Experimental ATHERO-SCLEROSIS

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experimental
ATHEROSCLEROSIS

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To the Memory of
Deborah V. Dauber, M.D.

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FOREWORD

"But medicine has long had all its means to hand, and has discovered both a principle and a method, through which the discoveries made over a long period are many and excellent, and through which full discovery will be made, if the enquirer be competent, conduct his researches with knowledge of the discoveries already made, and make them his starting point."

On Ancient Medicine,
A Hippocratic Tract, Author Unknown, Circa 450 B.C.
Cited by B. Farrington,
Greek Science, Its Meaning for Us (Thales to Aristotle), Penguin Books, Harmondsworth, Middlesex, England, 1944.

"Their obscurity [of the internal diseases], however, does not mean that they are our masters, but as far as is possible they have been mastered, a possibility limited only by the capacity of the sick to be examined and of researchers to conduct research. . . .

"When this information is not afforded, and nature herself will yield nothing of her own accord, medicine has found means of compulsion, whereby nature is constrained, without being harmed, to give up her secrets; when these are given up she makes clear to those who understand the art what course ought to be pursued."

The Art,
A Hippocratic Tract, Author Unknown, Circa 450 B.C.

"Knowledge and Human power are synonymous, since the ignorance of the cause frustrates the effect. . . .

"Now the true and lawful goal of the sciences is none other than this: that human life be endowed with new discoveries and powers."

Novum Organum,
Francis Bacon, 1620.

" 'Tis *Works,* not *Words: Things,* not *Thinking: Pyrotechnic,* not *Philology: Operation,* not merely *Speculation,* must justify us Physicians. Forebear then hereafter to be so wrongfully Satyrical against our Noble Experimentators, who questionless are entred into the right way of detecting the Truth of things."

George Thomson,
London, 1671.
Cited by B. J. Stern,
Society and Medical Progress,
Princeton University Press, Princeton, New Jersey, 1941.

I INTRODUCTION

ATHEROSCLEROSIS AND ARTERIOSCLEROSIS

THIS MONOGRAPH DEALS ONLY WITH ATHEROSCLEROSIS. A discussion of *other types of arteriosclerosis* is beyond its scope.

This subject delineation is not an arbitrary or artificial one. We emphasize the concept that the designation, *arteriosclerosis*, refers to several distinct pathologic entities. It is a generic term. It encompasses a number of different morbid processes, all of which produce thickening of the vessel wall. It includes alterations not necessarily associated with narrowing of the lumen, e.g., Mönckeberg's sclerosis.

When Lobstein first invented the term arteriosclerosis in 1833 (1), he used it precisely in this generic way. In his initial report on medial calcinosis (1903), Mönckeberg stressed that it was a pathologic entity separate and distinct from intimal arteriosclerosis (atherosclerosis) (2). In 1906 Klotz re-posed this problem of definition and classification: "What is arteriosclerosis? (a) is it an entity; or (b) are several distinct morbid conditions included under this one heading . . . ?" (3). He gave a clearcut answer to his question: "Let us preserve the broader meaning, and regard all scleroses or hardenings of the arteries as included under this general term, recognizing, if need be, distinct varieties" (3).

This view is still maintained by contemporary clinicians, pathologists and experimentalists (4–11). It has been reenforced by the data of Sappington and Cook (12). These workers studied various types of arteriosclerosis (diffuse in-

timal thickening, Mönckeberg's medial sclerosis, focal intimal atherosclerosis) in the radial, coronary, splenic, renal and cerebral arteries at different ages. Neither Mönckeberg's medial sclerosis nor diffuse intimal thickening was related to the presence or absence of atherosclerosis in the various arterial beds. Boyd recently emphasized such facts and indicated the errors arising from their neglect: "One reason why a perusal of the discussions in the literature is so confusing is that a number of different lesions are included under the one name of arteriosclerosis, so that now one, now another condition is being alluded to. Many authors use the term as synonymous with atheroma. This is quite justifiable as long as the reader is familiar with this usage. It is not really a disease but is rather what Clifford Allbutt calls an omnibus name including several main divisions, the anatomical result of several morbid processes . . . Accordingly we shall not consider the general condition known as hardening of the arteries, but the subject will be divided into three sections: atherosclerosis, Mönckeberg's sclerosis, and diffuse arteriolar sclerosis" (5).

Hueper has recently presented a more detailed breakdown of the various pathologic types of arterial "hardening" (4). Obviously final decision concerning the merit of one or another of these classifications must await more precise elucidation of the pathogenesis and etiology of each process. Nevertheless, sufficient knowledge is currently extant to validate our identifying several distinct entities among the arterioscleroses. And for the sake of clarity the use of the plural term, the *arterioscleroses*, may not be without value.

In 1904 Marchand coined the term, *atherosclerosis*, to designate the type of intimal arteriosclerosis which is the subject of this monograph (13). The prefix *athero* (Greek *athere*, meaning mush) was selected to designate the amorphous lipid accumulation in the intima which is the hallmark of the developed lesion.