# Heart failure

- Heart failure (cardiac failure) is not a disease but a syndrome, with many possible aetiologies and a complex pathogenesis, yet it may be simply defined as the failure of the heart to meet the normal perfusion demands of the body.

- The cardiac failure syndrome may also involve peripheral organ damage not directly caused by reduced blood supply, especially in skeletal muscle.

- Most cases of heart failure would be classified as ‘chronic compensated low-output left ventricular systolic failure’.

- The clinical features of left and right failure differ in certain crucial aspects, but many patients, especially the elderly, present with bilateral failure.

- The distinction between acute and chronic is important for management.

- The causes of heart failure may be considered in two broad groups:

**1.** Pump failure, with primary reduction in myocardial contractility.

**2.** Overloading, with either excessive afterload (pressure overload) or excessive preload(volume overload), which arise outside the heart and reduce contractility secondarily.

| Term | Comment/Typical cause |
|---|---|
| Acute | Sudden onset (e.g. myocardial infarction) |
| Chronic | Gradual onset, usually progressive course (e.g. valve disease) |
| Right | Lung disease (cor pulmonale) |
| Left | Untreated essential hypertension |
| Bilateral | Almost any cause (usually chronic) |
| Ventricular | Failure of ventricle(s) only (the usual form) |
| Atrial | Failure of atria only (uncommon) |
| Low output | Reduced contractility – most causes (usual form) |
| High output | Anaemia, thyrotoxicosis – due to excessive cardiac drive |
| Systolic | Reduced contractility → impaired emptying (usual variety) |
| Diastolic | Reduced ventricular compliance → impaired filling (less common) |
| Compensated | Compensation prevents symptoms at rest but cardiac reserve diminished |
| Decompensated | Cardiac reserve exhausted |
| Congestive (CHF, CCF) | Imprecise traditional term describing generalized oedema; usually implies bilateral ventricular failure |
| Cardiogenic shock | Acute severe decompensation: very low BP and CO; poor tissue perfusion |
| LVF/RVF | Left/right ventricular failure |

- The cardiomyopathies are a miscellaneous group in which diffuse damage occurs throughout the myocardium.

- They are either idiopathic or secondary to conditions such as infection, toxins (e.g. alcohol), inflammation or autoimmune disease.

- In dilated cardiomyopathy the myocardium becomes thin, weak and excessively enlarged, with a raised EDV and a low ejection fraction.

- This may arise as a consequence of, for example, infection, thyroid disease or alcohol abuse.

- In hypertrophic cardiomyopathy there is excessive thickening of the myocardium, leading to poor ventricular filling and obstructed ejection, particularly due to structural distortion around the valves, whereas in restrictive cardiomyopathy there is increased ventricular stiffness but little hypertrophy.

- Causes of diastolic failure include patchy ischaemic or senile fibrosis, restrictive cardiomyopathy and hypertrophic cardiomyopathy (e.g. owing to untreated hypertension).

| Haemodynamic defect | Cause | Side affected[a] | Acute or chronic |
|---|---|---|---|
| **Pump failure** | | | |
| Systolic failure | **Ischaemic heart disease** | L usually | Acute or chronic |
| | **Cardiomyopathy** | L ± R | Chronic |
| | Arrhythmias | L + R | Acute, chronic |
| | Infection, inflammation, alcohol | L + R | Acute, chronic |
| | Systemic disease (e.g. amyloidosis) | L + R | Chronic |
| | Diffuse fibrosis (senile, ischaemic) | L + R | Chronic |
| Diastolic failure | Ischaemia, cardiomyopathy, fibrosis | L + R | Chronic |
| **Excessive afterload** | **Hypertension – systemic** | L | Chronic |
| | – pulmonary (COPD) | R | Chronic |
| | **Valve stenosis** | L or R | Chronic |
| **Excessive preload** | | | |
| Obligatory | Vasodilatation: beri-beri, septicaemia | L + R | Chronic |
| Hypervolaemia | Fluid retention, e.g. renal failure, aldosteronism | R | Usually chronic |
| | Excess IV infusion | | |
| | Polycythaemia | | |
| Excessive demand | Regurgitation: valve incompetence | R or L | Chronic |
| | Hyperdynamic: anaemia, thyrotoxicosis | R | Chronic |

- The maladaptive changes in ventricular shape caused by dilatation and hypertrophy are termed remodelling, especially when they follow MI. Angiotensin may contribute to this process.

- Investigations are used in heart failure to confirm the diagnosis and exclude other possibile diagnoses, to determine the cause and any exacerbating or precipitating factors, to grade the extent of dysfunction, and to monitor the progress of treatment.

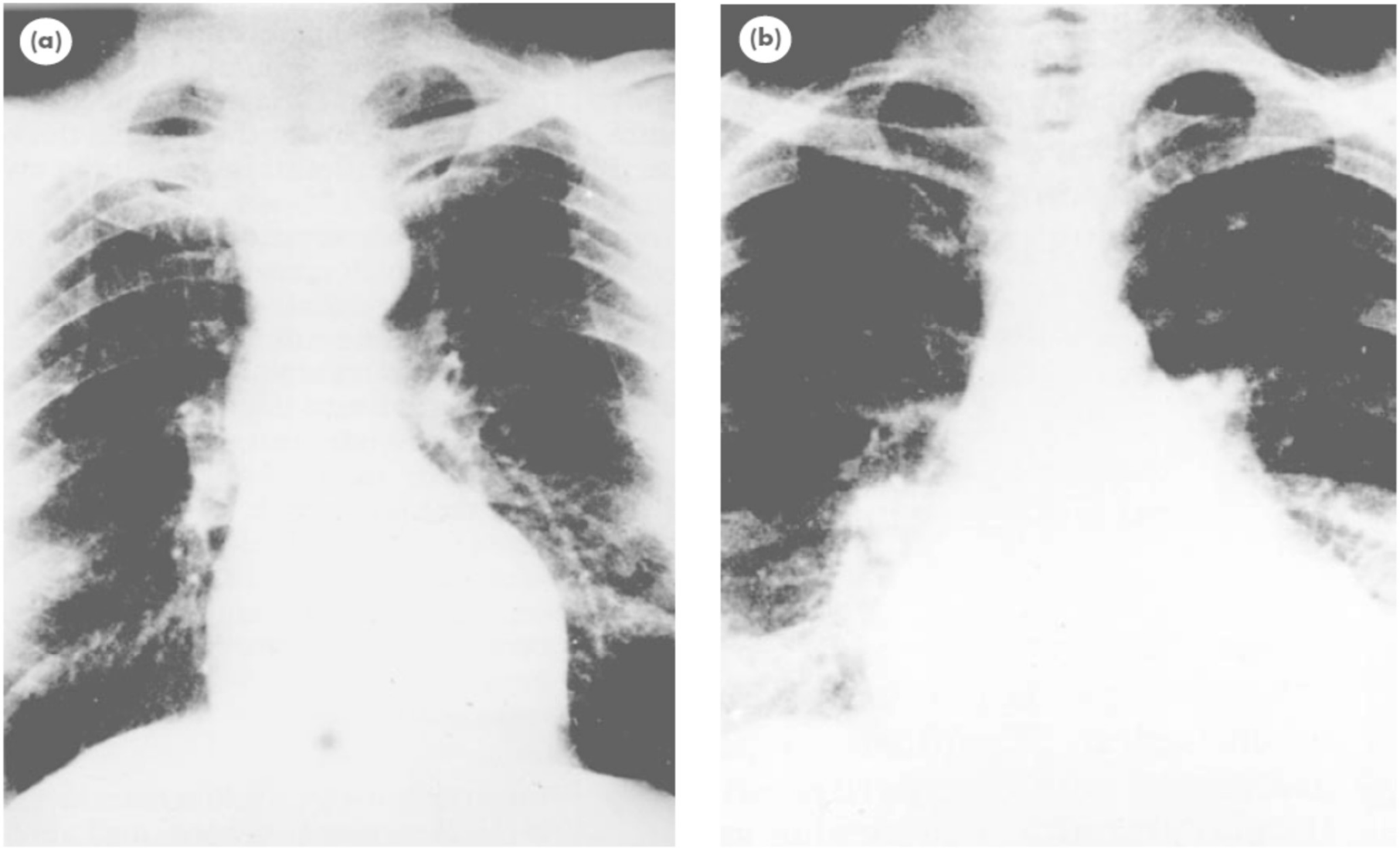
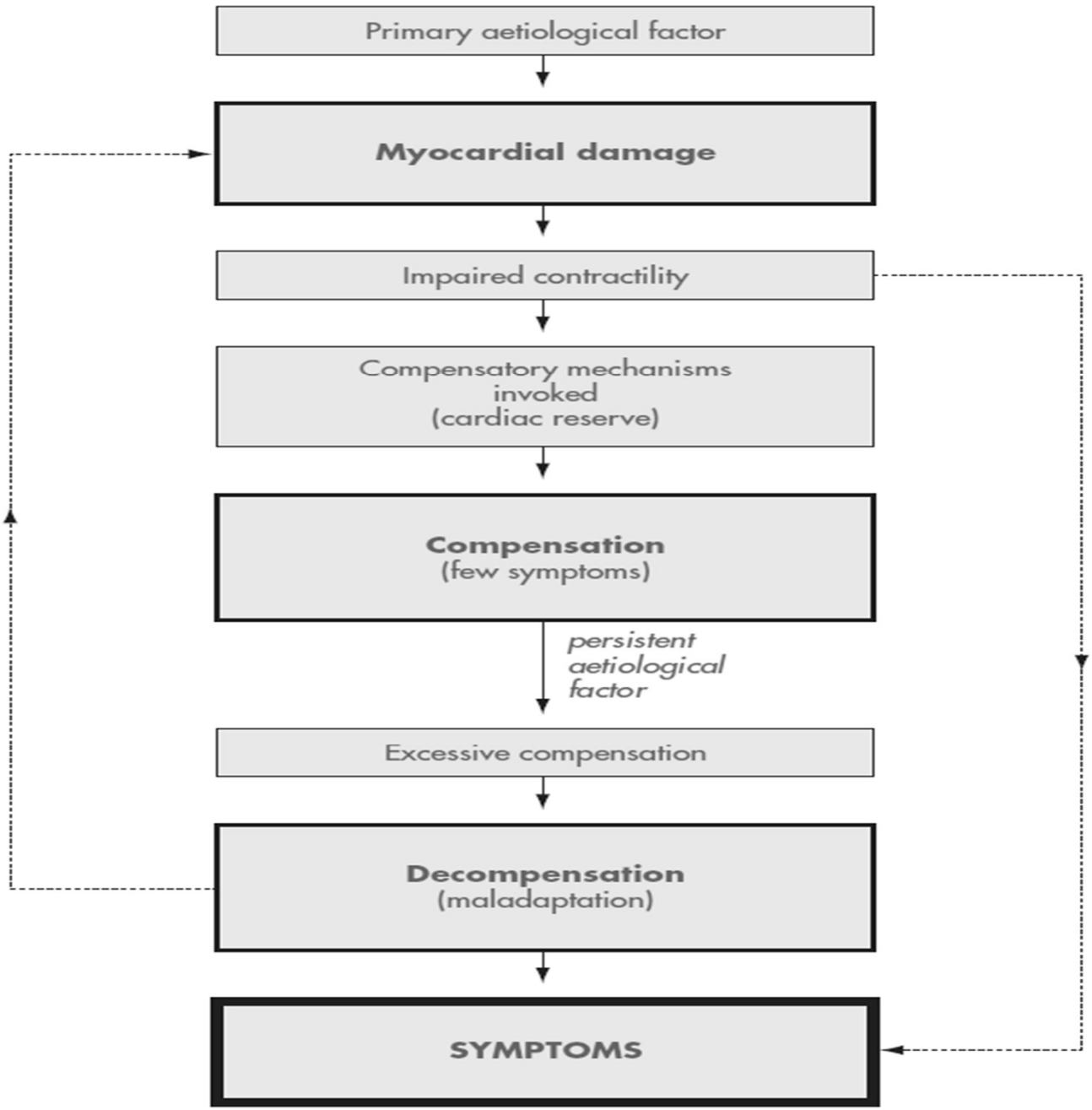
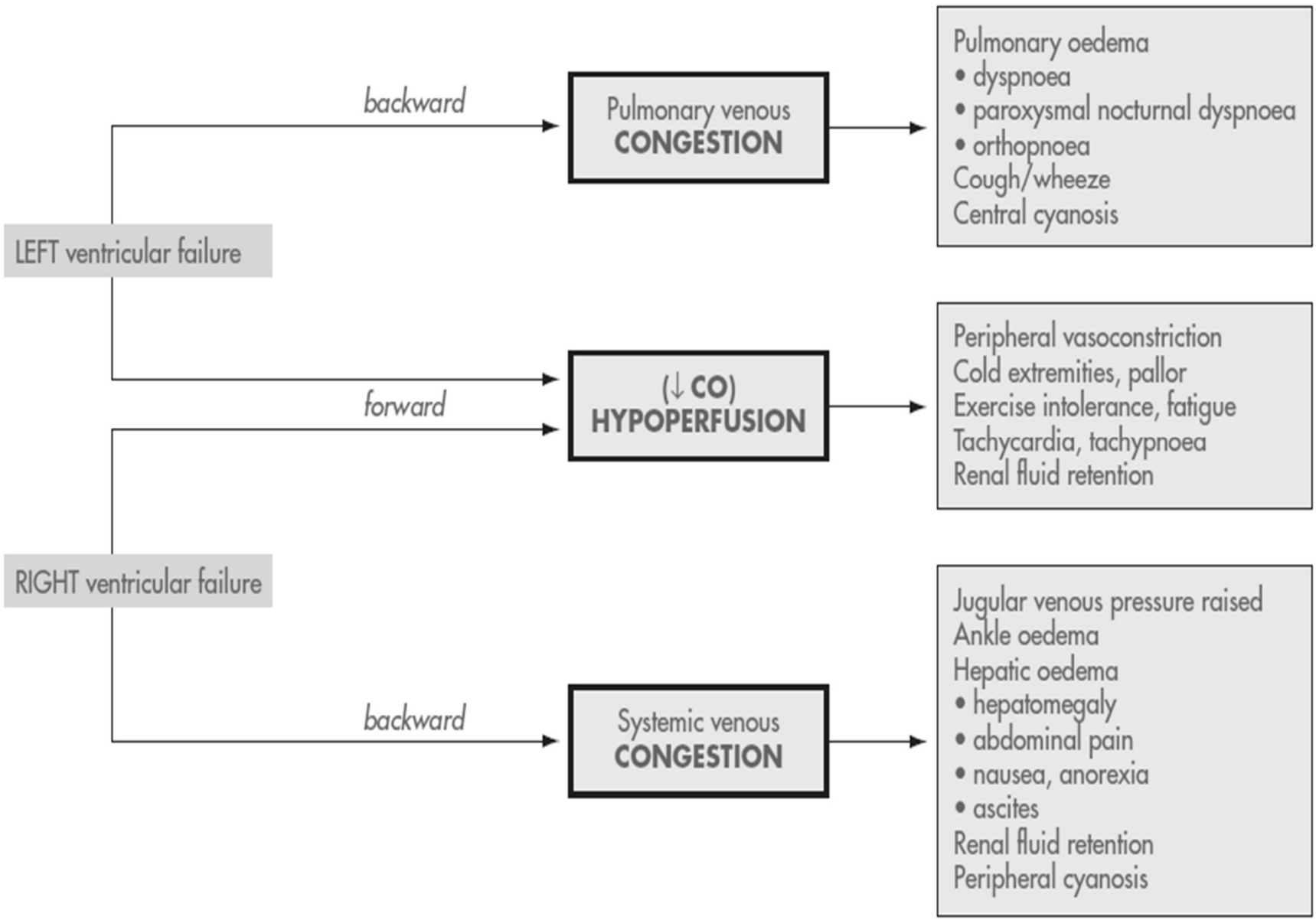



**Figure 4.12** Chest X-ray in heart failure. (a) Normal pattern. (b) Patient with severe heart failure. Note the increased width of the heart shadow indicating cardiac enlargement, and the diffuse shadowing at the lung bases indicating pulmonary oedema.


Primary aetiological factor
Myocardial damage
Impaired contractility
Compensatory mechanisms invoked (cardiac reserve)
Compensation (few symptoms)
persistent aetiological factor
Excessive compensation
Decompensation (maladaptation)
SYMPTOMS


LEFT ventricular failure
backward
Pulmonary venous CONGESTION
Pulmonary oedema
• dyspnoea
• paroxysmal nocturnal dyspnoea
• orthopnoea
Cough/wheeze
Central cyanosis
forward
(↓ CO) HYPOPERFUSION
Peripheral vasoconstriction
Cold extremities, pallor
Exercise intolerance, fatigue
Tachycardia, tachypnoea
Renal fluid retention
RIGHT ventricular failure
backward
Systemic venous CONGESTION
Jugular venous pressure raised
Ankle oedema
Hepatic oedema
• hepatomegaly
• abdominal pain
• nausea, anorexia
• ascites
Renal fluid retention
Peripheral cyanosis

**Class I.** Asymptomatic. No symptoms at ordinary physical activity (EF 40–50%).

**Class II**. Mild. Breathlessness and fatigue evident on strenuous exertion (EF 35–40%).

**Class III.** Moderate. Breathlessness and fatigue evident on moderate exertion (EF 30–35%).

**Class IV.** Severe. Breathlessness at rest (EF 30%).

- The management of heart failure involves correcting the consequences of low cardiac output and congestion, and addressing the various maladaptive pathophysiological responses that have complicated the clinical picture.

- Rather than attempting to

force the heart to maintain an unrealistic output while impaired and under maximal physiological stimulation, current practice favours two alternative strategies:

**1.** Reduce the load on the heart to match its reduced pumping ability.

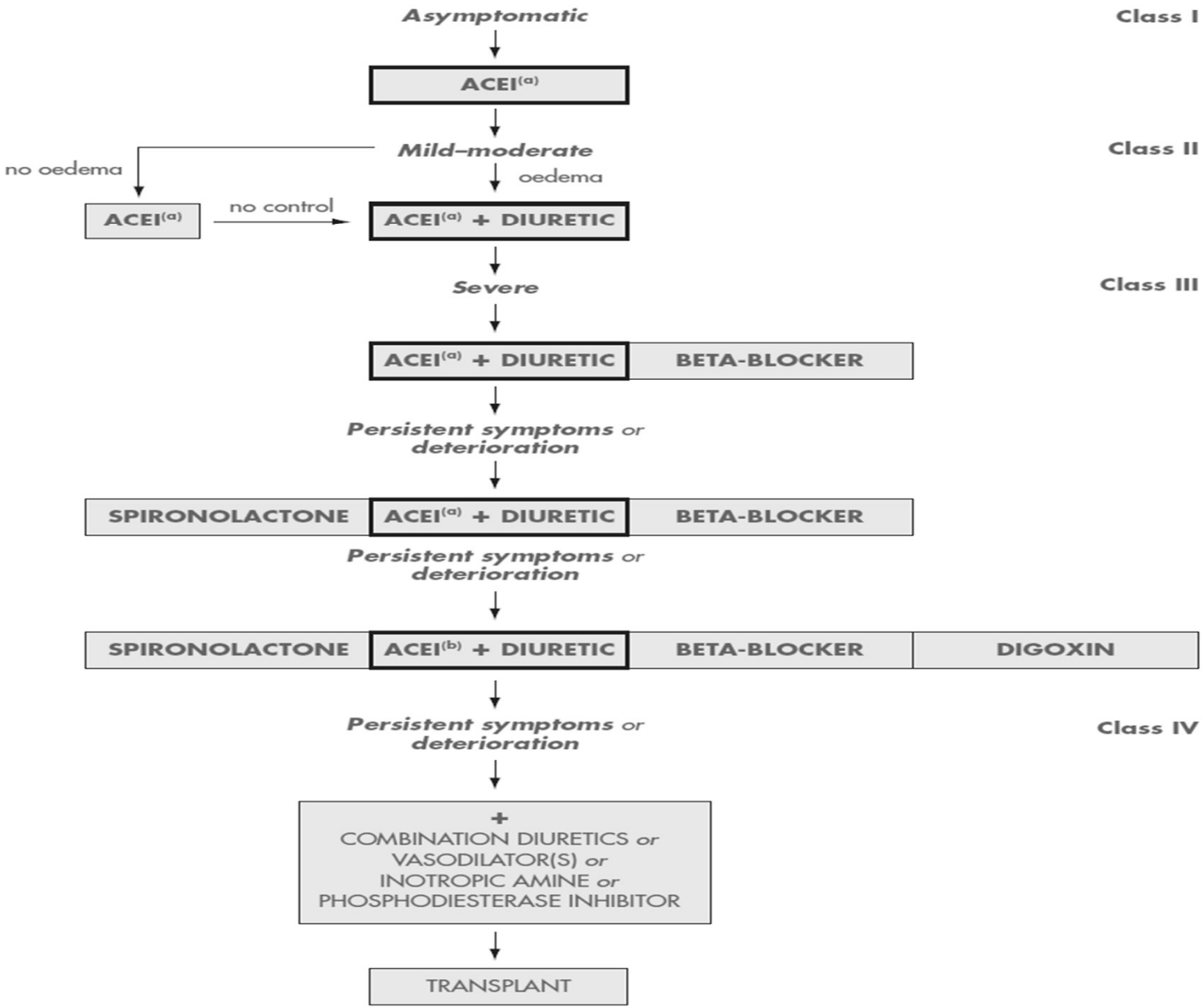
**2.** Limit the counterproductive compensatory mechanisms.

**Table 4.7** Predominant vascular sites of action of vasodilators used in heart failure

| Arterioles | Arterioles and veins | Veins |
|---|---|---|
| Hydralazine | ACEIs, ARAs | Nitrates |
| CCBs | Alpha-adrenergic blockers | |
| $Beta_2$-adrenergic agonists | Thiazide/loop diuretics | |
| Dopaminergic agonists | Nitroprusside | |

**Table 4.8** Actions of digoxin and other cardiac glycosides

| Pharmacological action | Effect on cardiovascular function | Site or mode of action |
|---|---|---|
| Positive inotropic | ↑ Contractility | ↓ Na/K-ATPase in myocyte |
| Negative chronotropic | ↓ Conduction velocity | Direct (AV node, etc.) |
| | ↓ Heart rate | ↑ Parasympathetic activity (vagus) |
| Reduced sympathetic activity (↓ noradrenaline). | ↓ Excessive myocardial stimulation | Restored baroreceptor sensitivity |
| | Peripheral vasodilatation | • ↓ central sympathetic activity<br>• ↓ noradrenaline (norepinephrine) level |
| Reduced renin secretion → angiotensin ↓ | ↓ Fluid retention | Kidney (juxtaglomerular apparatus) |
| | ↓ Peripheral vasoconstriction | • ↓ sympathetic stimulation?<br>• ↓ Na/K-ATPase reduces renin release? |


Asymptomatic
Class I
ACEI(a)
Mild–moderate
Class II
no oedema
oedema
ACEI(a)
no control
ACEI(a) + DIURETIC
Severe
Class III
ACEI(a) + DIURETIC
BETA-BLOCKER
Persistent symptoms or deterioration
SPIRONOLACTONE
ACEI(a) + DIURETIC
BETA-BLOCKER
Persistent symptoms or deterioration
SPIRONOLACTONE
ACEI(b) + DIURETIC
BETA-BLOCKER
DIGOXIN
Persistent symptoms or deterioration
Class IV
+
COMBINATION DIURETICS or
VASODILATOR(S) or
INOTROPIC AMINE or
PHOSPHODIESTERASE INHIBITOR
TRANSPLANT

# Diastolic failure

- This form of heart failure is especially difficult to treat, and there is as yet no reliable trial evidence.

- Efforts to increase diastolic time with cardiodepressants such as beta-blockers, or with CCBs such as verapamil, may be tried.

- Drugs that reduce preload (and hence diastolic filling) need to be used with great caution: this includes nitrates and diuretics.

# Hypertension:

- Hypertension is defined by persistent elevation of arterial blood pressure (BP).

- Patients with diastolic blood pressure (DBP) values <90 mm Hg and systolic blood pressure (SBP) values ≥140 mm Hg have isolated systolic hypertension.

**TABLE 10-1** Classification of Blood Pressure in Adults

| Classification | Systolic (mm Hg) | | Diastolic (mm Hg) |
|---|---|---|---|
| Normal | <120 | and | <80 |
| Prehypertension | 120–139 | or | 80–89 |
| Stage 1 hypertension | 140–159 | or | 90–99 |
| Stage 2 hypertension | ≥160 | or | ≥100 |

- Multiple factors may contribute to the development of primary hypertension, including:

✓ Humoral abnormalities involving the renin-angiotensin-aldosterone system, natriuretic hormone, or hyperinsulinemia;

✓ A pathologic disturbance in the CNS, autonomic nerve fibers, adrenergic receptors, or baroreceptors;

✓ Abnormalities in either the renal or tissue autoregulatory processes for sodium excretion, plasma volume, and arteriolar constriction;

✓ A deficiency in the local synthesis of vasodilating substances in the vascular endothelium, such as prostacyclin, bradykinin, and nitric oxide, or an increase in production of vasoconstricting substances such as angiotensin II and endothelin I;

✓ A high sodium intake and increased circulating natriuretic hormone inhibition of intracellular sodium transport, resulting in increased vascular reactivity and a rise in BP; and

✓ Increased intracellular concentration of calcium, leading to altered vascular smooth muscle function and increased peripheral vascular resistance.

- Patients with uncomplicated primary hypertension are usually asymptomatic initially.

- Patients with secondary hypertension may complain of symptoms suggestive of the underlying disorder.

- Hypertension is called malignant or accelerated (terms not strictly synonymous but often used so) when the DBP is above 120 mmHg and usually rising rapidly.

**Table 4.12** Risk factors and aetiological influences in hypertension

| Risk factor or aetiological influence | Possible rationale and comment |
|---|---|
| **Major** | |
| Family history | Inherited tendency – probably polygenic |
| Dietary Na high | Fluid retention; vascular wall oedema; ion pump defect (p. 214) |
| Obesity | Possible artefact of measurement (problem with arm cuff)? |
| | Greater perfusion demands of increased body mass |
| | Reducing weight can reverse borderline HPT |
| Alcohol | Unknown mechanism; possibly 30% of HPT related to alcohol abuse |
| Sedentary life | Unknown mechanism; regular exercise lowers BP |
| Renal disease | Overt or occult renal disease often implicated: cause or effect? |
| **Minor** | |
| Age | See text |
| Stress or type A personality | Overactive sympathetic nervous system → vasoconstriction and/or raised |
| | Difficult to quantify; effect may have been exaggerated |
| Dietary | |
| Ca, K, Mg ↓ | Some evidence, especially for K |
| Saturated fat ↑ | May induce vasoconstriction via endothelial interactions |
| Animal products | Vegetarians may have lower BP |
| Glucose intolerance | Complex interaction between insulin resistance, hyperlipidaemia and HI |
| Race | Increased average BP in urban Blacks: ↑ response to stress or dietary s |
| Smoking | **No** sustained effect on BP itself but greatly exacerbates atherosclerotic complications |

**Table 4.13** Causes of secondary hypertension

| Possible cause or underlying disease | Raised haemodynamic parameter | |
|---|---|---|
| | Peripheral resistance | Cardiac output |
| **Renal/endocrine** | | |
| Glomerular damage → ↓ GFR → fluid retention | − | + |
| Increased renin secretion → angiotensin ↑ (e.g. renal artery disease) | + | + |
| **Endocrine** | | |
| Phaeochromocytoma → adrenaline (epinephrine) – very rare | + | + |
| Cushing's disease/Conn's syndrome → aldosterone ↑ | − | + |
| **Vasomotor** | | |
| Increased intracranial pressure (e.g. trauma, tumour) | + | − |
| **Anatomic** | | |
| Aortic coarctation (constriction) | + | − |
| **Iatrogenic**, e.g.: NSAIDs, corticosteroids, oral contraceptives, sympathomimetics, MAOIs | + | + |

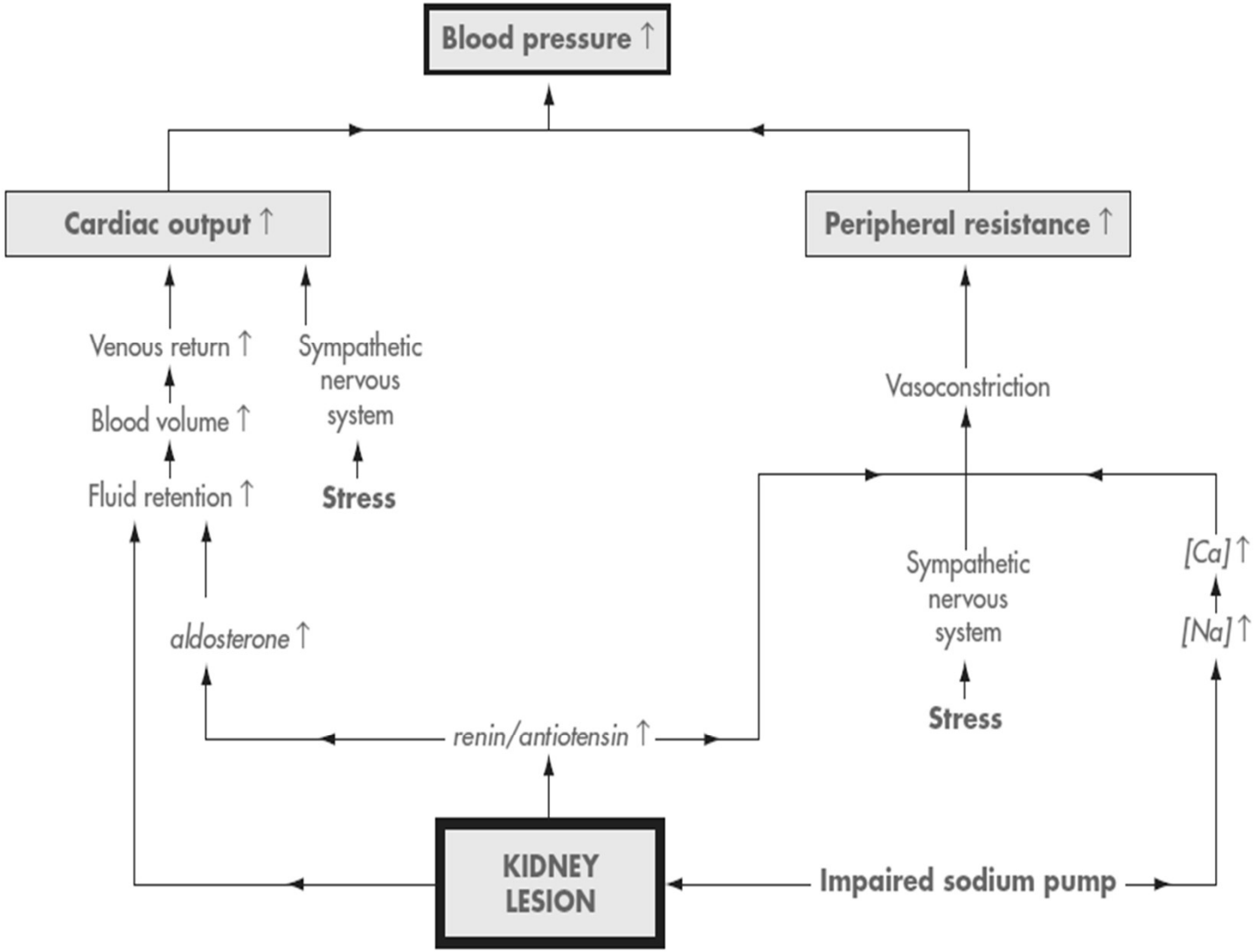



**Figure 4.20** Possible pathways in the pathogenesis of hypertension. [Ca], intracellular calcium concentration; [Na], intracellular sodium concentration.

Table 4.17 Complications of untreated hypertension

| Pathology | Pathogenesis | Clinical consequence |
|---|---|---|
| **Direct effects** | | |
| ↑ Peripheral resistance | Elevated LV afterload | LV failure |
| Arteriosclerosis | ↑ Wall stress, medial hypertrophy | Renovascular disease → renal failure |
| | | Haemorrhagic stroke, multiple infarcts |
| | | Dementia → hypertensive encephalopathy |
| | | Retinal damage |
| **Indirect effects** | | |
| Atherosclerosis | Possible: ↑ fat penetration, vessel wall damage, turbulent flow | Ischaemic heart disease |
| | | Peripheral vascular disease |
| | | Renal failure |
| | | Cerebrovascular disease → thrombotic stroke, multi-infarct dementia |

**Table 4.18** Signs of high cardiovascular risk in hypertensive patient, indicating need for earlier drug treatment in hypertension

| Risk factor for producing end-organ damage | Evidence of established end-organ damage |
|---|---|
| Hyperlipidaemia | Retinal damage |
| Smoking | Renal impairment |
| Diabetes mellitus | Cardiac enlargement or hypertrophy |
| Family history of CVD | Cardiac ischaemia (ECG) |
| Older patient | Angina/past MI |
| Male sex (younger patient) | Past stroke |
| | Peripheral vascular disease |

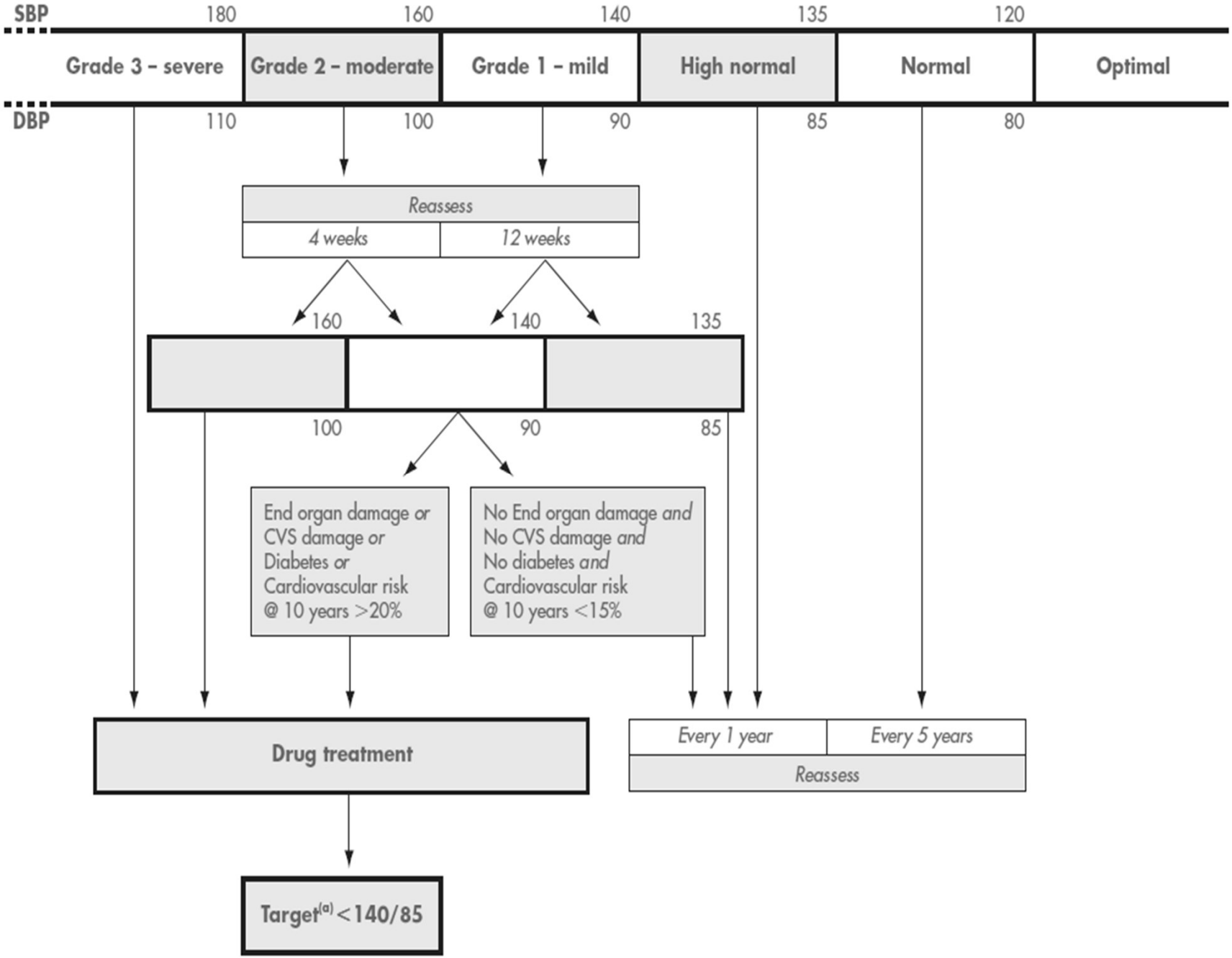
## Management:

- In addition to the level of the blood pressure itself, the patient's age and cardiovascular risk must be taken into account in balancing the likely benefits of intervention against the possible harms and reduced quality of life from lifelong drug therapy.

- Very severe hypertension (i.e. above 210/120 mmHg) represents a medical emergency, with the risk of encephalopathy, renal damage or haemorrhagic stroke.

- Nevertheless, this is not corrected too aggressively because a rapid fall in blood pressure can compromise cerebral perfusion.

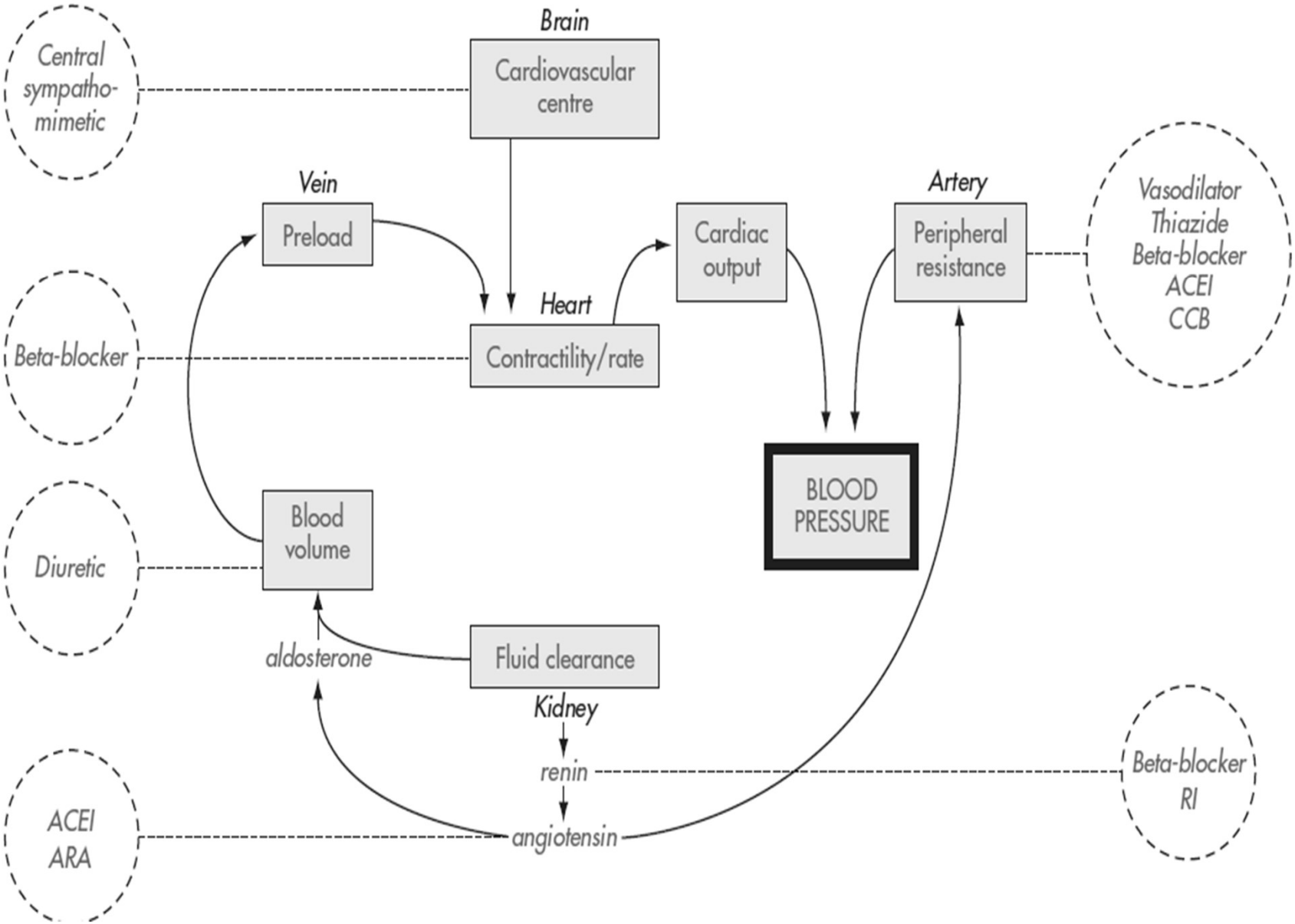
- Parenteral therapy is generally avoided, a smooth fall over a number of hours being preferred, and this can be attained effectively with oral therapy (e.g. ACEI, hydralazine, labetalol). IV


SBP
180
160
140
135
120
Grade 3 – severe
Grade 2 – moderate
Grade 1 – mild
High normal
Normal
Optimal
DBP
110
100
90
85
80
Reassess
4 weeks
12 weeks
160
140
135
100
90
85
End organ damage or
CVS damage or
Diabetes or
Cardiovascular risk
@ 10 years >20%
No End organ damage and
No CVS damage and
No diabetes and
Cardiovascular risk
@ 10 years <15%
Drug treatment
Every 1 year
Every 5 years
Reassess
Target[a] <140/85

## Principles of drug therapy in hypertension

- As few drugs as possible
- As few daily doses as possible
- Start with most suitable initial drug[a]
- Increase the dose gradually until adequate effect achieved
- If primary failure, substitute another suitable drug from different group
- If effectiveness declines, add another agent rather than substitute
- Combine agents acting by different mechanisms
- Combine agents tending to reduce each other's adverse actions
- Monitor adverse reactions and patient compliance regularly

# Proposed targets and haemodynamic actions of antihypertensive drugs.



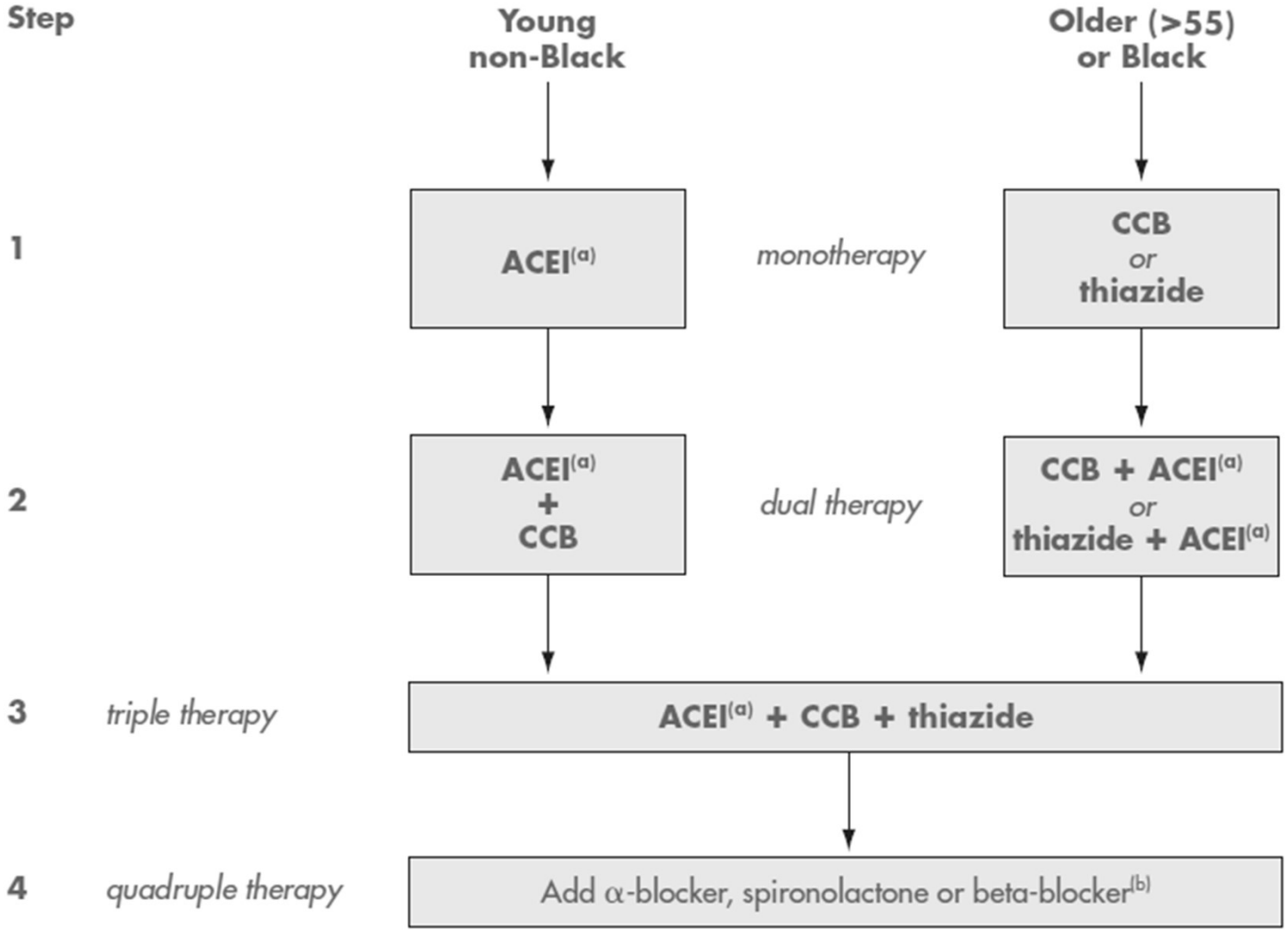
## Antihypertensive drugs classified haemodynamically

| Cardiac output reduced | Peripheral resistance reduced | Examples |
|---|---|---|
| Beta-blocker | Beta-blocker | Atenolol |
| Diuretics | Thiazide diuretic | Bendroflumethiazide |
| ACEI | ACEI | Captopril, enalapril |
| ARA | ARA | Losartan |
| RI | RI | Aliskiren |
| | CCB | Nifedipine, diltiazem |
| | Direct-acting vasodilator | Hydralazine, nitroprusside, minoxidil, diazoxide |
| | Alpha-blocker | Prazosin, doxazosin, labetalol, phentolamine |
| | Centrally acting sympathomimetic | Methyldopa, clonidine[b] |
| | Centrally acting selective imidazoline receptor agonist[a] | Clonidine[b], moxonidine |
| | Adrenergic neurone blocker[a,b] | Guanethidine |

## Specific indications, precautions and contra-indications of antihypertensive drugs

| Situation | Drugs to avoid/caution | Specific alternatives or recommendations[a] |
|---|---|---|
| Elderly | Sympatholytic (postural effect) | Thiazide, methyldopa |
| Young male | Thiazide, beta-blocker | ACEI[b], CCB |
| Black ethnic group | Beta-blocker, ACEI | – |
| Peripheral vascular disease | Beta-blocker, ? ACEI | Vasodilator |
| Vascular disease in elderly | ACEI | – |
| Angina | Vasodilator | Beta-blocker, CCB |
| Post-MI | – | Beta-blocker, ACEI |
| Heart failure, LVD | CCB esp. verapamil, diltiazem | Thiazide, ACEI, ? beta-blocker |
| Heart block | Beta-blocker, CCB | – |
| Hyperlipidaemia | Beta-blocker, thiazide[c] | ACEI, CCB, selective alpha-blocker |
| Diabetes (especially type 1) | Thiazide[c], beta-blocker[d] | ACEI, selective alpha-blocker |
| Obstructive pulmonary disease | Beta-blocker[d] | – |
| Pregnancy | Thiazide, ACEI | Methyldopa, labetalol, furosemide |
| Hepatic impairment | CCB | Methyldopa |
| Renal impairment: | | |
| – early | Thiazide | ACEI |
| – severe | ACEI | Furosemide, beta-blocker |
| Diabetic nephropathy | | ACEI |
| Renal artery stenosis | ACEI | – |
| High renin | – | ACEI |
| Thyrotoxicosis | – | Beta-blocker |
| Depression | Lipophilic beta-blockers, methyldopa, clonidine | – |
| Gout, hypokalaemia | Thiazide | – |
| Prostatic hypertrophy | – | Alpha-blocker |

# Drug selection in hypertension – recommendations of NICE and British Hypertension Society (2006).



# Potential interactions with antihypertensive therapy[a]

| | |
|---|---|
| **Drugs that elevate blood pressure** | |
| Vasoconstrictor sympathomimetics | Oral decongestants (e.g. phenylephrine, xylometazoline), bronchodilators especially non-specific[b], amphetamines |
| Drugs causing fluid retention | Corticosteroids, oral contraceptives, NSAIDs |
| **Drugs that lower blood pressure** | |
| CNS depressants | Tranquillizers, alcohol |
| Vasodilators | Nitrates, specific bronchodilators[b] |
| **Specific interactions** | |
| Beta-blockers | Verapamil, diltiazem → cardiac depression, failure |
| Alpha-blockers | Beta-blockers, diuretics → exaggerated first-dose hypotension |
| ACEIs | Potassium-sparing diuretics, potassium supplements → hyperkalaemia |