ARTERIAL DISEASE

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Foreword by
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TO OUR WIVES
MURIEL and JENNY

FOREWORD

The subject of this book is an important one for three reasons. First, many people, particularly men, die in middle age after the abrupt onset of pain in the chest and with manifestations before and after death suggesting infarction of the heart. Second, the cause of this disease is not understood, and therefore no preventive measures can be undertaken. Finally, a vast number of man-hours of scientific research, and a corresponding amount of wealth is being consumed in trying to answer this riddle. Unfortunately, the elementary facts concerning the disease in man are by no means clearly established. The critical onlooker may therefore be forgiven if he is a little doubtful whether some of this effort will have great relevance to the human problem just outlined.

It was because of this important consideration that Mitchell and Schwartz undertook the work that is set out in the first part of this book. I myself am delighted with this work for several reasons. It represents the joint effort of a physician and a pathologist to illuminate what happens during life by what can be seen after death, an effort that is nowadays too rare. They have compared the changes found in the coronary arteries with those in other arteries of comparable size and in the aorta. They have used the best methods yet described. They have avoided unnecessary and unverified assumptions. They have used the same methods to investigate patients dying with clinical or post-mortem evidence of infarction of the heart, and an unselected sample of those dying in hospital in the same city. Thus although this is not the first study of this subject it is in many ways the most complete. The story seems to be this.

The immediate cause of infarction of the heart is in most cases, though possibly not in all, a thrombus occluding a branch of a coronary artery, particularly the left anterior descending. The thrombus has a characteristic structure—clumps of platelets fringed with leucocytes and interlaced with a fibrin meshwork which often contains red cells or the ghosts of red cells. As the thrombus ages the nuclei disappear, and it becomes more uniform in composition. Later it becomes organized and recanalized. The longer the interval between the clinical attack and death, the less likely is there to be a fresh thrombus and the more likely is there to be a characteristic plaque of intimal thickening producing coronary stenosis. A unitary view

would imply that most stenosing plaques in coronary arteries represent the remnants of past thrombi of similar composition. An extrapolation of this hypothesis would be that most stenosing intimal plaques that occur in other arteries arise similarly.

A working hypothesis of the nature of this disease is thus that it is a disease in which leucocyte-platelet-fibrin thrombi occur episodically in arteries, especially at certain sites. These become organized and are incorporated into the intima as raised plaques. The media atrophies and the adventitia becomes vascular and infiltrated with cells. In this stage the disease is symptomless. Eventually a thrombus occludes a coronary artery, and the well known syndrome occurs which may or may not be fatal. This hypothesis resembles that of Rokitansky and Duguid, but differs in stressing that arterial thrombi contain platelets and leucocytes as well as fibrin. This is no more than a working hypothesis, but is as well substantiated as any other. If it is correct then the platelet, much neglected by current research projects, would seem to occupy a key position.

Finally, may I record my pleasure in being asked to write a foreword. As I have tried to indicate, this is careful, methodical work on an important subject which comes to a relatively novel, and I think probably correct, view of the nature of the disease. It is beautifully illustrated and presents new knowledge against a background of the old. It should make a substantial contribution to the advancement of knowledge in an important and hitherto poorly understood field.

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Some of our material has already appeared in scientific journals, and we are grateful to the following for permission to reproduce photographs, diagrams and data:

Figures 2.23, and 2.25, and the data on adventitial cellular infiltration—the Editor of *Circulation*, by permission of the American Heart Association.

Figures 3.1 to 4, 3.10 to 13 and the line diagrams in that chapter—the Editor, *Circulation Research*, by permission of the American Heart Association.

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PART TWO
ARTERIAL DISEASE—A REVIEW

INTRODUCTION

CHAPTER I

THE PROBLEM

'A man is as old as his arteries' (Cabanis *c.* 1800)

Despite increasing concern over the mortality and morbidity caused by cardiac infarction, stroke and limb gangrene, little progress has been made towards understanding their cause, or devising effective regimes for their treatment and prevention. Our failure to solve the problem of arterial disease may simply reflect the difficulties inherent in the task, but we consider that three remediable factors have contributed to our lack of progress:

1. The confusion which has been produced by the terms used to describe arterial lesions.
2. The way in which material has been selected for study.
3. The tendency to concentrate on one aspect of the disease or on one method of examination rather than studying the problem as an integrated whole.

1. TERMINOLOGY IN ARTERIAL DISEASE

Humpty Dumpty maintained that when he used a word it meant what he chose it to mean, neither more nor less, and there are those who would agree with him and who appear to believe that terminology is of little consequence. Although it may be possible to find one's way about a big city without knowing any of the street-names, when a group of people begin to compare notes on the best way to get from *A* to *B*, if they all have different names for the streets to be traversed, confusion is inevitable (Pappworth 1963). So it is in arterial disease, for when we attempt to compare findings within the same country at different times, to compare findings in different countries, to compare findings in different animal species or to integrate the results of workers from many disciplines, then the importance of the terms we use is inescapable. The present confused state has come about in two ways. First, by the transfer of terms from one discipline, where they had a precise and restricted implication, to other disciplines, where they are used more loosely or even in a completely different sense. In this way, terms such as 'infarction', 'thrombosis' and 'occlusion' have become labels for certain clinical events, whereas they are in reality descriptions of necropsy findings. Second, the use of terms which

have never had a precise or restricted meaning in any discipline, such as 'atheroma', 'atherosclerosis' and 'ischaemic' or 'degenerative' heart disease. These terms have been interpreted in many different ways, and are therefore virtually meaningless. If we are to advance our knowledge of arterial disease, then clinicians, pathologists, epidemiologists, statisticians, coagulation workers, veterinarians, biochemists and workers from many other disciplines must be able to understand each other; if the existing currency in terminology is debased, we must start afresh by looking, describing, classifying and comparing.

2. SELECTION OF MATERIAL FOR STUDY

Groups of patients studied in life and at necropsy have presented in a certain way, at a certain time and at a certain place because of an interplay of selection factors. We should recognize this, try to assess the effect of these factors on our findings and refrain from drawing conclusions about the whole from a highly selected sample. In particular the fallacy of apparent associations between diseases must be emphasized. For example, Hutchinson & Yates (1957) found that 40 per cent of a group of patients with strokes had significant narrowing of their neck arteries, and this has been thought to show that neck artery stenosis is an important causal factor in the production of strokes. As Schwartz & Mitchell (1961) found that a similar proportion of routine hospital necropsies showed the same amount of disease, this seems an unwarranted assumption. It is never enough to know that diseases A and B coexist; information is needed not only about the frequency of $A+B$ but also about A alone and B alone. Mainland (1953) has drawn attention to the fallacies inherent in this type of observation, but reports based on associations between diseases continue to appear, such as those on the relationship between liver disease and cardiac infarction (Hall, Olsen & Davis 1953; Howell and Manion 1960), and between duodenal ulceration and claudication (Eastcott 1962).

3. THE METHOD OF STUDY

No single investigator can master all the ways in which arterial disease can be studied, but all too often the boundaries of the examination are self-imposed, attention being given to those aspects of the material which are thought to be important. Thus as 'atherosclerosis' has been defined by some as a fatty disease of the intima (Hall 1957; Muir 1951), attention has been focused on lipids and on the intima, other chemical constituents and other parts of the arterial wall being correspondingly neglected. A narrow approach may be excellent if the original reasons for focusing attention in this way are correct; if not, it results in the omission of certain patients,