerebral infarction or haemorrhage, transient blindness or paralyses, seizures, stupor, or coma. Malignant hypertension often has a renal cause, and proteinuria, microscopic haematuria, red blood cell, and hyaline casts in urine are typical.

Asymptomatic high blood pressure

- This is a common occurrence, where an asymptomatic patient (either known hypertensive on treatment or previously not known to have hypertension), is found to have very high readings in the 'accelerated hypertension' range. If there are any signs of retinal involvement, they should be managed as per the 'malignant hypertension' or the 'accelerated hypertension' guidelines. However, if there is no target organ involvement, they should be evaluated for the cause of the high blood pressure.
- If a patient is already on antihypertensive medications, care should be taken to check compliance or worsening renal function. If the increase in blood pressure has occurred over time, it could simply reflect the need to up-titrate drug dosage, as the current dosage may not be sufficient. A history of illicit drug use should also be sought, as this can cause a sudden increase in blood pressure. Screening for a secondary cause is also important.
- If the patient is drug-naive, then they should be managed as per a newly diagnosed hypertensive, with screening for secondary causes, end organ damage, and cardiovascular risk.

Red flags

- Coarctation of aorta
- Pre-eclampsia
- Phaeochromocytoma
- Illicit drug use

Step-by-step diagnostic approach

Hypertension is usually asymptomatic, but patients may present with headaches, nosebleeds, visual symptoms, or neurological symptoms. The main aims of history-taking are to identify symptoms suggestive of a secondary cause, to establish concomitant risk factors for cardiovascular disease, and to seek any symptoms suggestive of target organ damage.[2] [3] [4] Often there are no physical signs. However, a full examination (including height and weight) is recommended, to look for any signs of an underlying condition or target organ damage. An absence of symptoms or end organ damage with a history of normal blood pressure readings outside the clinical environment may occur with pseudo-hypertension.

Baseline screening tests are useful in all patients to look for complications of hypertension. Specific tests are only recommended if the clinical suspicion of an underlying secondary cause is high, as the majority of patients will have essential (primary) hypertension.

Blood pressure measurement

Before a diagnosis of hypertension can be confirmed, it is essential that the blood pressure is checked correctly.[2] [3] [4] The patient should sit quietly for at least 5 minutes with the arm exposed and supported at the level of the heart, and the back resting against a chair. Ideally they should not have consumed caffeine or smoked tobacco within 30 minutes before testing. If an automatic machine is used, it needs be correctly calibrated, and calibration should be checked at least every 6 months. The width of the cuff should be equal to 80% of the arm circumference and cover two-thirds of the length of the arm (a small bladder can cause falsely elevated readings). The bell of the stethoscope should be used, and two readings should be taken 5 minutes apart. The cuff should be inflated to at least 20 mmHg above the pressure at which the radial pulse disappears, and should be deflated at a rate of approximately 3 mmHg/second in order to accurately identify the point at which Korokoff sounds can first be heard. Diastolic blood pressure in adults is measured as the point at which Korokoff sounds disappear (Phase V). In children, the pressure at which sounds become muffled is preferable (Phase IV). Elevated readings should be confirmed by 3 sets of readings at weekly intervals.

It is recommended that ambulatory 24-hour blood pressure monitoring or regular home monitoring be first used to document true hypertension outside the clinic setting, before therapy is initiated.[4] [19] [20] [21] A meta-analysis comparing clinic- and home-based blood pressure measurements with ambulatory blood pressure monitoring in adults found that neither clinic- nor home-based measurements had sufficient sensitivity and specificity to be used as a single diagnostic test, and that doing so may lead to substantial over-diagnosis.[22]

Concomitant cardiovascular risk factors

Establishing concomitant cardiovascular risk factors is essential to define overall cardiovascular risk.

- Smoking: enquiries should include type of cigarette or tobacco, quantity, and duration of habit. Patients have a tendency to under-report, and non-smokers may be exposed to passive cigarette smoking in the home if a partner is a heavy smoker.
- Diabetes mellitus: this is a strong risk factor for cardiovascular disease. The target blood pressure for a diabetic hypertensive patient is 130/80 mmHg.
- Known ischaemic heart disease or previous myocardial infarction.
- Previous cerebrovascular accident or transient ischaemic attack.
- Elevation of cholesterol or triglycerides: patients may be unaware of such elevation if they have never been tested.

Identification of a secondary cause

Although in the majority of patients hypertension is primary/essential, there are certain features that may lead to a suspicion of an underlying cause (secondary hypertension):

- Young patient (<40 years)

- Rapid onset of hypertension
- Sudden change in blood pressure readings when previously well controlled on a particular therapy
- Resistant hypertension that is unresponsive to pharmacological therapies.

If a secondary cause is suspected, then the presence of specific symptoms may suggest a particular cause and guide further investigations:

- Flash pulmonary oedema or widespread atherosclerosis may indicate renal artery stenosis
- Poor feeding in children, or cold legs, may indicate poor distal perfusion secondary to aortic coarctation
- Swelling and hypertension in a pregnant patient should raise suspicion of pre-eclampsia
- Oedema and reports of foamy urine in a non-pregnant patient may represent nephrotic syndrome
- A history of renal impairment, prostatic enlargement, previous urethral instrumentation, or renal calculi is consistent with obstructive uropathy or chronic kidney disease
- A family history of polycystic kidney disease, intracranial aneurysms, or subarachnoid haemorrhage in a young patient with hypertension is strongly suggestive of polycystic kidney disease
- Endocrine causes may present with numerous non-specific symptoms, but phaeochromocytoma usually has episodic symptoms consistent with a hyper-adrenergic state, such as panic attacks, sweating, palpitations, and abdominal cramps
- Symptoms of low potassium, such as headaches, nocturia, and paraesthesiae, may indicate hyperaldosteronism, although the majority of patients with this condition are normokalaemic
- Typical symptoms of Cushing's syndrome are depression, weight gain, hirsutism, easy bruising, and low libido
- Heat intolerance, sweating, palpitations, and weight loss may indicate an excess of thyroxine, while lethargy, constipation, weight gain, and depression are common findings with low circulating thyroxine levels
- Symptoms of bone pain, paraesthesiae, and myalgia may suggest hyperparathyroidism
- Excessive daytime sleepiness in an obese patient, who may also complain of erectile dysfunction and restless sleep, may be a symptom of obstructive sleep apnoea. Partners are likely to give a history of loud snoring
- Symptoms of a toxic cause include consumption of the oral contraceptive pill or NSAIDs, or chronic alcohol excess. There may be accompanying social, economic, or legal issues due to alcohol excess.[23]

Physical findings suggestive of a secondary cause include the following:

- Renal bruits may be audible with renal artery stenosis
- Enlarged kidneys may be palpated in polycystic kidney disease. There may be accompanying hepatomegaly or a hernia
- Arteriovenous fistulae may be present in a patient with end-stage kidney disease
- Flank tenderness or prostatic enlargement on rectal examination may suggest a cause of obstructive uropathy
- Facial oedema or limb oedema in a pregnant patient warrants urinary collection for proteinuria as suggestive of pre-eclampsia.
- Oedema in a non-pregnant patient might be due to nephrotic syndrome.
- Radio-femoral delay and a disparity in blood pressure readings between the arms may be demonstrated with coarctation of the aorta, along with systolic or continuous cardiac murmurs. Distal pulses may be weak or impalpable

- Cushing's syndrome has well defined features, typically described as a moon face, thin arms and legs, truncal obesity, striae, and skin thinning
- Isolated eyelid oedema with dry skin and a thick tongue may suggest hypothyroidism, while exophthalmos, proptosis, and lid lag suggest hyperthyroidism due to Graves' disease
- The deposition of calcium just inside the iris, or palpation of jaw tumours, raises the possibility of hyperparathyroidism
- Obesity, maxillomandibular abnormalities, and macroglossia predispose to obstructive sleep apnoea, and there may be sweating in paediatric patients
- Chronic alcohol excess can result in a myriad of signs, such as jaundice, hepatomegaly, spider nevi, ascites, and general neglect of appearance.

Target organ damage

Cardiovascular disease

- Symptoms of cardiac failure include shortness of breath, ankle oedema, paroxysmal nocturnal dyspnoea, and orthopnoea. Angina may also be reported. Examination may reveal cardiac murmurs, thrills, or heaves.
- Left ventricular hypertrophy diagnosed either by echocardiography or by electrocardiogram is a well-documented target organ damage. It has prognostic utility in patients with hypertension.[24]

Cerebrovascular disease

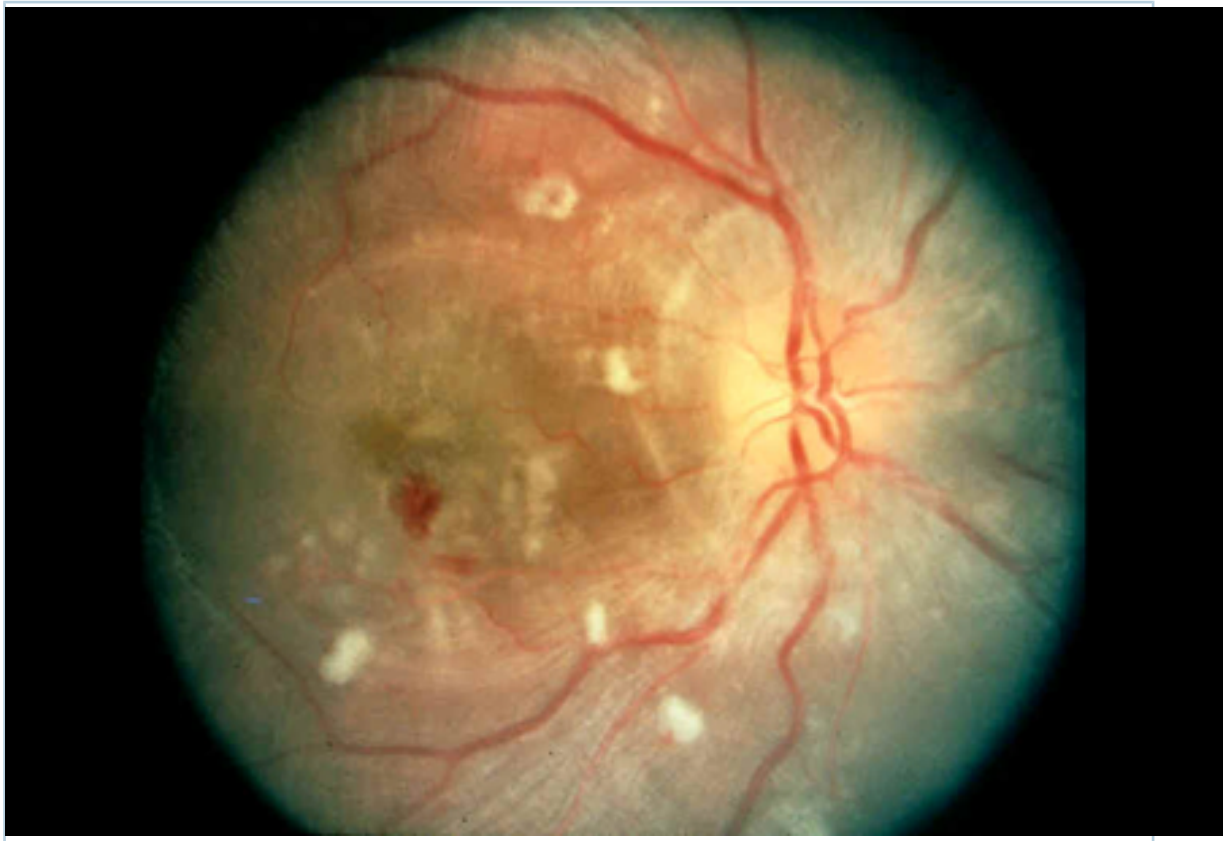
- Any history of symptoms suggestive of a TIA or CVA should be obtained. These may include speech difficulties, visual disturbance, or transient focal neurology.
- Carotid bruits may indicate carotid artery stenosis and warrant further duplex imaging to determine blood flow and degree of stenosis.
- There may be residual functional loss after a CVA.

Renal failure

- May be asymptomatic, but urinary symptoms such as decreased or increased frequency of urination, pruritus, lethargy, and weight loss may suggest renal damage.

Retinopathy

- This is often asymptomatic, but may present with visual loss or headaches.
- Hypertensive retinopathy on fundoscopy is characterised by:
    - arteriolar narrowing (graded 1 to 4 depending on the degree of narrowing);
    - arteriolar venous nipping (constriction of veins at crossing points);
    - 'cotton wool spots' on the retina (due to ischaemic changes);
    - flame haemorrhages or papilloedema.



Hypertensive retinopathy
From the collection of Sunil Nadar, MBBS, MRCP and Gregory Lip, MD, FRCP, FESC, FACC

Initial investigations

Baseline screening tests are useful in all patients to look for complications of hypertension.

- An ECG can be easily performed and is useful to seek signs of previous MI or left ventricular hypertrophy (a key prognostic factor). Echocardiography may be reserved for patients with clinical suspicion of cardiac failure or left ventricular hypertrophy.
- A chest x-ray is helpful to look for evidence of cardiomegaly, widening of the left subclavian border, and a double bulge at the site of the aortic knuckle. This may be seen in coarctation of the aorta, along with notching of the ribs due to large collateral circulation.
- Initial blood tests should include urea, electrolytes, and creatinine, with random blood sugar and serum cholesterol (as part of overall cardiovascular risk assessment). If diabetes is suspected, a fasting blood sugar test is required. Potassium levels may be low in hyperaldosteronism, but are usually normal.
- A urine dip test is performed to look for glycosuria and proteinuria, and the presence of casts may help to determine an underlying cause.

Subsequent investigations

Specific tests are only recommended if the clinical suspicion of an underlying secondary cause is high, as the majority of patients will have essential hypertension. Such tests include:

Blood tests

- Plasma renin and aldosterone levels if hyperaldosteronism suspected. Adrenal vein sampling to compare the ratio of renin to aldosterone in each kidney. A ratio >2 suggests an aldosterone-secreting tumour.[25] [26]
- Plasma renin activity is elevated in most patients with renal artery stenosis and is a good screening test.[27] A renal angiogram is the most specific and sensitive test.[28]
- Late-night salivary cortisol will be elevated in Cushing's disease, and this can be confirmed with the overnight dexamethasone suppression test.
- LFTs may be a useful screening tool if chronic alcohol excess and liver dysfunction are suspected.
- TFTs are useful screening tools if clinical history leads to suspicion of hyper- or hypothyroidism.
- Serum calcium levels can be measured if hyperparathyroidism is a possibility.

Urine tests

- 24-hour urine collection is useful for measuring catecholamines to exclude a phaeochromocytoma or to measure protein levels in suspected pre-eclampsia or nephrotic syndrome. However, in the case of pre-eclampsia and nephritic syndrome, a spot urine creatinine ratio can offer comparable results.

Imaging

- Ultrasound of kidneys and adrenal glands: a unilateral small kidney would be suspicious of chronic pyelonephritis or renal artery stenosis (causing renal atresia). Bilateral shrunken kidneys are consistent with chronic renal failure. Hydronephrosis may confirm an obstructive cause. This could be followed by a CT pyelogram if renal calculi are strongly suspected. Polycystic kidneys are easily visualised on abdominal ultrasound.
- CT of adrenals: this can be used to localise a phaeochromocytoma if urinary catecholamines are suggestive of the diagnosis. Alternatively, MRI can be offered.
- MRI: can be used to investigate renal artery stenosis if a renal angiogram is contra-indicated. It can identify and characterise an aortic coarctation, and be used to plan further treatment.[29] MRI is also useful for imaging the adrenals to localise a tumour in hyperaldosteronism or phaeochromocytoma.

Special tests

- Polysomnography is required for the diagnosis of obstructive sleep apnoea in patients with a consistent history, and a fibre-optic endoscopy is routinely performed in those patients in whom sleep apnoea is confirmed, as nasal polyps or tumours may be present.
- Renal biopsy: this is a definitive test to elicit the underlying cause of nephrotic syndrome in adults, but is rarely required in children.

Differential diagnosis overview

Common
Essential hypertension
Renal artery stenosis
Chronic kidney disease
Obstructive uropathy
Obstructive sleep apnoea
Uncommon
Coarctation of aorta
Pre-eclampsia
Glomerulonephritis
Nephrotic syndrome
Polycystic kidney disease
Phaeochromocytoma
Hyperaldosteronism
Cushing's disease/syndrome
Hyperthyroidism
Hypothyroidism
Hyperparathyroidism
Chronic alcohol excess
Medication
Illicit drug use
'White-coat hypertension'

Differential diagnosis

Common

◊ Essential hypertension

History	Exam	1st Test	Other tests
often asymptomatic; headaches, visual disturbance, nosebleeds, or neurological symptoms possible	may have signs of end organ damage; heave due to left ventricular hypertrophy, retinopathy, functional deficit following CVA; lack of signs to suggest a secondary cause	»**ECG:** normal, evidence of previous MI or left axis deviation with left ventricular hypertrophy »**urea/creatinine:** normal, or elevated with renal impairment »**serum cholesterol:** variable »**random blood glucose:** >8 mmol/L on non-fasting sample suggestive of comorbid diabetes and fasting blood sugar advised	

◊ Renal artery stenosis

History	Exam	1st Test	Other tests
often asymptomatic; headaches, visual disturbance, nosebleeds, or neurological symptoms possible; difficult-to-treat hypertension; peripheral vascular disease; may present with flash pulmonary oedema	bruit over the abdomen	»**plasma renin activity:** elevated	»**renal angiogram:** narrowing of renal artery »**renal MRI:** narrowing of renal artery

◊ Chronic kidney disease

History	Exam	1st Test	Other tests
known renal impairment; usually asymptomatic; may present with headaches, visual disturbances, neurological deficits (e.g., TIA or stroke), or nose bleeds, fatigue, nausea, anorexia; difficult-to-treat hypertension suggests possible renal cause[30]	features of chronic renal failure: oedema, arteriovenous fistulae, pale conjunctiva secondary to anaemia	»**urinalysis:** albuminuria, casts in the urine »**urea/creatinine:** elevated creatinine and urea »**renal ultrasound:** small kidneys	

Common

◊ Obstructive uropathy

History	Exam	1st Test	Other tests
variable depending on cause; may report previous urethral instrumentation, flank pain with nephrolithiasis, hesitancy, frequency, and poor stream with prostatic enlargement	variable; enlarged prostate on rectal examination, flank tenderness with renal calculi	»**renal ultrasound:** may show hydronephrosis or small kidneys with resultant chronic renal failure »**urea/creatinine:** elevated creatinine	»**non-contrast CT pyelogram:** demonstrates renal calculi if present

◊ Obstructive sleep apnoea

History	Exam	1st Test	Other tests
sleeping for long periods of time, loud snoring, excessive daytime sleepiness, restless sleep, erectile dysfunction, morning headaches, GORD, and weight gain	maxillomandibular abnormalities, sweating (paediatric patients), macroglossia	»**polysomnography:** respiratory disturbance index (RDI) or apnoea/hypopnoea index (AHI) 15 or more episodes/hour It may be a full night study or a split study. If a full night study is not carried out, the patient will need to return for continuous positive airway pressure (CPAP) titration. This determines CPAP pressures required, and ensures correct mask fit and patient tolerance. »**fibre-optic endoscopy:** may reveal nasal polyps or tumours	

Uncommon

◊ Coarctation of aorta

History	Exam	1st Test	Other tests
often asymptomatic; headaches, visual	disparity in the blood pressure readings between	»**ECG:** left ventricular hypertrophy »**echocardiogram:** left ventricular hypertrophy ± bicuspid aortic valve	»**MRI scan of aorta:** coarctation is clearly defined and used to plan further management

Uncommon

◊ Coarctation of aorta

History	Exam	1st Test	Other tests
disturbance, nosebleeds, or neurological symptoms possible; cold legs, sweating, poor feeding in children	both arms (left arm typically 20 mmHg lower than the right arm), radio-femoral delay, systolic or continuous murmurs over lateral chest wall, absence of pedal pulses	There is a 70% association between aortic coarctation and a bicuspid aortic valve. »**CXR:** widening of left subclavian border, double bulge above and below the usual site of the aortic knuckle, rib notching due to collaterals	

◊ Pre-eclampsia

History	Exam	1st Test	Other tests
pregnant woman, >20 weeks' gestation, usually >32 weeks' gestation, can be asymptomatic, may have facial or limb swelling, may have epigastric pain that radiates to the back	newly elevated BP >140/90 mmHg on 2 readings 6 hours apart, may have facial or limb pitting oedema	»**spot urine protein to creatinine ratio:** >30 »**24-hour urine collection:** >300 mg protein	

◊ Glomerulonephritis

History	Exam	1st Test	Other tests
nausea, malaise, weight loss, fever, features of underlying aetiology (e.g., arthralgia)	oedema with nephrotic features, hypervolaemia, signs of underlying aetiology; skin rash	»**urinalysis:** dysmorphic RBCs, sub-nephrotic proteinuria, and active sediment »**24-hour urine collection:** proteinuria is generally <3.5 g/day	»**renal biopsy:** characteristic findings on light and immunofluorescence microscopy

◊ Nephrotic syndrome

History	Exam	1st Test	Other tests
swelling of the legs, hands, face; foamy urine	hypoalbuminaemia, xanthelasma, oedema	»**spot urinary albumin to creatinine ratio:** >3.5 This corresponds to a 24-hour urine collection of 3.5 g of protein.[31]	»**renal biopsy:** variable Used in adults to establish underlying cause. Not routinely performed in children as minimal change disease is usually the cause.

Uncommon

◊ Nephrotic syndrome

History	Exam	1st Test	Other tests
		»**urinary microscopy:** cellular casts	

◊ Polycystic kidney disease

History	Exam	1st Test	Other tests
haematuria, headaches, abdominal pain, elevated BP often presenting feature in young patients (20 to 34 years); FHx of polycystic kidneys, or intracranial aneurysm, or subarachnoid haemorrhage	palpable kidneys; hepatomegaly, inguinal, incisional, and para-umbilical hernias are not uncommon	»**renal ultrasound:** 30 years of age: at least 2 unilateral or bilateral cysts; 30-59 years of age: 2 cysts in each kidney; >60 years of age: 4 cysts in each kidney. Large echogenic kidneys (without distinct macroscopic cysts) in a child at 50% risk for the disease are diagnostic »**urinalysis:** proteinuria, increased urinary albumin excretion, and haematuria are common Increased urinary albumin excretion indicates higher risk of progression to chronic kidney disease and correlates with a higher incidence of LVH.	

◊ Phaeochromocytoma

History	Exam	1st Test	Other tests
usually asymptomatic; may present with headaches, visual disturbances, neurological deficits (e.g., TIA or stroke), or nose bleeds; symptoms of the hyper-adrenergic state: palpitations, panic attacks, cold clammy skin, pallor, abdominal cramps[32]	no specific findings, features of target organ damage possible	»**urinary catecholamines, vanillylmandelic acid, and metanephrins:** levels twice the laboratory reference range are suggestive »**plasma metanephrins:** levels twice the laboratory reference range are suggestive Very sensitive, but less specific than urinary levels.[33]	»**CT or MRI of adrenals:** localisation of lesion if presence suggested by initial tests

Uncommon

◊ Hyperaldosteronism

History	Exam	1st Test	Other tests
usually asymptomatic (patients are typically normokalaemic); if serum potassium is low: headaches, tiredness, nocturia, paraesthesiae, muscle cramps, palpitations	no specific findings, features of target organ damage possible	»**plasma potassium:** normal; low, <3.0 mmol/L in 20% of patients Potassium can be falsely low with the use of diuretics.[25] »**plasma renin activity:** decreased The test has to be strictly standardised and done under specific conditions. Measurement should be done at 8 a.m. and the patient should have been strictly recumbent or upright for at least 2 hours. The blood must be transported rapidly at room temperature to the laboratory. If the samples are to be stored for batch testing, they should be rapidly centrifuged and frozen, to prevent degradation of the molecule.[34]	»**CT or MRI of adrenals:** localisation of adenoma/tumour »**adrenal vein sampling:** aldosterone to cortisol ratio >2 between sides suggestive of aldosterone-secreting tumour

◊ Cushing's disease/syndrome

History	Exam	1st Test	Other tests
psychiatric symptoms, weight gain, hirsutism, easy bruisability, decreased libido	supraclavicular fullness due to fat deposition, facial plethora, violaceous striae	»**late-night salivary cortisol:** elevated »**1 mg overnight dexamethasone suppression test:** >50 nanomol/L (1.8 microgram/dL) Patient given 1 mg at 11 p.m. and cortisol measured at 8 a.m. the next morning. Results affected by medications known to alter dexamethasone metabolism, such as phenytoin, carbamazepine, and rifampicin.	

Uncommon

◊ Cushing's disease/syndrome

History	Exam	1st Test	Other tests
		»**24-hour urinary free cortisol:** >50 micrograms/24 hours	

◊ Hyperthyroidism

History	Exam	1st Test	Other tests
heat intolerance, sweating, weight loss, palpitations, tremor	tachycardia, proptosis, exophthalmos, cardiac flow murmur	»**TSH:** suppressed Initial screening test. A lower-than-normal value suggests hyperthyroidism. Any level below 0.1 milli-international units/L may be associated with symptoms; however, clinically hyperthyroid patients will have undetectable levels 0.02 milli-international units/L or lower on highly sensitive assays. »**serum free T4:** elevated above normal range »**serum free or total T3:** elevated above normal range	

◊ Hypothyroidism

History	Exam	1st Test	Other tests
weight gain, lethargy, depression, constipation	dry skin, bradycardia, thick tongue, eyelid oedema	»**serum TSH:** elevated above normal range »**free serum T4:** below normal range	

◊ Hyperparathyroidism

History	Exam	1st Test	Other tests
fatigue, anxiety, depression, bone pain, paraesthesiae, myalgia	band keratopathy (deposition of calcium just inside the iris on eye	»**serum calcium:** elevated If high-normal and high suspicion, should be	

Uncommon

◊ Hyperparathyroidism

History	Exam	1st Test	Other tests
	examination), fibro-osseous jaw tumours on palpation (uncommon)	re-checked on separate day after fasting. Diagnosis only requires elevated serum calcium and intact serum PTH levels. Fasting and avoidance of venous stasis in blood draw will aid in accuracy. »**serum PTH levels:** normal or elevated	

◊ Chronic alcohol excess

History	Exam	1st Test	Other tests
CNS excitability on withdrawal of alcohol, dependency behaviour, tolerance; social, economic, or legal problems	jaundice, hepatomegaly, evidence of cirrhosis; spider nevi, ascites	»**diagnostic interview:** Structured Clinical Interview for DSM (SCID) can be administered by non-clinicians and can replace a psychiatric interview; at least 2 of the 11 DSM-5 criteria for alcohol-use disorder must be present »**GGT, ALT, and AST:** elevated	

◊ Medication

History	Exam	1st Test	Other tests
current use of oral contraceptive pill or chronic use of NSAIDs	no specific examination findings	»**trial discontinuation of medication:** elevated BP resolves If oral contraceptive pill is discontinued, alternative contraceptive options should be discussed.	

Uncommon

◊ Illicit drug use

History	Exam	1st Test	Other tests
hx of use of vasoactive illicit drug (e.g., cocaine, metamfetamine) and/or non-compliance with prescribed medications; nervousness, restlessness, tremors, anxiety, irritability; hostility and exaggerated strength; headache; abdominal pains; hallucinations, convulsions, delirium, unconsciousness, seizures	constricted or dilated pupils, cold extremities, tachycardia; nervousness, restlessness, tremors, anxiety, and irritability; rise in body temperature/hyperthermia; enhanced reflexes; irregular respiration	»**urinary toxicology:** positive for illicit drug (e.g., cocaine or methamfetamine) Usually available by contacting the local poisons unit. »**serum toxicology:** positive for illicit drug (e.g., cocaine or methamfetamine) Usually available by contacting the local poisons unit.	

◊ 'White-coat hypertension'

History	Exam	1st Test	Other tests
asymptomatic, elevated blood pressure readings in clinic but normal readings at home or outside hospital environment	no evidence of end organ damage as hypertension is not sustained outside clinical environment	»**24-hour blood pressure monitoring:** normal 'White-coat hypertension' is recognised as a rise in blood pressure when measured in the clinical environment while remaining normal at other times. Usually due to anxiety.	

DIAGNOSIS

Diagnostic guidelines

Europe

Hypertension in adults: diagnosis and management

Published by: National Institute for Health and Care Excellence
Last published: 2016
Summary: This clinical guideline updates and replaces the previous guideline of 2006. It offers evidence-based advice on the care and treatment of adults with primary hypertension, and provides new and updated recommendations on diagnosis, antihypertensive drug treatment, and treatment monitoring.

Europe

Guidelines for the management of arterial hypertension

Published by: European Society of Cardiology
Last published: 2013
Summary: This guideline provides a comprehensive overview of the management of this condition.

European Society of Hypertension Practice Guidelines for home blood pressure monitoring

Published by: European Society of Hypertension
Last published: 2010

North America

Hypertension Canada's 2016 education program guidelines for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension

Published by: Canadian Hypertension Education Program
Last published: 2016

2014 evidence-based guideline for the management of high blood pressure in adults

Published by: Eighth Joint National Committee (JNC 8)
Last published: 2014
Summary: Evidence-based recommendations regarding the management of high blood pressure. This guideline did not re-define high blood pressure, as the guideline panel thought that the 140/90 mmHg definition from the JNC 7 guideline remained reasonable.

Update: ambulatory blood pressure monitoring in children and adolescents

Published by: American Heart Association
Last published: 2014

VA/DOD clinical practice guideline for the diagnosis and management of hypertension in the primary care setting

Published by: Department of Veterans Affairs; Department of Defense
Last published: 2014

North America

Resistant hypertension: diagnosis, evaluation, and treatment

Published by: American Heart Association
Last published: 2008

Key articles

- Williams B, Poulter NR, Brown MJ, et al. Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004-BHS IV. J Hum Hypertens. 2004;18:139-185. Full text Abstract
- Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J. 2013;34:2159-2219. Full text Abstract
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Images

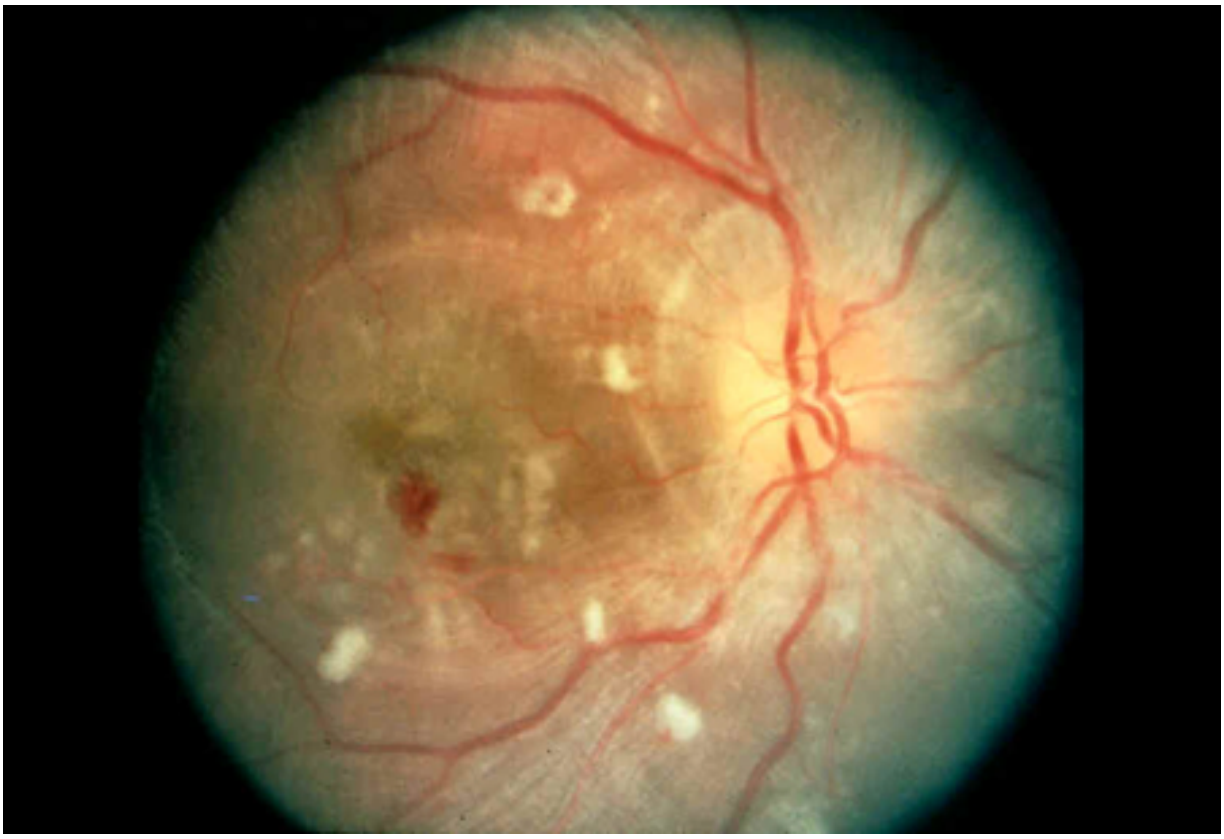

Figure 1: Hypertensive retinopathy

From the collection of Sunil Nadar, MBBS, MRCP and Gregory Lip, MD, FRCP, FESC, FACC

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Contributors:

// Authors:

Sunil Nadar, MBBS, MRCP

Consultant Cardiologist
Good Hope Hospital, Honorary Senior Lecturer , University of Birmingham, Birmingham, UK
DISCLOSURES: SN is an author of a number of references cited in this monograph.

Gregory Lip, MD, FRCP, FESC, FACC

Professor of Cardiovascular Medicine
University of Birmingham, Visiting Professor of Haemostasis, Thrombosis and Vascular Sciences, University of Aston, Birmingham, UK
DISCLOSURES: GL is a consultant for Bayer/Janssen, BMS/Pfizer, Biotronik, Medtronic, Boehringer Ingelheim, Microlife, and Daiichi-Sankyo; he is also a speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Microlife, Roche, and Daiichi-Sankyo. GL is an author of references cited in this topic.

// Peer Reviewers:

Rod Jackson, MD, PhD

Professor of Epidemiology
Head of the Section of Epidemiology & Biostatistics, School of Population Health, University of Auckland, Auckland, New Zealand
DISCLOSURES: RJ declares that he has no competing interests.

Alan Wilkinson, MD, FRCP

Professor of Medicine
David Geffen School of Medicine at UCLA, Los Angeles, CA
DISCLOSURES: AW declares that he has no competing interests. Unfortunately we have since been made aware that Professor Wilkinson is deceased.

Michael Schachter, MB, BSc, FRCP

Department of Clinical Pharmacology
St Mary's Hospital, Imperial College, London, UK
DISCLOSURES: MS declares that he has no competing interests.