PATHOLOGY OF THE CARDIOMYOPATHIES

BRIAN McKINNEY

ANALYTICAL METHODS APPLIED TO AIR POLLUTION MEASUREMENTS

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Brian McKinney
M.D., M.R.C.Path.
Wellcome Trust Research Fellow;
Honorary Lecturer in Pathology,
Royal Free Hospital, London

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Foreword

This book on the pathology of the cardiomyopathies by Dr. Brian McKinney is an important contribution to the medical literature. The cardiomyopathies constitute a significant portion of diseases of the heart. They are being recognized more throughout the world as physicians learn about diseases of the myocardium. McKinney has had a profound interest in diseases of the myocardium for many years. His interest has not been limited entirely to pathology but has also included the related clinical manifestations of, and research devoted to, cardiomyopathies. The chapters of this book reflect his extensive knowledge. Students of heart disease will readily find the presentations to reflect these many interests and personal contributions to the field. The clinician as well as the pathologist will appreciate this book and learn a great deal from it.

McKinney has included most, if not all, of the causes of heart muscle disease in his monograph. He has used the term 'cardiomyopathy' literally, i.e. as the term implies: heart muscle pathology. His general approach to the pathology of cardiomyopathies is certainly helpful to the physician. Regardless of cause, the clinical manifestations that follow damage to the myocardium are quite similar. There are some cardiologists who limit the term 'cardiomyopathy' to disease of the myocardium of unknown cause. This relatively narrow or limited approach seems to me to be less effective in the management of all the cardiomyopathies of known cause, many preventable and many curable if recognized early. For example, myocardial disease due to hyperthyroidism or anaemia is certainly preventable and many are curable if recognized early. McKinney's concepts and approach to heart disease emphasize prevention and cure. The importance of prevention and cure is even more appreciated when it is realized that cardiomyopathy is disease of the myocardium itself, i.e. the tissue that does the work. The health of the power source of the pump must be preserved for good health.

The book is clearly written, the illustrations are excellent and the bibliographies supporting each disease entity are well selected. McKinney has properly devoted more pages in his book to the more common types of cardiomyopathies without neglecting the less common ones.

McKinney has rendered a great service to cardiology and medicine in general. This is an important book in pathology and is concerned with an organ responsible for the most deaths in many nations of the world. The clinician must understand the pathological basis of the diseases he treats. This book provides an excellent and much needed source of this information. McKinney is to be thanked and congratulated—he has produced a good book.

GEORGE E. BURCH

Preface

Since first becoming interested in endomyo cardial fibrosis in Uganda in 1959, I found that I was unable to obtain any book which was devoted entirely to a complete survey of cardiomyopathies, either clinically or pathologically. Much information on these diseases has been published but it is widely scattered in reports of symposia which have been held in different parts of the world, and in odd chapters and sections in textbooks on cardiology and cardiovascular pathology.

Subsequently, I found that many other people were faced with a similar problem. Pathologists or cardiologists, particularly those working for higher examinations, have often asked me to recommend a suitable book and I have had to say that there appears to be none available.

I was, therefore, very pleased when the opportunity to write such a book presented itself to me in 1970, particularly as, by then, I had amassed a great deal of material on cardiomyopathies and had become acquainted with many pathologists and cardiologists who were, like myself, particularly interested in this subject.

I should like to thank the many pathologists who have lent me slides and photographs of some of their specimens to use as illustrations in this book. These workers are listed in detail on the following pages. I am also deeply grateful to the following pathologists who have read and criticized sections of the manuscript of this book before it was finally submitted for publication:

Professor Norman Woody of Tulane University, New Orleans—Chagas' disease. Professor George Burch, also of Tulane University, New Orleans—Alcoholic cardiomyopathy. Professor Charlos Arribada of Chile—Cardiac toxoplasmosis. Dr Merton Sandler, London—Carcinoid heart disease. Dr Peter Hopper, London—Bacterial and viral infections. Dr Joyce Skinner, London—Fungal diseases and the remaining parasitic diseases. The late Professor E. Bajusz, McGill University—Hereditary cardiomyopathies in hamsters. Professor

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I should also like to thank my secretary, Mrs Sheila Meering, for dealing with the great amount of correspondence with very many people, which this book has entailed; Miss Linda Turney, for typing the manuscript; Mr George Brocklebank for much of the technical work; and Mr Cedric Gilson and the other members of the photographic department of the Royal Free Hospital who spent much time and energy in taking and printing photographs for me.

Lastly, I would like to thank the British Heart Foundation for a grant to allow me to obtain specimens of many of the tropical cardiomyopathies and another grant so that I could buy a Vickers Patholux microscope, with which I was able to take many of the photographs that are included in this book; and the Wellcome Trust for personal support over many years and without whose help this work could not have been carried out.

B. McK.

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Figures 2.5, 2.6 and 2.9: Zoltawska (1971); *Journal of Clinical Pathology*
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Figures 4.5–4.10: Ferrans *et al.* (1972); *Acta pathologica et microbiologica scandinavica*
Figures 5.1, 5.10 and 5.11: Spach *et al.* (1966); *American Heart Journal*
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Figures 11.9–11.11, and 11.13: Anselmi *et al.* (1966); *American Heart Journal*
Figures 12.2–12.9: Roberts, Liegler and Carbone (1969); *American Journal of Medicine*
Figures 13.1, 13.3 and 13.4: Pomerance (1965); *British Heart Journal*
Figures 13.18, 13.20 and 13.21: O'Donnell and Mann (1966); *American Heart Journal*
Figures 14.1–14.5: Rubler and Fleischer (1967) and Fleischer and Rubler (1968); *American Journal of Cardiology*
Figures 14.10–14.12: Engel, Erlandson and Smith (1964); *Circulation*
Figures 15.11–15.14: Ferrans *et al.* (1965); *American Heart Journal*
Figures 16.3, 16.4 and 16.6: Skause, Berg and Westfelt (1959); *Acta medica scandinavica*
Figures 16.1, 16.5 and 16.9: Sterns *et al.* (1966); *British Heart Journal*

Figures 16.14–16.18: Fine and Morales (1971); *Archives of Pathology*
Figures 16.23, 16.24, 16.26 and 16.27: Aikat and Nirodi (1971): *Journal of Pathology and Bacteriology*
Figures 17.1–17.4, 17.10, 17.11, 17.14 and 17.16: Deodhar and Chatty (1969): *Archives of Pathology*
Figures 17.13, 17.15 and 17.17: Bonenfant, Miller and Roy (1967): *Canadian Medical Association Journal*
Figures 18.5, 18.6, 18.8–18.10: Bajusz (1969); *American Heart Journal*

Contents

One

Introduction

During the past twenty-five years the importance of heart disease of unknown or unusual origin has become obvious. Previously the only agents commonly regarded as causing damage to the myocardium were coronary artery obstruction, causing myocardial infarction, or rheumatic myocarditis.

Many cases of cardiac disease have since been recognized which are not due to either of these causes. This originally became evident probably because of reports of idiopathic cardiac disease arising from all parts of the world, but chiefly, from differing parts of Africa. Although cases of cardiac failure (due to various causes such as alcohol) have been known for many years, this has not been generally appreciated and it is only recently that it has become evident that many cases of heart failure are due to a cardiomyopathy—involvement of the heart muscle; and not due to an infarct, ischaemic heart disease or rheumatic carditis. The terms most frequently applied in description of heart muscle disease of unknown or unusual origin are: idiopathic myocardial hypertrophy, idiopathic cardiomegaly, cardiomyopathy and/or myocardiopathy, although there are many other even more non-specific terms such as myocardioses (commonly used by many continental writers).

All these terms may be misleading. In general pathology 'cardiac hypertrophy' implies that the cardiac enlargement has been caused by an increase in the size of the cardiac muscle fibres. According to this definition many obscure heart diseases, such as some cases of endomyocardial fibrosis, must be excluded.

The myocardium may be affected by a number of inflammatory, degenerative or neoplastic processes; the principal manifestations of which may, however, be located in other parts of the body.

This book will be limited to describing conditions where the disease involving the myocardium is of such clinical significance as to produce cardiac enlargement, congestive heart failure or both. The

term commonly accepted for the description of this type of cardiac disease is *cardiomyopathy.*

DEFINITION

The word cardiomyopathy simply means disease of the heart muscle, and was first used by Brigden (1957) in his St Cyres Lecture. He went further, however, in confining his description to that group of diseases of the myocardium which were of unknown aetiology and did not have a basis of coronary occlusion as their principal aetiological origin.

Goodwin *et al.* (1961) describe cardiomyopathies as 'sub-acute or chronic disorder of the heart muscle of unknown or obscure aetiology, often with associated endocardial and sometimes with pericardial involvement but not atherosclerotic in origin'.

Robin (1961), however, calls them 'a broad group of diseases of diverse etiology, that specifically involve the myocardium to produce abnormalities of structure, abnormalities of function or both. The end result of many of these diseases may be the development of myocardial fibrosis'.

The definition accepted by the WHO study group on cardiomyopathies states that: 'the name indicates conditions of different—frequently, unknown or unclear, etiology in which the dominant feature is cardiomegaly, and cardiac failure. It excludes heart diseases resulting from damage to the valvular strictures of the heart, and from disorder of coronary, systemic or pulmonary vessels.'

This definition deliberately omits reference to the duration of the disease process in view of the inadequate knowledge of their natural history.

At present there are three descriptions of the cardiomyopathies which are commonly accepted by different groups of cardiologists and pathologists.

(1) Goodwin (1966) divides all types of cardiomyopathies into four groups (*Figure 1.1*).

The largest group of cases, for which he uses the descriptive term 'congestive cardiomyopathy', include all those types of cardiomyopathy which present, clinically, in congestive cardiac failure with a large heart, gallop rhythm and often with evidence of valvular insufficiency (Goodwin *et al.*, 1961). Most cases of idiopathic cardiomegaly will present in this way, but not all cases presenting as 'congestive cardiomyopathy' will consist of patients with this disease.

The second most common type is *hypertrophic obstructive cardiomyopathy* (in North America this is known as idiopathic hypertrophic

subaortic stenosis); this being an inherited disorder characterized by marked ventricular hypertrophy without dilatation.

The third type, *constrictive* (*restrictive*) *cardiomyopathy*, resembles constrictive pericarditis with diastolic filling, difficulty due to myocardial rigidity, infiltration and often endocardial involvement. This type of cardiomyopathy is rare; the most common cause being amyloid infiltration.

The last type, *obliterative cardiomyopathy*, describes disorders in which obliteration of the cavities of the ventricles is associated with

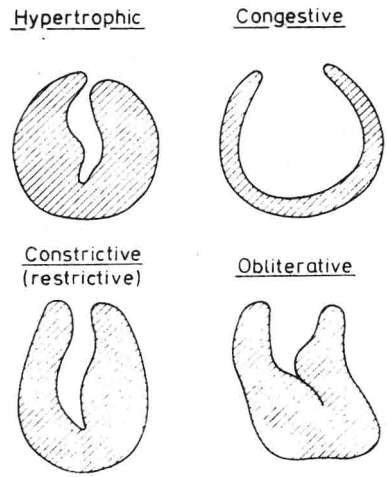

Figure 1.1. Diagram to show gross differences in ventricular form in four types of cardiomyopathy (*Goodwin, 1970*)

atrioventricular valve regurgitations as in endomyocardial fibrosis (Davies, 1948) and in Loeffler's (1936) eosinophilic fibroplastic endocarditis.

(2) Hudson (1970) has proposed that the definitions of the terms for cardiomyopathy should include all diseases of the endocardium, pericardium and myocardium, irrespective of functional characteristics and whether or not of recognized origin.

(3) Mattingly (1965) uses the term cardiomyopathies to include all disease of the myocardium alone, whether or not of recognized aetiology but, of course, not including that due to coronary artery disease. This is the definition which is generally accepted by most North American and European workers in this field.

CLASSIFICATION

The many conditions, which fall into the broad category of cardiomyopathies, make it very difficult to construct a simple system for classification.

Several classifications have been proposed, some of them depending on aetiology (Emmanuel, 1970), some on clinical or pathological features (Carlisle, 1971); or whether the disease involves primarily processes affecting other organs as well as, and often before, the heart (Fejfar, 1970).

One group of workers employs the term 'primary myocardial disease' as inclusive not only of the idiopathic disorders of the myocardium but also of more generalized diseases when the myocardium is the principle site of involvement. In other classifications (Fowler, 1964) the term primary myocardial disease is used only to refer to the idiopathic disorder which, in actual fact, probably represents a heterogeneous group of diseases which, in many instances, begin as myocarditis.

In the classification proposed below, the cardiomyopathies are divided into those which are thought to be 'primary', i.e., those in which the disease process involves the heart alone and those which are 'secondary', i.e., the cardiomyopathy is part of a generalized disease process which affects other parts of the body, either before or after the heart is involved. This definition, of course, excludes the changes which may be found in the body which have been caused by congestive cardiac failure.

A certain group of heart diseases of unknown aetiology, for example, some types of cardiomyopathies producing symptoms or signs of obstruction, show no cardiac muscle hypertrophy or enlargement. This fact does not seem to fit with the term 'myocardiopathy'. Finally, 'cardiomyopathy' means a disorder of the heart muscle and therefore it is unfit to include those forms of heart disease where the lesion is principally of the endocardium or valves—as, for example, in a case of bacterial endocarditis.

In considering all these terms, I suggest the use of the word 'cardiomyopathy'. This term is not completely satisfactory as it means any disorder of the heart. However, if the word has a definite meaning, others will know to what one is referring. In this respect I do not think the definition proposed by Korb (1973) can be improved upon. 'Cardiomyopathies are heart diseases of unknown or unusual etiology, associated with pathological processes within the myocardium or endocardium or both and including certain lesions of the conduction system.' This definition excludes such common

aetiological categories as coronary, valvular, hypertensive and pulmonary heart disease. Constrictive pericarditis and other forms of pericardial disease, and cardiac malformations, should also not be included.

Concerning the classification, it seems reasonable to start by dividing cardiomyopathies into primary and secondary forms. A *primary cardiomyopathy* means that the heart alone is affected by a disease process of either known or unknown aetiology, while *secondary cardiomyopathies* comprise a group of conditions where the heart is involved as part of a generalized underlying disease process. Additionally, one must include heart diseases of unusual or unknown aetiology involving the heart only, for example, primary tumours of the endocardium or myocardium.

From the viewpoint of clinicians the best classification is that proposed by Goodwin (1966) where, as stated above, he divided the cardiomyopathies into the following four groups: (1) congestive cardiomyopathies; (2) hypertrophic cardiomyopathies, with and without obstruction; (3) constrictive cardiomyopathies; and (4) obliterative cardiomyopathies.

The classification given below does not consider clinical aspects purposely, because it seems impossible to mix morphological, geographical and functional concepts of a disease.

This classification of myocardial disease—cardiomyopathies—includes such common aetiological categories as the following.

PRIMARY CARDIOMYOPATHIES

(1) Endocardial fibro-elastosis
(2) Hypertrophic obstructive cardiomyopathy
(3) Primary myocardial disease
(4) Familial cardiomyopathies

(a) Metabolic storage disease
  (i) Pompe's disease (glycogen)
  (ii) Refsum's disease (phytannic acid)
  (iii) Fabry–Anderson's disease (glycolipid)
  (iv) Hurler's syndrome, i.e., gargoylism (mucopolysaccharidosis)
  (v) Haemochromatosis (iron)
  (vi) Oxalosis (calcium oxalate)
  (vii) Pseudoxanthoma elasticum

(b) The muscular dystrophies and myotonia congenita
(c) Friederich's ataxia
(d) Sickle-cell anaemia

(5) Tropical cardiomyopathies. The term includes both endomyocardial fibrosis and cardiomegaly of unknown origin
(6) Peri-partal and post-partal cardiomyopathies

SECONDARY CARDIOMYOPATHIES

(1) Inflammatory

(a) Viral infection: Coxsackie, psittacosis, rubella, rubeola, smallpox, vaccinia, infectious mononucleosis, infectious hepatitis, varicella, mumps, rabies, yellow fever, atypical pneumonia, herpes zoster, cytomegalic inclusion body disease

(b) Rickettsial infection: typhus, scrub typhus, Q fever, Bartonelliasis

(c) Bacterial infection: infections of the upper respiratory tract, diphtheria, streptococcal infections, infections of the lower respiratory tract, meningococcal, haemophilus, salmonellosis, brucellosis, tetanus, tuberculosis, clostridia, gonococcal, tularaemia

(d) Spirochaetal infection: leptospirosis, syphilis

(e) Fungal infection: aspergillosis, actinomycosis, histoplasmosis, blastomycosis, cryptococcosis, candidiasis, coccidioidomycosis

(f) Parasitic infection:

(i) *Protozoal*—Chagas' disease (*Trypanosoma cruzi*), African trypanosomiasis (*T. gambiense* and *T. rhodesiense*), toxoplasmosis, malaria

(ii) *Metazoal*—cysticercosis, trichiniasis, schistosomiasis, filariasis, ascariasis, strongyloidiasis, visceral larva migrans, heterophydiasis, paragonimiasis

(2) 'Collagen' diseases

(a) Rheumatic heart disease
(b) Rheumatoid arthritis
(c) Ankylosing spondilitis
(d) Scleroderma
(e) Systemic lupus erythematosus
(f) Myasthenia gravis
(g) 'Loeffler's disease'
(h) Periarteritis nodosa
(i) Dermatomyositis

(3) Idiopathic

(a) Sarcoidosis

(b) Giant-cell myocarditis
(c) Amyloidosis

(4) Endocrine abnormalities
(a) Thyrotoxicosis
(b) Myxoedema
(c) Phaeochromocytoma
(d) Acromegaly
(e) Hyperparathyroidism producing myocardial calcification

(5) Nutritional causes
(a) Starvation and malnutrition (including kwashiorkor)
(b) Anaemia
(c) Beriberi

(6) Alcoholic heart disease

(7) Poisons
(a) Carbon monoxide
(b) Scorpion sting
(c) Snake bite
(d) *Argemone mexicana* (epidemic dropsy)
(e) Cobalt
(f) Arsenic
(g) Antimony

(8) Drugs
(a) Immunosuppressive drugs, i.e., Methotrexate
(b) Daunrubicin
(c) Emetine
(d) Phenylbutazone
(e) Sulphonamides
(f) Antibiotics
(g) Paracetamol
(h) Other anaesthetic agents
(i) Phenylthiazine and derivatives
(j) Lithium carbonate
(k) Adrenaline, noradrenaline and isoproterenol

(9) Physical trauma
(a) Temperature and humidity
(b) Radiant energy
(c) Electricity
(d) Ionizing radiation