Cardiomyopathy

Thomas D. Giles
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PREFACE

Cardiomyopathy — disease of heart muscle — is an important and common clinical concern. Cardiomyopathy is both simple and complex: simple because disease of the heart muscle, the driving force of the cardiac pump, and the resulting consequence, is an easily understood concept; complex because of the myriad of etiologic factors and the varied and subtle pathophysiologic profiles. This dichotomy — the simple and complex nature of cardiomyopathy — may be confusing but is also fascinating for those interested in heart disease.

Cardiomyopathy was a relatively neglected subject for many years. Chronic myocarditis was considered the only cause of heart muscle disease. Interest in the cardiomyopathies evolved slowly until the 1900s when outstanding clinicians led the way in characterizing these diseases; Henry Christian, Thomas Mattingly, and George Burch from the United States and Wallace Brigden and John Goodwin from the United Kingdom. Countless others from throughout the world have added to the current state of knowledge of this important group of diseases.

This book is intended to aid in understanding the spectrum of cardiomyopathy by blending simple and complex aspects of heart muscle disease. Thus, section I presents a systematic approach to cardiomyopathy followed by more detailed descriptions in sections II and III. Or, the book may serve as a source of reference for those interested in a particular aspect of cardiomyopathy. In both instances the book is intended to be complementary to standard general textbooks of cardiology and medicine. The book is written with medicine residents, cardiologists in training, practicing internists and cardiologists, internists and cardiologists in an academic setting, and pathologists with a special interest in cardiac disease in mind.

We are grateful to each author for his contribution. The editors have tried to carefully mold the direction of the book while permitting the authors to retain some individuality. We thank them for their patience and understanding.

The following are owed a debt of gratitude by the editors and authors in bringing this book to fruition: Patricia Giles; Louise Roffidal, RN; and C. Thorpe Ray, MD.

Thomas D. Giles
Gary E. Sander

CONTENTS

SECTION I
GENERAL ASPECTS OF CARDIOMYOPATHY

1

A Perspective on Nosology and Incidence of Cardiomyopathy

Thomas D. Giles

"What's in a name? That which we call a rose
By any other name would smell as sweet"
— WILLIAM SHAKESPEARE

Cardiomyopathy means, literally, "disease of heart muscle."[1] Despite this simple definition, the proposed classifications of cardiomyopathy are numerous.[1–7] In fact, it has been suggested that the cardiomyopathies are in danger of being classified into oblivion.[8]

Two major sources of contention have resulted from attempts to classify the cardiomyopathies: the inclusion of heart muscle disease of known cause as a cardiomyopathy and the decision as to which known causes of heart muscle disease are acceptable and which are nonacceptable. However, the restriction of the definition of cardiomyopathy, as some have suggested,[2] to myocardial disease of unknown cause, appears to serve no useful purpose; the terms "idiopathic" or "cryptogenic" are suitable modifiers when cardiomyopathy exists without a clue as to etiology (eg, viruses) or pathophysiology (eg, ischemia). Moreover, many cardiomyopathies have more than one cause, ie, they are pluricausal. The challenge for the future is defining the cause of each of the cardiomyopathies: *every cardiomyopathy has a cause(s).*

The designation of a cardiomyopathy as *primary* (the heart alone is the obvious diseased organ) or *secondary* (the heart is diseased as part of a generalized illness) is arbitrary; systemic manifestations may

be associated with any cardiomyopathy. Some clinicians use the term *primary* as synonymous with *idiopathic*.

To recognize some causes of cardiomyopathy, eg, viruses, while ignoring the existence of others, eg, cardiomyopathy due to valvular heart disease, is also arbitrary. Valvular heart disease produces permanent myocardial changes wnich, in turn, produce chronic cardiac dysfunction (see chapter 20). Every physician who cares for patients with heart disease is familiar with an unexpected poor result following valve replacement because an unappreciated factor, discovered after the fact, was significant myocardial disease. Hypertension and atherosclerotic coronary artery disease are other examples of etiologies of cardiomyopathy frequently not recognized. Thus, a broad definition of cardiomyopathy will be used throughout this book. It is not unreasonable to consider the myocardium separately when assessing heart disease.

Too often, if one etiology of cardiomyopathy is established, eg, atherosclerotic coronary artery disease, then another, eg, alcoholic cardiomyopathy, may not be considered. Moreover, the epidemic of atherosclerotic coronary artery disease in some Western countries may dull the enthusiasm for identifying other contributing etiologies for heart disease. In fact, cardiomyopathy, in many individuals, has multiple causes.

The nomenclature used for a particular cardiomyopathy generally reflects the degree to which the etiology and pathophysiology are known and understood. Thus, the nosology of cardiomyopathy is dynamic and will continue to be until all causes of cardiomyopathy are determined.

In this book, the emphasis will be on etiology, pathophysiology, and suspected associations with a contributing pathophysiologic factor (Table 1-1). As indicated above, *idiopathic* will be used to indicate that the etiology of a particular cardiomyopathy is unknown. *Idiopathic cardiomyopathy* is always a diagnosis of exclusion.

Modification of the clinicopathologic classification of cardiomyopathy proposed by Goodwin[9] has value for the clinician. The classification is of value primarily from the viewpoint of differential diagnosis and will be discussed further in chapter 5.

Certain types of cardiomyopathy as they are discussed in this book require clarification. Viral cardiomyopathy, alcoholic cardiomyopathy, and postpartal cardiomyopathy often have clinical presentations indistinguishable from the idiopathic dilated type. In fact, viruses and alcohol may account for a large number of otherwise unexplained cardiomyopathies. Viruses produce both acute and chronic myocardial effects and appreciation of the magnitude of the role that these agents play in causing cardiomyopathy continues to evolve. *Alcoholic cardio-*

myopathy may result from both metabolic and toxic factors. *Postpartal cardiomyopathy* may be included in the idiopathic category; however, the association with the postpartal period would seem to justify a separate discussion until the pathophysiology is better understood.

Ischemic cardiomyopathy is referred to by some as "cardiomyopathic syndrome resulting from coronary artery disease." The spectrum of disease begins when myocardial ischemia first occurs and not just when the heart has suffered repeated infarctions. Thus, myocardial dysfunction resulting from an unfavorable supply of blood flow to the heart relative to need caused by obstructive changes in the coronary circulation defines the entity and includes transient luminal narrowing, eg, coronary artery spasm. *Senile* cardiomyopathy is related to the poorly understood aging process and is, therefore, difficult to separate from other diseases. *Hyperergopathic cardiomyopathy* (cardiomyopathy of overwork) is primarily related to systemic and pulmonary arterial hypertension and valvular heart disease.

THE INCIDENCE OF CARDIOMYOPATHY

The cardiomyopathies are common throughout the world. However, reporting is inconsistent because nomenclature, classification, and theories concerning etiology and pathogenesis vary considerably. In 1968, the World Health Organization suggested the term "idiopathic cardiomegaly."[10] Table 1-2 gives an indication of the incidence using this procedure.[11] However, as is evident from a comparison of Tables 1-1 and 1-2, vast numbers of patients would go unreported if this definition of cardiomyopathy was used. In 1980, the WHO/ISFC Task Force suggested a division into "cardiomyopathy" and "specific heart muscle diseases."[2] Although the classification will increase the reporting of cardiomyopathy, many cardiomyopathies, eg, those secondary to coronary atherosclerosis, will continue to go unreported.

Moreover, the clinician's diagnosis is somewhat determined by standard disease coding classification. For example, the Ninth Revision of the International Classification of Disease provides the following categories for cardiomyopathy: endomyocardial fibrosis, hypertrophic obstructive cardiomyopathy, obscure cardiomyopathy of Africa, endocardial fibroelastosis, other primary cardiomyopathies, alcoholic cardiomyopathy, and secondary cardiomyopathy, unspecified. Such a restricted coding classification discourages the clinician from considering cardiomyopathy as a diagnosis for the purpose of reporting morbidity and mortality. Thus, it is not surprising that in 1982, only 10,345 deaths in 410,000 days of hospital care were attributed to cardiomyopathy.[12]

Unfortunately, much of the data concerning the incidence of

Table 1-1
Types of Cardiomyopathy*

I. Idiopathic Cardiomyopathy
  A. Dilated ("fibrotic," "congestive")
    1. Familial
    2. Sporadic
    3. Associated with idiopathic mitral valve prolapse
  B. Hypertrophic
    1. With asymmetric septal hypertrophy
    2. Without asymmetric septal hypertrophy
  C. Nondilated; nonhypertrophic
    1. Endomyocardial fibrosis
      a. Löffler's fibroplastic endocarditis

II. Specific Cardiomyopathy
  A. Alcoholic cardiomyopathy
  B. Infectious cardiomyopathy
    1. Viral
    2. Bacterial
    3. Rickettsial
    4. Protozoal
    5. Metazoal
    6. Probable infectious origin
      a. Lyme disease
      b. Whipple's disease
  C. Metabolic cardiomyopathy
    1. Endocrine diseases associated with cardiomyopathy
      a. Hyperthyroidism and hypothyroidism
      b. Myxedema
      c. Acromegaly
      d. Hypoparathyroidism
      e. Hyperparathyroidism
      f. Other endocrine disorders
    2. Diabetes mellitus
    3. Electrolyte disturbances
      a. Potassium
      b. Phosphate
      c. Magnesium
      d. Deficiency of other electrolytes
    4. Nutritional
      a. Thiamine deficiency (beriberi)
      b. Starvation cardiomyopathy
      c. Protein deficiency
      d. Other nutritional causes
  D. Immunologically mediated cardiomyopathy
    1. Postvaccinial
    2. Serum sickness
    3. Urticaria
    4. Transplant rejection
  E. Toxic cardiomyopathy
    1. Drugs
    2. Heavy metals (cobalt, cadmium, etc)

3. Poisons
4. Anesthetic gases
5. Foods

F. Cardiomyopathy associated with "collagen vascular diseases"
1. Rheumatoid arthritis
2. Systemic lupus erythematosus
3. Progressive systemic sclerosis
4. Polymyositis

G. Cardiomyopathy associated with deposition of abnormal material
1. Amyloidosis
   a. Immunocytic dyscrasia
   b. "Senile" cardiac
   c. Other
2. Hemochromatosis
3. Glycogen storage disease

H. Granulomatous cardiomyopathy (sarcoidosis)

I. Cardiomyopathy due to physical agents
1. Extreme cold and heat
2. Ionizing radiation
3. Electric shock
4. Nonpenetrating chest injury

J. Cardiomyopathy associated with neuromuscular disorders
1. Friedreich's disease
2. Progressive muscular dystrophy
   a. Duchenne's dystrophy
   b. Limb-girdle (Erb's dystrophy)
   c. Fascioscapulohumeral (Landouzy-Déjérine dystrophy)
3. Myotonic dystrophy

K. Primary tumor of the myocardium (myxoma)

L. Senile cardiomyopathy

M. Postpartal cardiomyopathy

N. Cardiomyopathy associated with other diseases of the cardiovascular system
1. Ischemic
2. Hyperergopathic
   a. Hypertensive cardiomyopathy
   b. Valvular heart disease

*This list contains most of the recognized cardiomyopathies, but is not inclusive.

cardiomyopathy is gathered from findings at necropsy, and necropsy data only partially reflect the true incidence of cardiomyopathy even at death. For example, patients with neoplastic diseases treated with doxorubicin hydrochloride may not have cardiomyopathy listed as a complication if the manifestations are mild. After the patient dies, unless cardiomyopathy dominates the clinical picture, the myocardial changes may go unreported.

It appears that in countries where the incidence of coronary artery disease is low, other types of cardiomyopathy are widely recognized.[13,14] Compared to ischemic heart disease, cardiomyopathy was coded as the cause of death in only 2% of cases in whites and 5%

Table 1-2
Incidence of Cardiomyopathy Using WHO Definition

	Years	Idiopathic Cardiomegaly (%)	Endomyocardial Fibrosis (%)	Chagas' Disease (%)
Autopsy Material				
1. Bahia, Brazil	1950–1963	6.7	—	47.9
2. Ribeirao Preto, Brazil	1960–1964	?	—	44.0
3. Sao Paulo, Brazil	—	4.3	—	13.0
4. Cali, Colombia	—	12.0	—	—
5. Kingston, Jamaica	1959–1965	4.1	—	—
6. Kampala, Uganda	1965–1967	3.5	9.2	—
7. Lyon, France	—	13.0*	—	—
8. Japan	1958–1964	3.3	—	—
Clinical Material				
9. Ibadan, Nigeria	1964–1965	29	11	—
10. Kampala, Uganda	1962–1963	13.5	11.1	—
11. Mombasa, Kenya	1960	4.3	10.8	—
12. Bulawayo, Rhodesia	—	7.3	—	—
13. Johannesburg, South Africa	1957	37.5	—	—
14. Trivandrum, Kerala (India)	"Recent"	6.7	1.3	—
15. Karachi, Pakistan	1958–1963	2.7	—	—

Reproduced with permission from Burch GE, Giles TD: Incidence of cardiomyopathy, in Bajusz E, Rona G (eds): *Recent Advances in Cardiac Structure and Metabolism. Cardiomyopathies*. Baltimore, University Park Press, 1973, vol 2, p 63.
*Primary, degenerative, and senile cardiomyopathies.

in blacks in the United States between 1970 and 1982.[12] Thus, *atherosclerotic* heart disease may mask the incidence of other types of cardiomyopathy in countries where the incidence of atherosclerosis is high. It is apparent that the incidence of atherosclerosis is now substantial in most of the world, including the developing countries (Figure 1-1).[15] Importantly, the onset of atherosclerosis may take place in the early years of life only to be manifested in middle age or older.

Clearly, systemic arterial *hypertension* continues to be a major cause of cardiomyopathy throughout many areas of the world (Figure 1-2).[16] From 8% to 18% of adults have blood pressures above 160 mmHg systolic and/or 95 mmHg diastolic, except in China where a lower prevalence is reported.

Some instances of a high incidence of *idiopathic* cardiomyopathy

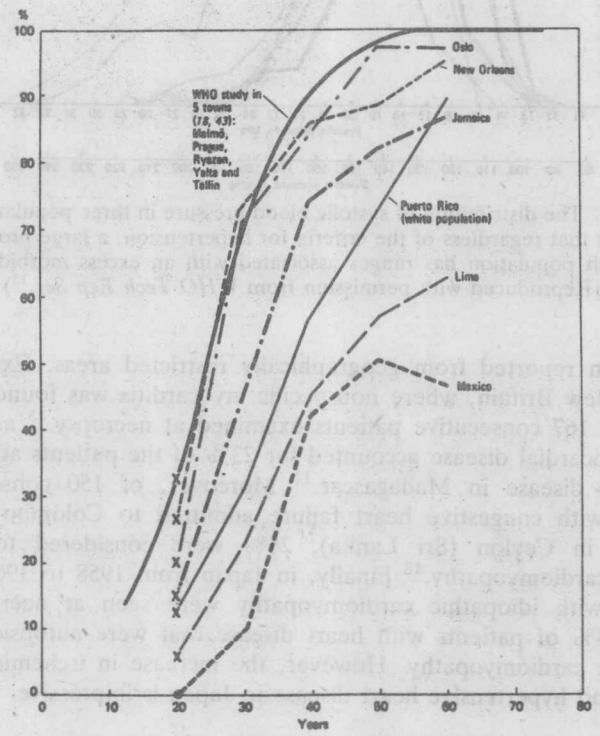

Figure 1-1 Results of necropsy studies showing the "incidence" of atherosclerotic plaques in some developed and developing populations related to age. X = prevalence rates at age 20 years. (Reproduced with permission from *WHO Tech Rep Ser.*[14])

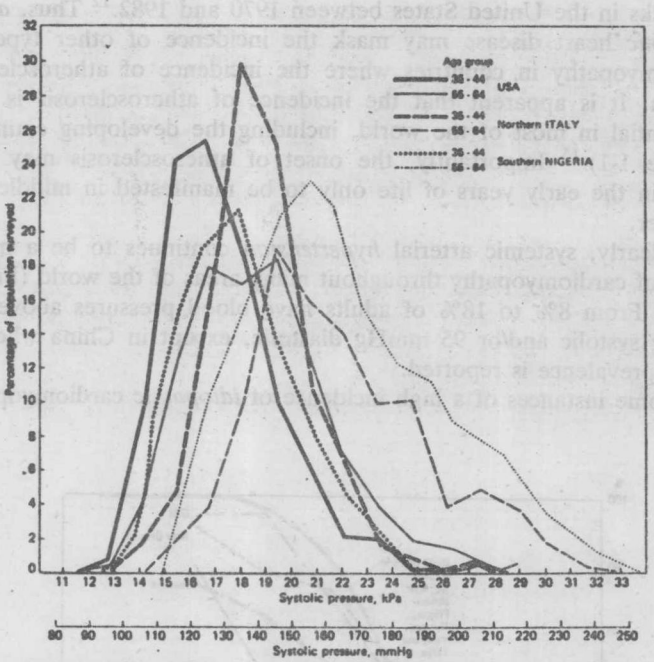

Figure 1-2 The distribution of systolic blood pressure in three populations. It is apparent that regardless of the criteria for hypertension, a large proportion of the adult population has ranges associated with an excess morbidity and mortality. (Reproduced with permission from *WHO Tech Rep Ser.*[15])

have been reported from geographically restricted areas. Examples include New Britain, where nonspecific myocarditis was found in 19 (11%) of 167 consecutive patients examined at necropsy,[15] and primary myocardial disease accounted for 23% of the patients admitted for heart disease in Madagascar.[17] Moreover, of 150 consecutive patients with congestive heart failure admitted to Colombo South Hospital in Ceylon (Sri Lanka), 26% were considered to have primary cardiomyopathy.[18] Finally, in Japan from 1958 to 1967, 512 patients with idiopathic cardiomyopathy were seen at necropsy.[19] Thus, 4.4% of patients with heart disease that were autopsied had idiopathic cardiomyopathy. However, the increase in ischemic heart disease and hypertensive heart disease in Japan is impressive.

North America and Europe

In North America and Europe, *ischemic* cardiomyopathy is the most common type of heart muscle disease.[20] Data from the United States

exemplified the role of hypertension in producing heart disease independent of its role as a risk factor for coronary atherosclerosis (Figure 1-3). Although the next most common form of cardiomyopathy is "idiopathic," it is likely that *alcohol* abuse and *infections*, especially viral, are the true culprits. Using the restricted definition of cardiomyopathy, between 1970 and 1978, the age adjusted rate for cardiomyopathy among persons 35 to 70 in the United States increased from 17 to 65 per million for white males and 5 to 24 per million for white females; non-white males increased from 61 to 157 per million and non-white females from 20 to 65 per million.[12] These figures probably illustrate the problem of reporting rather than the incidence of cardiomyopathy. In England, using the restrictive definition of dilated cardiomyopathy, ie, of unknown cause, the prevalence was 8.317 per 100,000 population.[21] In Malmo, Sweden an incidence of cardiomyopathy of 3 per 100,000 per year of the hospital population was

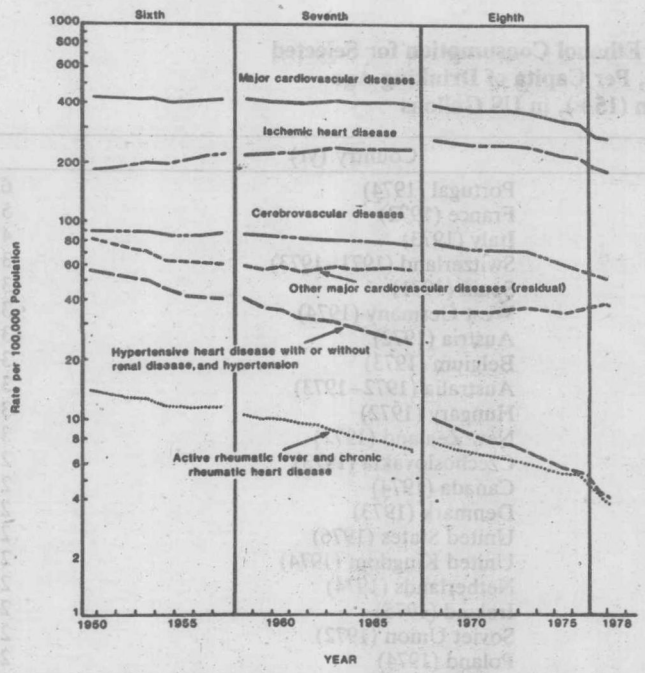

Figure 1-3 Age-adjusted death rates for major cardiovascular diseases and components, United States, 1950–1978 (Vital Statistics of the United States, National Center for Health Statistics). Although ischemic heart disease accounts for the majority of cardiovascular disease, hypertension and "other" major cardiovascular disease affect substantial numbers. Also, many of these disease categories substantially interact.