DEFINITION

1. The cardiomyopathies are a heterogeneous group of diseases in which the common feature is myocardial dysfunction. They are a complex group and currently the focus of much research so that present understanding is not definitive. They were reclassified by a WHO/ISFC Task Force in 1995.

2. The "true" cardiomyopathies are idiopathic or of unknown origin while the term "specific" cardiomyopathies covers heart muscle disease secondary to specific cardiac or systemic disorders. By definition, myocardial disorders occurring as part of ischaemic, valvular, hypertensive or congenital heart disorders and pericardial abnormalities are excluded.

3. The most commonly used clinical classification is based on pathophysiology rather than aetiology.

4. The three main groups are:

    4.1. **dilated cardiomyopathy**
    4.2. **hypertrophic cardiomyopathy**
    4.3. **restrictive cardiomyopathy**

CLINICAL MANIFESTATIONS

5. **Dilated cardiomyopathy** - This the most common form (90% of cases). It is characterised by dilatation and impaired contraction of the left, or both ventricles. Presentation is usually with heart failure which is often progressive. Arrhythmias, thromboembolism and sudden death are common and may occur at any age.

6. **Hypertrophic cardiomyopathy** - This condition is characterised by left and/or right ventricular hypertrophy, which is usually asymmetric and involves the interventricular septum. Contractile function is preserved or enhanced. Typically, the left ventricular volume is normal or reduced. Myocardial ischaemia of multifactorial origin may occur but the condition is often asymptomatic and consistent with long life. However arrhythmias are not uncommon and there is a constant risk of sudden death.

7. **Restrictive cardiomyopathy** - This is the least common variety. It is characterised by abnormal diastolic function; the ventricular walls are excessively rigid and impede ventricular filling. The ventricles have normal or near normal systolic function and wall thickness. There are therefore similarities with constrictive pericarditis and differentiation is essential because of the potential for successful surgical treatment of the latter. Interstitial fibrosis may be present.

8. The distinction between these three functional categories is not absolute and often there is overlap. In particular, patients with hypertrophic cardiomyopathy also have increased wall stiffness due to the myocardial hypertrophy and so exhibit some of the features of restrictive cardiomyopathy. Not all cases fit neatly into this classification. Two important conditions are arrhythmogenic right ventricular cardiomyopathy and peripartum cardiomyopathy.

9. **Arrhythmogenic right ventricular cardiomyopathy** - This disorder is familial and progressive with a predominance in young males. A recessive form is described. The usual presentation is arrhythmia, particularly multiple ectopic beats or right ventricular tachycardia and is a cause of sudden death in previously symptom-free young people.

10. **Peripartum cardiomyopathy** - Cardiac dilatation and unexplained heart failure may develop during the last trimester of pregnancy or within six months of delivery. The signs and symptoms are similar to those in patients with idiopathic dilated cardiomyopathy and the mortality rate may be as high as 25 to 50%.

11. In general most specific cardiomyopathies are of the dilated variety, the exception being the group attributed to infiltrative disorders such as amyloidosis, haemochromatosis, neoplasia, sarcoidosis, Fabry disease and the fibroplastic disorders. These tend to have mainly restrictive effects.

AETIOLOGY

CARDIOMYOPATHIES OF UNKNOWN ORIGIN –TRUE CARDIOMYOPATHIES

12. By definition, the true cardiomyopathies are idiopathic. However with greater understanding of genetic and immunological mechanisms the size of this group is diminishing. A range of clinical presentations is seen.

13. **Dilated cardiomyopathy** may be idiopathic, familial/genetic or associated with recognised cardiovascular disease where the degree of myocardial dysfunction is disproportionate to the abnormal loading conditions or the extent of ischaemic damage. Single gene mutations in the structural proteins of the myocyte or mitochondrial DNA are recognised causes of dilated cardiomyopathy. The role of familial factors is increasingly recognised and as many as 30% of cases will have other family members with evidence of left ventricular dysfunction or enlargement.

14. **Hypertrophic cardiomyopathy** is now recognised in many cases as being caused by mutations in genes coding for myofibrillary proteins. The characteristic finding is inappropriate myocardial hypertrophy occurring in the absence of any obvious cause (such as aortic stenosis or systemic hypertension). Affected individuals are heterozygous. There is variation in the distribution of myocardial involvement which may be localised or affect the whole of the left (and sometimes right) ventricles.

15. **Restrictive cardiomyopathy** - This entity may be caused by a diffuse fibrosis of unknown origin. Another form of the condition may have a familial basis.

16. **Arrhythmogenic right ventricular cardiomyopathy** - This condition is familial with autosomal dominant inheritance and incomplete penetrance.

17. **Peripartum cardiomyopathy** - The cause of this disorder is unknown, although the current view is that it is multifactorial in origin. It is rare, and so far little research has been performed. The prognosis for future pregnancies is closely related to whether the heart size returns to normal after delivery.

SPECIFIC CARDIOMYOPATHIES

18. The specific cardiomyopathies originate from specific cardiac disorders or from systemic disorders. The causes may be grouped as follows:

    18.1. **Inflammatory causes** (infective) including viral, rickettsial, bacterial, fungal agents.
    Inflammatory causes (non-infective) including collagen diseases, Kawasaki.

    18.2. **Metabolic causes** (nutritional) including thiamine, selenium deficiency, obesity, scurvy etc.
    Metabolic causes (endocrine) including acromegaly, thyrotoxicosis, myxoedema, diabetes.
    Metabolic causes (altered metabolism) including gout, porphyria.

    18.3. **Toxic** causes including alcohol, phenothiazines, lead, chloroquine, phosphorus, mercury, corticosteroids, cocaine and certain chemotherapeutic agents, e.g. doxorubicin.

    18.4. **Infiltrative causes**, including amyloidosis, haemochromatosis, neoplasia, sarcoidosis, Fabry disease.

    18.5. **Fibroplastic disorders**, including endomyocardial fibrosis, endocardial fibroelastosis, carcinoid.

    18.6. **Haematological disorders**, including sickle cell anaemia, polycythaemia vera, leukaemia.

    18.7. **Hypersensitivities** to various agents, including certain antibiotics, phenylbutazone.

    18.8. **Genetic disorders**, including Duchenne muscular dystrophy, Friedrich's ataxia.

    18.9. **Miscellaneous acquired conditions** including obesity.

    18.10. **Physical agents**, including therapeutic radiation

19. Some of the commoner specific cardiomyopathies are discussed below.

ALCOHOLIC CARDIOMYOPATHY

20. Chronic excessive consumption of alcohol is the major cause of dilated cardiomyopathy in the Western world and accounts for upwards of one-third of all cases. Stopping alcohol consumption early in the course of alcoholic cardiomyopathy may halt the progression or even reverse left ventricular contractile dysfunction, unlike other specific cardiomyopathies which are often marked by progressive clinical deterioration.

21. Alcohol may result in myocardial damage by two basic mechanisms: (1) a direct toxic effect of alcohol or its metabolites; and (2) nutritional effects, most commonly in association with thiamine deficiency. The distinguishing features of each include peripheral vasodilatation and high output heart failure, often right-sided, in the former and reduced contractility with typically left-sided low-output failure in the latter.

22. Alcohol results in acute as well as chronic depression of myocardial contractility and may produce reversible cardiac dysfunction even when ingested by normal non alcohol-dependent individuals. The reason for the transition from the reversible acute effects to permanent myocardial damage is unclear.

AMYLOIDOSIS

23. Amyloidosis results from the deposition of a material consisting of unique twisted B-pleated sheet fibrils formed from various proteins. It may affect almost any organ. It may be senile, hereditary, or due to immunocyte dyscrasia (malfunctioning of cells normally involved in the response to infection) and it may be associated with chronic inflammatory disorders or malignant neoplasms. Involvement of the heart may occur in any variety of the condition although clinically significant amyloidosis is most common in patients with immunocyte dyscrasia.

24. Cardiac amyloidosis is commoner in men and is rare before the age of 30 years. The most common presentation is that of restrictive cardiomyopathy with right ventricular failure and arrhythmia.

DIABETES MELLITUS

25. Diabetes mellitus increases the risk of congestive cardiac failure from all causes and it appears that this is attributable to factors other than atheroma and coronary heart disease. The coincidence of diabetes and cardiomyopathy is substantial and interstitial fibrosis and arteriolar hyalinisation are the most frequent abnormalities found. The severity of dysfunction is related to the degree of diabetes control.

ENDOMYOCARDIAL DISORDERS

26. Endomyocardial fibrosis is a form of secondary restrictive cardiomyopathy, occurring most commonly in certain ethnic groups in tropical countries, where it accounts for 10 to 20% of deaths due to heart disease. Loeffler's endocarditis (hypereosinophilic syndrome) with which it shares many similarities is associated with a hypereosinophilia of unknown cause. The end-stage intense endocardial fibrotic thickening in both diseases produces restrictive features. The aetiology is unknown.

HAEMOCHROMATOSIS

27. Haemochromatosis is characterised by the excessive deposition of iron in a variety of parenchymal tissues, including the heart, pancreas, and liver. Causes include chronic liver disease, a defect in haemoglobin synthesis, chronic excessive intake of iron over a number of years, or as a familial or idiopathic disorder. The severity of cardiac involvement varies widely and only roughly parallels that in other organs. It manifests itself as a mixed dilated/restrictive cardiomyopathy with both systolic and diastolic dysfunction and is thought to be due to toxicity of the free iron moiety.

HIV

28. The heart is involved in up to 50% of people with AIDS but symptoms arise in only 10% and death attributable to heart disease occurs in only 5%. The cause is complex and probably multifactorial. It may arise secondary to myocarditis due to a wide variety of opportunistic cardiotoxic organisms or may be attributable to human immunodeficiency virus itself by means of an immunocyte mediated reaction. Antiviral drugs have also been implicated in the process, including zidovudine and interferon. The changes are those of dilated cardiomyopathy.

NEUROMUSCULAR DISORDERS

29. The inherited neuromuscular disorders are associated with varying degrees of heart muscle involvement. In Duchenne's progressive muscular dystrophy cardiac involvement is uncommon, but if it occurs the resulting congestive cardiac failure is often refractory to treatment. In myotonic dystrophy a variety of conductive abnormalities may occur and syncope and sudden death are major hazards. In limb-girdle dystrophy and fascioscapulohumeral dystrophy cardiac involvement is uncommon and seldom severe. Cardiac involvement is common in Friedreich's ataxia where a hypertrophic pattern may occur.

SARCOIDOSIS

30. Sarcoidosis is a granulomatous disorder of unknown cause. Almost any tissue may be involved although the skin, reticulo-endothelial system and lungs are most commonly affected. Diffuse pulmonary fibrosis may result in fatal right heart failure. Clinical manifestations of sarcoid heart disease are present in less than 5% of patients and may cause heart block, congestive cardiac failure, ventricular arrhythmias and sudden death. Features of restrictive and dilated cardiomyopathy may coexist because both increased stiffness of the ventricular wall and diminished contractile function may be present.

THERAPEUTIC CHEST IRRADIATION

31. The prevalence of radiation-induced cardiomyopathy is increasing, associated with the increased survival of many malignancies. The majority of affected individuals are Hodgkin's disease survivors, followed by cases of non-Hodgkin's lymphoma, oesophageal, lung and breast cancer and metastatic seminoma. Radiation dosage (total) is likely to be in the region of 60Gy or even higher. Pericardial disease is the commonest expression of radiation damage but restrictive cardiomyopathy may occur, with congestive heart failure.

CONCLUSION

32. The cardiomyopathies are a diverse group of disorders of heart muscle whose origin is uncertain (true cardiomyopathies) or secondary to cardiac or systemic disorders (specific cardiomyopathies). Heart muscle disease due to ischaemic, valvular, hypertensive and pericardial abnormalities and congenital heart disease is excluded under the present classification.

33. They may cause a dilated, hypertrophic or restrictive pattern of heart dysfunction.

34. They may present with arrhythmia, with signs and symptoms of right- or left cardiac failure. In many types there is a risk of sudden premature death.

35. The aetiology of the true cardiomyopathies is by definition unknown, although genetic and immunological causes are gradually being clarified. Specific cardiomyopathies may be caused by a wide variety of agents; inflammatory, metabolic, toxic, infiltrative, fibroplastic, haematological, hypersensitisation and neuromuscular.

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