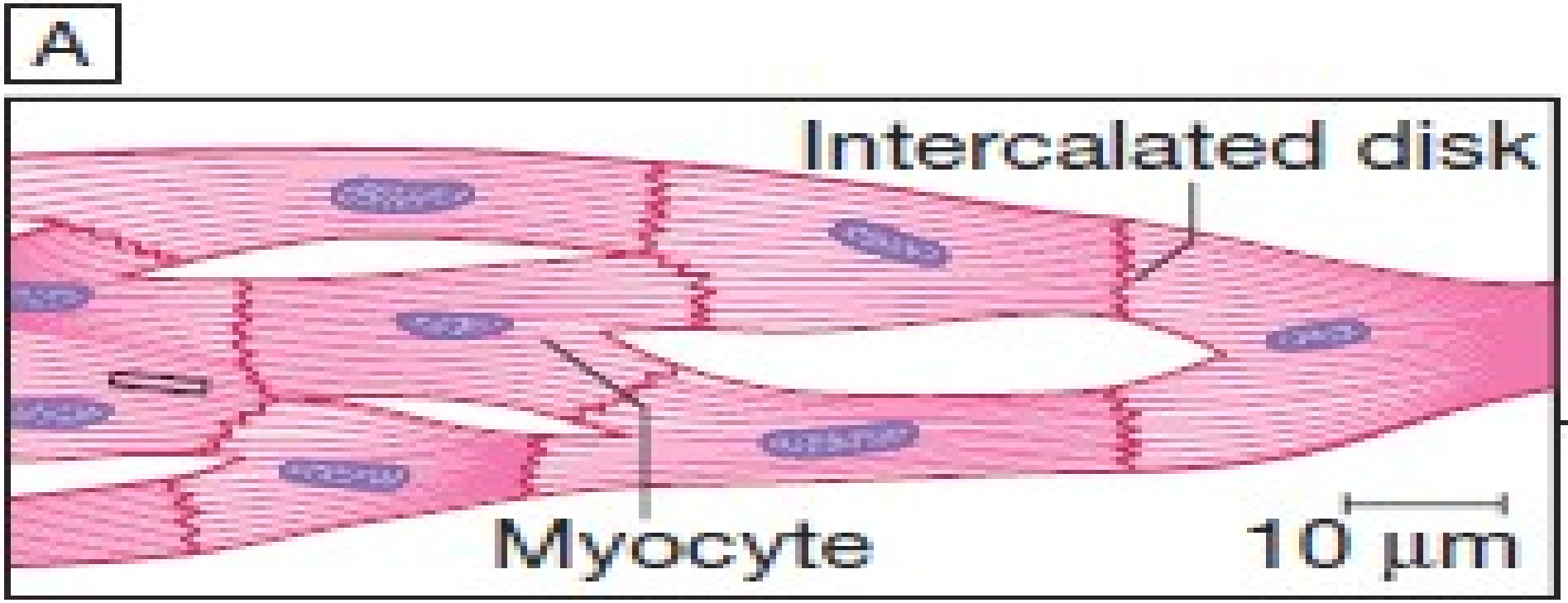
DISEASES OF THE MYOCARDIUM

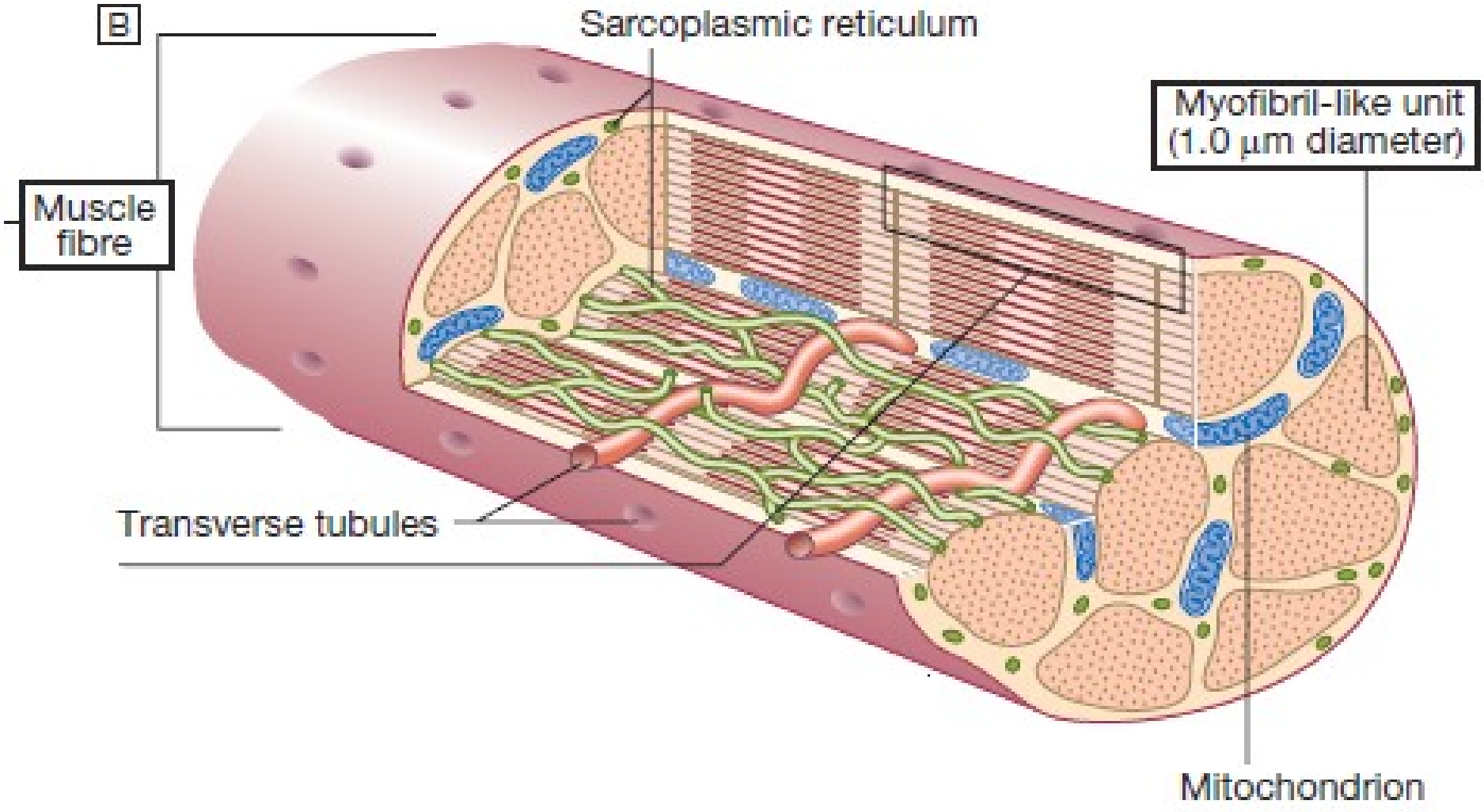
Learning objectives

- 1-Histology and physiology
- 2-Causes of myocarditis
- 3-Clinical features of myocarditis
- 4-Investigations
- 5-Management and prognosis in myocarditis
- 6-Types and pathophysiology of each type of cardiomyopathy
- 7-Causes of cardiomyopathy
- 8-Presentations
- 9-Investigations
- 10-Treatment

Myocardial contraction

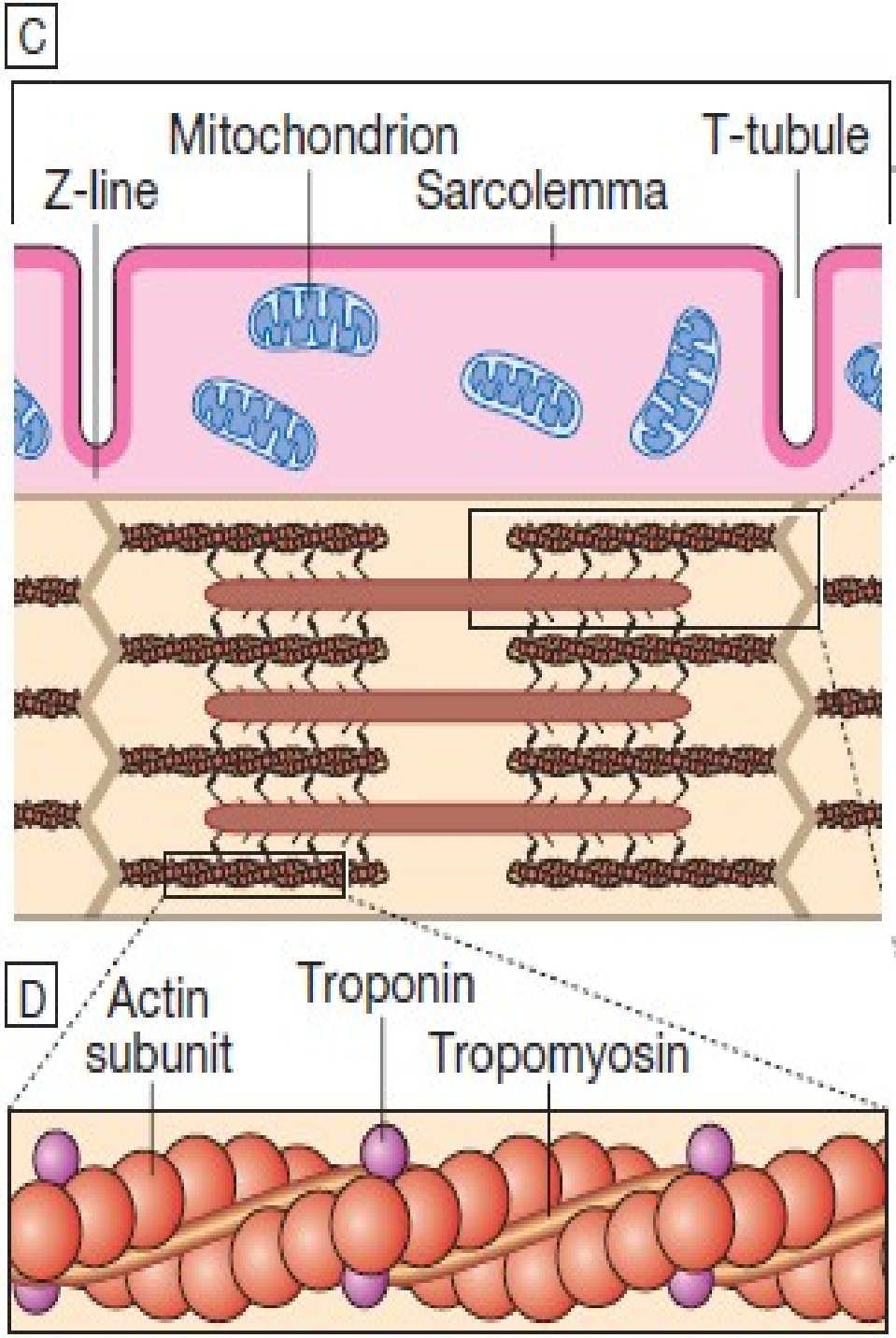


A- Myocardial cells (myocytes) are about 50–100 µm long; each cell branches and interdigitates with adjacent cells. Myocytes are joined together through intercalated Discs, an intercalated disc permits electrical conduction via gap junctions, and mechanical conduction via the fascia adherens, to adjacent cells



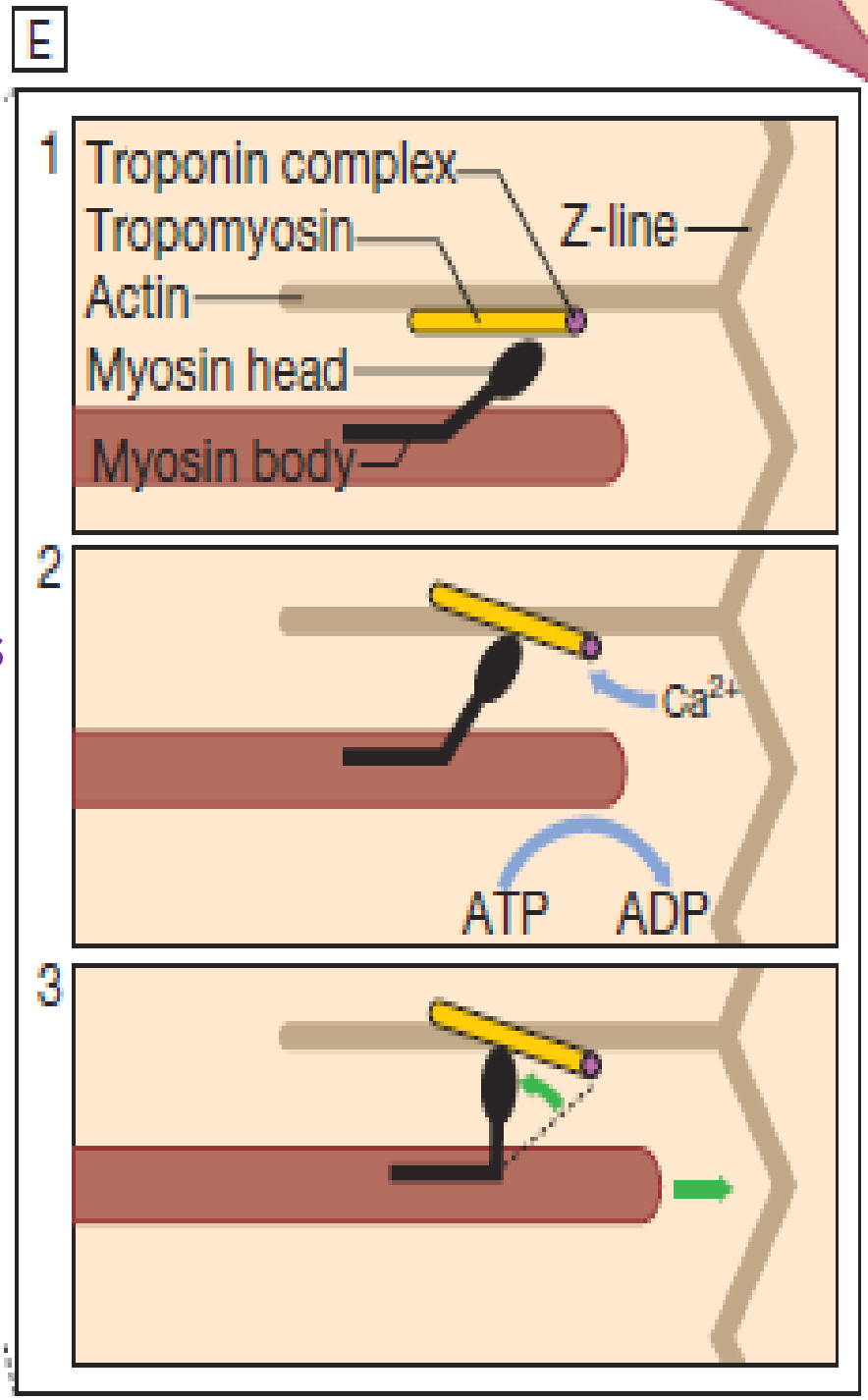
B- Within the myocytes, myofibrils are composed of longitudinal and transverse tubules extending from the sarcoplasmic reticulum.

The basic unit of contraction is the sarcomere (2 µm long), which is aligned to those of adjacent myofibrils, giving a striated appearance due to the Z-lines. Actin filaments are attached at right angles to the Z-lines and interdigitate with thicker parallel myosin filaments. C- The expanded section shows a schematic of an individual sarcomere with thick filaments composed of myosin and thin filaments composed primarily of actin. D- Actin filaments are composed of troponin, tropomyosin and actin subunits.



The cross-links between actin and myosin molecules contain myofibrillar adenosine triphosphatase (ATPase), which breaks down adenosine triphosphate (ATP) to provide the energy for contraction.

E- The three stages of contraction, resulting in shortening of the sarcomere. (1) The actin-binding site is blocked by tropomyosin. (2) ATP-dependent release of calcium ions, which bind to troponin, displacing tropomyosin. The binding site is exposed. (3) Tilting of the angle of attachment of the myosin head, resulting in fibre shortening. (ADP = adenosine diphosphate; ATP = adenosine triphosphate)



Myocarditis

This is an acute inflammatory condition that can have an infectious, toxic or autoimmune aetiology.

Causes:

1- Viral infections are the most common causes, such as Coxsackie and influenza A and B viruses. Susceptibility is increased by corticosteroid treatment, immunosuppression, radiation, previous myocardial damage and exercise. Some bacterial and protozoal infections may be complicated by myocarditis; for example Lyme disease (*Borrelia burgdorferi)*.

2- Toxic causes include drugs, which may directly injure the myocardium (e.g. cocaine, lithium and anti-cancer drugs, such as doxorubicin) or may cause a hypersensitivity reaction associated myocarditis (e.g. penicillins and sulphonamides, lead and carbon monoxide).

3- Autoimmune: such as systemic lupus erythematosus and rheumatoid arthritis.

Clinical features

Which classified by four distinct clinical presentations:

Fulminant myocarditis follows a viral prodrome or influenza-like illness, and results in severe heart failure or cardiogenic shock.

Acute myocarditis presents over a longer period with heart failure; it can lead to dilated cardiomyopathy.

Chronic active myocarditis is rare and associated with chronic myocardial inflammation.

Chronic persistent myocarditis is a focal myocardial infiltrates and can cause chest pain and arrhythmia without causing ventricular dysfunction.

Investigations:

In myocarditis ECG changes are common but nonspecific.

Biochemical markers of myocardial injury (e.g. troponin I and T, creatine kinase) may be elevated in the early phases.

Echocardiography may reveal left ventricular dysfunction that is sometimes regional (due to focal myocarditis).

Cardiac MRI may show diagnostic patterns of myocardial inflammation or infiltration.

Endomyocardial biopsy is sometimes used to confirm the diagnosis.

Management and prognosis

In most patients, myocarditis is self-limiting and the immediate prognosis is good. However, death may occur due to a ventricular arrhythmia or rapidly progressive heart failure.

Specific antimicrobial therapy may be used if a causative organism has been identified.

Treatment for cardiac failure or arrhythmias may be required and patients should be advised to avoid intense physical exertion because there is some evidence that this can induce potentially fatal ventricular arrhythmias.

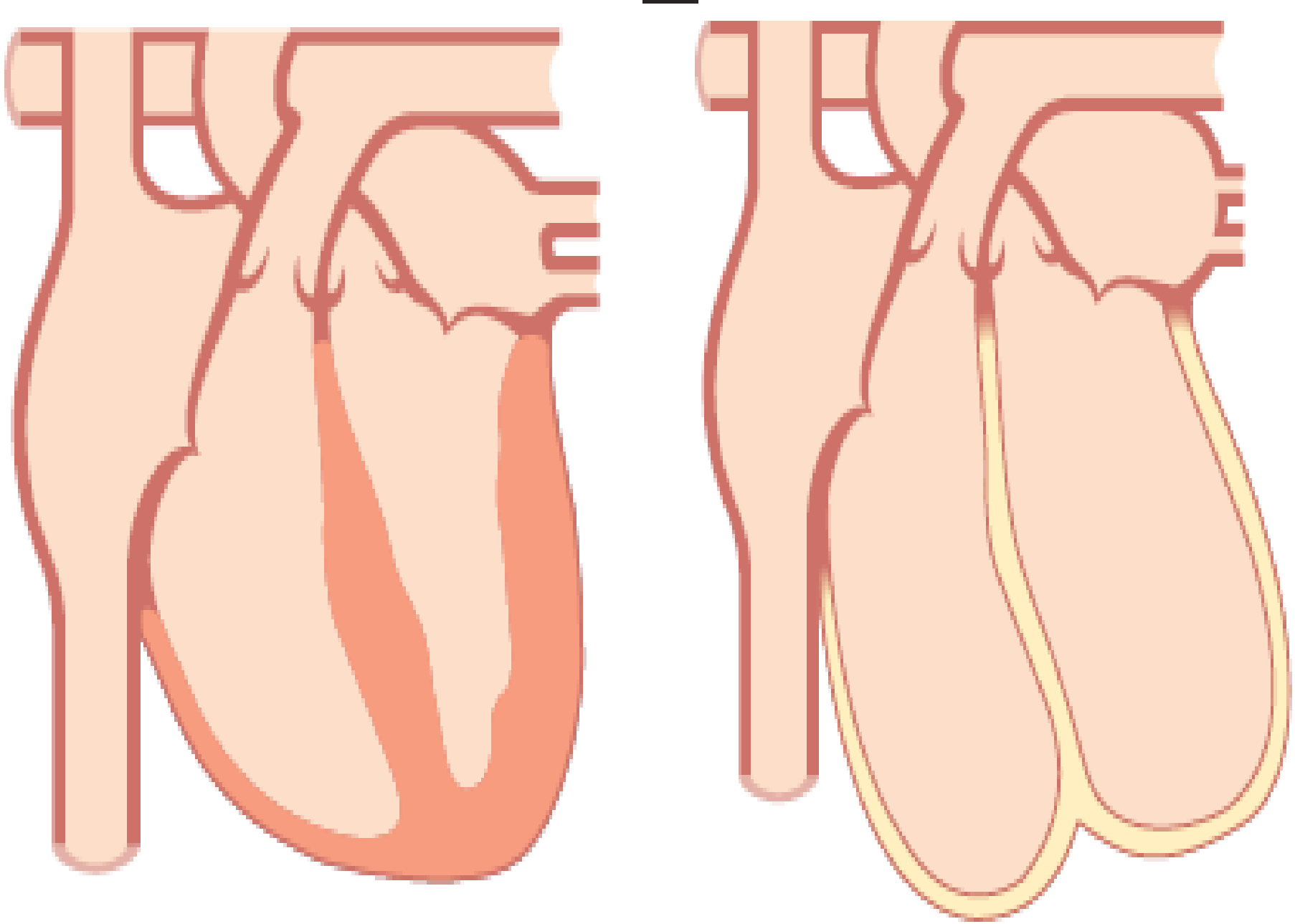
Cardiomyopathies

Cardiomyopathies are a heterogeneous group of diseases of the myocardium associated with structural and functional abnormalities.

1- Dilated cardiomyopathy:

This is characterised by dilatation and impaired contraction of the LV and often the RV, with reduce LV wall thickness and ‘functional’ mitral and tricuspid incompetence. A diagnosis of dilated cardiomyopathy should only be made when coronary artery disease has been excluded.

Histological changes are variable but include myofibrillary loss, interstitial fibrosis and T-cell infiltrates.



Normal heart

Dilated cardiomyopathy

Causes: Alcohol, autosomal dominant inheritance in 25%, X-linked inherited skeletal muscular dystrophies (e.g. Becker and Duchenne). Finally, a late autoimmune reaction to viral myocarditis.

Clinical features: Men are affected more than twice as often as women.

Most patients present with heart failure. The cardiac examination reveals a laterally displaced apex. S3 gallop is common; murmurs of mitral and tricuspid regurgitation are frequently heard because of dilation of the mitral and tricuspid annuli caused by ventricular enlargement. Crackles indicating pulmonary edema may be present over the lung fields.

Arrhythmia, thromboembolism and sudden death may occur at any stage.

Investigations: CXR: cardiomegaly, pulmonary venous congestion, and pleural effusions.

Serum B-type natriuretic peptide (BNP) levels are elevated.

ECG: nonspecific ST- and T-wave abnormalities.

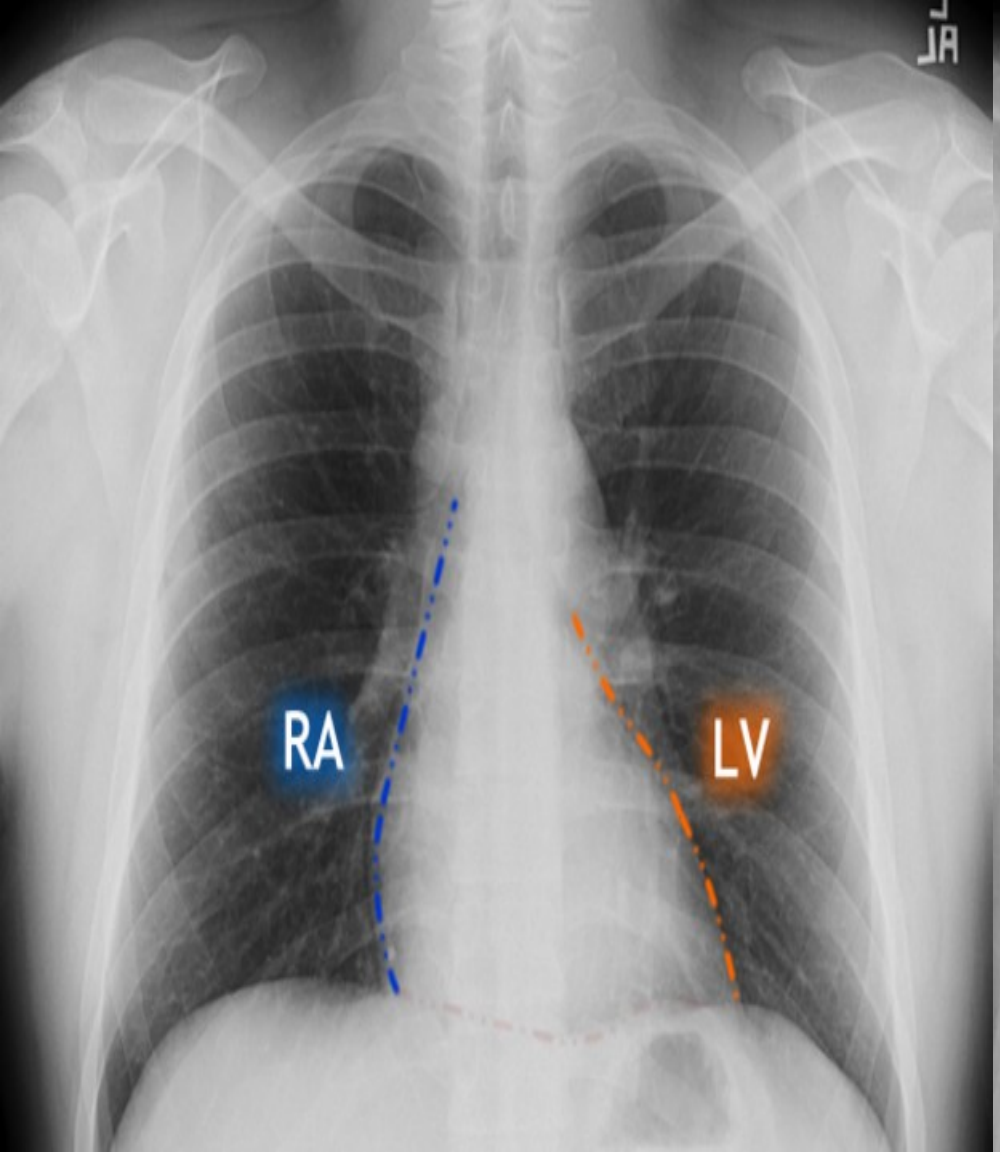
Echocardiography: assessment of ventricular size and function, valvular function, presence of a ventricular thrombus.

Similar information can be now obtained with MRI.

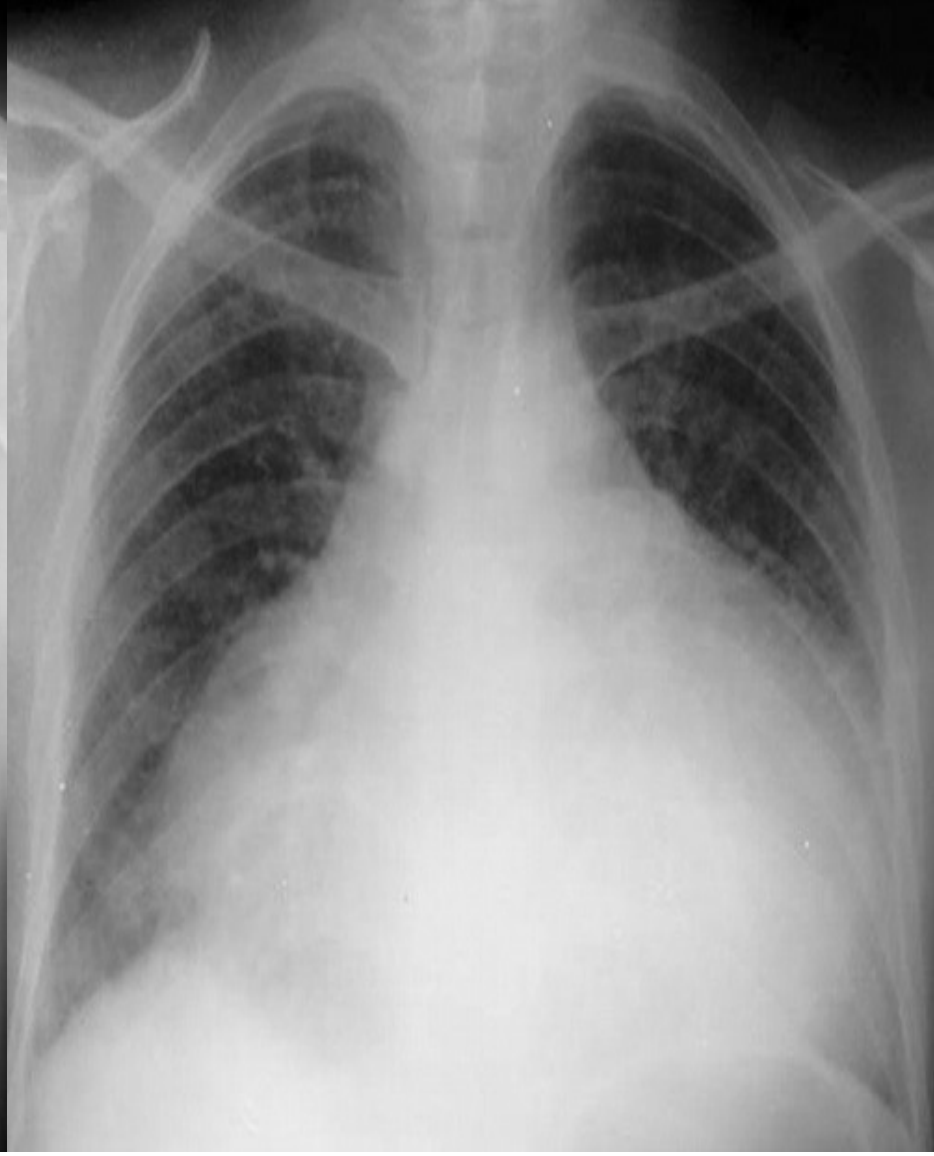
Treatment: is aimed at controlling the resulting heart failure.

The risk of sudden arrhythmic death is substantially reduced by medical therapy with β-blockers and angiotensin receptor. Some patients may be considered for implantation of a cardiac defibrillator and/or cardiac resynchronisation therapy

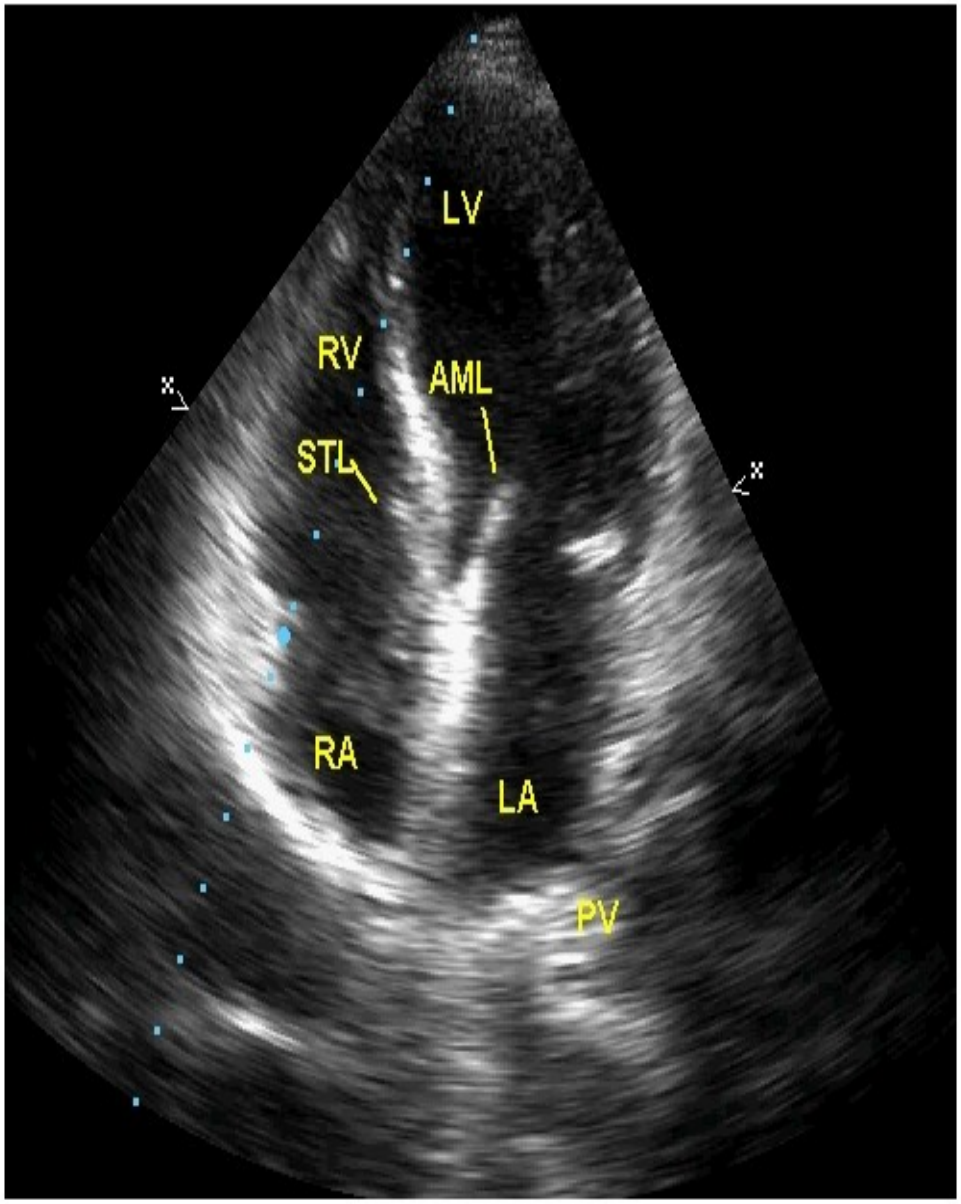
cardiac transplantation may be indicated.



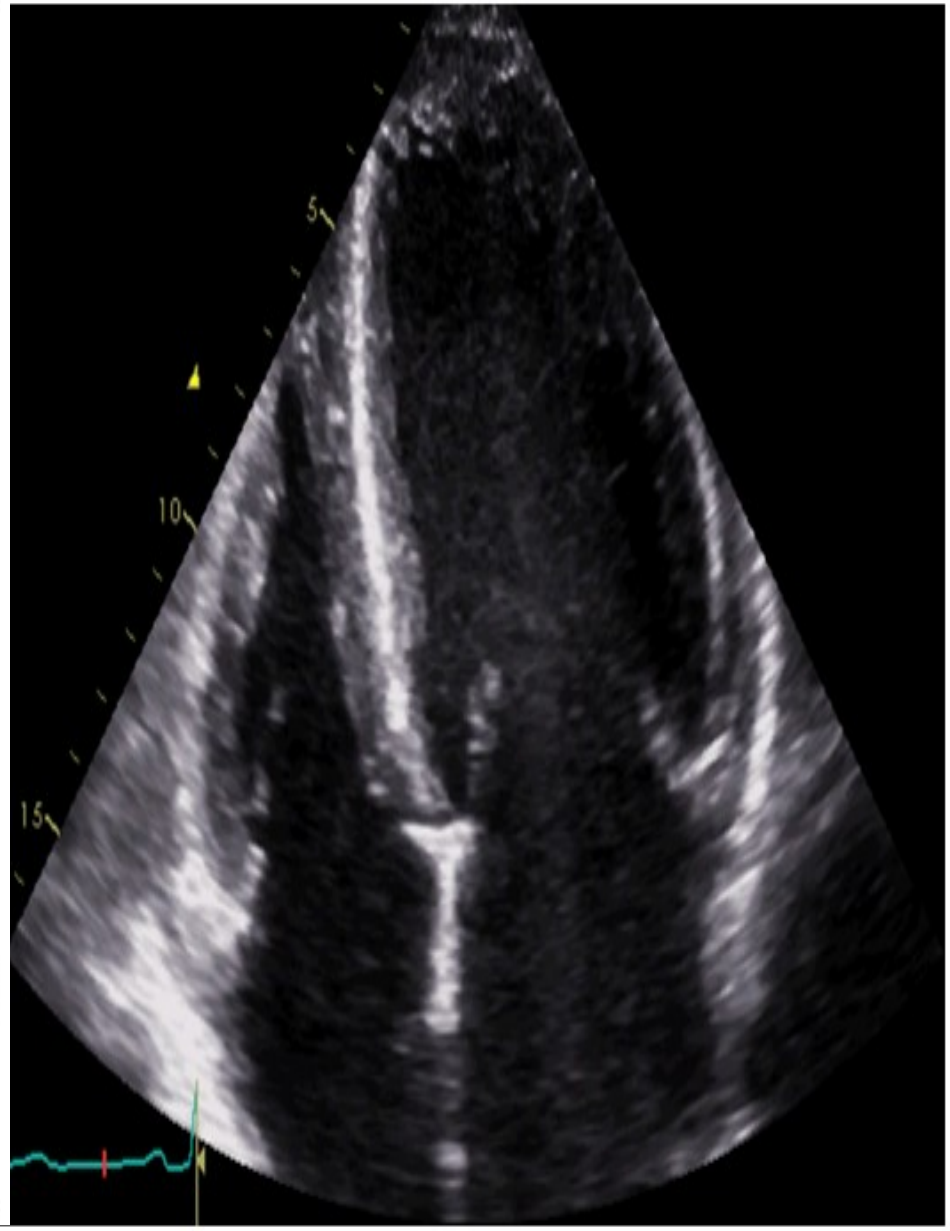
Chest x-ray normal heart borders and lungs



Chest x-ray of patient with dilated cardiomyopathy



Normal echocardiogram apical four chamber view



Echocardiography showing dilated chambers of the heart

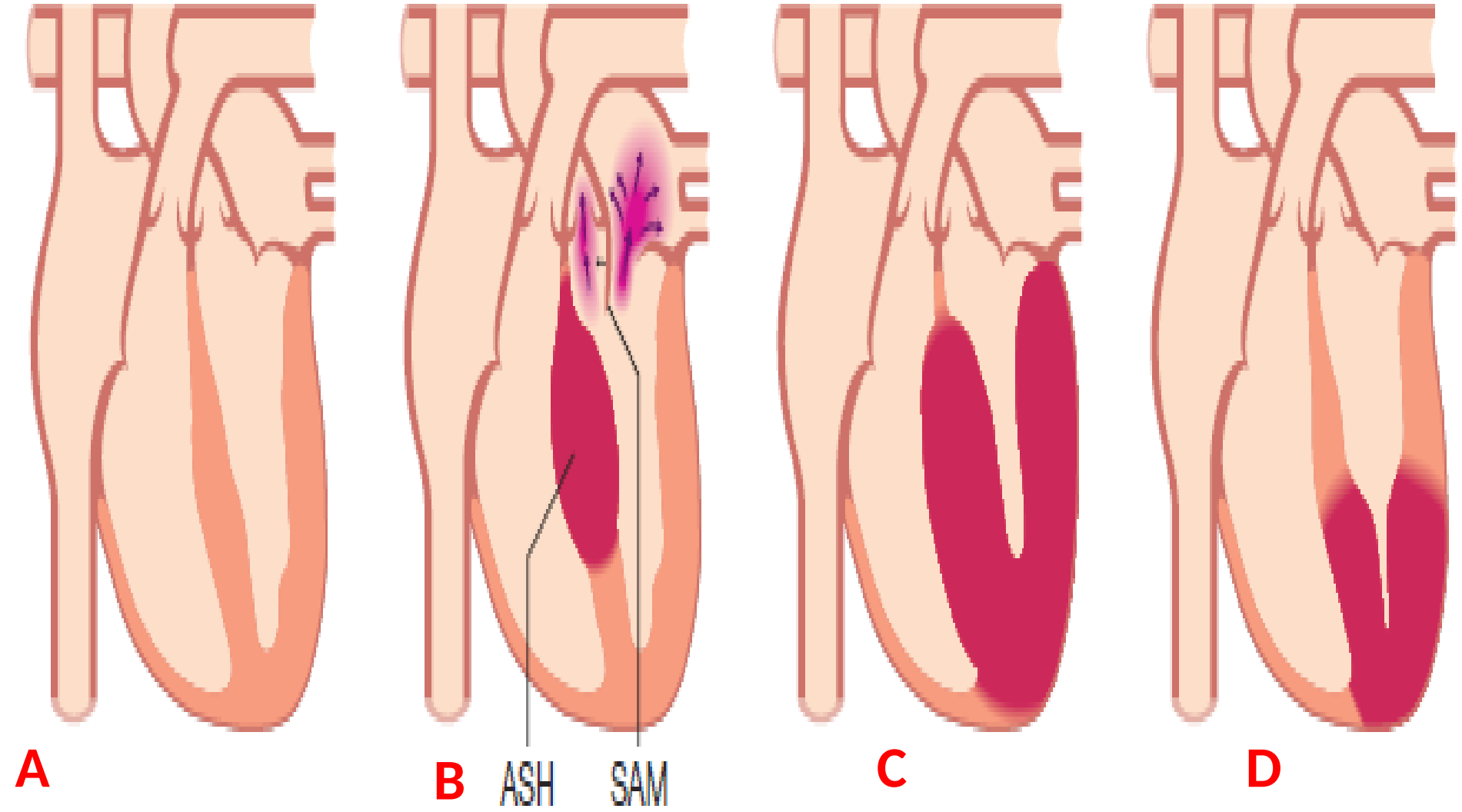
2- Hypertrophic cardiomyopathy

It is characterised by inappropriate and elaborate left ventricular hypertrophy with malalignment of the myocardial fibres and myocardial fibrosis.

The hypertrophy may be generalised or confined largely to the interventricular septum (asymmetric septal hypertrophy), or other regions e.g. apical hypertrophic cardiomyopathy, a variant which is common in the Far East.

It is the most common form of cardiomyopathy, with a prevalence of approximately 100 per 100 000.

Pathophysiology: Heart failure may develop because the stiff noncompliant ventricles impede diastolic filling. Septal hypertrophy may also cause dynamic left ventricular outflow tract obstruction (hypertrophic obstructive cardiomyopathy, HOCM) and mitral regurgitation due to abnormal systolic anterior motion of the anterior mitral valve leaflet. Sudden death typically occurs during or just after vigorous physical activity commonly due to ventricular arrhythmias.



A- Normal heart. B- Hypertrophic cardiomyopathy: asymmetric septal hypertrophy (ASH) with systolic anterior motion of the mitral valve (SAM), causing mitral reflux and dynamic left ventricular outflow tract obstruction. C- Hypertrophic cardiomyopathy: concentric hypertrophy. D- Hypertrophic cardiomyopathy: apical hypertrophy.

Causes: Hypertrophic cardiomyopathy is a genetic disorder, usually with autosomal dominant transmission. It is due to a single point mutation in one of the genes that encode sarcomeric contractile proteins.

There are three common groups of mutation with different phenotypes:

1. Beta-myosin heavy chain= associated with left ventricular hypertrophy.
2. Troponin mutations= associated with little, and sometimes even no, hypertrophy but marked myocardial fibre disarray, an abnormal vascular response (e.g. exercise-induced hypotension) and a high risk of sudden death.
3. Myosin-binding protein C mutations= present late in life and are often associated with hypertension and arrhythmia.

Clinical features: Symptoms and signs are similar to those of aortic stenosis, except that, in hypertrophic cardiomyopathy, the character of the arterial pulse is jerky.

Symptoms

- Angina on effort
- Dyspnoea on effort
- Syncope on effort
- Sudden death

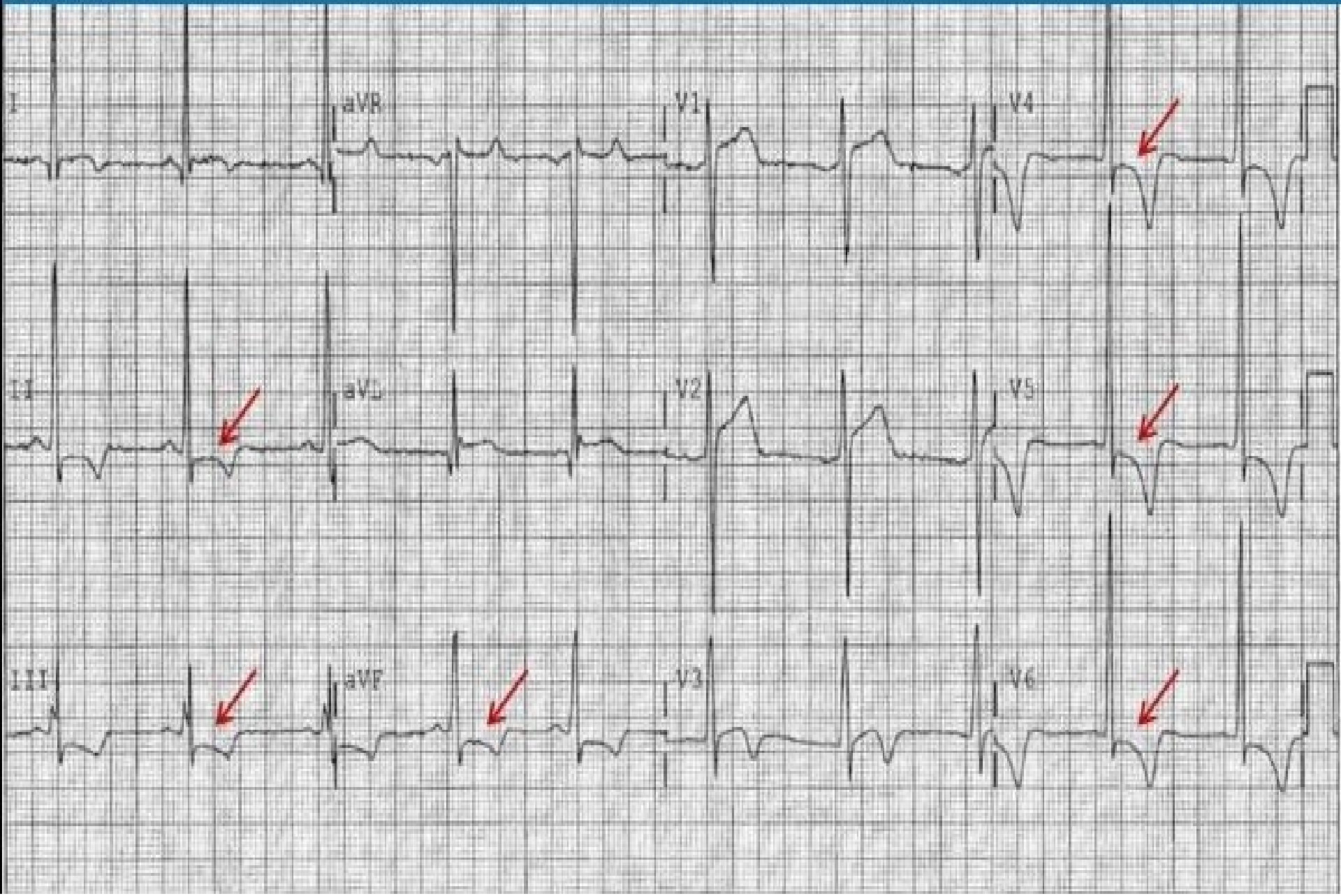
Signs

- Jerky pulse*
- Palpable left ventricular hypertrophy
- Double impulse at the apex (palpable fourth heart sound due to left atrial hypertrophy)
- Mid-systolic murmur at the base*
- Pansystolic murmur (due to mitral regurgitation) at the apex

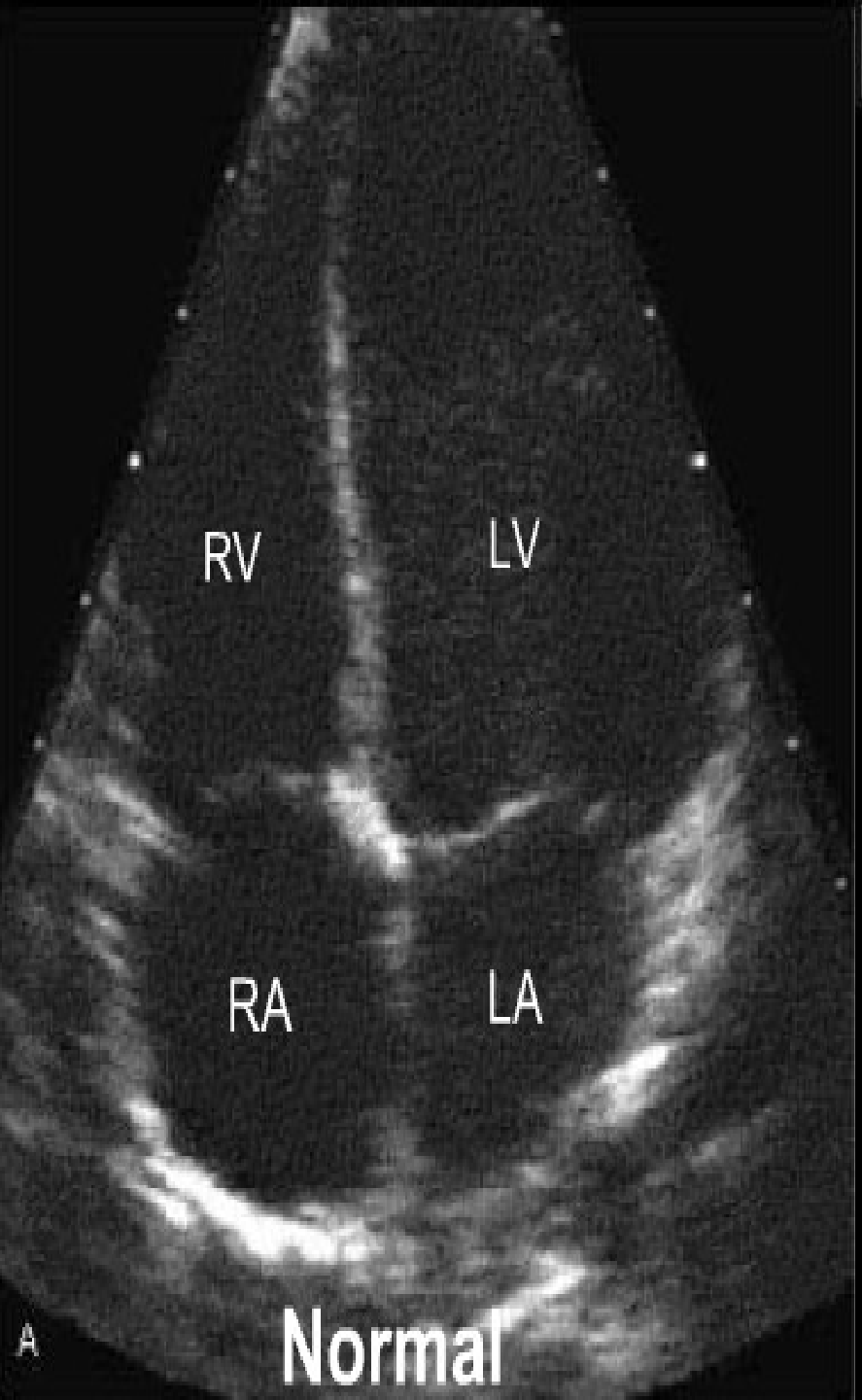
*Signs of left ventricular outflow tract obstruction may be augmented by standing up (reduced venous return), inotropes and vasodilators (e.g. sublingual nitrate).

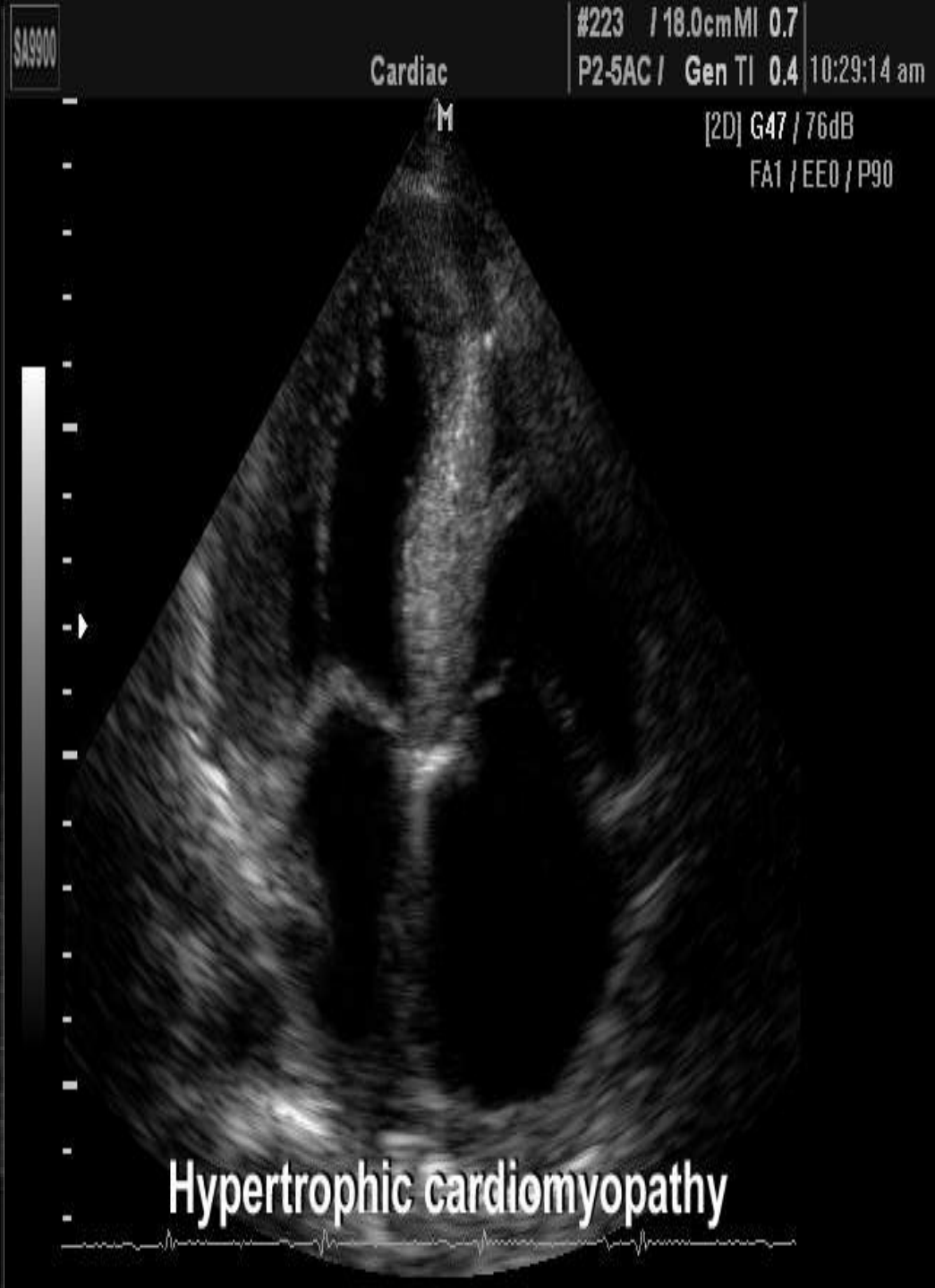
Investigations:

- The ECG is abnormal and shows features of left ventricular hypertrophy with a wide variety of often bizarre abnormalities (e.g. pseudo-infarct pattern, deep T-wave inversion).
- Echocardiography and MRI are helpful in confirming the diagnosis and allow for evaluation of the degree and location of the hypertrophy, the presence and degree of outflow obstruction, and the presence of systolic anterior motion of the anterior mitral leaflet.
- Genetic testing may facilitate diagnosis and, in some cases, is helpful in screening relatives of affected individuals.



ECG in a patient with hypertrophic cardiomyopathy. Note deep T wave inversion and ST depression in the inferolateral leads.


RV
LV
RA
LA
A
Normal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Cardiac
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#223 / 18.0cm MI 0.7
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Hypertrophic cardiomyopathy

Treatment:

- Beta-blockers, rate-limiting calcium antagonists (e.g. verapamil) and disopyramide can help to relieve symptoms and sometimes prevent syncopal attacks.
- Arrhythmias are common and often respond to treatment with amiodarone.
- Outflow tract obstruction can be improved by partial surgical resection (myectomy) or by iatrogenic infarction of the basal septum (septal ablation) using a catheter delivered alcohol solution.
- An implantable cardiac defibrillator should be considered in patients with clinical risk factors for sudden death.
- Digoxin and vasodilators may increase outflow tract obstruction and should be avoided.

3- Arrhythmogenic right ventricular cardiomyopathy

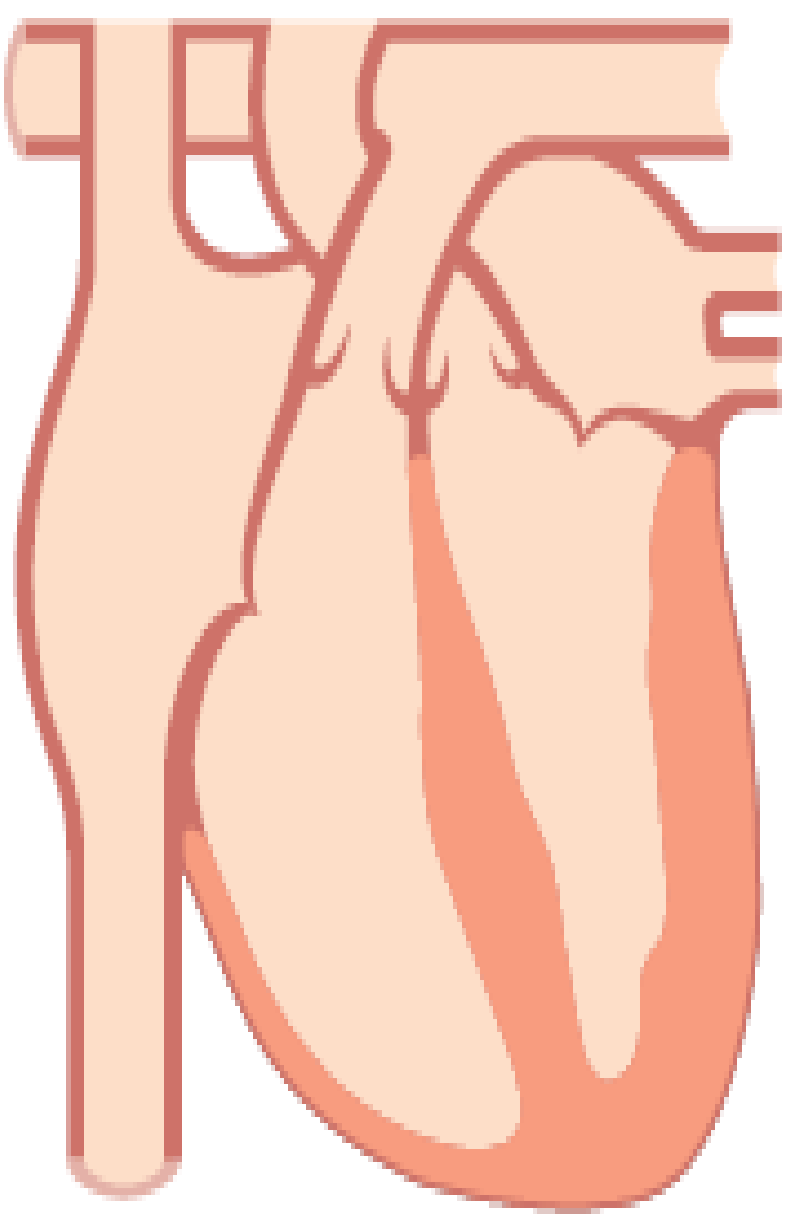
In this condition, patches of the right ventricular myocardium are replaced with fibrous and fatty tissue.

It is inherited as an autosomal dominant trait and has a prevalence of approximately 10 per 100 000.

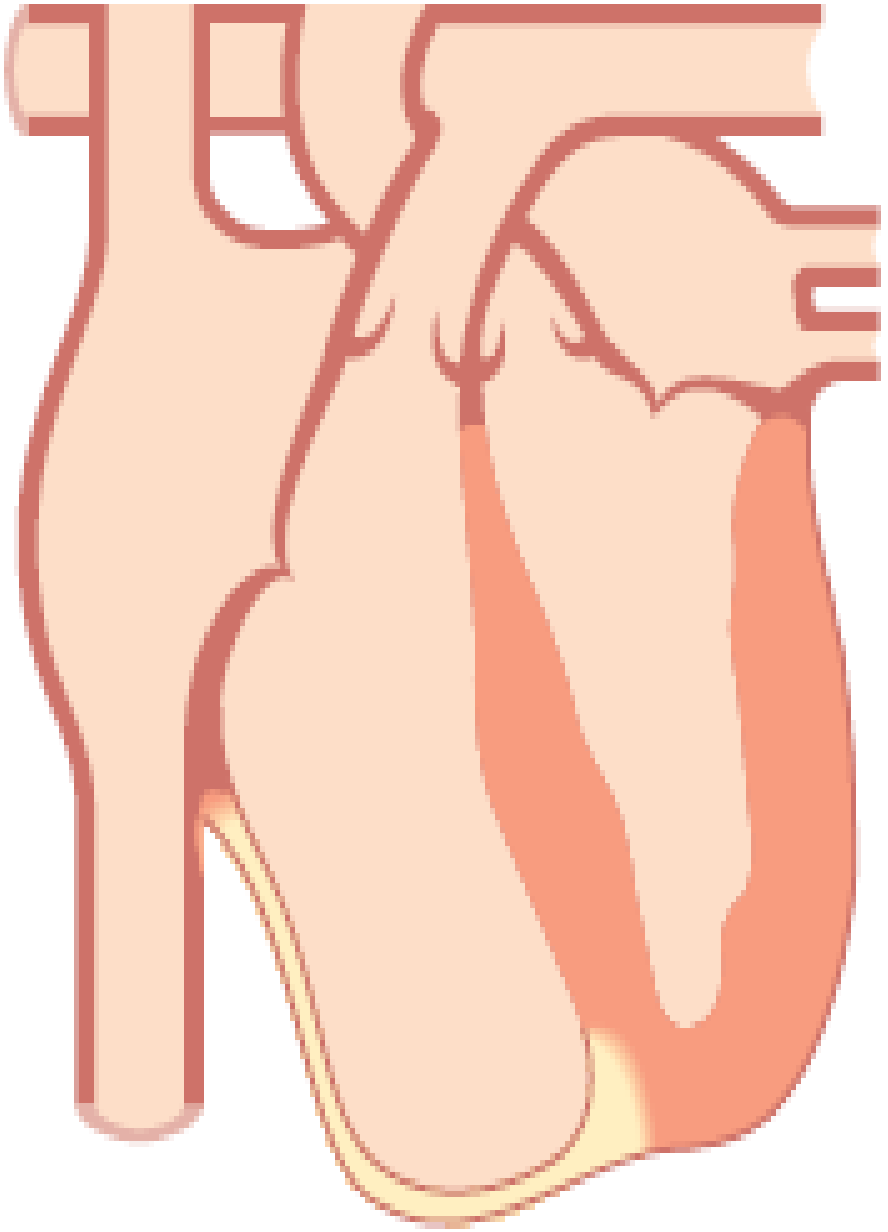
The dominant clinical problems are ventricular arrhythmias, sudden death and right-sided cardiac failure.

ECG typically shows a slightly broadened QRS complex and inverted T waves in the right precordial leads. MRI is a useful diagnostic tool and is used, along with the 12-lead ECG and ambulatory ECG monitoring, to screen the first-degree relatives of affected individuals.

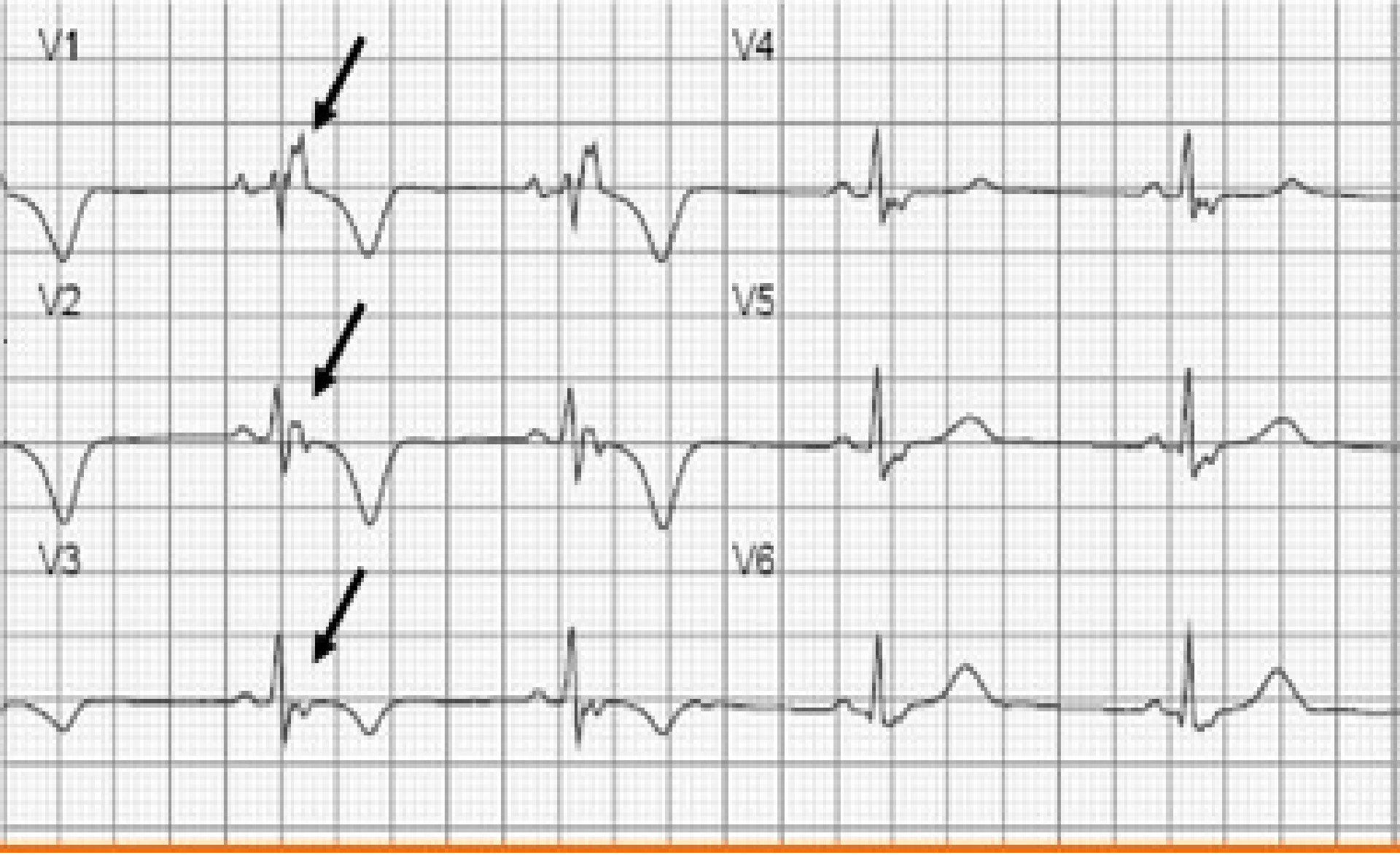
Patients at high risk of sudden death can be offered an implantable cardiac defibrillator.



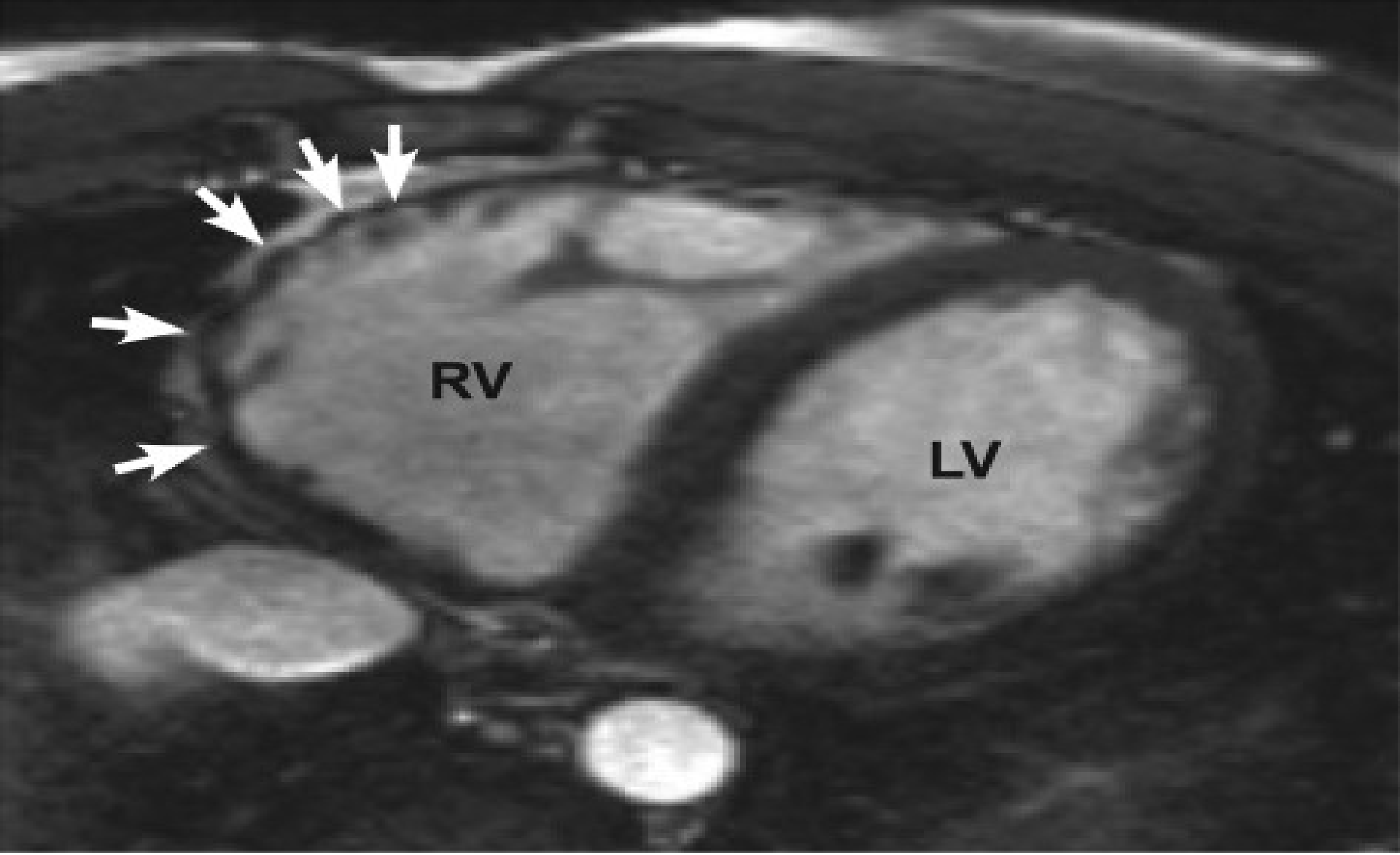
Normal heart



Arrhythmogenic right ventricular cardiomyopathy



Chest ECG leads of Arrhythmogenic right ventricular cardiomyopathy during regular sinus rhythm, with an epsilon wave (arrow) in leads V1-V3 (major criterion), right precordial QRS prolongation >110 msec (major criterion), and T-wave inversion in leads V1-V3 (minor criterion).



MRI findings of Arrhythmogenic right ventricular cardiomyopathy include morphologic changes such as right ventricular dilatation, wall thinning, and aneurismal outpouchings, as well as abnormal tissue characteristics such as myocardial fibrosis and fatty infiltration.

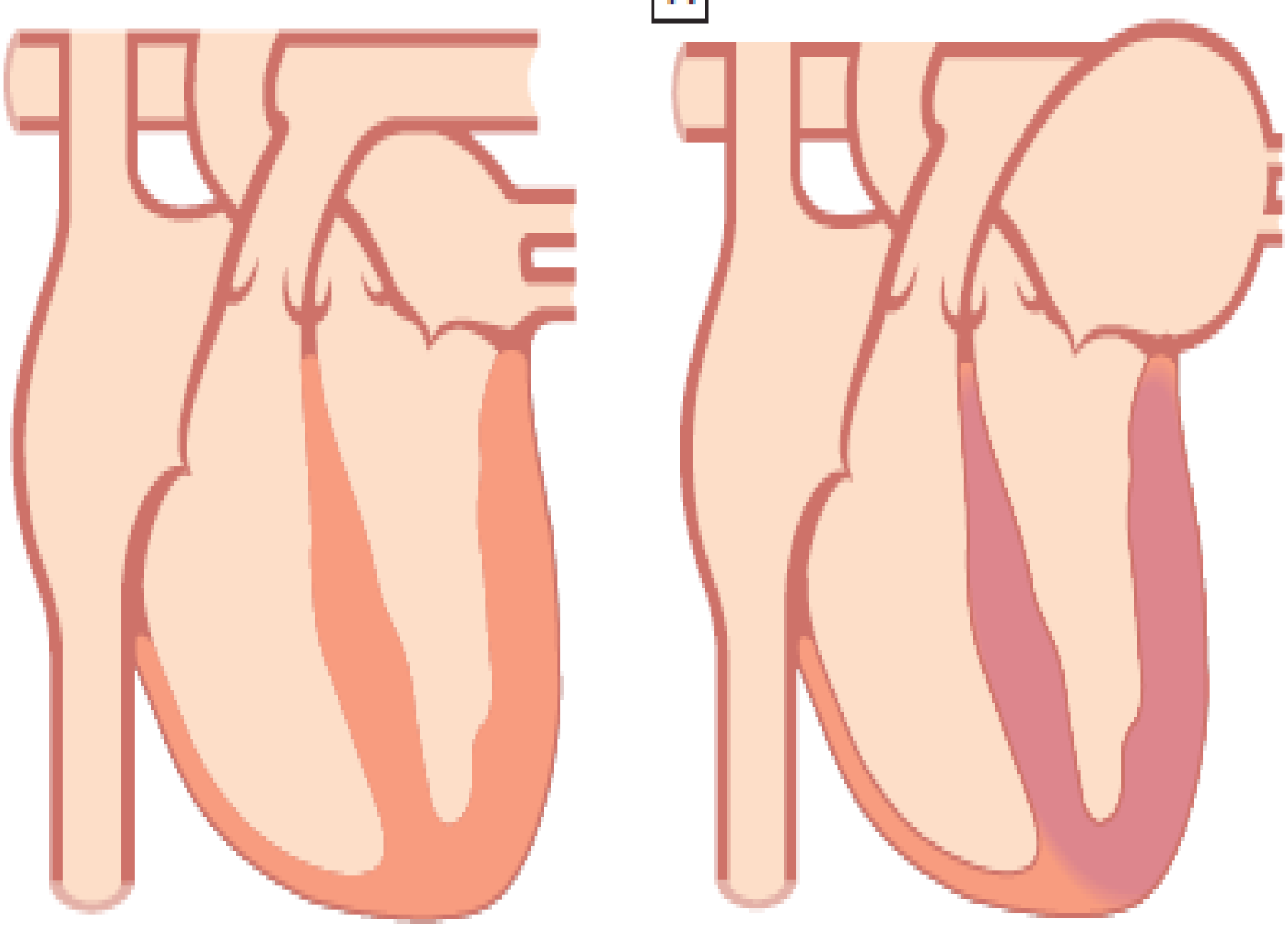
4- Restrictive cardiomyopathy

In this rare condition, ventricular filling is impaired because the ventricles are ‘stiff’. This leads to high atrial pressures with atrial hypertrophy, dilatation and, later, atrial fibrillation.

Causes: Amyloidosis, other forms of infiltration (e.g. glycogen storage diseases), idiopathic perimyocyte fibrosis and a familial form of restrictive cardiomyopathy.

Diagnosis can be very difficult and requires complex Doppler echocardiography, CT or MRI, and endomyocardial biopsy.

Treatment is symptomatic but the prognosis is usually poor and transplantation may be indicated.



Normal heart

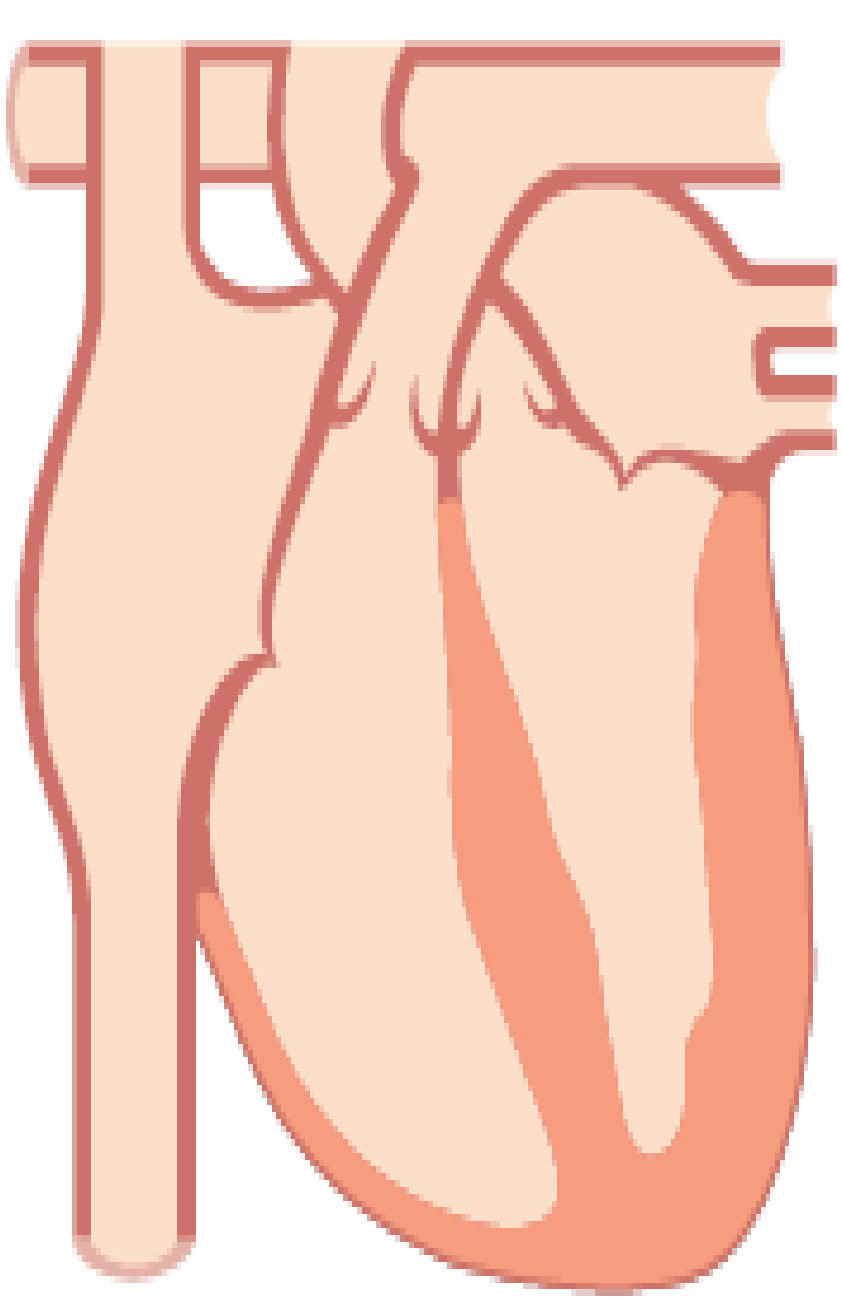
Restrictive cardiomyopathy

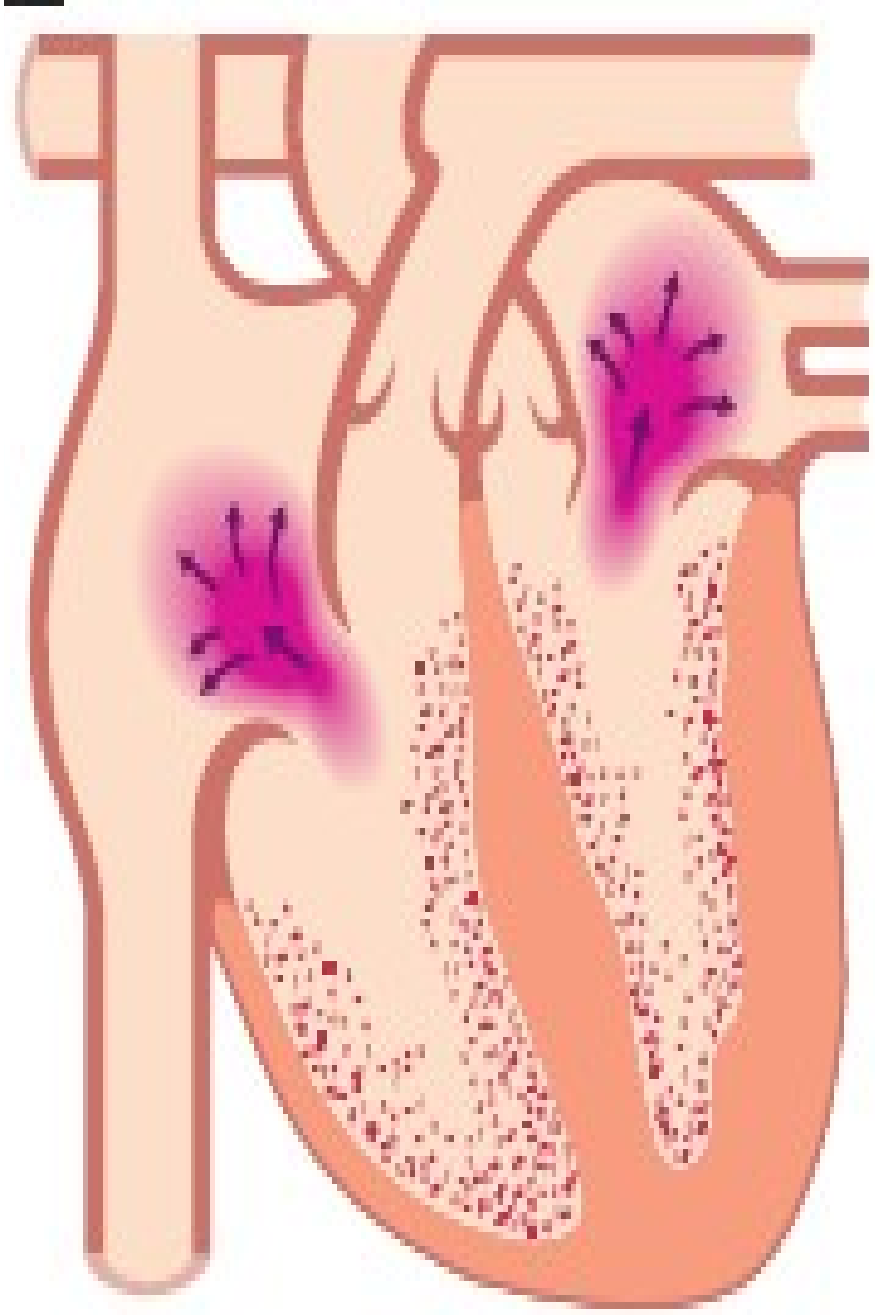
5- Obliterative cardiomyopathy

This is a rare form of restrictive cardiomyopathy characterised by thrombosis and fibrosis, with gradual obliteration of the ventricular cavities (e.g. endomyocardial fibroelastosis)

The mitral and tricuspid valves become regurgitant. Heart failure and pulmonary and systemic embolism are prominent features. It can sometimes be associated with eosinophilia.

Mortality is high: 50% at 2 years. Anticoagulation and antiplatelet therapy are used, and diuretics may help symptoms of heart failure. Surgery (tricuspid and/or mitral valve replacement with decortication of the endocardium) may be helpful in selected cases.





Normal heart

Obliterative cardiomyopathy

Thanks