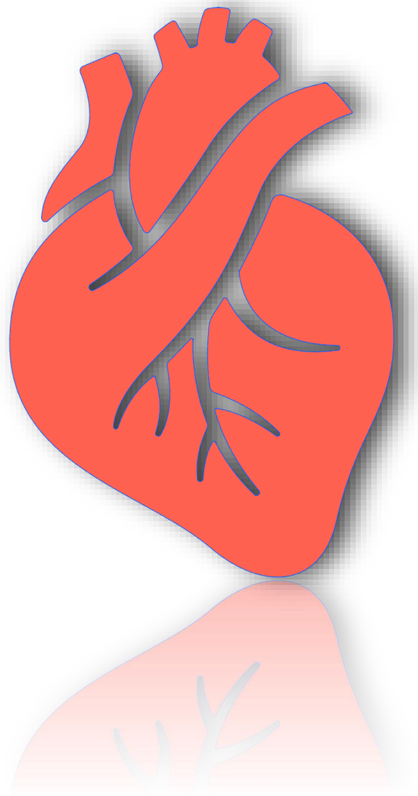


Heart failure

Sami Mukhlif Al-obaidy
Interventional Cardiologist and Senior Lecturer
FIBMS Cardiol , CABM(Med.), D.M(Med) , D.M (Chest Disease) ,MBChB , MESC

Heart failure

Clinical syndrome that develops when there is a **mismatch** between cardiac output and body demand .
Every syndrome has an exacerbation and each exacerbation has distinct cause.

- Heart failure describes the clinical syndrome that develops when the heart cannot maintain adequate output, or can do so only at the expense of elevated ventricular filling pressure. In mild to moderate forms of heart failure, symptoms occur only when the metabolic demand increases during exercise or some other form of stress. In severe heart failure, symptoms may be present at rest. In clinical practice, heart failure may be diagnosed when a patient with significant heart disease develops the signs or symptoms of a low cardiac output, pulmonary congestion or systemic venous congestion at rest or on exercise. Three types of heart failure are recognised.

- **Left heart failure**

This is characterised by a reduction in left ventricular output and an increase in left atrial and pulmonary venous pressure. If left heart failure occurs suddenly – for example, as the result of an acute MI – the rapid increase in left atrial pressure causes pulmonary oedema. If the rise in atrial pressure is more gradual, as occurs with mitral stenosis, there is reflex pulmonary vasoconstriction, which protects the patient from pulmonary oedema. However, the resulting increase in pulmonary vascular resistance causes pulmonary hypertension, which in turn impairs right ventricular function.

- **Right heart failure**

This is characterised by a reduction in right ventricular output and an increase in right atrial and systemic venous pressure. The most common causes are chronic lung disease, pulmonary embolism and pulmonary valvular stenosis. The term ‘cor pulmonale’ is used to describe right heart failure that is secondary to chronic lung disease.

- **Biventricular heart failure**

In biventricular failure, both sides of the heart are affected. This may occur because the disease process, such as dilated cardiomyopathy or coronary heart disease, affects both ventricles or because disease of the left heart leads to chronic elevation of the left atrial pressure, pulmonary hypertension and right heart failure.

- **Epidemiology**

Heart failure predominantly affects older people; the prevalence is 1.6% in the UK adult population but affects more than 10% in those aged 80–89 years. In the UK, most patients admitted to hospital with heart failure are more than 70 years old; they typically remain hospitalised for a week or more and may be left with chronic disability. Although the outlook depends, to some extent, on the underlying cause of the problem, untreated heart failure generally carries a poor prognosis; approximately 50% of patients with severe heart failure due to left ventricular dysfunction will die within 2 years because of either pump failure or malignant ventricular arrhythmias. The most common causes are coronary artery disease and myocardial infarction but almost all forms of heart disease can lead to heart failure. An accurate diagnosis is important because treatment of the underlying cause may reverse heart failure or prevent its progression.

Pathogenesis

Heart failure occurs when cardiac output fails to meet the demands of the circulation. Cardiac output is determined by preload (the volume and pressure of blood in the ventricles at the end of diastole), afterload (the volume and pressure of blood in the ventricles during systole) and myocardial contractility, forming the basis of Starling’s Law

- Ventricular dysfunction
- High- output failure
- Valvular disease
- Arrhythmias

BP = CO x SVR

CO = SV x HR

Depends on arteriolar tone

SV = preload. — afterload

Preload
End diastolic volume, pressure. Filling pressure or atrial pressure

Afterload
End systolic volume, pressure .
Resistance against ventricular ejection

EF = SV / end diastolic volume

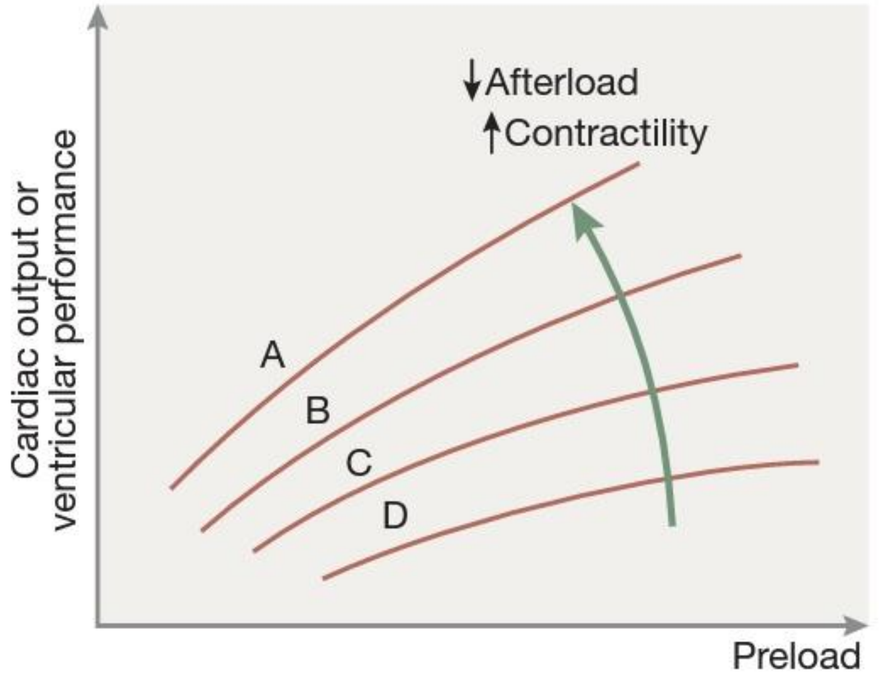


Fig. 16.24 Starling's Law. Normal (A), mild (B), moderate (C) and severe (D) heart failure. Ventricular performance is related to the degree of myocardial stretching. An increase in preload (end-diastolic volume, end-diastolic pressure, filling pressure or atrial pressure) will therefore enhance function; however, overstretching causes marked deterioration. In heart failure, the curve moves to the right and becomes flatter. An increase in myocardial contractility or a reduction in afterload will shift the curve upwards and to the left (green arrow).

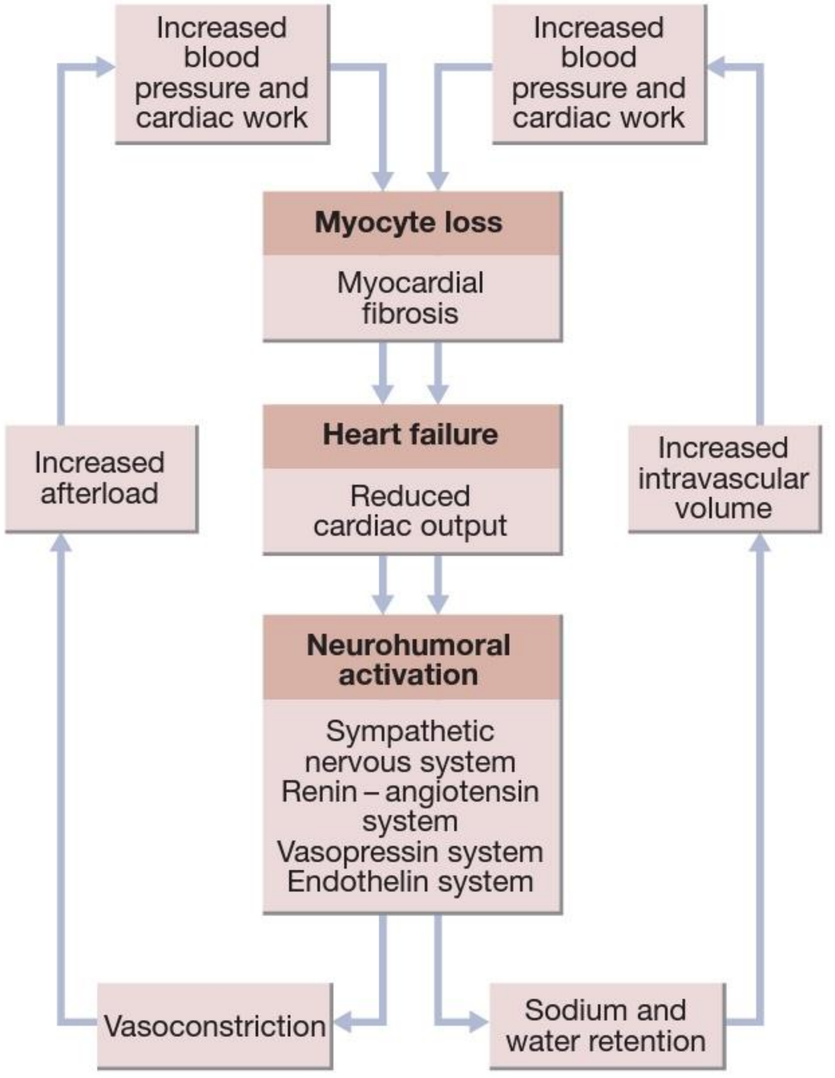
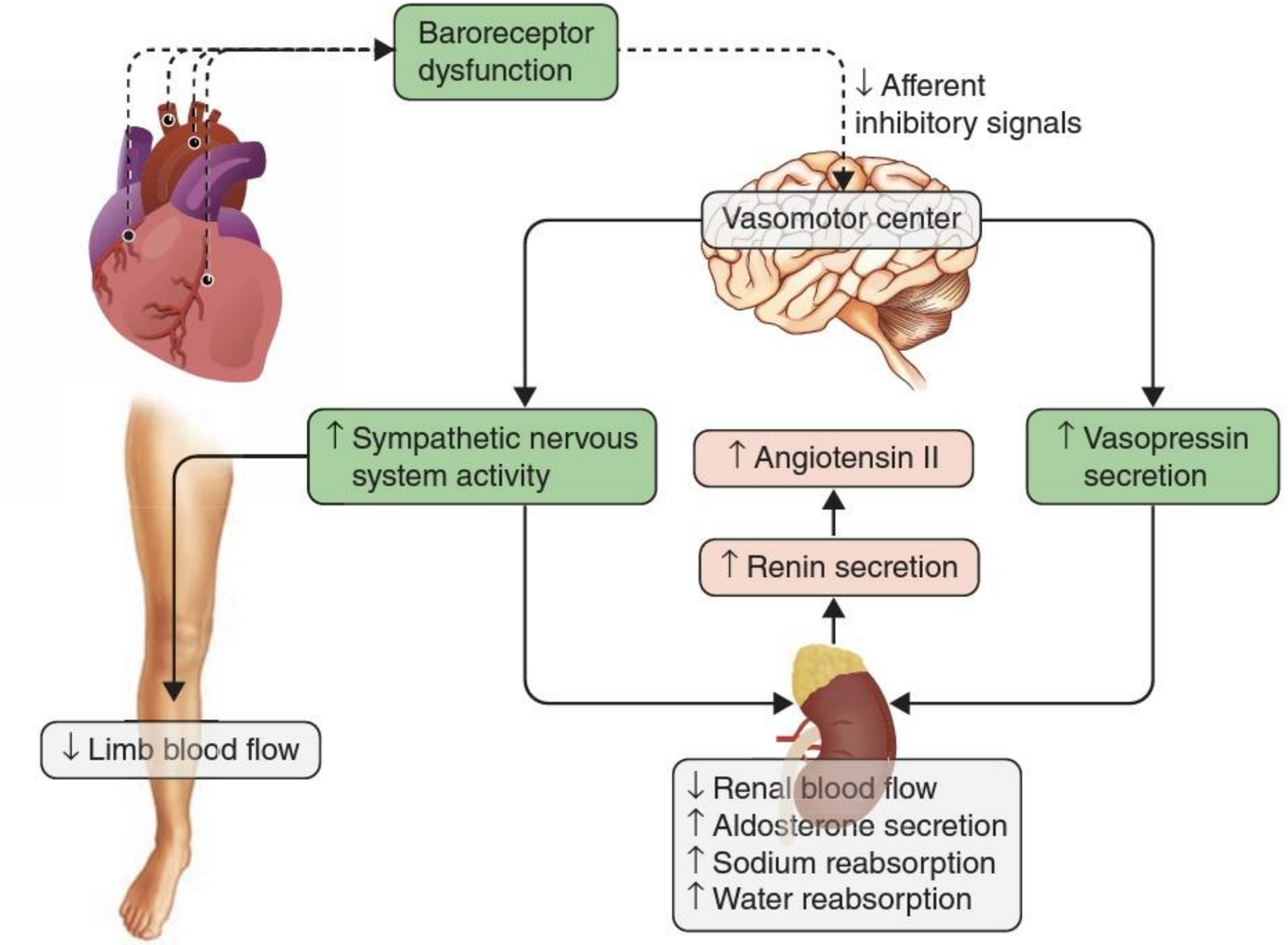


Fig. 16.25 Neurohumoral activation and compensatory mechanisms in heart failure. There is a vicious circle in progressive heart failure.


Baroreceptor dysfunction
↓ Afferent inhibitory signals
Vasomotor center
↑ Sympathetic nervous system activity
↑ Angiotensin II
↑ Vasopressin secretion
↑ Renin secretion
↓ Limb blood flow
↓ Renal blood flow
↑ Aldosterone secretion
↑ Sodium reabsorption
↑ Water reabsorption

- **Ventricular dysfunction**

Ventricular dysfunction is the most common cause of heart failure. This can occur because of impaired systolic contraction due to myocardial disease, or diastolic dysfunction where there is abnormal ventricular relaxation due to a stiff, non-compliant ventricle. This is most commonly found in patients with left ventricular hypertrophy. Systolic dysfunction and diastolic dysfunction often coexist, particularly in patients with coronary artery disease. Ventricular dysfunction reduces cardiac output, which, in turn, activates the sympathetic nervous system (SNS) and renin–angiotensin–aldosterone system (RAAS). Under normal circumstances, activation of the SNS and RAAS supports cardiac function but, in the setting of impaired ventricular function, the consequences are negative and lead to an increase in both afterload and preload . A vicious circle may then be established because any additional fall in cardiac output causes further activation of the SNS and RAAS, and an additional increase in peripheral vascular resistance. Activation of the RAAS causes vasoconstriction and sodium and water retention. This is primarily mediated by angiotensin II, a potent constrictor of arterioles, in both the kidney and the systemic circulation .

- **Ventricular dysfunction**

Activation of the SNS also occurs and can initially sustain cardiac output through increased myocardial contractility and heart rate. Prolonged sympathetic stimulation has negative effects, however, causing cardiac myocyte apoptosis, cardiac hypertrophy and focal myocardial necrosis. Sympathetic stimulation also contributes to vasoconstriction and predisposes to arrhythmias. Sodium and water retention is further enhanced by the release of aldosterone, endothelin-1 (a potent vasoconstrictor peptide with marked effects on the renal vasculature) and, in severe heart failure, vasopressin (antidiuretic hormone, ADH).

- **Natriuretic peptides** are released from the atria in response to **atrial dilatation** and compensate to an extent for the sodium-conserving effect of aldosterone, but this mechanism is overwhelmed in heart failure. Pulmonary and peripheral oedema occur because of high left and right atrial pressures, and are compounded by sodium and water retention, caused by impairment of renal perfusion and by secondary **hyperaldosteronism**. If the underlying cause is a myocardial infarction, cardiac contractility is impaired and SNS and RAAS activation causes hypertrophy of non-infarcted segments, with thinning, dilatation and expansion of the infarcted segment . This leads to further deterioration in ventricular function and worsening heart failure.

- **High-output failure** Sometimes cardiac failure can occur in patients without heart disease due to a large arteriovenous shunt, or where there is an excessively high cardiac output due to beri-beri, severe anaemia or thyrotoxicosis.

- **Valvular disease** Heart failure can also be caused by valvular disease in which there is impaired filling of the ventricles due to mitral or tricuspid stenosis; where there is obstruction to ventricular outflow, as occurs in aortic and pulmonary stenosis and hypertrophic cardiomyopathy; or as the result of ventricular overload secondary to valvular regurgitation.

16.12 Mechanisms of heart failure

Cause	Examples	Features
Reduced ventricular contractility	Myocardial infarction (segmental dysfunction)	In coronary artery disease, 'akinetic' or 'dyskinetic' segments contract poorly and may impede the function of normal segments by distorting their contraction and relaxation patterns
	Myocarditis/cardiomyopathy (global dysfunction)	Progressive ventricular dilatation
Ventricular outflow obstruction (pressure overload)	Hypertension, aortic stenosis (left heart failure) Pulmonary hypertension, pulmonary valve stenosis (right heart failure)	Initially, concentric ventricular hypertrophy allows the ventricle to maintain a normal output by generating a high systolic pressure. Later, secondary changes in the myocardium and increasing obstruction lead to failure with ventricular dilatation and rapid clinical deterioration
Ventricular inflow obstruction	Mitral stenosis, tricuspid stenosis	Small, vigorous ventricle; dilated, hypertrophied atrium. Atrial fibrillation is common and often causes marked deterioration because ventricular filling depends heavily on atrial contraction
Ventricular volume overload	Left ventricular volume overload (mitral or aortic regurgitation) Ventricular septal defect Right ventricular volume overload (atrial septal defect) Increased metabolic demand (high output)	Dilatation and hypertrophy allow the ventricle to generate a high stroke volume and help to maintain a normal cardiac output. However, secondary changes in the myocardium lead to impaired contractility and worsening heart failure
Arrhythmia	Atrial fibrillation	Tachycardia does not allow for adequate filling of the heart, resulting in reduced cardiac output and back pressure
	Tachycardia	Prolonged tachycardia causes myocardial fatigue
	Complete heart block	Bradycardia limits cardiac output, even if stroke volume is normal
Diastolic dysfunction	Constrictive pericarditis	Marked fluid retention and peripheral oedema, ascites, pleural effusions and elevated jugular veins
	Restrictive cardiomyopathy	Bi-atrial enlargement (restrictive filling pattern and high atrial pressures). Atrial fibrillation may cause deterioration
	Left ventricular hypertrophy and fibrosis	Good systolic function but poor diastolic filling
	Cardiac tamponade	Hypotension, elevated jugular veins, pulsus paradoxus, poor urine output

16.13 Factors that may precipitate or aggravate heart failure in pre-existing heart disease

- Myocardial ischaemia or infarction
- Intercurrent illness
- Arrhythmia
- Inappropriate reduction of therapy
- Administration of a drug with negative inotropic (β-blocker) or fluid-retaining properties (non-steroidal anti-inflammatory drugs, glucocorticoids)
- Pulmonary embolism
- Conditions associated with increased metabolic demand (pregnancy, thyrotoxicosis, anaemia)
- Intravenous fluid overload

Clinical assessment

- Heart failure may develop suddenly, as in MI, or gradually, as in valvular heart disease. When there is gradual impairment of cardiac function, several compensatory changes take place. The term compensated heart failure is sometimes used to describe the condition of those with impaired cardiac function, in whom adaptive changes have prevented the development of overt heart failure. However, a minor event, such as an intercurrent infection or development of atrial fibrillation, may precipitate acute heart failure in these circumstances . Similarly, acute heart failure sometimes supervenes as the result of a decompensating episode, on a background of chronic heart failure; this is called acute-on-chronic heart failure.

- **Acute left heart failure**

Acute left heart failure presents with a sudden onset of dyspnoea at rest that rapidly progresses to acute respiratory distress, orthopnoea and ultimately respiratory failure. Often there is a clear precipitating factor, such as an acute MI, which may be apparent from the history. The patient appears agitated, pale and clammy. The peripheries are cool to the touch and the pulse is rapid, but in some cases there may be an inappropriate bradycardia that aggravates the acute episode of heart failure. The BP is usually high because of SNS activation, but may be normal or low if the patient is in cardiogenic shock. The jugular venous pressure (JVP) is usually elevated, particularly with associated fluid overload or right heart failure. In acute heart failure, there has been no time for ventricular dilatation and the apex is not displaced. A ‘gallop’ rhythm, with a third heart sound, is heard quite early in the development of acute left-sided heart failure. A new systolic murmur may signify acute mitral regurgitation or ventricular septal rupture. Chest examination may reveal crepitations at the lung bases if there is pulmonary oedema, or crepitations throughout the lungs if this is severe. There may be expiratory wheeze. Patients with acute-on-chronic heart failure may have additional features of chronic heart failure . Potential precipitants, such as an upper respiratory tract infection or inappropriate cessation of diuretic medication, may be identified on clinical examination or history-taking.

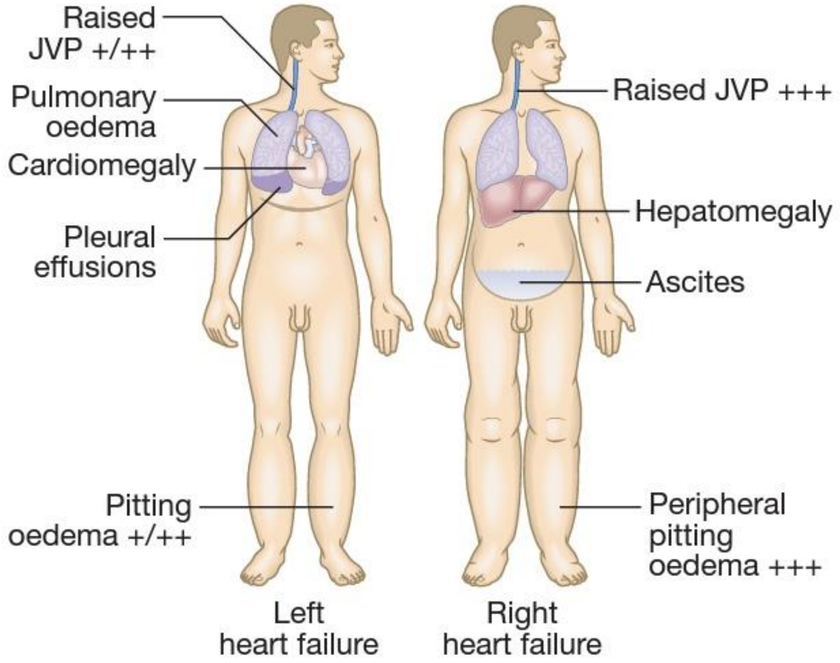


Fig. 16.26 Clinical features of left and right heart failu
(JVP = jugular venous pressure)

4.5 New York Heart Association classification of heart failure symptom severity

Class	Description
I	No limitations. Ordinary physical activity does not cause undue fatigue, dyspnoea or palpitation (asymptomatic left ventricular dysfunction)
II	Slight limitation of physical activity. Such patients are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnoea or angina pectoris (symptomatically 'mild' heart failure)
III	Marked limitation of physical activity. Less than ordinary physical activity will lead to symptoms (symptomatically 'moderate' heart failure)
IV	Symptoms of congestive heart failure are present, even at rest. With any physical activity, increased discomfort is experienced (symptomatically 'severe' heart failure)

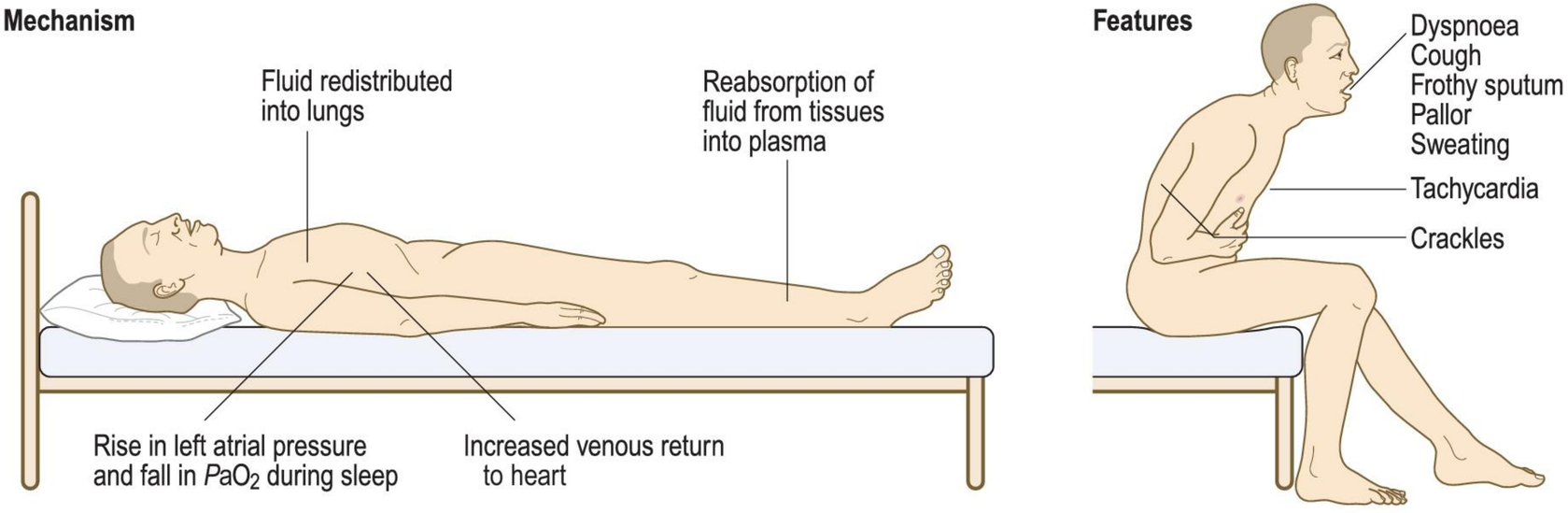


Fig. 4.3 Paroxysmal nocturnal dyspnoea.

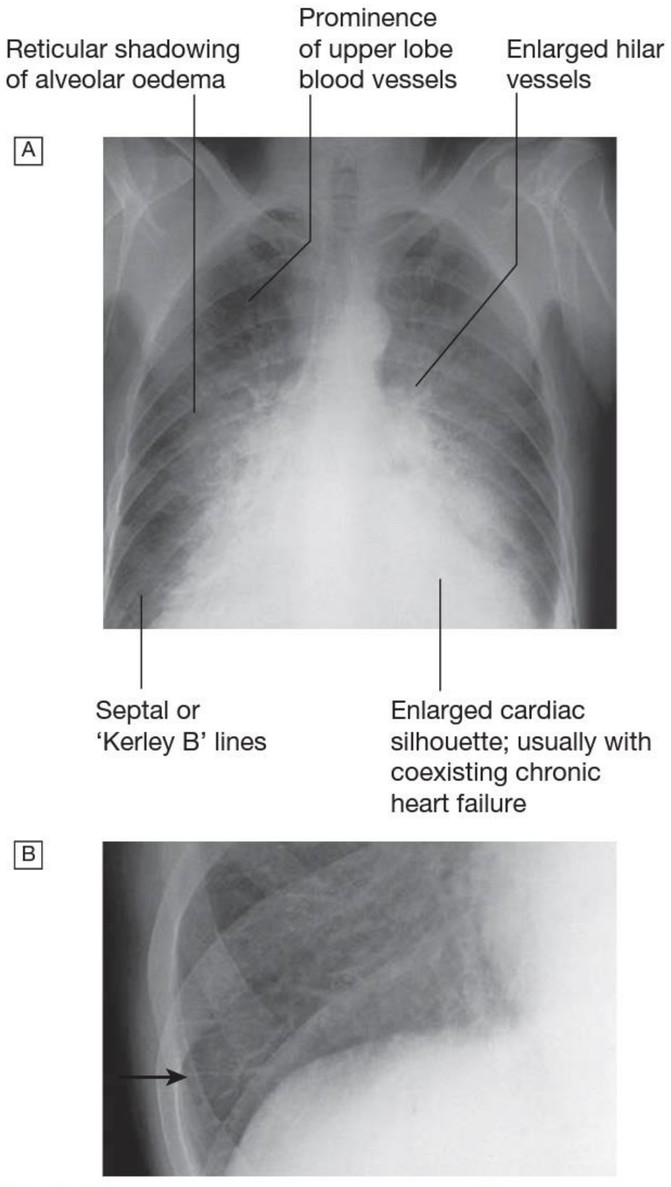
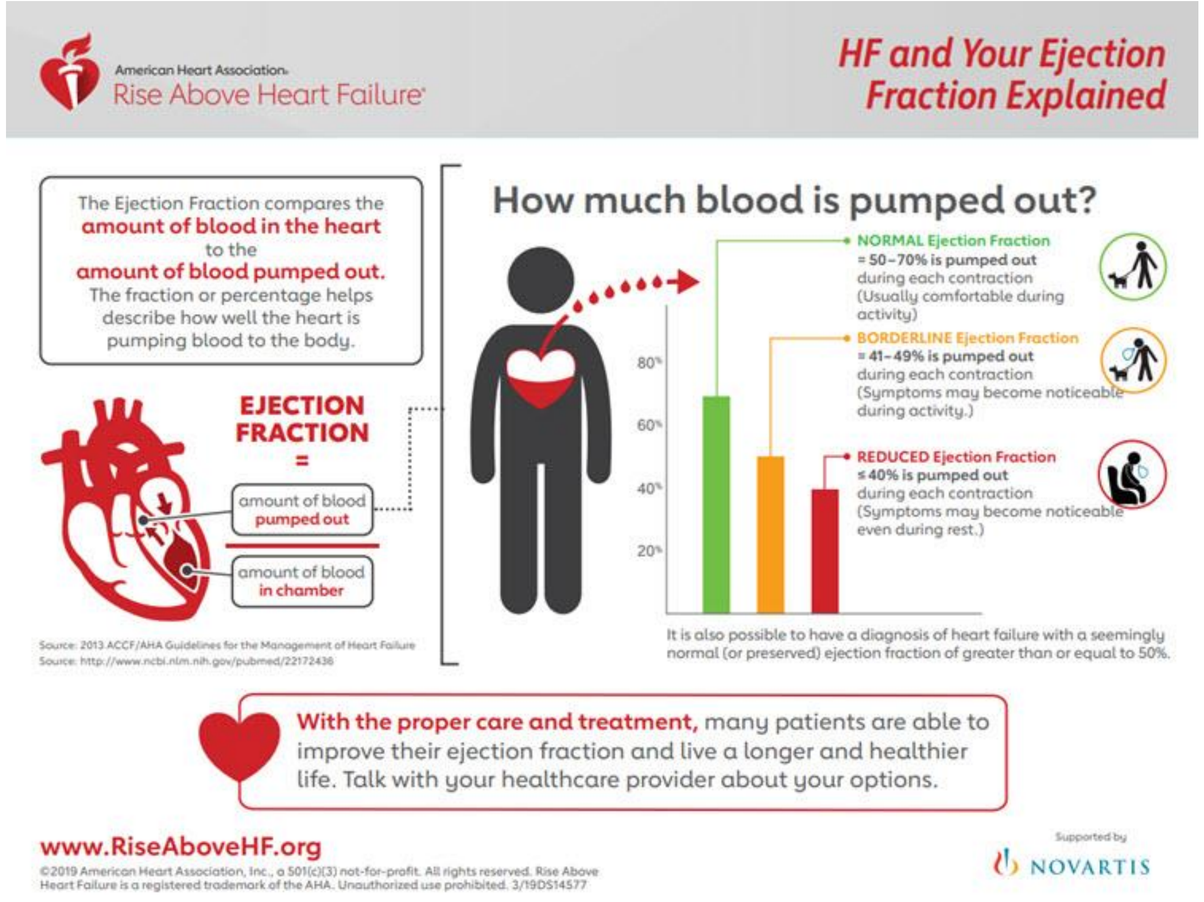
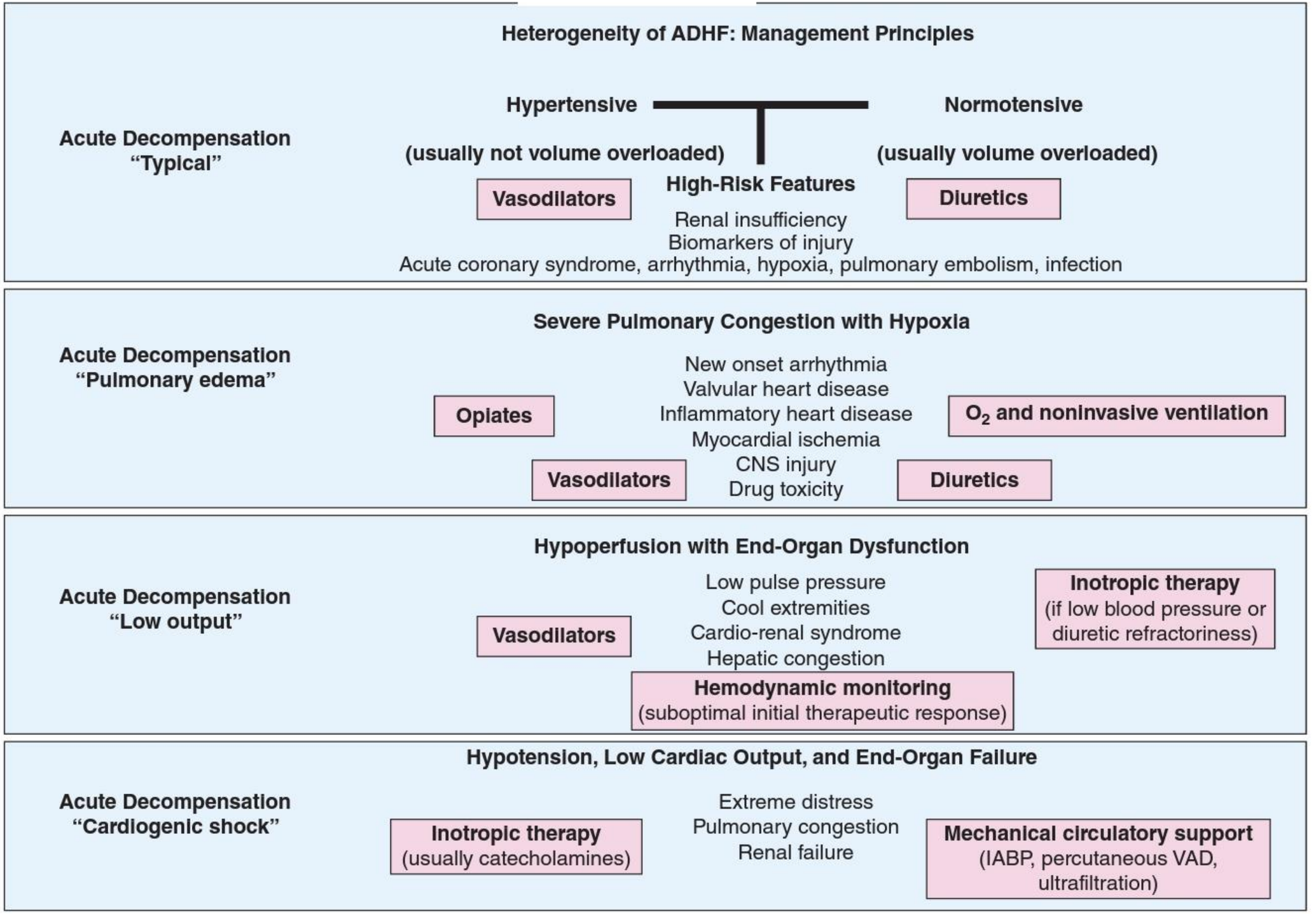


Fig. 16.27 Radiological features of heart failure. A Chest X-ray of a patient with pulmonary oedema. B Enlargement of lung base showing septal or 'Kerley B' lines (arrow).




Heterogeneity of ADHF: Management Principles
Acute Decompensation "Typical"
Hypertensive
(usually not volume overloaded)
Normotensive
(usually volume overloaded)
Vasodilators
High-Risk Features
Renal insufficiency
Biomarkers of injury
Acute coronary syndrome, arrhythmia, hypoxia, pulmonary embolism, infection
Diuretics
Severe Pulmonary Congestion with Hypoxia
Acute Decompensation "Pulmonary edema"
New onset arrhythmia
Valvular heart disease
Inflammatory heart disease
Myocardial ischemia
CNS injury
Drug toxicity
Opiates
O2 and noninvasive ventilation
Vasodilators
Diuretics
Hypoperfusion with End-Organ Dysfunction
Acute Decompensation "Low output"
Low pulse pressure
Cool extremities
Cardio-renal syndrome
Hepatic congestion
Vasodilators
Inotropic therapy
(if low blood pressure or diuretic refractoriness)
Hemodynamic monitoring
(suboptimal initial therapeutic response)
Hypotension, Low Cardiac Output, and End-Organ Failure
Acute Decompensation "Cardiogenic shock"
Extreme distress
Pulmonary congestion
Renal failure
Inotropic therapy
(usually catecholamines)
Mechanical circulatory support
(IABP, percutaneous VAD, ultrafiltration)

16.15 Management of acute pulmonary oedema

Action	Effect
Sit the patient up	Reduces preload
Give high-flow oxygen	Corrects hypoxia
Ensure continuous positive airway pressure (CPAP) of 5–10 mmHg by tight-fitting mask	Reduces preload and pulmonary capillary hydraulic gradient
Administer nitrates:* IV glyceryl trinitrate (10–200 μg/min) Buccal glyceryl trinitrate 2–5 mg	Reduces preload and afterload
Administer a loop diuretic: Furosemide (50–100 mg IV)	Combats fluid overload

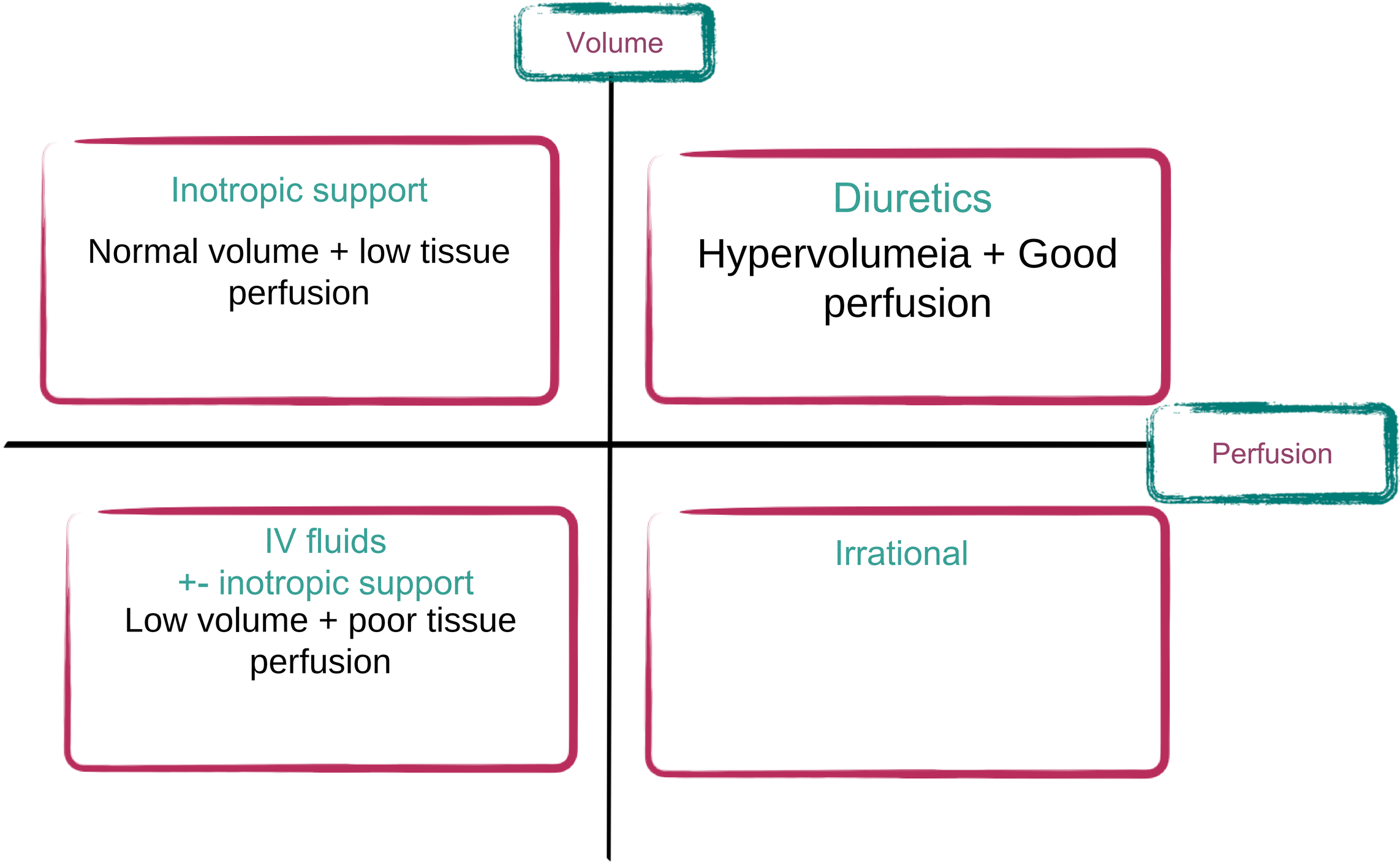
*The dose of nitrate should be titrated upwards every 10 mins until there is an improvement or systolic blood pressure is <110 mmHg.

Perfusion axis

- Bp
- Capillary refilling
- Temperature
- Skin color

Volume axis

- JVP
- Basil crackles
- Pleural effusions
- Ascites
- Leg edema
- Mucous membrane


Volume
Inotropic support
Normal volume + low tissue perfusion
Diuretics
Hypervolumeia + Good perfusion
Perfusion
IV fluids
+- inotropic support
Low volume + poor tissue perfusion
Irrational

- **Management of acute heart failure**

Acute heart failure with pulmonary oedema is a medical emergency that should be treated urgently. The patient should initially be kept rested upright, with continuous monitoring of cardiac rhythm, BP and pulse oximetry. Intravenous opiates can be of value in distressed patients but must be used sparingly, as they may cause respiratory depression and exacerbation of hypoxaemia and hypercapnia.

If these measures prove ineffective, inotropic agents such as dobutamine (2.5–10 μg/kg/min) may be required to augment cardiac output, particularly in hypotensive patients. An intra-aortic balloon pump may be beneficial in patients with acute cardiogenic pulmonary oedema and shock.

Chronic heart failure

- Patients with chronic heart failure commonly follow a relapsing and remitting course, with periods of stability and episodes of decompensation, leading to worsening symptoms that may necessitate hospitalisation. The clinical picture depends on the nature of the underlying heart disease, the type of heart failure that it has evoked, and the changes in the SNS and RAAS that have developed . Low cardiac output causes **fatigue and poor effort tolerance**; the peripheries are cold and the BP is low. To maintain perfusion of vital organs, blood flow is diverted away from skeletal muscle and this may contribute to fatigue and weakness. **Poor renal perfusion leads to oliguria and uraemia**. Pulmonary oedema due to left heart failure presents with dyspnoea and inspiratory crepitations over the lung bases. In contrast, right heart failure produces a **high JVP with hepatic congestion and dependent peripheral oedema.** In ambulant patients the oedema affects the lower legs, whereas in bed-bound patients it collects around the thighs and sacrum. Ascites or pleural effusion may occur . Heart failure is not the only cause of oedema . Chronic heart failure is sometimes associated with marked weight loss (**cardiac cachexia**), caused by a combination of anorexia and impaired absorption due to gastrointestinal congestion, poor tissue perfusion due to a low cardiac output, and skeletal muscle atrophy due to immobility.

16.14 Differential diagnosis of peripheral oedema

- Cardiac failure: right or combined left and right heart failure, pericardial constriction, cardiomyopathy
- Chronic venous insufficiency: varicose veins
- Hypoalbuminaemia: nephrotic syndrome, liver disease, protein-losing enteropathy; often widespread, can affect arms and face
- Drugs:
  - Sodium retention: fludrocortisone, non-steroidal anti-inflammatory drugs
  - Increasing capillary permeability: nifedipine, amlodipine
- Idiopathic: women > men
- Chronic lymphatic obstruction

Complications of heart failure

- **Renal failure** is caused by poor renal perfusion due to low cardiac output and may be exacerbated by diuretic, ACE inhibitor and angio tensin receptor blocker (ARB) therapies.

- **Hypokalaemia** may be caused by potassium-losing diuretics, and also by hyperaldosteronism due to activation of the renin–angiotensin system and impairment of aldosterone metabolism from hepatic congestion. Most of the body's potassium is intracellular and there may be substantial depletion of potassium stores, even when the plasma concentration is in the reference range.

- **Hyperkalaemia** may be due to the effects of drugs that promote renal resorption of potassium, in particular the combination of ACE inhibitors, ARBs and mineralocorticoid receptor antagonists. These effects are amplified if there is renal dysfunction due to low cardiac output or atherosclerotic renal vascular disease.

- **Hyponatraemia** is a feature of severe heart failure and is a poor prognostic sign. It may be caused by diuretic therapy, inappropriate water retention due to high vasopressin secretion, or failure of the cell membrane ion pump due to intracellular energy depletion.

- **Impaired liver function** is caused by hepatic venous congestion and poor arterial perfusion, which frequently cause mild jaundice and abnormal liver function tests; reduced synthesis of clotting factors can make anticoagulant control difficult.

- **Thromboembolism**. Deep vein thrombosis and pulmonary embolism may occur due to the effects of low cardiac output and enforced immobility. Systemic embolism, including stroke, occurs in patients with atrial fibrillation or flutter, or with intracardiac thrombus complicating mitral stenosis, MI or left ventricular aneurysm.

- **Atrial and ventricular arrhythmias** are very common and may be related to electrolyte changes such as hypokalaemia and hypomagnesaemia, myocardial fibrosis and the pro-arrhythmic effects of sympathetic activation. Atrial fibrillation occurs in approximately 20% of patients with heart failure and causes further impairment of cardiac function. Ventricular ectopic beats and non-sustained ventricular tachycardia are common findings in patients with heart failure and are associated with an adverse prognosis.

- **Sudden death** occurs in up to 50% of patients with heart failure and is most often due to ventricular fibrillation

Long Term Management Of Heart Failure

- The aims of treatment in chronic heart failure are to improve cardiac function by increasing contractility and coordination of the myocardium, by optimising preload or decreasing afterload, and controlling cardiac rate and rhythm .

- This can be achieved by using drug treatments, implantable device therapy, coronary revascularisation, and in resistant cases, mechanical assist devices or cardiac transplantation.

16.16 General measures for the management of heart failure

Education

- Explanation of nature of disease, treatment and self-help strategies

Diet

- Good general nutrition and weight reduction for the obese
- Avoidance of high-salt foods and added salt, especially for patients with severe congestive heart failure

Alcohol

- Moderation or elimination of alcohol consumption; alcohol-induced cardiomyopathy requires abstinence

Smoking

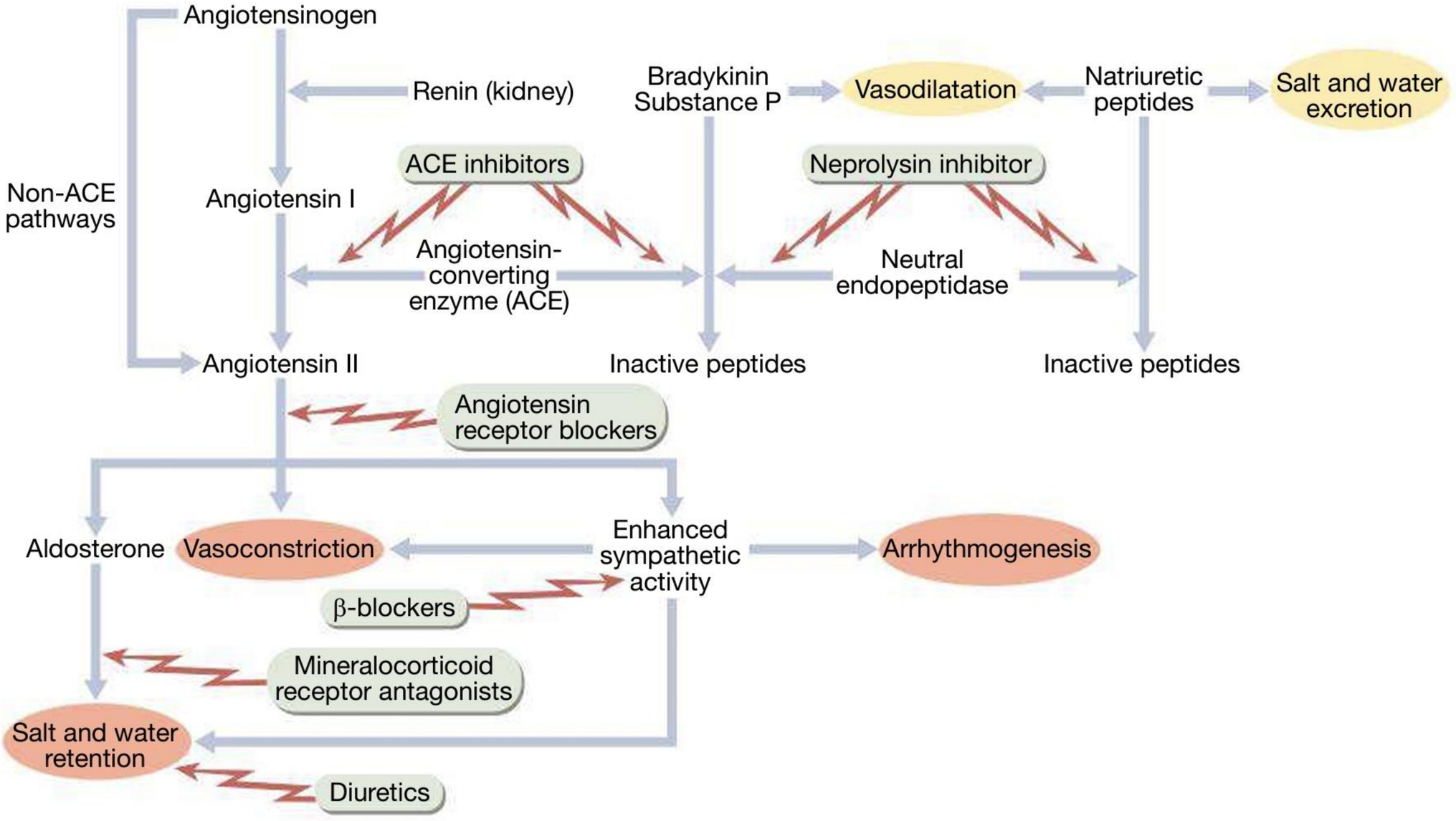
- Cessation

Exercise

- Regular moderate aerobic exercise within limits of symptoms

Vaccination

- Consideration of influenza and pneumococcal vaccination


Angiotensinogen
Renin (kidney)
Bradykinin
Substance P
Vasodilatation
Natriuretic
peptides
Salt and water
excretion
Non-ACE
pathways
Angiotensin I
ACE inhibitors
Neprolysin inhibitor
Angiotensin-
converting
enzyme (ACE)
Neutral
endopeptidase
Angiotensin II
Inactive peptides
Inactive peptides
Angiotensin
receptor blockers
Aldosterone
Vasoconstriction
Enhanced
sympathetic
activity
Arrhythmogenesis
β-blockers
Mineralocorticoid
receptor antagonists
Salt and water
retention
Diuretics

- **Diuretics**

Diuretics **promote urinary sodium and water excretion, leading to a reduction in blood plasma volume**, which in turn **reduces preload** and improves pulmonary and systemic venous congestion. They may also **reduce afterload and ventricular volume**, leading to a fall in ventricular wall tension and increased cardiac efficiency iency. Although a fall in preload (ventricular folling pressure) normally reduces cardiac output, patients with heart failure are beyond the apex of the Starling curve, so there may be a substantial and beneficial cial fall in filling pressure with either no change or an improvement in cardiac output . Over-diuresis can cause excessive volume depletion, resulting in a fall in cardiac output with hypotension, lethargy and renal failure. This is especially likely in patients with a marked diastolic component to their heart failure .

Oedema may persist, despite oral loop diuretic therapy, in some patients with severe chronic heart failure, particularly if there is renal impairment. Under these circumstances an intravenous infusion of a loop diuretic, such as furosemide (5–10 mg/hr), may initiate a diuresis. Combining this with a thiazide diuretic, such as bendroflumethiazide (5 mg daily), may augment the diuresis but care must be taken to avoid an excessive fluid loss, **hyponatraemia** and **hypokalaemia**.

- **Mineralocorticoid receptor antagonists**, such as spironolactone and eplerenone, are potassium-sparing diuretics that are of particular benefit in patients with heart failure with severe left ventricular systolic dysfunction. **They improve long-term clinical outcome in individuals with severe heart failure or heart failure following acute MI** but may cause hyperkalaemia, particularly when used with an ACE inhibitor.

- Originally developed as a treatment for type 2 diabetes mellitus, sodium-glucose co-transporter 2 (SGLT-2) inhibitors block the resorption of glucose in the nephron of the kidney to cause an osmotic diuresis. Their use is associated with reduced hospitalisations for heart failure and lower mortality in patients with heart failure irrespective of the presence of diabetes. However, they are associated with an increased risk of genitourinary tract infections and diabetic ketoacidosis.

- **Angiotensin-converting enzyme inhibitors**

Angiotensin-converting enzyme (ACE) inhibitors **play a central role in the management of heart failure since they interrupt the vicious circle of neurohumoral activation that is characteristic of the disease by preventing the conversion of angiotensin I to angiotensin II**. This, in turn, **reduces peripheral vasoconstriction**, activation of the sympathetic nervous system , and salt and water retention due to aldosterone release, as well as preventing the activation of the renin–angiotensin system caused by diuretic therapy. In moderate and severe heart failure, ACE inhibitors can produce a substantial improvement in effort tolerance and in mortality. **They can also improve outcome and prevent the onset of overt heart failure in patients with poor residual left ventricular function following MI.** Adverse effects of ACE inhibitors include hypotension and renal impairment, especially in patients with bilateral renal artery stenosis or those with pre-existing renal disease. An increase in serum potassium concentration may also occur, which can be beneficial in offsetting the hypokalaemia associated with loop diuretic therapy. In stable patients without hypotension (systolic BP over 100 mmHg), ACE inhibitors can usually be safely started in the community. In other patients, however, it is usually advisable to withhold diuretics for 24 hours before starting treatment with a small dose of a long-acting agent, preferably given at night). Renal function and serum potassium must be monitored and should be checked 1–2 weeks after starting therapy.

- **Angiotensin receptor blockers**

Angiotensin receptor blockers (ARBs) act by blocking the action of angiotensin II on the heart, peripheral vasculature and kidneys. **In heart failure they produce beneficial haemodynamic changes similar to those of ACE inhibitors but are generally better tolerated.** They have comparable effects on mortality and are a useful alternative for patients who cannot tolerate ACE inhibitors. They should be started at a low dose and titrated upwards, depending on response . Unfortunately, they share all the more serious adverse effects of ACE inhibitors, including renal dysfunction and hyperkalaemia. While ARB are normally used as an alternative to ACE inhibitors, they can be combined in patients with resistant or recurrent heart failure.

- **Neprilysin inhibitors** The only drug currently in this class is sacubitril, a small-molecule inhibitor of neutral endopeptidase, or neprilysin, which is responsible for the breakdown of the endogenous diuretics ANP and BNP as well as vasoactive peptides such as bradykinin and substance P . If used in combination with the ARB in an initial oral dose of 24 mg **sacubitril** and 26 mg valsartan daily, it produces additional symptomatic and mortality benefits over ACE inhibition and is increasingly being used in preference to ACE inhibitors in patients with chronic heart failure.

- **Vasodilators** These drugs are valuable in chronic heart failure, when ACE inhibitors or ARBs are contraindicated. Venodilators, such as nitrates, reduce preload. Arterial dilators, such as hydralazine, reduce afterload . Their use is limited by pharmacological tolerance and hypotension.

- **Beta-adrenoceptor antagonists (β-blockers):** Beta-blockade helps to counteract the deleterious effects of enhanced sympathetic stimulation and reduces the risk of arrhythmias and sudden death. When initiated in standard doses β-blockers may precipitate acute-on-chronic heart failure, but when given in small incremental doses they can increase ejection fraction, improve symptoms, reduce the frequency of hospitalisation and reduce mortality in patients with chronic heart failure. A typical regimen is bisoprolol, starting at 1.25 mg daily and increased gradually over 12 weeks to a target maintenance dose of 10 mg daily. Beta-blockers are more effective at reducing mortality than ACE inhibitors, with a relative risk reduction of 33% versus 20%, respectively.

- **Ivabradine** acts on the I f inward current in the SA node, resulting in reduction of heart rate. Typical dosages are 2.5–5 mg twice daily, increasing to 7.5 mg twice daily if necessary. It reduces hospital admission and mortality rates in patients with heart failure due to moderate or severe left ventricular systolic impairment. In trials, its effects were most marked in patients with a relatively high heart rate (over 77/min), so ivabradine is best suited to patients who cannot take β-blockers or whose heart rate remains high despite β-blockade. It is ineffective in patients with atrial fibrillation .

- **Digoxin** in maintenance doses of 0.0625–0.25 mg daily can be used to provide rate control in patients with heart failure and atrial fibrillation. In patients with severe heart failure (NYHA class III–IV, digoxin reduces the likelihood of hospitalisation for heart failure, although it has no effect on long-term survival.

- **Amiodarone** is a potent anti-arrhythmic drug that has little negative inotropic effect and may be valuable in patients with poor left ventricular function. It is effective only in the treatment of symptomatic arrhythmias and should not be used as a preventative agent in asymptomatic patients. Amiodarone is used for prevention of symptomatic atrial arrhythmias and of ventricular arrhythmias when other pharmacological options have been exhausted.

Non pharmacological treatment

- **Implantable cardiac defibrillators** :These devices are indicated in patients with heart failure who have had, or who are at high risk of, life-threatening ventricular arrhythmias, since they reduce the risk of sudden death. Cardiac resynchronisation therapy devices In patients with marked conduction system disease, especially left bundle branch block, there is uncoordinated left ventricular contraction which exacerbates heart failure.

- **Cardiac resynchronisation therapy (CRT)** : uses pacemaker technology to overcome dyssynchronous contraction by pacing the LV and RV simultaneously . This improves cardiac output and is associated with improved symptoms and reduced mortality.

- **Coronary revascularisation** :Coronary artery bypass surgery or percutaneous coronary intervention may improve function in areas of the myocardium that are ‘hibernating’ because of inadequate blood supply, and can be used to treat carefully selected patients with heart failure and coronary artery disease. If necessary, ‘hibernating’ myocardium can be identified by stress echocardiography and specialised nuclear or magnetic resonance imaging.

- **Cardiac transplantation**

Cardiac transplantation is an established and successful treatment for patients with intractable heart failure. Coronary artery disease and dilated cardiomyopathy are the most common indications. The use of transplantation is limited by the efficacy of modern drug and device therapies, as well as the availability of donor hearts, so it is generally reserved for young patients with severe symptoms despite optimal therapy. Conventional heart transplantation is contraindicated in patients with pulmonary vascular disease due to long-standing left heart failure, complex congenital heart disease such as Eisenmenger syndrome, or primary pulmonary hypertension because the RV of the donor heart may fail in the face of high pulmonary vascular resistance. However, heart–lung transplantation can be successful in patients with Eisenmenger syndrome, and lung transplantation has been used for primary pulmonary hypertension. Although cardiac transplantation usually produces a dramatic improvement in the recipient's quality of life,

- **serious complications may occur:**

- **Rejection**. In spite of routine therapy with ciclosporin A, azathioprine and corticosteroids, episodes of rejection are common and may present with heart failure, arrhythmias or subtle ECG changes. Cardiac biopsy is often used to confirm rm the diagnosis before starting treatment with high-dose corticosteroids.

- **Accelerated atherosclerosis**. Recurrent heart failure is often due to progressive atherosclerosis in the coronary arteries of the donor heart. This is not confined to patients who underwent transplantation for coronary artery disease and is probably a manifestation of chronic rejection. Angina is rare because the heart has been denervated.

- **Infection**. Opportunistic infection with organisms such as cytomegalovirus or Aspergillus remains a major cause of death in transplant recipients.

- **Ventricular assist devices** Because of the limited supply of donor organs, ventricular assist devices (VAD) may be employed as a bridge to cardiac transplantation and as short-term restoration therapy following a potentially reversible insult such as viral myocarditis. In some patients, VADs may be used as a long-term therapy if no other options exist. These devices assist cardiac output by using a roller, centrifugal or pulsatile pump that, in some cases, is implantable and portable. They withdraw blood through cannulae inserted in the atria or ventricular apex and pump it into the pulmonary artery or aorta. They are designed not only to unload the ventricles but also to provide support to the pulmonary and systemic circulations. Their more widespread application is limited by high complication rates (haemorrhage, systemic embolism, infection, neurological and renal sequelae), although some improvements in survival and quality of life have been demonstrated in patients with severe heart failure.

Long term management

- Diuretic therapy

A. Loop diuretic : sodium and water excretion—> decrease plasma volume—> decrease preload—> improves venous congestion… fall in bp .(furosemide, Bumetanide, Torasemide)

B. Thiazides……. can be combined with loop diuretic but we should take care to avoid excessive diuresis

C. Mineralocorticoid receptor antagonists(spironolactone , eplerenone) **improve long-term clinical outcome in individuals with severe heart failure or heart failure following acute MI but may cause hyperkalaemia, particularly when used with an ACE inhibitor.**

D. sodium-glucose co-transporter 2 (SGLT-2) == osmotic diuresis … reduces hospitalization

- ACEI : **play a central role in the management of heart failure since they interrupt the vicious circle of neurohumoral activation**

- **improve outcome and prevent the onset of overt heart failure in patients with poor residual left ventricular function following MI.**

- **Side effects: symptomatic hypotension (first dose) , renal impairment , hyperkalemia ,,, Cough**

- **ARB** : similar effects of the ACEI

- Side effects similar to ACEI except well tolerated and no cough

- Neprilysin inhibitors The only drug currently in this class is sacubitril, a small-molecule inhibitor of neprilysin, which is responsible for the breakdown of the endogenous diuretics ANP and BNP. Used in combination with the ARB valsartan (sacubitril–valsartan), it has been shown to produce additional symptomatic and mortality benefit over ACE inhibition and is now recommended in the management of resistant heart failure.

- **Beta - blockers** : counteract the deleterious effects of enhanced sympathetic stimulation and reduces the risk of arrhythmias and sudden death .

- Cardioselective beta blocker (bisoprolol , metoprolol succinate, carvedolol , atenolol)

- Contraindications (asthma, bradycardia, patient taking Calicium channel blocker)

- Digoxin…. Not used except in HF associated with AF , or NYAHA III, IV
- Ivabradine (reduces the HR when BB is contraindicated) , reduces hospital admission in patient with moderate to severe HF
- Amiodarone : treatment and prevention of arrhythmias