Hypertension (High Blood Pressure, HBP)—Classification and Clinical Signs

See online here

With a prevalence of approximately 50 %, arterial hypertension is a very common disease. Blood pressure is a risk factor of secondary diseases such as stroke, CHD and cardiac insufficiency. Social connections, as well as a relationship between hypertension, body weight, and age, are apparent. Many individuals with hypertension are not treated at all or receive insufficient therapy and, in many cases, are not aware they have the disease.

Definition of Hypertension

Hypertension relates to a blood pressure which is higher than the following limits:

- Systolic > 130 mm Hg
- Diastolic > 80 mm Hg

If the patients' blood pressure exceeds the levels above, they can benefit from blood pressure-lowering therapy.

Epidemiology of Hypertension

Widespread hypertension

Approximately a quarter of the world's population suffers from arterial hypertension, and about half of all the individuals afflicted are not aware of their condition.

In more than 50% of the patients who are aware of their hypertension, the disease is not

managed at all or only treated inadequately.

The prevalence of arterial hypertension increases with age and body weight. The disease affects men more frequently than women. Post-menopausal women, however, are generally affected as well.

Etiology of Hypertension

Based on the etiology of this disease, arterial hypertension is divided into primary and secondary hypertension.

Primary hypertension

The majority of individuals with hypertension (**> 90%**) suffer from primary hypertension, which is **idiopathic,** which means that the diagnosis is based on the principle of exclusion.

The **risk factors** associated with primary hypertension that usually occur in individuals over the age of 30 years include:

- Nutritional factors such as excess weight, alcohol consumption, and a diet high in sodium
- Stress factors
- Smoking
- Advanced age
- Lower social status

Secondary hypertension

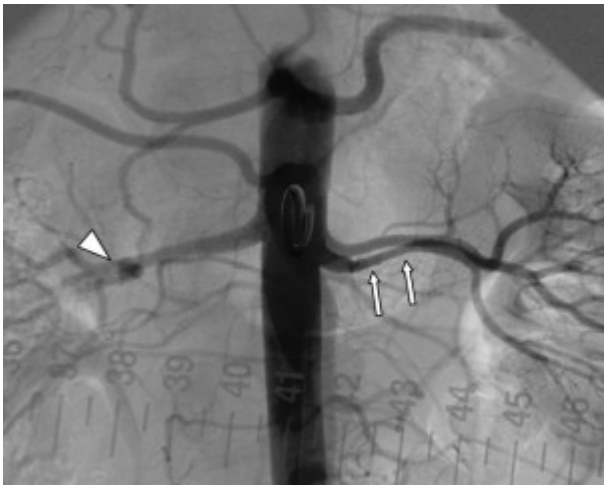


Image: 'Angiography of renal artery stenosis' by Zeina AR, Vladimir W, Barmeir E. License: CC BY 2.0

Secondary hypertension is triggered by other diseases, such as sleep apnea syndrome, aortic isthmus stenosis, and atherosclerosis. Neurogenic, psychogenic, and iatrogenic forms of the disease are also known. Iatrogenic factors include, among others, ovulation inhibitors and NSAR drugs. Exposure to drugs and toxins, such as excessive licorice consumption, may also induce secondary hypertension.

Other forms of secondary hypertension include renal hypertension caused by diseases of renal parenchyma or renal artery stenosis as well as **endocrine**

hypertension, i.e. in cases of primary and secondary hyperaldosteronism, pheochromocytoma, Cushing syndrome, or thyrotoxicosis.

Another type of arterial hypertension is the **hypertensive disease of pregnancy**. Among the risk factors for pregnancy-related hypertension include increasing maternal age and multi-fetal pregnancies.

Hypertensive disorders of pregnancy include a variety of diseases occurring in pregnancy, such as:

- Gestational hypertension (hypertension not associated with proteinuria)
- Pre-eclampsia (hypertension associated with proteinuria)
- Eclampsia (pre-eclampsia with at least one convulsion episode)

Classification of Hypertension

Hypertension is divided into several stages. An increase in blood pressure as a result of physical exertion does not count as hypertension.

Disproportional increase in blood pressure with little exertion is referred to as **unstable hypertension**.

Life-threatening form of arterial hypertension is accompanied by diastolic blood pressure above 120 mmHg that drops less than 10% overnight and is referred to as **malignant hypertension**.

The following table provides an overview of the different stages of hypertension according to the WHO classification:

Stage	Systolic pressure in mmHg	Diastolic Pressure in mmHg
Normal	< 120	< 80
Elevated	120–129	< 80
Stage 1 Hypertension	130–139	80–89
Stage 2 Hypertension	≥ 140	≥ 90

Pathophysiology of Hypertension

Development of hypertension

Arterial hypertension develops due to a **disturbance of the regulatory mechanism** that usually maintains blood pressure constant. The disturbances include **increased peripheral resistance, an increase in cardiac output,** or a combination of both.

During the progression of the disease, several compensatory mechanisms occur, consistently maintaining the blood pressure at an elevated level. In order to maintain cardiac output, cardiac hypertrophy occurs which helps to permanently withstand the increased pressure. The resistant vessels hypertrophy as well. The **baroreceptor reflex** that usually registers increased levels of blood pressure is shifted, allowing higher blood pressure values to be considered normal.

The kidneys play a role in this compensatory process as well. Even though renal blood flow and glomerular filtration rate are constant for the most part, an increase in sodium excretion **(pressure natriuresis)** accompanies the increase in blood pressure in order to counteract hypertension. The effects of renin release as well as the changes in renal

sodium reabsorption, for instance, on pressure natriuresis, are the topic of this discussion.

Clinical Signs of Hypertension

Symptoms of hypertension

Symptoms of arterial hypertension frequently manifest themselves rather late.

Typical symptoms include:

- Early morning headache
- Sleep disorders, dizziness
- Nosebleeds
- Ringing in the ears
- Non-specific cardiac symptoms
- Palpitations

In cases of secondary hypertension, symptoms of the individual underlying disease accompany those of hypertension.

Progression and Special Forms of Hypertension

Special forms of arterial hypertension include isolated office hypertension and isolated ambulatory hypertension.

Isolated office hypertension

Isolated office hypertension, also referred to as '**white-coat hypertension'**, is characterized by readings ≥ 130/80 mm Hg in the physician's office, while measurements obtained at home and during blood pressure monitoring are normal.

Isolated ambulatory hypertension

Isolated ambulatory hypertension is also referred to as **masked hypertension**. In these cases, blood pressure readings at the office are normal; however, readings at home or during blood pressure monitoring are elevated ≥ 130/80 mm Hg. Isolated ambulatory hypertension is linked to factors such as male gender, younger patients as well as smoking, alcohol consumption, and stress. Isolated ambulatory hypertension involving individuals already undergoing treatment for hypertension is referred to as **masked uncontrolled hypertension (MUCH)**.

Diagnosis of Hypertension

Medical history and physical examination

Gathering a patient's medical history is essential to determine possible symptoms and identify previous values of blood pressure measured as well as possible risk factors. It is also necessary to inquire about the patient's current and past medications, because the use of NSAR drugs, ovulation inhibitors, and corticosteroids, for instance, may contribute to elevated blood pressure. Previous illnesses must also be investigated along with the patient's family history.

The patient’s physical examination includes not only the measurement of blood pressure but also radial and femoral pulse recordings as well as abdominal auscultation, which may indicate renal artery stenosis.

Furthermore, it is essential to look for signs of cardiac insufficiency and renal failure. The fundus of the eye should be examined as well.

Measuring blood pressure

The focal point of diagnosing arterial hypertension is the non-invasive **measurement of blood pressure according to Riva Rocci,** who invented the cuff-based version of the mercury sphygmomanometer for blood pressure measurement. Elevated blood pressure must be established by taking at least three readings on two different days: The first readings are frequently 10% higher than subsequent readings.

In order to diagnose forms of white-coat hypertension—or to rule this form out—and to establish permanently elevated blood pressure, **ambulatory blood pressure monitoring** (ABPM) over a period of 24 hours is appropriate. The average daytime measurement should be below 135/85 mm Hg and the average nighttime measurement below 120/70 mmHg. The average 24-hour reading should be below 130/80 mm Hg.

Laboratory diagnostics

Blood parameters including Hb and **HcT** may be used to evaluate anemia due to underlying renal disease. Renal function may be tested by measuring **creatinine** and **eGFR levels**. **Potassium levels** yield more information if Conn’s syndrome is suspected. Furthermore, other parameters such as **cholesterol, triglycerides**, and **glucose** indicate the risk for atherosclerosis.

In order to evaluate the presence of endocrine hypertension, parameters such as **T3**, **T4**, **TSH**, **aldosterone**, and **renin** may be measured.

Urinalysis is another test option because **microalbuminuria** may be an early indicator of renal damage, especially in diabetic patients. Determining glucose levels is necessary to rule out potential diabetes mellitus. **Nitrite levels** may reveal urinary tract infections, and **catecholamine levels** combined with severely high diastolic blood pressure (> 110 mm Hg) are indicators of pheochromocytoma.

Instrument-based diagnostics

Instrument-based diagnostics is primarily used to diagnose secondary hypertension. ECG screening can be used to rule out left ventricular damage or coronary heart disease. Chest x-rays may be used to determine the presence of any dilatation.

Echocardiography is used to determine the ventricular circumference and to exclude any abnormal or defective pump function of the heart. Carotid Doppler sonography, renal sonographies or color duplex sonographies of the renal arteries may also be an option in specific conditions.

Therapy of Hypertension

Non-pharmacological measures

Blood pressure-lowering therapy may begin with non-pharmacological measures unless a hypertensive crisis or emergency exists. Non-pharmacological therapy includes:

- Weight reduction until a BMI of approximately 25 kg/m² is achieved
- Diet low in sodium, with no more than 5–6 g NaCl per day
- Switch to a Mediterranean diet
- Lifestyle measures to reduce hypertension—abstinence or reduced smoking, alcohol, and coffee intake

Medications that may cause hypertension should no longer be used. In addition, **dynamic conditioning training** to include sports such as swimming, jogging, or bicycling should be pursued three to four times per week.

Aside from these general measures, diseases that may cause secondary hypertension must be treated. According to the European society of hypertension (ESH), the target blood pressure values in individuals under the age of 60 years (source: JNC 8) are **below 130/80 mm Hg;** in patients older than 60, the target values are below 150/90 mm Hg.

Pharmacological therapy

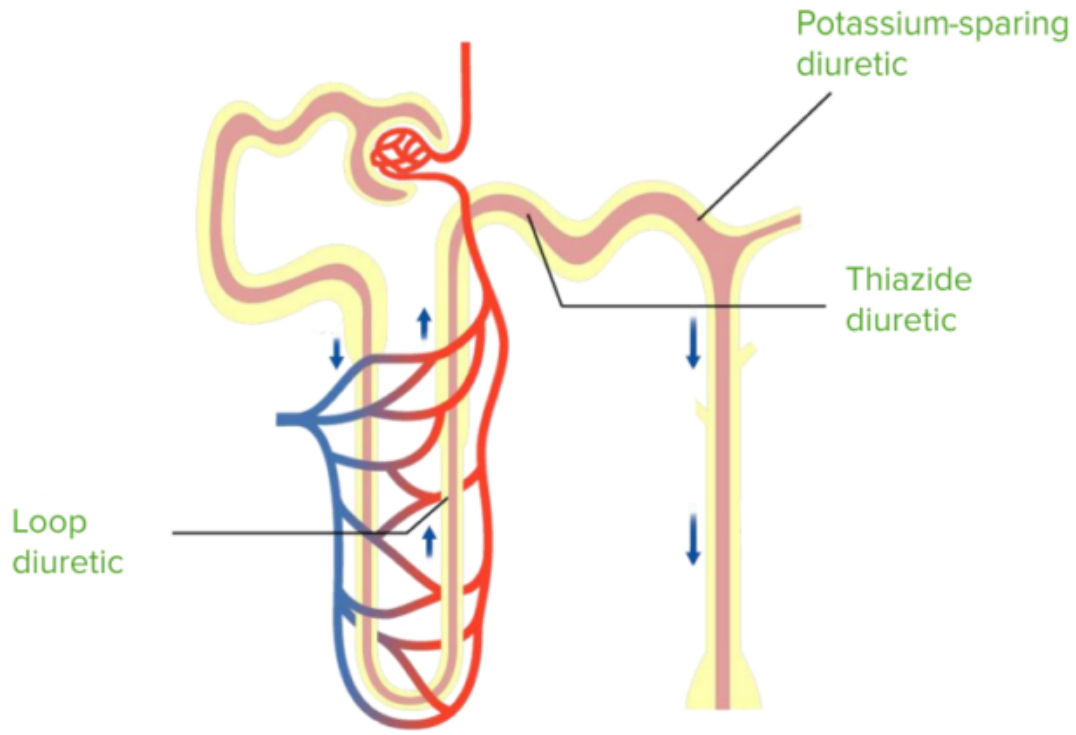
Pharmacological therapy may be started as monotherapy. However, if blood pressure values strongly deviate from normal values (> 140/80 mm Hg), or in cases of comorbidities, primary combination therapy should be initiated.

First-line medications include:

- Diuretics
- Beta-blockers
- ACE inhibitors
- AT1 receptor blockers
- Long-acting calcium channel blockers

Diuretics

Primary sites of action



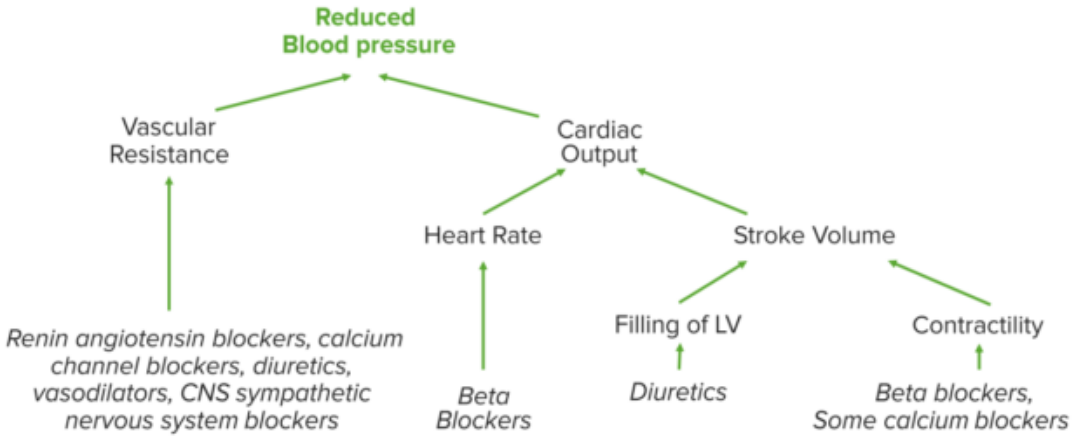
Thiazide Diuretics

- Excellent first-line therapy alone and in combination with other agents
- Generic and therefore inexpensive
- Shown to reduce cardiovascular events, for example, stroke, in patients with hypertension
- Chlorothiazide, Chlorthalidone, HCTZ, Indapamide, and Metolazone

Adverse effects (AEs) of thiazide diuretics

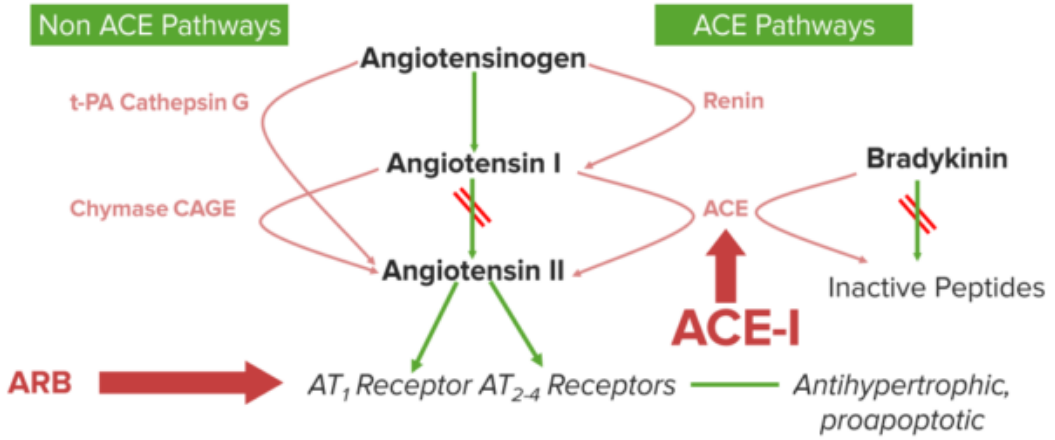
- Hypokalemia — low blood potassium level — particularly a problem with chlorthalidone (dose-related, may affect the clinical outcome)
- Glucose intolerance = diabetic tendency
- Gout
- Kidney damage

Antihypertensive drugs: hemodynamic mechanism of BP reduction



Renin-angiotensin-aldosterone system

The kidney is central to blood pressure control via the juxtaglomerular apparatus. Baroreceptors in the arterial system inform the central nervous system concerning the level of blood pressure. The signals transmitted by the baroreceptors alter the activity of the autonomic nervous system. Renin initiates a biochemical sequence that eventually converts angiotensinogen produced in the liver into angiotensin, a strong vasoconstrictor. Angiotensin stimulates the release of aldosterone from the adrenal gland, which causes renal retention of salt (NaCl) and water. Angiotensin stimulates the release of antidiuretic hormone from the pituitary gland, which leads to water retention by the kidney.

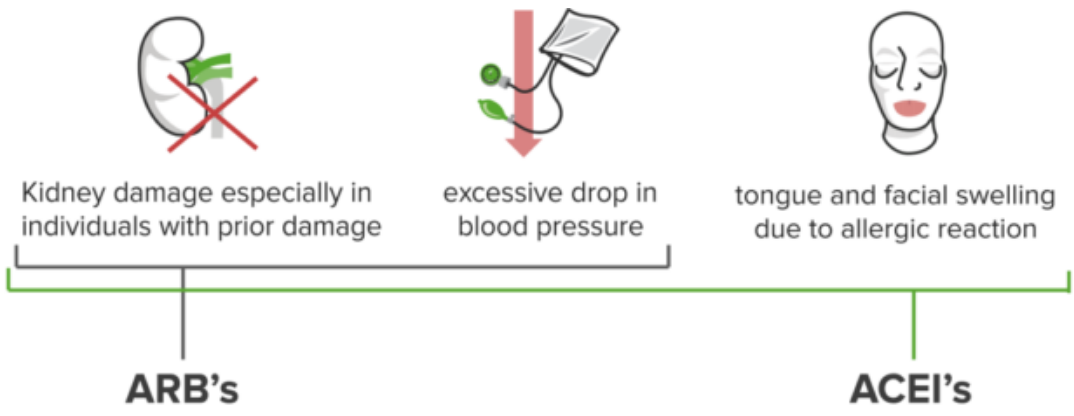


This system is part of the body's defense against dehydration and/or blood loss. The goal is to restore blood volume to normal as quickly as possible.

Angiotensin-converting enzyme blockers (ACEI) and angiotensin receptor blockers (ARB)

- Captopril—ACEI
- Enalapril—ACEI
- Lisinopril—ACEI
- Ramipril—ACEI
- Losartan—ARB
- Candesartan—ARB
- Valsartan—ARB

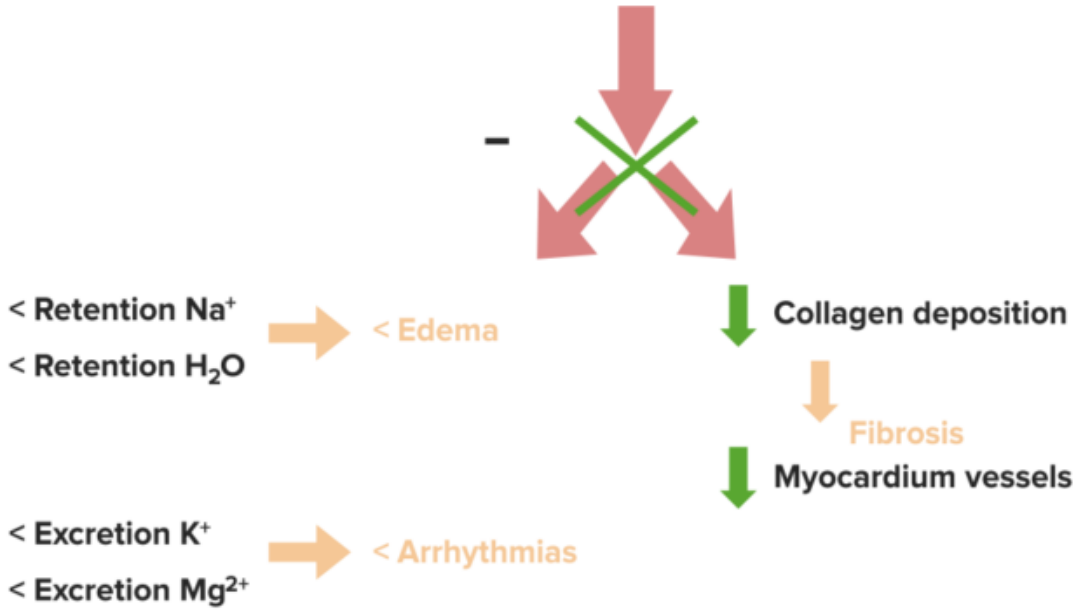
Adverse effects of ACEI and ARB — 1st line Rx



Aldosterone antagonists: mechanism of action

- Inhibition of aldosterone binding to receptors in kidneys, heart blood vessels, and brain
- Blockade of aldosterone in renal tubule → increased Na^+Cl^- and water excretion and potassium retention

Aldosterone inhibitors: spironolactone



Beta-blockers

Beta-blockers slow the heart rate and block the sympathetic nerve stimulation to the kidney (< renin release) and the peripheral nerves (< vascular resistance). They are second-line agents for hypertension.

- Propranolol
- Metoprolol
- Atenolol
- Carvedilol
- Bisoprolol
- Labetalol

Adverse events

Fluid retention worsening heart failure is more likely to occur during initiation and the first several months; later, the heart failure improves. Other adverse events are daily weight gains requiring careful adjustment of diuretics. Hypotension is more likely with carvedilol. The risk of bradycardia and heart block is 5—10% as the dose is increased. Fatigue and weakness may resolve with time or reduction in dose. Asthma may worsen or develop.

Calcium channel blockers

Calcium channel blockers are first-line medications in patients with abnormal kidney function. They dilate arterioles (resistance vessels) and thereby decrease vascular resistance.

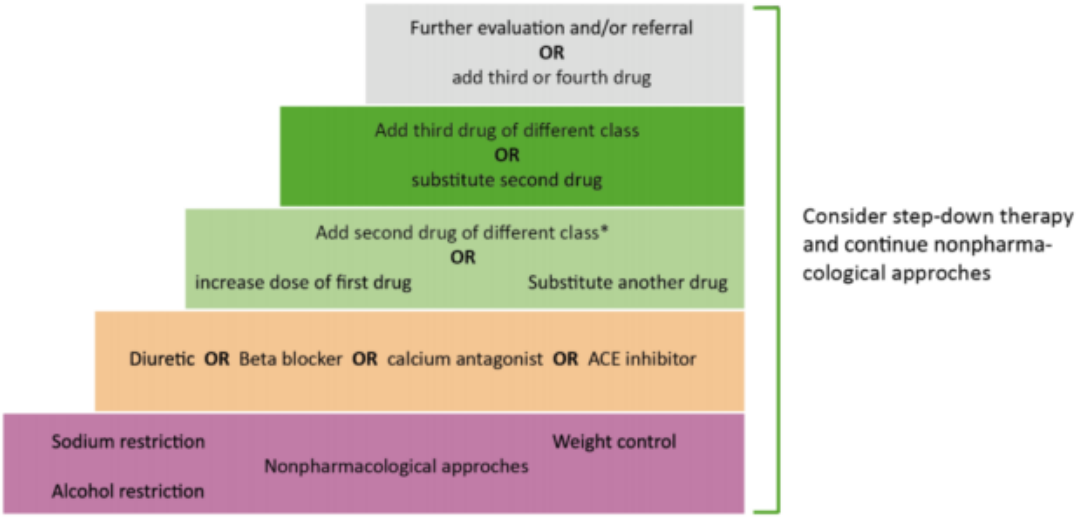
At the doses used in humans, calcium channel blockers only dilate arterioles, without affecting the electrical system of the heart (or the cardiac conduction system). They

dilate arterioles and also decrease the rate of transmission of electrical impulses in the heart muscle. Because of their effect on the electrical activity of the heart, they are often used to control arrhythmias.

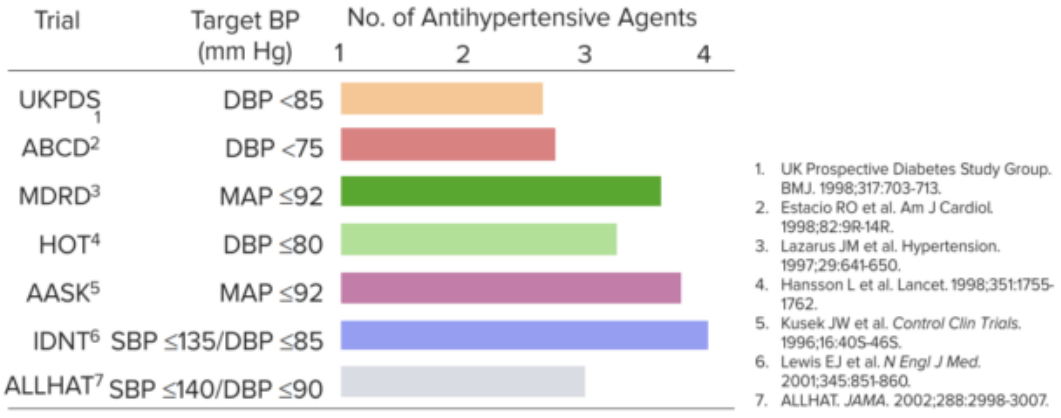
Other forms of pharmacological therapy

Other drugs occasionally used in the treatment of hypertension

- Minoxidil: very potent blood vessel dilator; also used to grow hair
- Clonidine: blocks sympathetic nerve activity in the brain and leads to reduced vascular resistance
- Alpha-blockers: peripheral sympathetic receptor blockers in vascular smooth muscle



The average number of antihypertensive agents used to achieve target blood pressure



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Possible drug combination

Dual combinations may include, for instance, a diuretic along with a beta-blocker, a long-acting calcium channel blocker, ACE inhibitors, or AT1 receptor blockers.

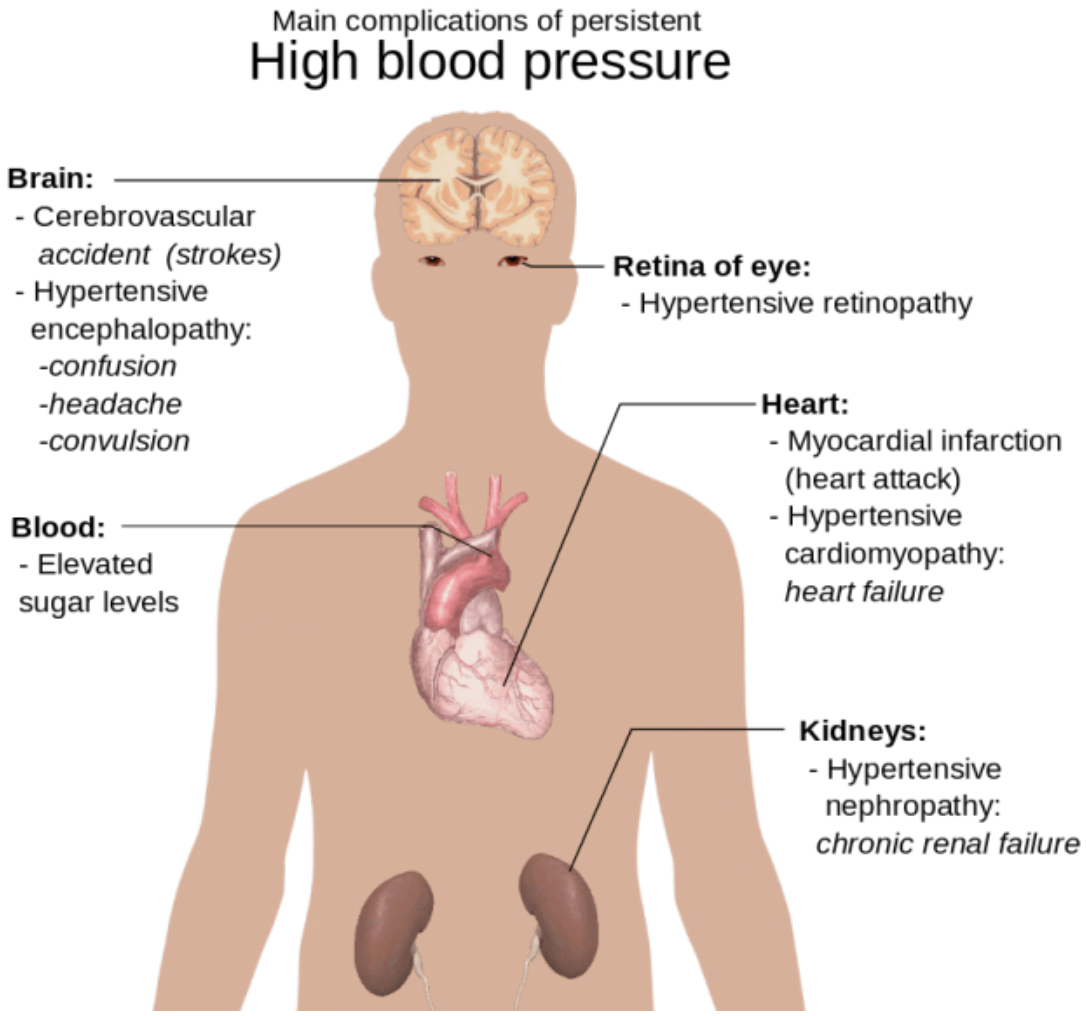
Alternatives include the combination of a calcium channel blocker with a beta-blocker, ACE inhibitors or AT1 receptor blockers.

N.B. Calcium channel blockers of the non-dihydropyridine variety must **not** be administered in combination with beta-blockers as they may promote bradycardia or atrioventricular block (AV block)!
Depending on the individual comorbidities, the respective medications may either gain or lose significance. In the case of hypertension combined with cardiac insufficiency, diuretics are an option. ACE inhibitors may also be used in cases of cardiac insufficiency but also with diabetic nephropathy. In the case of existing cardiac insufficiency, beta-blockers are indicated as well.

The use of individual medications is dictated by factors such as side effects, individual tolerability, and interactions with other medications already used by the patient. Triple combinations are another alternative in the event the dual combination does not have the desired efficacy.

Isolated systolic hypertension may be treated similar to the treatment for systolic and diastolic hypertension.

Complications of Hypertension



Dangers of hypertension

The challenge with arterial hypertension is that, most often, it is not diagnosed for a long time and is not treated at all or only to an insufficient degree. In addition, lack of patient compliance due to illness may hinder therapy, which leads to **secondary diseases,** frequently affecting **the heart**, **the kidneys**, **the brain,** and **the eyes** or manifestations involving the **vessels of the lower extremities**. These diseases frequently result from atherosclerosis involving the affected sections of vessels.

Important secondary cardiac diseases, in the context of **hypertensive heart disease,** include **left ventricular hypertrophy and left ventricular insufficiency** as well as **coronary heart disease**. Cardiac hypertrophy occurs in order to withstand the increased pressure. The critical heart weight is 500 g. If this weight is exceeded, the heart muscle can no longer be supplied sufficiently, resulting in left ventricular insufficiency.

As a result of atherosclerotic changes in the coronary blood vessels, the coronary reserve is impaired to the extent that in individuals with hypertension, the increased cardiac output with effort may not be adequate. Therefore, it may frequently result in **angina pectoris**, myocardial infarction or sudden cardiac arrest.

Hypertensive nephropathy is accompanied by damage to the kidneys, which may lead to microalbuminuria associated with endothelial damage, similar to the damage in diabetic patients. Years of arterial hypertension may lead to **pronounced nephrosclerosis** with **terminal kidney failure**.

Arterial hypertension may result in transient ischemic attacks (TIAs) as well as cerebral infarction, hypertensive hemorrhage, or acute hypertensive encephalopathy. The risk of suffering a stroke can significantly be lowered with antihypertensive therapy.

Hypertensive retinopathy is generally attributed to extensive atherosclerosis of the vessels in the retina. Vascular diseases caused by hypertension include **peripheral arterial disease**, **abdominal aortic aneurysm** as well as **aortic dissection**.

Prevention of Hypertension

Preventative approaches include the elimination of risk factors or their reduction.

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Notes