

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

Module 3. Current practice of internal medicine.

Contents module № 1.

**Theme 1. Management of the patients
with hypertension**

Guidelines for students and interns

Модуль 3. Сучасна практика внутрішньої медицини.

Змістовний модуль №1.

**Тема 1. Ведення пацієнта
з артеріальною гіпертензією**

*Методичні вказівки
для студентів та лікарів-інтернів*

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1. Module title: «Current practice of internal medicine»

2. Theme title: « Management of patients with hypertension»

3. Theme aims

General Outcome

The students should be able to describe main links of pathogenesis, clinical features, diagnostic and treatment of arterial hypertension .

The aim of this topic is to provide the student with an opportunity to:

- provide a basic overview of the pathophysiology, diagnosis, and classification of hypertension;
- evaluate theories of pathogenesis of hypertension referring to renal & vascular physiology;
- appreciate the epidemiology of hypertension;
- discuss the roles of age, sex, lifestyle, type of diabetes and genetics in the development of hypertension.

Have an advanced understanding of the CV & renal outcomes of hypertension.

Apply risk assessment to select patients for active treatment to reduce progression of CV disease

Evaluate guideline-based management strategies for the treatment of hypertension.

Develop an individualized pharmacotherapy and monitoring plan for the management of hypertension

4. Specific Learning Outcomes:

Upon successful completion of this unit, the students should be able to:

1. Describe the classifications of hypertension.
2. Describe the main mechanism of etiopathogenesis.
3. Describe the main clinical features of hypertension.
4. List and describe the group of drugs that are used in the treatment of hypertension and give specific examples of each.
5. Make a treatment plan of patient with hypertension.
6. Assess the relevant differences between hydrochlorothiazide and chlorthalidone in the management of hypertension.
7. Distinguish within class differences among β -blockers and their ability to reduce CV and other clinical outcomes in patients with hypertension.
8. Apply special considerations and analyze clinical controversies surrounding the treatment of hypertension in the elderly.

5. Specification of the theoretical question for training of “Management of the patients with hypertension”

Student must know:

1. What is the definition of hypertension?
2. What are the main causes of hypertension?

3. What are the main pathogenetic links of hypertension?
4. What are the main types of hypertension?
5. What are the clinical features of hypertension?
6. What laboratory tests are used in patients with hypertension?
7. What imaging studies are used in patients with hypertension?
8. What treatment methods are used to decrease the blood pressure in patients hypertension?
9. What treatment methods are used in the treatment of hypertension in the elderly?
10. What treatment methods are used in the treatment of hypertension during the pregnancy?

Tests and assignments for self-assessment basic level of knowledge: multiple choice questions (choose the correct answer/statement)

For each clinical scenario below, give the most likely cause for the clinical findings. Each option may be used only once.

Question 1. A 30-year-old woman presenting with hypertension is found to have hypokalaemia and a mild metabolic alkalosis.

Question 2. An anxious 26-year-old woman presents with episodes of chest pain and palpitations precipitated by stress and smoking. Her 24-hour urine shows elevated catecholamines.

Question 3. A 45-year-old woman presents with weight gain, muscle weakness and hirsutism. On examination she is hypertensive and has pedal edema.

Question 4. A 40-year-old man is brought to A&E with severe headache. On examination he has papilloedema and fundal haemorrhages. His BP is 220/145 mmHg.

Question 5. Hypertension in a 75 year old who is a heavy smoker with widespread peripheral vascular disease.

A. Cushing's Syndrome

B. Systemic Sclerosis

C. Coarctation Of The Aorta

D. Conn's Syndrome

E. Pregnancy

F. Polycystic Kidneys

G. Malignant Hypertension

H. Hyperparathyroidism

I. Renal Artery Stenosis

J. Portal Hypertension

K. Pheochromocytoma

ANSWERS

1	2	3	4	5
D	K	A	G	I

Definition

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 percent of the adult population. 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.

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 140/90mmHg.

However, most people will have a blood pressure of < 140/90 mm Hg but may still experience hypertension-related disease. The risk to an individual may correlate with the severity of the hypertension. Panel 1 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 severity⁵ (*table 2*). Again, these are arbitrary figures that do not address the presence of co-morbidities such as diabetes, hypercholesterolemia and smoking, which might enhance the risk of cardiovascular disease for any given blood pressure reading.

Hypertension may be classified by etiology 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 percent of all cases of hypertension. Secondary hypertension, where a cause can be identified, accounts for less than 5 percent of cases (*table 3*).

Essential hypertension is now recognized 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 percent 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.

Epidemiology

Age. The prevalence of hypertension increases with age. The prevalence of hypertension to be 3.3 percent in those aged under 40 years, 27.9 percent in those aged 40-79 years and 49.9 percent 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 populations 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. The prevalence of hypertension in African Americans is 50 percent 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.

Sex Women are less likely than men to develop hypertension at an early age. The third national health and nutrition examination survey found the prevalence of hypertension to be 12 percent for white men and 5 percent 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 percent compared with 50 percent 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 percent increase in the incidence of hypertension per decade.

Etiology.

Pathophysiology. Arterial blood pressure is a product of cardiac output and total 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 counter balanced 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, vasodilatation 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 fibers 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 percent patients with isolated systolic hypertension have records of previous diastolic hypertension. 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." The association between salt intake and hypertension is more pronounced in the older population. There is a significant

Table1.1

Predicting risk

<p>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.</p>
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Risk Assessment

The risk for cardiovascular disease in patients with hypertension is determined not only by the level of blood pressure but also by the presence or absence of target organ damage or other risk factors such as smoking, dyslipidemia and diabetes, as shown in Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). These factors independently modify the risk for subsequent cardiovascular disease, and their presence or absence is determined during the routine evaluation of patients with hypertension (i.e., history, physical examination, laboratory tests).

Cardiovascular Risk Factors/Target Organ Damage

Major Risk Factors

- Hypertension
- Age (older than 55 for men, 65 for women)*
- Diabetes mellitus**
- Elevated LDL cholesterol
- Low HDL cholesterol**
- Estimated glomerular filtration rate (GFR) less than 60 mL/min
- Microalbuminuria
- Family history of premature cardiovascular disease (men younger than 55 or women younger than 65)
 - Obesity** (body mass index greater than or equal to 30 kg/m², waist circumference greater than 40 inches for men and greater than 35 inches in women)

- Physical inactivity
- Tobacco usage, particularly cigarettes

Target Organ Damage

- Heart
- Left ventricular hypertrophy
- Angina/prior myocardial infarction
- Prior coronary revascularization
- Heart failure
- Brain
- Stroke or transient ischemic attack
- Dementia

Chronic kidney disease

Peripheral arterial disease

- Retinopathy

* *Increased risk begins at approximately 55 and 65 for men and women, respectively. Adult Treatment Panel III used earlier age cutpoints to suggest the need for earlier action.*

** *Components of the metabolic syndrome. Reduced HDL and elevated triglycerides are components of the metabolic syndrome. Abdominal obesity is also a component of metabolic syndrome.*

A point scale approach for estimating 10-year coronary heart disease risk can also be used (*fig. 1*).

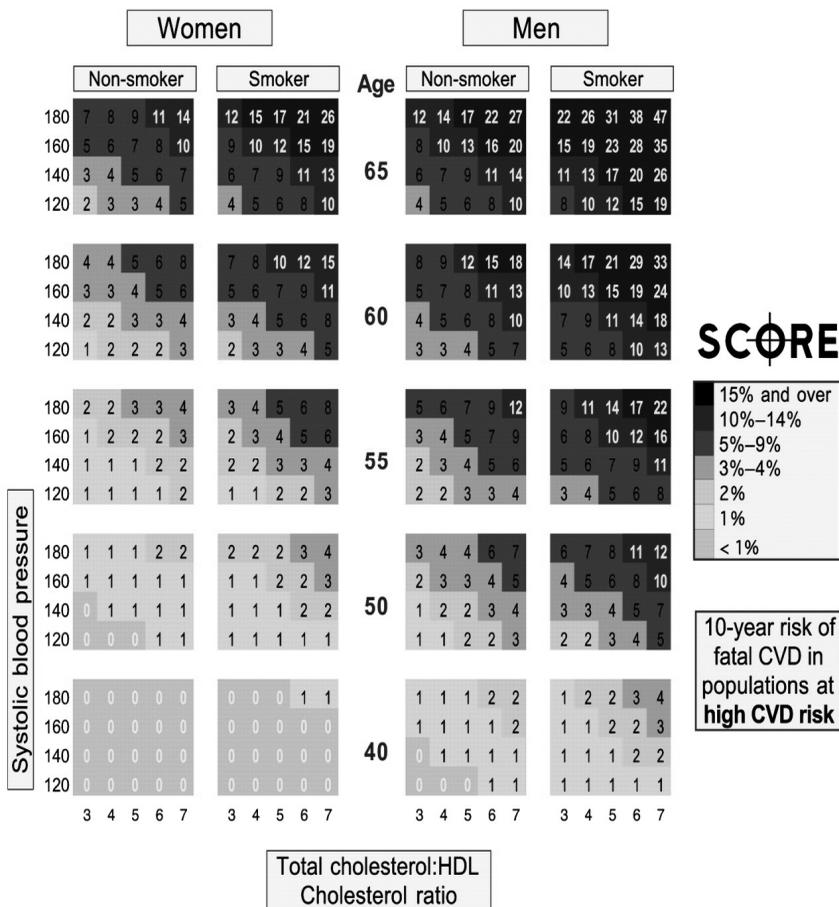


Fig 1. "Ten-Year Cardiovascular Disease Risk Calculator"
(Risk Assessment)

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.

Table 2

**High blood pressure is classified in stages,
as indicated in this table**

Classification	Sistolik (mmHg)	Diastolik (mmHg)
Normal	< 120	< 80
Prehypertension	120–139	80–89
Stage 1	140–159	90–99
Stage 2	160–179	100–109
Stage 3	≥ 180	≥ 110

Hypertensive nephrosclerosis (hardening of the blood vessels in the kidney) is 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 edema and microhemorrhages. 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.

Secondary hypertension

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

Renal (50 percent of cases)

■ Renal parenchyma disease:

- glomerular nephritis;
- polycystic disease.

■ Renovascular disease.

Endocrine (20 percent of cases).

■ Acromegaly.

Vascular

- Coarctation of the aorta.
- Vasculitis.

Other

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

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.

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 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 hemorrhages, macular edema, exudates and eventually papilledema. The severity of hypertensive retinopathy is divided into four grades with Grade IV being the most severe and associated with malignant hypertension.

Table 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 hematuria.
- Echocardiogram.

Additional investigations

- Chest X-ray.
- Echocardiogram.
- Carotid ultrasound.
- Quantitative proteinuria (if dipstick test positive).
- Ankle-brachial BP index.
- Fundoscopy.
- Glucose tolerance test (if fasting plasma glucose >5.6 mmol/L (100 mg/dL).

- Home and 24 hours ambulatory BP monitoring.
- Pulse wave velocity measurement (where available).

Extended evaluation (domain of the specialist)

- Further search for cerebral, cardiac, renal and vascular damage.

Mandatory in complicated hypertension.

- Search for secondary hypertension when suggested by history, physical examination or routine tests: measurement of renin, aldosterone, corticosteroids, catecholamines in plasma and/or urine; arteriographies; renal and adrenal ultrasound; computer-assisted tomography; magnetic resonance imaging.

Investigations

Unless a secondary cause of hypertension is suspected, routine investigations for essential hypertension are carried out, as listed in Table 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 hematuria can be seen in hypertensive renal disease but is not as good an indicator of the disease as the presence of proteinuria. Hematuria 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 ischemia, 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. If a secondary cause is suspected then further investigations may be warranted (*table 5*).

Lifestyle management. The mainstay of treatment of hypertension is pharmacological intervention. 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 percent 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.

Table 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

Diet. A reduction in salt intake of 100 mmol/day can reduce systolic blood pressure by 6 mmHg and diastolic pressure by 2mmHg." Some patients are particularly sensitive to salt reduction and can achieve systolic pressure reductions of over 10 mmHg. 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 3 mmHg. 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. Reassuringly, no adverse outcomes were seen with increased potassium and potassium chloride can be considered as a safe alternative to sodium chloride.

Table 6

Lifestyle modifications to prevent and manage hypertension*

Modification	Recommendation	Approximate Systolic BP Reduction (Range)**
Weight reduction	Maintain normal body weight (body mass index 18.5 to 24.9 kg/m ²)	5 to 20 mm Hg/10 kg
Adopt Dietary Approaches to Stop Hypertension (DASH) eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat.	8 to 14 mm Hg
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mmol per day (2.4 g sodium or 6 g sodium chloride).	2 to 6 mm Hg
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30-45 minutes per day, most days of the week)	4 to 8 mm Hg
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks (e.g., 24 oz. beer, 10 oz. wine, or 3 oz. 80 proof whiskey) per day in most men and to no more than one drink per day in women and lighter-weight persons.	2 to 4 mm Hg

**For overall cardiovascular risk reduction, stop smoking*

***The effects of implementing these modifications are dose- and time-dependent and could be greater for some individuals.*

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. 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 important 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.

PHARMACOLOGICAL MANAGEMENT

Target blood pressures The optimal systolic blood pressure (SBP) is <140mmHg and the optimal diastolic blood pressure (DPB) is <85mmHg. A target SBP of 130mmHg and DPB of <80mmHg should be considered for patients with established atherosclerotic cardiovascular disease, diabetes or chronic renal failure. Guidance on initiating pharmacological treatment is summarized in Table 7.

Table 7.

Target blood pressures for pharmacological treatment

Initial blood pressure	Complications*	Action
Systolic \geq 220mmHg or or diastolic \geq 160 mmHg	No	Treat immediately
Systolic 180-219mmHg or diastolic 110-119mmHg	No	Confirm over one to two weeks and treat if these readings are sustained
Systolic 160-179mmHg or diastolic 100-109mmHg	Yes	Confirm over three to four weeks and treat if these readings are sustained
Systolic 160-179mmHg or diastolic 100-109mmHg	No	Advise lifestyle changes initially reassess weekly and treat if these leadings are sustained on repeat measurements over four to 12 weeks
Systolic 140-159mmHg or diastolic 90-99mmHg	No	Confirm in within 12 weeks and treat if these 1 readings are sustained
Systolic 140-159mmHg or diastolic 90-99mmHg	Yes	Advise lifestyle changes and reassess monthly.Treat persistent mild hypertension if the 10-year cardiovascular disease risk is 20 percent

Regardless of the severity of hypertension, all patients should be offered lifestyle advice to reduce their blood pressure. This includes advice on smoking cessation, weight reduction, exercise, alcohol intake and diet.

Drug classes Commonly used classes of antihypertensive drugs are the thiazide diuretics (e.g., bendroflumethiazide), beta-blockers (e.g., propranolol, atenolol), angiotensin-converting enzyme inhibitors (e.g., captopril, enalapril), angiotensin II antagonists (e.g., candesartan, losartan), calcium channel blockers (e.g., amlodipine, nifedipine) and alpha-blockers (e.g., doxazosin).

Less commonly used drugs include vasodilator and centrally acting antihypertensives and, rarely, guanethidine, which is indicated for the treatment of hypertensive crisis.

Thiazide diuretics

Thiazide diuretics are moderately potent diuretics which lower blood pressure by inhibiting sodium reabsorption at the beginning of the distal convoluted tubule in the kidney, increasing sodium excretion and urine volume. Thiazides also have a direct vasodilatory effect on arterioles, sustaining the antihypertensive effect. They are well absorbed following oral administration, widely distributed and metabolized in the liver.

The diuretic effect of thiazides occurs within one to two hours of administration and continues for 12-24 hours, allowing once daily administration.

The antihypertensive effect occurs at low thiazide doses and there is no additional benefit to blood pressure from increasing the dose, although additional diuresis can occur at higher doses.

The effects of thiazides on the renal tubule depend on the extent of their excretion, so thiazides may be less effective in patients with renal impairment.

Side effects Increased urinary excretion with thiazide diuretics can lead to hypokalemia, hyponatraemia and hypomagnesaemia. Hypercalcaemia can occur due to reduced excretion of calcium. Interference with the excretion of uric acid can cause hyperuricaemia, so thiazides should be used with caution in patients with gout. Thiazide diuretics can also cause hyperglycaemia due to impaired glucose tolerance (insulin resistance) leading to an increased risk of non-insulin dependent diabetes mellitus.

Other less common side effects include hyperlipidaemia, causing increases in low density lipoprotein and triglycerides and a reduction in high density lipoprotein (HDL). Up to 25 percent of men treated with thiazide diuretics may experience impotence, which is usually reversible on withdrawal of treatment.

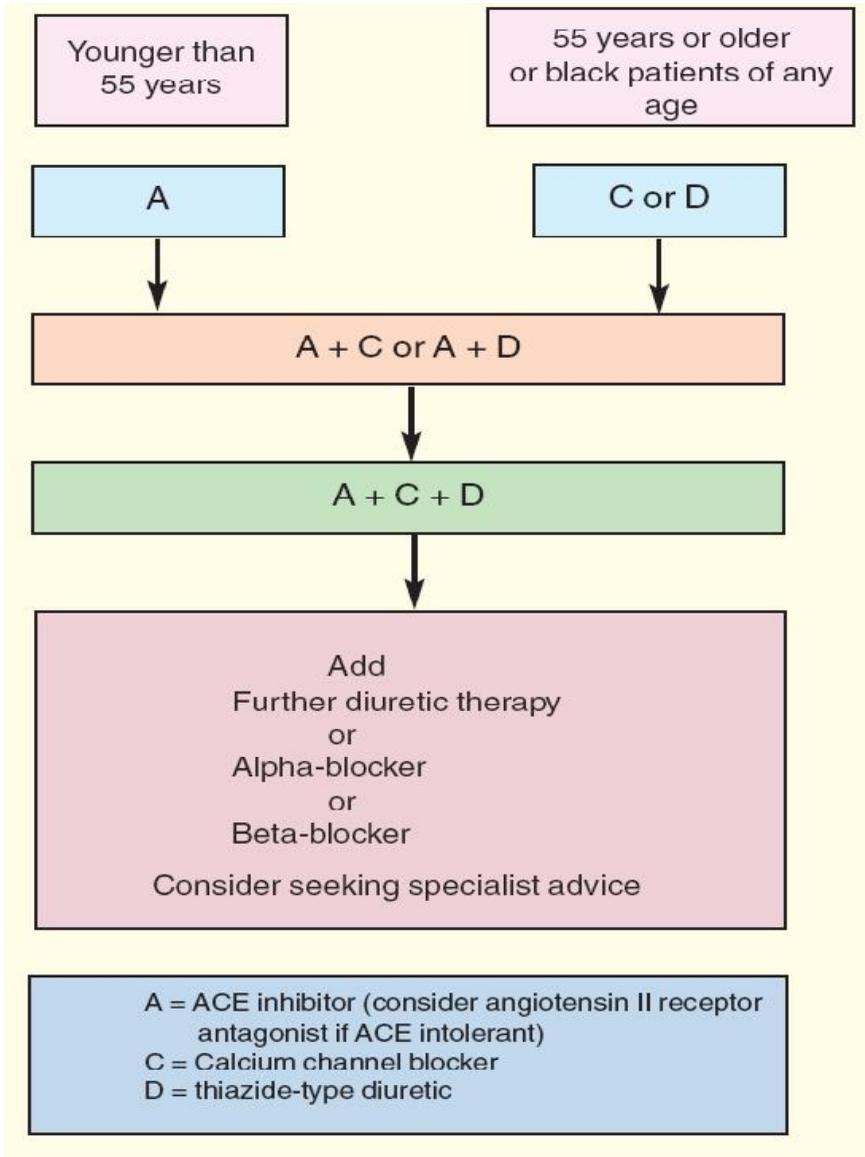


Fig. 2. Diagrammatic representation of the National Institute for Health and Clinical excellence guidelines for the treatment of hypertension

Beta-blockers

Beta-blockers block beta-adrenoreceptors in the body. These receptors are subclassified as beta-1 receptors or beta-2 receptors. Beta-1 receptors are mainly located in the heart and beta-2 receptors are mostly found in the lung, peripheral blood vessels, and skeletal muscle. However, beta-2 receptors can be found in the heart and beta-1 receptors can also be found in the kidney. Beta-receptors are also found in the brain.

Stimulation of beta-receptors in the brain and periphery promotes the release of neurotransmitters which increase sympathetic nervous system activity. Stimulation of beta-1 receptors in the sino-atrial node and the myocardium increases heart rate and force of contraction. Stimulation of beta-receptors in the kidney promotes renin release, increasing the activity of the renin-angiotensin-aldosterone system. The overall effect of stimulation of these receptors is increased cardiac output, increased peripheral vascular resistance and an increase in aldosterone-mediated sodium and water retention.

Treatment with beta-blockers antagonises all of these effects resulting in a reduction in blood pressure, although the principal anti hypertensive mechanism of this group of drugs is unclear.

Selective beta-blockers (commonly called cardioselective beta-blockers), for example bisoprolol, primarily act on beta-1 receptors. However they are not specific for beta-1 receptors so should be used with caution in patients with a history of asthma and bronchospasm. Non-selective beta-blockers (eg. propranolol) block both beta-1 and beta-2 receptors.

Beta-blockers with partial agonist activity (sometimes known as intrinsic sympathomimetic activity), e.g. acebutolol, act as a beta-stimulant when adrenergic activity is minimal (e.g. during sleep) but exert a beta-blocking effect when adrenergic activity is increased (e.g. during exercise). This has the benefit of reducing bradycardia during the day. Some beta-blockers, such as labetalol and carvedilol, also block the effects of peripheral alpha-adrenoreceptors. Others, such as celiprolol, exert beta-2 agonist or vasodilator activity.

Beta-blockers are excreted hepatically or renally depending on the water or lipid solubility of each drug. Those eliminated by the liver usually require multiple daily dosing while those excreted renally generally have longer half-lives and can be administered once daily. Beta-blockers should never be abruptly stopped but should be withdrawn gradually, especially in patients with angina, or rebound symptoms can occur.

Side effects Blockade of beta-2 receptors in the bronchi can precipitate bronchospasm, even when cardioselective beta-blockers are used. Other adverse effects of beta-blockers include bradycardia, impairment of myocardial contractility, and cold extremities caused by vasoconstriction from blockade of beta-2 receptors in the smooth muscle of peripheral blood vessels.

Awareness of hypoglycaemia in some patients with insulin-dependent diabetes mellitus can be reduced. This is because beta-blockers block sympathetic nervous system activity which is responsible for the warning signs of hypoglycaemia. Reduced sympathetic outflow may also account for the feelings of malaise experienced by some patients taking beta-blockers.

Vivid dreams and nightmares can occasionally occur, especially with lipid soluble beta-blockers such as propranolol. Impotence can also occur. The non-selective beta-blockers can cause an increase in serum triglyceride levels and a decrease in HDL.

Table 8

Antihypertensive treatment: preferred drugs

<i>Subclinical Organ Samage</i>	
LVH	ACEI, CA, ARB
Asymptomatic atherosclerosis	CA, ACEI
Microalbuminuria	ACEI, ARB
Renal dysfunction	ACEI, ARB
<i>Clinical Event</i>	
Previous stroke	Any BP lowering agent
Previous MI	BB, ACEI, ARB
Angina pectoris	BB, CA
Heart failure	Diuretics, BB, ACEI, ARB, antialdosterone agents
Atrial fibrillation	
Recurrent	ARB, ACEI
Permanent	BB, non-dihydropyridine CA
ESRD/proteinuria	ACEI, ARB, loop diuretics
Peripheral artery disease	CA
<i>Condition</i>	
ISH (elderly)	Diuretics, CA
Metabolic syndrome	ACEI, ARB, CA
Diabetes mellitus	ACEI, ARB
Pregnancy	CA, methyl dopa, BB
Blacks	Diuretics, CA

Abbreviations: LVH: left ventricular hypertrophy; ISH: isolated systolic hypertension; ESRD: renal failure; ACEI: ACE inhibitors; ARB: angiotensin receptor antagonists; CA: calcium antagonists; BB: beta-blockers

ACE inhibitors

Angiotensin-converting enzyme (ACE) inhibitors competitively inhibit the formation of angiotensin II from its inactive precursor angiotensin I, which is found in the blood, blood vessels, kidney, heart, adrenal gland and brain.

Angiotensin II is a potent vasoconstrictor which also promotes aldosterone release and central and peripheral sympathetic activity. Inhibiting its formation therefore reduces blood pressure. If the renin-angiotensin-aldosterone system is already activated (e.g. due to sodium depletion, or diuretic therapy), the antihypertensive effect of ACE inhibitors will be greater.

ACE is also responsible for the breakdown of kinins including bradykinin, which have a vasodilatory effect. Inhibition of this breakdown effect results in a more pronounced antihypertensive effect.

There are significant pharmacokinetic differences between the ACE inhibitors. Captopril is rapidly absorbed but has a short duration of action, so is useful for initial assessment of how a patient will respond to ACE inhibition. The first dose of an ACE inhibitor should be administered at night because a profound drop in blood pressure may occur; this effect is enhanced in patients with low sodium levels.

Angiotensin II antagonists.

Angiotensin II receptors are found in blood vessels and other targets. They are subclassified into AT₁ and AT₂ receptors. The AT₁ receptor mediates the pharmacological responses of angiotensin II, such as vasoconstriction and aldosterone release, and is therefore the target for drug treatment. The role of the AT₂ receptor is less well understood.

Many tissues contain enzyme pathways which are capable of converting angiotensin I into angiotensin II without using ACE. Therefore there may be advantages in blocking the renin-angiotensin system via the AT₁ receptor antagonist pathway with an angiotensin II receptor antagonist.

Angiotensin II receptor antagonists have many properties similar to those of ACE inhibitors, although they do not inhibit the breakdown of kinins. Because of the renal effects, ACE inhibitors and angiotensin II receptor antagonists are contraindicated in bilateral renal artery stenosis and in severe stenosis of the artery supplying a single functioning kidney.

Side effects of ACE inhibitors and angiotensin-II receptor antagonists

Before starting treatment with an ACE inhibitor or angiotensin II receptor antagonist a patient's renal function and electrolyte levels should be checked. This monitoring should continue during treatment because both classes of drug can occasionally impair renal function.

Both ACE inhibitors and angiotensin II receptor antagonists cause hyperkalemia due to reduced aldosterone production, so potassium supplements and potassium sparing diuretics should be avoided in these patients.

One difference between the two classes is that a dry cough is a common side effect of ACE inhibitors, exhibited in up to 15 per cent of patients.

Angiotensin II receptor antagonists are not associated with the cough because they do not interfere with the inhibition of bradykinin breakdown.

Calcium channel blockers.

Calcium channel blockers (less correctly called calcium channel antagonists) reduce calcium ion influx into myocardial cells, the cells within the specialized conducting system of the heart, and the cells of vascular smooth muscle. The effect of this is to reduce myocardial contractility, depress the formation and propagation of electrical impulses within the heart and promote vasodilator activity, interfering with the constriction of vascular smooth muscle. All of these are calcium ion-dependent processes.

There are three classes of calcium channel blockers: the dihydropyridines (eg. nifedipine and amlodipine); the phenylalkalamines (verapamil) and the benzothiazepines (diltiazem). The dihydropyridines have distinct peripheral vasodilator properties so are effective antihypertensives while verapamil and diltiazem have cardiac effects and are used to reduce heart rate and prevent angina.

All calcium channel blockers are metabolised by the liver.

Side effects Facial flushing, headache and swelling of the ankles are often seen, due to the vasodilatory effect of the dihydropyridine calcium channel blockers. Abdominal pain and nausea may also occur.

The gastrointestinal tract is also affected by the influx of calcium ions so calcium channel blockers often cause gastrointestinal disturbances, which may include constipation.

Table 9.

New NICE guidelines⁷ The most recent guidance from the National Institute for Health and Clinical Excellence on the treatment of hypertension is as follows

Step 1. In hypertensive patients aged 55 years or older or in black patients of any age, first choice therapy should be a calcium channel blocker or thiazide-type diuretic. In patients under 55 years, the first choice for initial therapy should be an angiotensin-converting enzyme (ACE) inhibitor (or an angiotensin II receptor antagonist if ACE inhibitors are not tolerated).

Step 2. If an additional drug is required adding an ACE inhibitor to a calcium channel blocker or a diuretic (or vice versa) is recommended.

Step 3. If treatment with three drugs is required then the combination of an ACE inhibitor (or angiotensin II receptor antagonist), calcium channel blocker and thiazide-type diuretic should be used.

Step 4. If a fourth drug is required then a higher dose of thiazide diuretic, should be considered, or an alternative diuretic, beta-blocker or alpha blocker.

All drug doses should be up-titrated as per the British National Formulary.

Alpha-blockers

Alpha-blockers (alpha-1 adrenoreceptors blocking agents) block peripheral alpha-1 adrenoreceptors, causing vasodilatory effects due to relaxation of vascular smooth muscle. They are indicated for resistant hypertension.

Side effects Alpha-blockers can cause postural hypotension, which is commonly seen after administration of the first dose. Alpha-blockers may be beneficial in older men because they may improve symptoms of prostate enlargement.

Other groups

Vasodilator antihypertensive drugs (eg, hydralazine, minoxidil) lower blood pressure by relaxation of vascular smooth muscle. Centrally acting antihypertensives (eg, clonidine, methyldopa, moxonidine) act on alpha-2 adrenoreceptors or related receptors in the brainstem, reducing sympathetic outflow to the heart, blood vessels and kidneys, leading to a reduction in blood pressure.

Side effects Vasodilator antihypertensives can cause fluid retention. Liver function tests should be monitored during treatment with hydralazine because it is hepatically cleared. Hydralazine has also been associated with systemic lupus erythematosus, Monoxidil has been associated with hypertrichosis (hirsutism) and so may be unsuitable for use in women.

Centrally acting agents are not specific or selective enough to avoid central nervous system side effects such as sedation, dry mouth and drowsiness, which commonly occur.

Methyldopa has a similar mechanism of action to clonidine but can cause immunological side effects, including pyrexia, hepatitis and hemolytic anemia.

Choice of therapy

An update of the National Institute for Health and Clinical Excellence guideline on hypertension was published 2007 year, together with the British Hypertension Society, as recently published clinical trials provided further evidence for the treatment of hypertension.

The main changes to the NICE guideline are that beta-blockers are no longer the recommended first line treatment for any patient group. Beta-blockers were found to be less effective at reducing major cardiovascular events, especially stroke, than other types of antihypertensives.

Atenolol was the beta-blocker used in most of the studies. When the trials which used atenolol were excluded from the review, the evidence base for the use of beta-blockers in the treatment of hypertension was much weaker than for the other drug classes. It was concluded that, in the absence of other compelling indications for a beta-blocker (e.g., angina), they should not be recommended as an initial treatment for hypertension.

Beta-blockers were also found to be less effective than ACE inhibitors or dihydropyridine calcium channel blockers in reducing the risk of diabetes, especially in patients already taking a thiazide diuretic. If a patient taking beta-blockers requires a second drug, an ACE inhibitor or calcium channel blocker should be added, rather than a thiazide.

Special considerations

Pregnancy Centrally acting agents have a poor CNS profile. However, methyldopa is used in pregnancy, due to its long-term safety data and beta-blockers are used in the third trimester. Intravenous labetalol is reserved for use in pregnancy in a hypertensive crisis. A controlled release formulation of nifedipine has also been used in pregnancy but is unlicensed.

Hypertension in pregnancy

- Hypertensive disorders in pregnancy, particularly pre-eclampsia, may adversely affect neonatal and maternal outcomes.

- Non-pharmacological management (including close supervision and restriction of activities) should be considered for pregnant women with Systolic BP (SBP) 140 to 149 mmHg or Diastolic BP (DBP) 90 to 95 mmHg. In the presence of gestational hypertension (with or without proteinuria) drug treatment is indicated at BP levels $\geq 140/90$ mmHg. SBP levels ≥ 170 or DBP ≥ 110 mmHg should be considered an emergency requiring hospitalization.

- In non-severe hypertension, oral methyldopa, labetalol, calcium antagonists and (less frequently) beta-blockers are drugs of choice.

- In pre-eclampsia with pulmonary oedema, nitroglycerine is the drug of choice. Diuretic therapy is inappropriate because plasma volume is reduced.

- As emergency, intravenous labetalol, oral methyldopa and oral nifedipine are indicated. Intravenous hydralazine is no longer the drug of choice because of an excess of perinatal adverse effects. Intravenous infusion of sodium nitroprusside is useful in hypertensive crises, but prolonged administration should be avoided.

- Calcium supplementation, fish oil and low dose aspirin are not recommended. However, low dose aspirin may be used prophylactically in women with a history of early onset pre-eclampsia.

Ethnic group. Thiazide diuretics and the dihydropyridine calcium channel blockers are more effective than beta-blockers in Afro-Caribbean patients. ACE inhibitors and angiotensin II antagonists have been shown to increase the risk of stroke in this group of patients and are therefore not recommended as first line therapy.

Table 10

Compelling and possible contraindications to use of antihypertensive drugs

	Compelling	Possible
Thiazide diuretics	Gout	Metabolic syndrome Glucose intolerance Pregnancy
Beta-blockers	Asthma Atrioventricular (A-V) block (grade 2 or 3)	Peripheral artery disease Metabolic syndrome Glucose intolerance Athletes and physically active patients Chronic obstructive pulmonary disease
Calcium antagonists (dihydropyridines)		Tachyarrhythmias Heart failure
Calcium antagonists (verapamil, diltiazem)	A-V block (grade 2 or 3) Heart failure	
Angiotensin-converting enzyme (ACE) inhibitors	Pregnancy Angioneurotic oedema Hyperkalaemia Bilateral renal artery stenosis	
Angiotensin receptor antagonists	Pregnancy Hyperkalaemia Bilateral renal artery stenosis	
Diuretics (antialdosterone)	Renal failure Hyperkalaemia	

Elderly The thiazide diuretics or dihydropyridine calcium channel blockers should be the first line therapy in elderly people. However, attention should be paid to renal function during treatment with a thiazide because the elderly are more at risk of renal impairment. Patients over 80 years old should be offered the same treatment as patients aged over 55 years.

- Randomized trials in patients with systolic-diastolic or isolated systolic hypertension aged ≥ 60 years have shown that a marked reduction in cardiovascular morbidity and mortality can be achieved with antihypertensive treatment.

- Drug treatment can be initiated with thiazide diuretics, calcium antagonists, angiotensin receptor antagonists, ACE inhibitors, and beta-blockers, in line with general guidelines. Trials specifically addressing treatment of isolated systolic hypertension have shown the benefit of thiazides and calcium antagonists but subanalysis of other trials also show efficacy of angiotensin receptor antagonists.

- Initial doses and subsequent dose titration should be more gradual because of a greater chance of undesirable effects, especially in very old and frail subjects.

- BP goal is the same as in younger patients (i.e. <140/90mmHg or below if tolerated). Many elderly patients need two or more drugs to control BP and reductions to <140mmHg systolic may be particularly difficult to obtain.

- Drug treatment should be tailored to the risk factors, target organ damage and associated cardiovascular and non-cardiovascular conditions that are frequent in the elderly. Because of the increased risk of postural hypotension, BP should always be measured also in the erect posture.

- In subjects aged 80 years and over, evidence for benefits of antihypertensive treatment is as yet inconclusive. However, there is no reason for interrupting a successful and well tolerated therapy when a patient reaches 80 years of age.

Diabetes Patients with diabetes may require a combination of antihypertensive drugs to achieve their optimal target blood pressure. ACE inhibitors are the initial treatment of choice because they can delay the progression of microalbuminuria to nephropathy. Patients with diabetic nephropathy should be treated with an ACE inhibitor or an angiotensin II receptor antagonist to minimise the risk of further renal deterioration, even if their blood pressure is normal.

Antihypertensive treatment in diabetics

- Where applicable, intense non-pharmacological measures should be encouraged in all diabetic patients, with particular attention to weight loss and reduction of salt intake in type 2 diabetes.

- Goal BP should be <130/80mmHg and antihypertensive drug treatment may be started already when BP is in the high normal range.

- To lower BP, all effective and well tolerated drugs can be used. A combination of two or more drugs is frequently needed.

- Available evidence indicates that lowering BP also exerts a protective effect on appearance and progression of renal damage. Some additional protection can be obtained by the use of a blocker of the renin-angiotensin system (either an angiotensin receptor antagonist or an ACE inhibitor).

- A blocker of the renin-angiotensin system should be a regular component of combination treatment and the one preferred when monotherapy is sufficient.

- Microalbuminuria should prompt the use of antihypertensive drug treatment also when initial BP is in the high normal range. Blockers of the renin-angiotensin system have a pronounced antiproteinuric effect and their use should be preferred.

- Treatment strategies should consider an intervention against all cardiovascular risk factors, including a statin.

- Because of the greater chance of postural hypotension, BP should also be measured in the erect posture.

Renal disease ACE inhibitors can reduce or abolish glomerular filtration and can cause severe and progressive renal failure. They are therefore contraindicated in patients with bilateral renal artery stenosis. However, ACE inhibitors are unlikely to have an adverse effect on overall renal function in patients with unilateral renal artery stenosis. A dihydropyridine calcium channel blocker can be added if further blood pressure lowering is required, but thiazide diuretics may be ineffective.

Antihypertensive therapy in patients with renal dysfunction

- Renal dysfunction and failure are associated with a very high risk of cardiovascular events.

- Protection against progression of renal dysfunction has two main requirements:

- Strict BP control (<130/80mmHg and even lower if proteinuria is >1 g/day)

- Lowering proteinuria to values as near to normal as possible

- To achieve the BP goal, combination therapy of several antihypertensive agents (including loop diuretics) is usually required.

- To reduce proteinuria, an angiotensin receptor blocker, an ACE inhibitor or a combination of both are required.

- There is controversial evidence as to whether blockade of the renin-angiotensin system has a specific beneficial role in preventing or retarding nephrosclerosis in non-diabetic non-proteinuric hypertensives, except perhaps in Afro-American individuals. However, inclusion of one of these agents in the combination therapy required by these patients appears well founded.

- An integrated therapeutic intervention (antihypertensive, statin and antiplatelet therapy) has to be frequently considered in patients with renal damage because, under these circumstances, cardiovascular risk is extremely high.

Systolic hypertension Isolated systolic hypertension (ISH) is defined as an SBP of greater than 160mmHg with a DBP less than 90mmHg. Patients with ISH should be offered the same treatment as patients with raised SBP and raised DBP, because ISH carries the same risk of complications.

The dihydropyridine calcium channel blockers have been used in the treatment of isolated systolic hypertension in the elderly, especially where a thiazide diuretic is contraindicated.

Accelerated hypertension. Accelerated or very severe hypertension, defined as a DBP of greater than 140 mmHg, requires urgent medical attention. Beta-blockers such as atenolol or labetalol or the dihydropyridine calcium channel blockers are indicated for this condition. DBP should be reduced to 100 – 110 mmHg during the first 24 hours. Blood pressure should be reduced further over the next two to three days using a combination of diuretics, vasodilators and ACE inhibitors, if required.

If intravenous treatment is required then sodium nitroprusside or glyceryl trinitrate is recommended.

Causes of resistant hypertension

- Poor adherence to therapeutic plan
- Failure to modify lifestyle including:
 - Weight gain

Heavy alcohol intake (NB: binge drinking)

• Continued intake of drugs that raise BP (liquorice, cocaine, glucocorticoids, non-steroid anti-inflammatory drugs, etc.)

- Obstructive sleep apnoea
- Unsuspected secondary cause
- Irreversible or scarcely reversible organ damage
- Volume overload due to:
 - Inadequate diuretic therapy
 - Progressive renal insufficiency
 - High sodium intake
 - Hyperaldosteronism

Causes of spurious resistant hypertension

- Isolated office (white-coat) hypertension
- Failure to use large cuff on large arm
- Pseudohypertension

Monotherapy versus combination therapy

• Regardless of the drug employed, monotherapy allows to achieve BP target in only a limited number of hypertensive patients.

• Use of more than one agent is necessary to achieve target BP in the majority of patients. A vast array of effective and well tolerated combinations is available.

• Initial treatment can make use of monotherapy or combination of two drugs at low doses with a subsequent increase in drug doses or number, if needed.

• Monotherapy could be the initial treatment for a mild BP elevation with a low or moderate total cardiovascular risk. A combination of two drugs at low doses should be preferred as first step treatment when initial BP is in the grade 2 or 3 range or total cardiovascular risk is high or very high.

- Fixed combinations of two drugs can simplify treatment schedule and favour compliance.

- In several patients BP control is not achieved by two drugs, and a combination of three or more drugs is required.

- In uncomplicated hypertensives and in the elderly, antihypertensive therapy should normally be initiated gradually. In higher risk hypertensives, goal BP should be achieved more promptly, which favours initial combination therapy and quicker adjustment of doses.

Antihypertensive treatment in patients with cerebrovascular disease

- In patients with a history of stroke or transient ischemic attacks, antihypertensive treatment markedly reduces the incidence of stroke recurrence and also lowers the associated high risk of cardiac events.

- Antihypertensive treatment is beneficial in hypertensive patients as well as in subjects with BP in the high normal range. BP goal should be <130/80 mmHg.

- Because evidence from trials suggests that the benefit largely depends on BP lowering **per se**, all available drugs and rational combinations can be used. Trial data have been mostly obtained with ACE inhibitors and angiotensin receptor antagonists, in association with or on the top of diuretic and conventional treatment, but more evidence is needed before their specific cerebrovascular protective properties are established.

- There is at present no evidence that BP lowering has a beneficial effect in acute stroke but more research is under way. Until more evidence is obtained antihypertensive treatment should start when post-stroke clinical conditions are stable, usually several days after the event. Additional research in this area is necessary because cognitive dysfunction is present in about 15% and dementia in 5% of subjects aged ≥ 65 years.

- In observational studies, cognitive decline and incidence of dementia have a positive relationship with BP values. There is some evidence that both can be somewhat delayed by antihypertensive treatment.

Antihypertensive treatment in patients with coronary heart disease and heart failure

- In patients surviving a myocardial infarction, early administration of beta-blockers, ACE inhibitors or angiotensin receptor antagonists reduces the incidence of recurrent myocardial infarction and death. These beneficial effects can be ascribed to the specific protective properties of these drugs but possibly also to the associated small BP reduction.

- Antihypertensive treatment is also beneficial in hypertensive patients with chronic coronary heart disease. The benefit can be obtained with different drugs and drug combinations (including calcium antagonists) and appears to be

related to the degree of BP reduction. A beneficial effect has been demonstrated also when initial BP is <140/90 mmHg and for achieved BP around 130/80 mmHg or less.

- A history of hypertension is common while a raised BP is relatively rare in patients with congestive heart failure. In these patients, treatment can make use of thiazide and loop diuretics, as well as of beta-blockers, ACE inhibitors, angiotensin receptor antagonists and antialdosterone drugs on top of diuretics. Calcium antagonists should be avoided unless needed to control BP or anginal symptoms.

- Diastolic heart failure is common in patients with a history of hypertension and has an adverse prognosis. There is at present no evidence on the superiority of specific antihypertensive drugs.

The metabolic syndrome

The metabolic syndrome is characterized by the variable combination of visceral obesity and alterations in glucose metabolism, lipid

- metabolism and BP. It has a high prevalence in the middle age and elderly population.

- Subjects with the metabolic syndrome also have a higher prevalence of microalbuminuria, left ventricular hypertrophy and arterial stiffness than those without the metabolic syndrome. Their cardiovascular risk is high and the chance of developing diabetes markedly increased.

- In patients with a metabolic syndrome diagnostic procedures should include a more in-depth assessment of subclinical organ damage. Measuring ambulatory and home BP is also desirable.

- In all individuals with metabolic syndrome, intense lifestyle measures should be adopted. When there is hypertension drug treatment should start with a drug unlikely to facilitate onset to diabetes. Therefore a blocker of the renin-angiotensin system should be used followed, if needed, by the addition of a calcium antagonist or a low-dose thiazide diuretic. It appears desirable to bring BP to the normal range.

- Lack of evidence from specific clinical trials prevents firm recommendations on use of antihypertensive drugs in all metabolic syndrome subjects with a high normal BP. There is some evidence that blocking the renin-angiotensin system may also delay incident hypertension.

- Statins and antidiabetic drugs should be given in the presence of dyslipidemia and diabetes, respectively. Insulin sensitizers have been shown to markedly reduce new onset diabetes, but their advantages and disadvantages in the presence of impaired fasting glucose or glucose intolerance as a metabolic syndrome component remain to be demonstrated

Treatment of associated risk factors

Lipid-lowering agents

- All hypertensive patients with established cardiovascular disease or with type 2 diabetes should be considered for statin therapy aiming at serum total and LDL cholesterol levels of, respectively, < 4.5 mmol/l (175 mg/dl) and < 2.5 mmol/l (100 mg/dl), and lower, if possible.

- Hypertensive patients without overt cardiovascular disease but with high cardiovascular risk ($\geq 20\%$ risk of events in 10 years) should also be considered for statin treatment even if their baseline total and LDL serum cholesterol levels are not elevated.

Antiplatelet therapy

- Antiplatelet therapy, in particular low-dose aspirin, should be prescribed to hypertensive patients with previous cardiovascular events, provided that there is no excessive risk of bleeding.

Low-dose aspirin should also be considered in hypertensive patients without a history of cardiovascular disease if older than 50 years, with

- a moderate increase in serum creatinine or with a high cardiovascular risk. In all these conditions, the benefit-to-risk ratio of this intervention (reduction in myocardial infarction greater than the risk of bleeding) has been proven favourable.

- To minimize the risk of haemorrhagic stroke, antiplatelet treatment should be started after achievement of BP control.

Glycaemic control

- Effective glycaemic control is of great importance in patients with hypertension and diabetes.

- In these patients dietary and drug treatment of diabetes should aim at lowering plasma fasting glucose to values ≤ 6 mmol/l (108 mg/dl) and at a glycated haemoglobin of <6.5%.

10. Tests and assignments for self-assessment final level of knowledges.

CHOOSE THE SINGLE BEST ANSWER FOR EACH QUESTION

1. A 35-year-old man has hypertension, which has been difficult to control with medication. Periodically, he experiences periods when he develops intense symptoms including racing heart, lightheadedness, flushing, diaphoresis, clammy skin, headache, and a sense of impending doom. He has gone to the emergency department of a local hospital several times during these episodes, but by the time he is seen several hours later, the symptoms have long passed, and nothing can be found on physical examination or serum chemistry studies. The patient's physician orders a 24-hour urine to be collected, which is found to contain significantly elevated levels of vanillylmandelic acid. This compound is a degradation product of which of the following?

- A. *Acetylcholine.* C. *Epinephrine.* E. *Testosterone.*
B. *Cholesterol.* D. *Serotonin.*

2. A 41-year-old woman comes to the physician's office complaining of fatigue, muscle weakness, cramping, headaches, polydipsia, and polyuria. She has been treated for hypertension for 6 years, and her doctors have told her that she has renal problems. Beta-blockers, calcium channel blockers, and diuretics have been used to control her hypertension. There is a family history of renal disease and hypertension. Her blood pressure is 240/140 mm Hg and her pulse is 85/min. The remainder of her examination is normal. A routine chemical panel shows hypokalemia, hypernatremia, and metabolic alkalosis. Pathologic examination of this patient would most likely reveal which of the following findings?

- A. *Adrenal adenoma.* D. *Multiple adrenal adenomas.*
B. *Adrenal carcinoma.* E. *Unilateral nodular adrenal hyperplasia.*
C. *Bilateral nodular hyperplasia.*

3. A 34-year-old man undergoing a routine physical examination is found to have a blood pressure of 165/105 mm Hg. The measurement is repeated 40 minutes later, and is 162/103 mm Hg. The physician asks the patient to return the next week and the week following, and each time repeats the evaluation yielding the following results: 170/102, 168/107, 175/108, 167/102 mm Hg. This patient's blood pressure should be classified as which of the following?

- A. *Optimal.* D. *Stage 1 (mild) hypertension.*
B. *Normal.* E. *Stage 2 (moderate) hypertension.*
C. *High-normal.* F. *Stage 3 (severe) hypertension.*

4. Patients with hypertension would be most likely to have which of the following findings on renal biopsy?

- / A. Crescent formation.
- / B. Hyaline arteriosclerosis.
- / C. Kimmelstiel-Wilson nodules.

- / D. Papillary necrosis.
- / E. Subepithelial electron-dense humps.

5. A 19-year-old woman presents to her doctor's office for an annual physical examination. She has been previously healthy and is currently doing well without complaints. She is a non-smoker and has no significant past medical history or family history. Her temperature is 36.9 C (98.5 F), blood pressure is 160/90 mm Hg (confirmed in all extremities), pulse is 84/min, and respirations are 16/min. Her pulses are symmetric and equal, her cardiac and pulmonary examinations are unremarkable, and there is an abdominal bruit with a systolic and diastolic component.

Serum chemistry reveals:

Sodium	145 mEq/L
Potassium	3.1 mEq/L
Chloride	102 mEq/L
Bicarbonate	28 mEq/L
Blood urea nitrogen	14 mg/dL
Creatinine	1.0 mg/dL
Glucose	80 mg/dL

Which of the following is the most likely cause of her elevated blood pressure?

- / A. Coarctation of the aorta.
- / B. Cushing syndrome.
- / C. Pheochromocytoma.
- / D. Renovascular hypertension.
- / E. Thyrotoxicosis.

ANSWERS

1	2	3	4	5
C	A	E	B	D



INDICATIVE READING LIST

1. Henry Richard Black, William J. Elliott// Hypertension: a companion to Braunwald's heart disease// Elsevier Health Sciences, 2007, 615 p.
2. G. Murphy Joseph Mayo Clinic Cardiology: Concise Textbook, 3rd ed. 2007
3. Ong K.L., Cheung B.M., Man Y.B., et al: Prevalence, awareness, treatment, and control of hypertension among United States adults 1999-2004. Hypertension. 2007, 49: (1): 69-75.
4. Sarafidis P.A., Li S, Chen S.C., et al: Hypertension awareness, treatment, and control in chronic kidney disease. Am J Med. 2008, 121: (4): 332-340.
5. Mancia G, De Backer G, Dominiczak A, et al: ESH-ESC Task Force on the Management of Arterial Hypertension: 2007 ESH-ESC Practice Guidelines for the Management of Arterial Hypertension. J Hypertens. 2007, 25: (9): 1751-1762.

Навчальне видання

**Модуль 3. Сучасна практика внутрішньої медицини.
Змістовний модуль №1.
Тема 1. Ведення пацієнта
з артеріальною гіпертензією**

*Методичні вказівки
для студентів та лікарів-інтернів*

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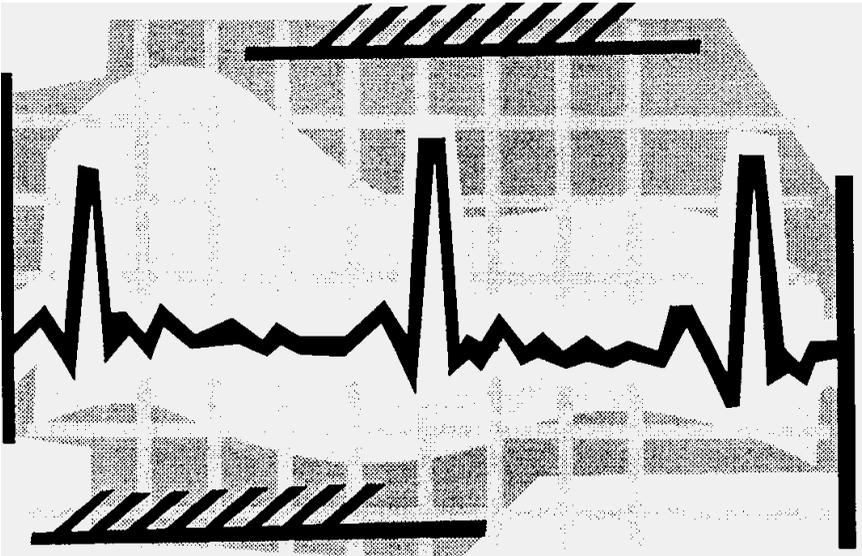
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Свідоцтво про внесення суб'єкта видавничої справи до Державного реєстру видавництв, виготовників і розповсюджувачів видавничої продукції серії ДК № 3242 від 18.07.2008 р.

**Module 3. Current practice of internal medicine.
Contents module № 1.**

**Theme 1. Management of the patients
with hypertension**

Guidelines for students and interns



**Модуль 3.
Сучасна практика внутрішньої медицини.
Змістовний модуль №1.
Тема 1. Ведення пацієнта
з артеріальною гіпертензією**

*Методичні вказівки
для студентів та лікарів-інтернів*