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*The Clinical  
Aspects of*  
**ARTERIOSCLEROSIS**



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## Foreword

THE GREAT problems of medicine are functions of time, place and economic development. In primitive societies, the major challenges derive from the noxious effects of undernutrition and the infective and traumatic hazards of the environment. These causes of morbidity and mortality recede *pari passu* with advancing culture. The result is that a higher proportion of the population reaches the time of life in which the endogenous processes of physical deterioration inherent in all living substance attain significant intensity. Economic advance, at least in contemporary Occidental Civilization, most often brings in its wake a diet containing more animal lipids. From the evidence available at present, it appears likely that this combination of an aging population and a diet rich in animal lipid has created a milieu favorable to the development of atherosclerosis. But whether or not this pathogenesis is factual, there can be no doubt of the enormous increase in the frequency of atherosclerosis in the Western World. In the thirty-five years that the writer has practiced medicine in New York City, an infinitesimal moment in medical evolution, the augmented incidence of coronary thrombosis and other atherosclerotic diseases has been all too evident; it has not been a matter of improved diagnosis, for my teachers of three decades ago were well acquainted with the clinical manifestations of coronary disease and certainly with its post mortem recognition. There is no doubt that in the Western World atherosclerosis has succeeded to the grisly title of *Captain of the Men of Death* held in the past by such redoubtable scourges as starvation, war, tuberculosis, malaria, bubonic plague and pneumonia. Moreover, the greater case incidence of arteriosclerotic disease does not fully measure the increment in the proportion of the contemporary physician's effort which is devoted to the victims of arteriosclerosis. For the introduction of intensive sodium restriction and mercurial diuretics has greatly prolonged the average duration of life in coronary disease and the antibiotics have done the same for sufferers from cardiac, cerebral and other localizations of arteriosclerosis. Diabetic and hypertensive patients live longer than before, and the late stages of both diseases are dominated by the consequences of arteriosclerosis. The result is that a startling proportion of the patients in the medical, neurological and psychiatric wards are there because of arteriosclerotic disease.

The enormity of the challenge presented by the arteriosclerotic maladies has of course called forth a corresponding increase in clinical and experimental investigation. The resulting literature is gargantuan and scattered

throughout the journals of every branch of medicine as well as in numerous monographs dealing primarily with experimental investigation, pathological anatomy or the clinical aspects of arteriosclerotic disease of the heart, brain, extremities or other individual organs. But the practitioner must deal every day with arteriosclerotic disease in various organs. It is hardly feasible for him to keep abreast of this vast scattered literature, or for the specialist to follow the publications in fields other than his own. Dr. Rinzler's book integrates in a single volume the totality of the clinical aspects of arteriosclerosis in coordination with recent basic investigations along morphological, physiological, biochemical, geopathological, and epidemiologic lines. He has surveyed the enormous literature and subjected it to critical analysis in the light of his own extensive studies and experience. The pathogenesis of arteriosclerosis is still very much sub judice, but in the forty odd years since Anitschkow first rendered rabbits atheromatous by feeding cholesterol, a great deal has been achieved by investigation along diverse paths, and this is judiciously evaluated by Dr. Rinzler. He presents the evidence which negates the formerly dominant nihilistic view that atherosclerosis is an almost inevitable concomitant of senescence and shows that it is a potentially reversible process. The major objective of Dr. Rinzler's book, however, is the elucidation of the clinical aspects of arteriosclerosis, and in this he has succeeded in superlative fashion. Diagnosis, prognosis and treatment of the arteriosclerotic diseases are all covered in the light of both an exhaustive survey of the world literature and his own experience and work. Especially noteworthy and detailed are the sections on arteriosclerotic heart disease, quantitatively the most important of the arteriosclerotic diseases, which Dr. Rinzler has studied intensively for many years and to the understanding of which he has substantially contributed. The discussion of cerebral arteriosclerosis is illuminated by the addition of the point of view of the internist to this primarily neurologic subject.

The profession is indebted to Dr. Rinzler for undertaking and successfully accomplishing the tremendous task of elucidating present-day knowledge of arteriosclerosis and its consequences. In his book, medical student and practitioner will find a comprehensive, authoritative and judiciously evaluated presentation of which is known of the nature, clinic and treatment of the arteriosclerotic diseases.

ARTHUR M. FISHBERG, M.D.

*New York, New York*

## Preface

THE UPSURGE in interest in arteriosclerosis over the past decade from the experimental and therapeutic viewpoint, plus the reported increase in incidence of arteriosclerosis because of the longer life span, prompted this book which deals with a holistic approach to the clinical problems in arteriosclerosis. I have stressed the arteriosclerotic patient as seen by the general practitioner, in particular, by emphasizing the diagnosis and therapy of the major and minor manifestations of arteriosclerosis from head to foot. However, the specialist, especially in the medical branches, may find the text of general interest.

The greater part of the book has been devoted to the cardiac, cerebral and peripheral vascular manifestations of arteriosclerosis, and, rightfully so, since these organs are most commonly involved in this disease and account for the highest incidence of morbidity and mortality. The chapter on General Considerations represents an attempt to orient the reader in the present-day direction of thought with regard to the etiology, to the abnormalities in the biochemical processes, and to the co-related diseases.

Acknowledgments, as alluded to in the inscriptions, are due to many of my colleagues. My original interest in the clinical aspects of arteriosclerosis began in 1941 when, under the aegis of Dr. Harry Gold, I was permitted to attend the meetings of a Committee of the New York Heart Association which was planning the study of the life history of arteriosclerosis. Dr. Janet Travell and I also began at this time a collaboration, both at Dr. Gold's Cardiac Clinic at Beth Israel Hospital and at the Department of Pharmacology at Cornell University Medical College, of studies on cardiac pain and on coronary dilator drugs which led to the publication of a monograph on Cardiac Pain in 1951. Dr. Travell, Dr. Gold and Dr. McKeen Cattell, Professor of Pharmacology at Cornell University Medical College, have shown interest, kindness and have been of utmost help beyond the call of duty in the pursuit of my studies. The Cornell Conferences on Therapy, conducted by the Department of Pharmacology, have been a great source of instruction in therapeutic matters.

Dr. Arthur Fishberg, Director of Medicine at Beth Israel Hospital, was kind enough to review the text in the early stages of its writing. His ward service rounds and teachings have contributed greatly to my understanding of the in-patient problems in arteriosclerosis. Dr. Abraham Schlossman critically reviewed the section on retinal aspects of arteriosclerosis. Dr. Abraham Geffen, of the Department of Radiology at Beth Israel Hospital, kindly supplied some of the roentgen films used in this book. For several years after

1946, Dr. Seymour Rogers was the surgical half of the team in the Peripheral Vascular Clinic at Beth Israel Hospital, and we worked together until Dr. Rogers left New York.

I am grateful to Dr. Howard A. Rusk, Director of the Department of Physical Medicine and Rehabilitation at Bellevue Hospital, for permitting the studies of drug therapy in the treatment of hemiplegia and of the rehabilitation of the cardiac, and for the opportunity to observe, on his service, the cerebro-vascular and spinovascular complications of arteriosclerosis. Dr. Arthur C. Corcoran, of the Cleveland Clinic, was most helpful with suggestions for improving the text just before it went to press. The arduous task of proofreading the text was assumed by my wife, Rita. For this and much more, I give her my heartfelt thanks.

It is with great appreciation that I would like to acknowledge the grants from The National Heart Institute of the United States Public Health Service, The Josiah Macy, Jr., Foundation and the Loyal League Philanthropies, which directly or indirectly made possible our clinical studies.

My secretaries through the years of the writing of the text have been Corinne Futterman, Linda Dubester, Irene Friedman and Myrna Cassin.

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# Contents

	<i>Page</i>
FOREWORD . . . . .	vii
PREFACE . . . . .	ix
<i>Chapter</i>	
I. GENERAL CONSIDERATIONS . . . . .	3
Definition of Arteriosclerosis . . . . .	3
The Incidence of Arteriosclerosis . . . . .	3
The Heritage of Arteriosclerosis . . . . .	12
The Pathology of Arteriosclerosis . . . . .	13
The Pathogenesis of Arteriosclerosis . . . . .	16
Biochemistry of Arteriosclerosis . . . . .	20
Diet and Arteriosclerosis . . . . .	26
Anti-Arteriosclerotic Agents . . . . .	30
Sex and Arteriosclerosis . . . . .	34
Race and Arteriosclerosis . . . . .	37
Hypertension and Arteriosclerosis . . . . .	38
Diabetes Mellitus and Arteriosclerosis . . . . .	38
Corneal Arcus and Arteriosclerosis . . . . .	39
Xanthelasma, Xanthoma and Arteriosclerosis . . . . .	39
Intramuscular Vessels and Arteriosclerosis . . . . .	40
References . . . . .	40
II. CARDIAC ASPECTS OF ARTERIOSCLEROSIS . . . . .	52
Blood Supply of the Heart . . . . .	52
Nerve Pathways of the Heart . . . . .	53
Coronary Circulation and Arteriosclerosis . . . . .	56
The Natural History of Coronary Artery Disease . . . . .	56
The Clinical Aspects of Coronary Atherosclerotic Disease . . . . .	60
Objective Tests for Diagnosis of Effort Angina . . . . .	63
The Ballistocardiogram in Coronary Artery Disease . . . . .	66
Stress Tests for Use in Patients With Chest Pain and Normal Rest- ing Electrocardiograms . . . . .	69
Stress Tests With Drugs . . . . .	75
Anoxemia Test . . . . .	78
Critique of Stress Tests . . . . .	80
The Exercise and Anoxemia Ballistocardiogram . . . . .	81
Tobacco, the Ballistocardiogram and Coronary Artery Disease . . . . .	81
Blood Tests in the Diagnosis of Coronary Insufficiency . . . . .	82
Prognosis of Angina Pectoris . . . . .	82
References . . . . .	83



<i>Chapter</i>	<i>Page</i>
III. DIFFERENTIAL DIAGNOSIS OF CHEST PAIN . . . . .	89
Lesions of the Vascular System . . . . .	89
Lesions of the Muscular System . . . . .	92
Lesions of the Nervous System . . . . .	93
Lesions of the Bones . . . . .	95
Lesions of the Respiratory System . . . . .	96
Lesions of the Gastrointestinal Tract . . . . .	97
Lesions of the Mediastinum . . . . .	100
Lesions of the Pericardium . . . . .	101
Hematologic Diseases . . . . .	101
Lesions of the Diaphragm . . . . .	102
Functional Cardiovascular Disorder . . . . .	102
References . . . . .	103
IV. TREATMENT OF THE PATIENT WITH EFFORT ANGINA . . . . .	108
Drug Therapy . . . . .	111
Coronary Vasodilators . . . . .	112
Miscellaneous Agents . . . . .	118
References . . . . .	127
V. SURGICAL THERAPY . . . . .	134
Interrupting Sensory Pathways . . . . .	140
References . . . . .	155
VI. CONGESTIVE HEART FAILURE . . . . .	160
References . . . . .	172
VII. DISORDERS OF THE HEART BEAT IN CORONARY ARTERY DISEASE . . . . .	176
Drug Therapy in Disorder of the Heart Beat . . . . .	176
Specific Disorders of Heart Beat . . . . .	178
References . . . . .	184
VIII. ACUTE MYOCARDIAL INFARCTION . . . . .	186
Complications of Acute Myocardial Infarction . . . . .	200
Prognosis of Acute Myocardial Infarction . . . . .	205
References . . . . .	209
IX. CEREBRAL ASPECTS OF ARTERIOSCLEROSIS . . . . .	217
Blood Supply . . . . .	217
Cerebral Roentgenology, Angiography and Arteriosclerosis . . . . .	221
Cerebral Circulation and Arteriosclerosis . . . . .	224
Cerebral Arteriosclerosis . . . . .	225
Cerebrovascular Accidents . . . . .	229
Vascular Lesions of the Brain Stem . . . . .	233
Spinovascular Accidents . . . . .	243
Differentiation of Cerebral Hemorrhage From Cerebral Thrombosis . . . . .	244
Treatment of Hemiplegia . . . . .	245
Treatment of Parkinson's Syndrome . . . . .	250
References . . . . .	253

Chapter	Page
X. AORTIC ASPECTS OF ARTERIOSCLEROSIS . . . . .	261
Blood Supply . . . . .	261
Arteriosclerosis of the Thoracic Aorta . . . . .	261
Occlusion of the Aorta . . . . .	261
Thromboarteriosclerosis of the Abdominal Aorta . . . . .	262
Arteriosclerotic Aneurysms . . . . .	267
Mesenteric Thrombosis . . . . .	270
Innominate Artery Thrombosis . . . . .	271
References . . . . .	271
XI. PERIPHERAL VASCULAR ASPECTS OF ARTERIOSCLEROSIS . . . . .	274
Blood Supply . . . . .	274
Types of Peripheral Arteriosclerotic Disease . . . . .	274
Monckeberg's Arteriosclerosis . . . . .	274
Arteriosclerosis Obliterans . . . . .	276
Treatment of Arteriosclerosis Obliterans . . . . .	280
Acute Arterial Occlusion . . . . .	290
Peripheral Arterial Embolism . . . . .	291
Peripheral Arterial Arteriosclerotic Aneurysms . . . . .	292
References . . . . .	293
XII. RETINAL ASPECTS OF ARTERIOSCLEROSIS . . . . .	298
Ophthalmoscopic Signs of Arteriosclerosis . . . . .	298
Retinal Arteriosclerosis With and Without Hypertension . . . . .	301
Circulatory Disturbances of the Retina . . . . .	302
Anticoagulants for Occlusive Vascular Disease of the Retina . . . . .	303
Stellate Ganglion Blocks . . . . .	306
Diabetic Retinopathy . . . . .	306
References . . . . .	306
XIII. RENAL ASPECTS OF ARTERIOSCLEROSIS . . . . .	310
Blood Supply . . . . .	310
Diabetic Glomerulosclerosis . . . . .	310
Renal Artery Sclerosis and Thrombosis . . . . .	311
References . . . . .	311
XIV. PULMONARY ASPECTS OF ARTERIOSCLEROSIS . . . . .	314
Blood Supply . . . . .	314
Clinical Aspects . . . . .	314
References . . . . .	316
XV. CONCLUSIONS . . . . .	317
References . . . . .	318
INDEX . . . . .	319

*The Clinical Aspects of*  
ARTERIOSCLEROSIS

*No man is an Iland, intire of itselfe.*

JOHN DONNE

*I live not in myself, but I become*

*Portion of that around me:*

BYRON

*I am a part of all that I have met.*

TENNYSON

## General Considerations

**T**HE CLINICAL problems in vascular disease due to arteriosclerosis arise from occlusive intimal disease (atherosclerosis) (1) of the small and medium-sized arteries (2) and statistically affect mainly the heart, brain and lower extremities (3). However, a "head to foot" approach to the problem of the patient with arteriosclerosis must be made since arterial insufficiency or occlusion may, under suitable circumstances, be found in any artery (4-6). It is the purpose of this volume to deal with the clinical aspects of arteriosclerosis primarily from the points of view of diagnosis and therapy.

### DEFINITION OF ARTERIOSCLEROSIS

Moschcowitz (7) defines arteriosclerosis as a progressive and irreversible affection of the arteries in which hyperplasia of one or more of the structural elements is a primary reaction, with deposition of lipids, collagenous tissue, hyalin and calcium as a secondary reaction, the totality of both components resulting in thickening, dilatation, deformity, and loss of elasticity of the walls. Arteriosclerosis is to be regarded as a generic term (8) which includes such entities as atherosclerosis, Mönckeberg's sclerosis, atheromatosis and hyperplastic arteriosclerosis. Atheromatosis (9) indicates a degenerative lesion in which lipid material, particularly cholesterol, is accumulated in the intima. This is a reversible condition. Atherosclerosis indicates the presence not only of lipid material and often calcium, but also of reactive connective tissue proliferation. Here the primary target is the intima and the goal, complete occlusion of the arterial lumen. True Mönckeberg's sclerosis is associated with calcification of the medial coat and not necessarily with lesions of the intima. Hyperplastic arteriosclerosis (10, 11) refers to the normal involutionary process which arteries undergo from birth to maturity. Arteriosclerosis is to be regarded as an exaggerated phase dependent on such factors as intravascular pressure, normal and increased, the composition of the blood, perivascular stresses and fixations, the vascular supply of the blood vessel walls and tissue permeability.

### THE INCIDENCE OF ARTERIOSCLEROSIS

Arteriosclerosis is found in 25 per cent of people between 40 and 49 years, 48 per cent of people between 50 and 59 years, 78 per cent of people between 60 and 69 years, and 90 per cent of people over 70 years of age. In 1951 (12) the total deaths from all causes in the United States were

1,481,000. Cardiovascular diseases accounted for 767,000 (51.8 per cent) of these deaths. Arteriosclerotic heart disease, including coronary disease, caused 338,000 (44.1 per cent) deaths. General arteriosclerosis resulted in 37,000 (4.8 per cent) deaths. Vascular lesions affecting the central nervous system (mixed hypertension and arteriosclerosis) caused 158,000 (20.6 per cent) deaths. In the year 1951, *cardiovascular disease caused over half of all deaths, and arteriosclerosis and hypertension caused over 90 per cent of all deaths from cardiovascular disease.*

Statistics gathered by the New York Heart Association in 1952 indicated that 500,000 of the 8,000,000 population of New York City were suffering from diseases of the heart and circulation. Of a total of 81,239 deaths,

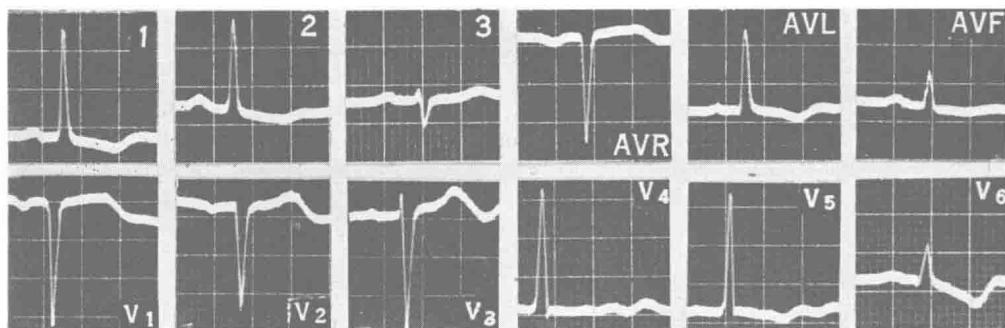


Fig. 1. Electrocardiogram of a 59-year-old white male with arteriosclerotic heart disease taken in 1955, showing non-specific myocardial damage. The electrocardiogram was normal in 1950 and during the 5 ensuing years, without a clinical acute myocardial infarction, the T waves gradually became inverted.

42,729 were due to disease of the heart and circulation, with diseases of the heart resulting in 35,684 deaths and vascular lesions of the central nervous system causing 5,560 deaths. The number of attacks of coronary occlusion that occur annually has been estimated to be between 500,000 (13) and 1,000,000 (14, 15). Gould (9) estimated that in 1953 there were approximately 600,000 persons living in the United States who had had one or more myocardial infarctions.

**The co-occurrence of arteriosclerosis in various parts of the body. Patients under 40 years of age:** Berlin (16) found no evidence of clinical coronary artery disease in 11 cases of cerebral thrombosis in young adults. One patient examined at autopsy showed no disease of the coronary arteries.

Gertler (17) in discussing myocardial infarction in patients under 40 years of age, does not mention any clinical atherosclerosis elsewhere in the body. Yater (18) presented autopsy data on 450 patients of from 18 to 39 years of age who died of coronary thrombosis. Clinical evidences of cerebral or peripheral vascular disease were absent. Cerebral arteriosclerosis

at autopsy was present in a mild to moderate degree in 10 patients. Arteriosclerosis of the kidneys were found in 6 patients. In a few patients in whom there was considerable atherosclerosis of the aorta, the first portion of the intercostal arteries, lumbar arteries, celiac artery, mesenteric artery or renal arteries was also involved. In 191 patients there was atherosclerosis of the aorta, but in 103 the lesions were comparatively insignificant. Yater concluded that coronary artery sclerosis in this series was a specific disease in the coronary arteries and was not a part of generalized arteriosclerosis.

It would seem that in those under 40 years of age, the clinical manifestations of atherosclerosis appear in a single organ. This is to be contrasted

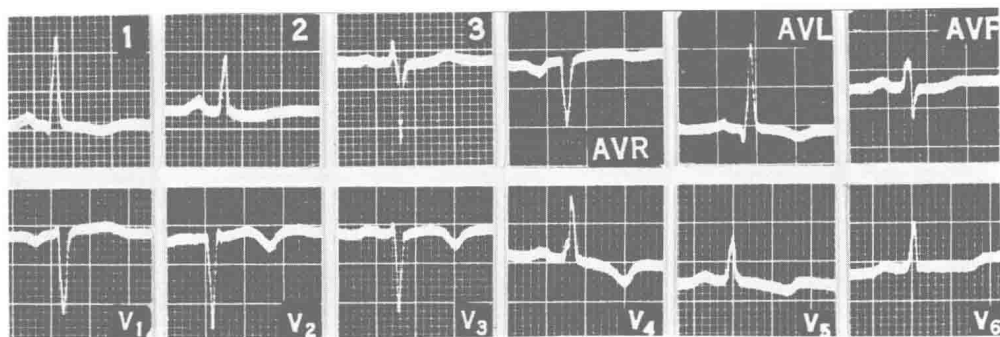


Fig. 2. Electrocardiogram of a 58-year-old white female illustrating a previous anterior wall infarction,  $Q_1T_1$  pattern.

with the clinical finding of simultaneous atherosclerosis in various parts of the body in the older age groups.

**The co-occurrence of arteriosclerosis in various parts of the body. Patients over 40 years of age:** Boas and Epstein (19) studied the prevalence of manifest atherosclerosis of a working union population of 32,000 male and female garment workers over 40 years of age by examination of 343 men and 225 women who represented a sample of this total union population. The average age of the men was 60 years, and of the women, 54 years.

Their method of examination for the presence of atherosclerosis is presented in detail as an example of the techniques useful in the diagnosis of atherosclerosis:

Each examination includes the following: family and medical history; dietary history, complete physical examination, 12-lead electrocardiogram, postero-anterior chest roentgenograms and lateral roentgenograms of the abdomen for evidence of aortic calcifications, blood tests (glucose, cholesterol, phospholipid, uric acid, serological test for syphilis), and urine examination.

The diagnosis of atherosclerosis is made whenever evidence of coronary, peripheral, or cerebral artery disease or aortic calcifications, alone or in combination, are found.



The diagnosis of coronary disease is based on a definite history of angina pectoris or myocardial infarction or on the following characteristic electrocardiographic signs:  $Q_1T_1$  patterns,  $Q_3T_3$  patterns with concomitant changes in Lead aVf, abnormal Q waves (Q being 20% or more of QRS in Leads I and/or II, 30% or more of QRS in Leads  $V_5$  and/or  $V_6$ , or 60% or more in Lead aVf), widening of the QRS interval to 0.12 second or more in the absence of undue cardiac hypertrophy, or S-T elevations or depressions of

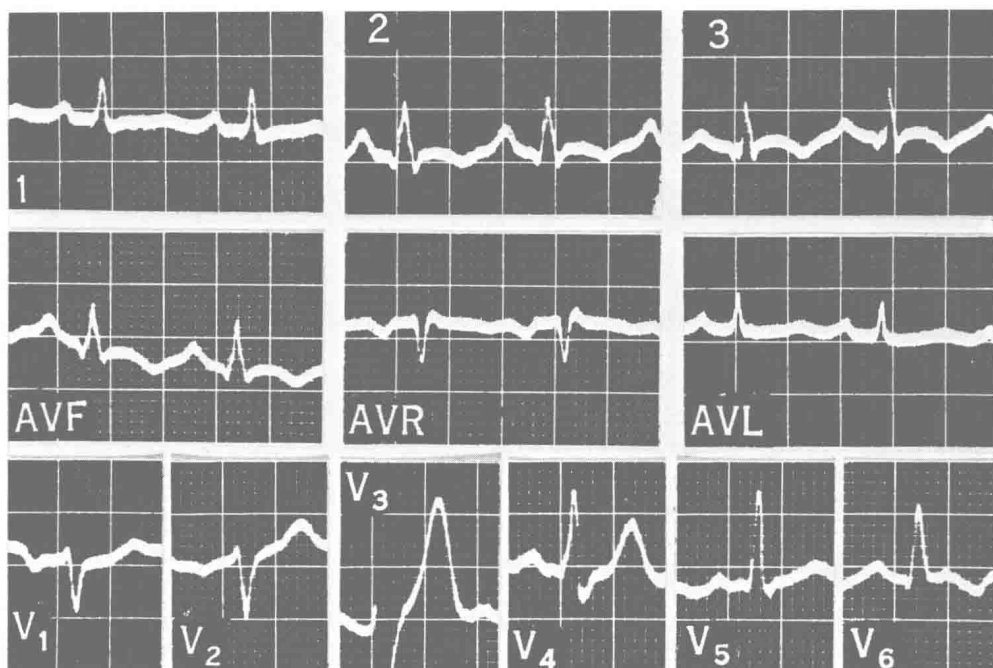


Fig. 3. Electrocardiogram of a 53-year-old white male illustrating a previous posterior wall infarction,  $Q_3T_3$  pattern.

2 mm. or more in one or more leads, unaccounted for by left ventricular strain, digitalis, or transient causes [Figs. 1-5].

Peripheral artery disease is diagnosed when two or more pulses in one leg or one or more pulses in each leg are absent in the femoral, popliteal, anterior, or posterior tibial arteries. No importance is attached to absent pulsations in the dorsalis pedis arteries. It is agreed that the absence of pulsations in the major arteries is the most reliable single sign of occlusive arterial disease in the legs. It is occasionally difficult to be certain whether a given pulsation is present, diminished, or absent. In such cases, postural color changes and, despite their limited value, oscillometric readings have been used as additional guides. Symptoms of intermittent claudication, without objective signs of arterial insufficiency, are not considered diagnostic of peripheral artery disease, since true occlusive disease rarely if ever occurs unless there is absence or diminution of peripheral pulsations.

Cerebral atherosclerosis is diagnosed from a history of a major stroke or an attack of sudden transient dizziness, aphasia, or mental confusion, accompanied by unilateral palsy, or signs of residual lesions of the central nervous system.

Aortic calcifications are diagnosed from postero-anterior 6-ft. (1.8 meter) chest plates and lateral views of the abdomen [Figs. 6 and 7]. The chest films are slightly overpenetrated in order to reveal calcifications more clearly; on an average, 66 kv., 300 ma., with an exposure of 1/10 second is used. Lateral roentgenograms of the abdomen are taken with a Bucky grid at a distance of 36 in. (90 cm.), using 100 ma., and exposure of 2 seconds, and an average of 85 kv., depending on size of the patient. Calcification of the thoracic aorta is diagnosed if definite crescentic shadows are seen in the

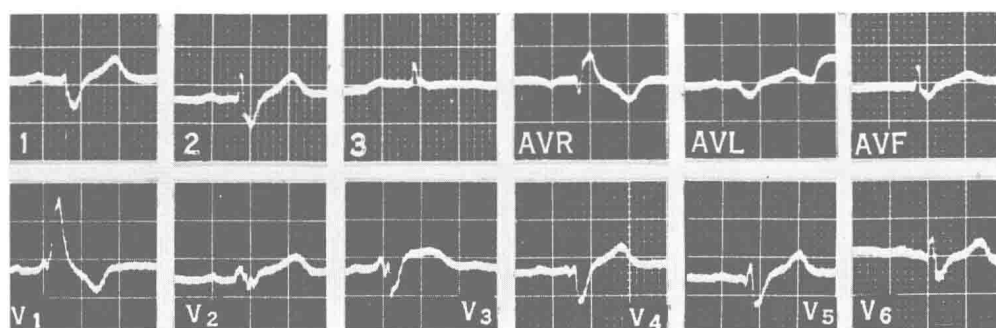


Fig. 4. Electrocardiogram of a 49-year-old white male illustrating a right bundle branch block.

aortic knob. Calcification of the abdominal aorta is diagnosed in the presence of single linear densities at least 1 cm. long or multiple streaks, in line or parallel, in the proper location. Advanced calcification that outlines the aorta is easily recognized.

Using these standards, 33 per cent of the men and 23 per cent of the women had one or more lesions of atherosclerosis in various parts of the body. Ten per cent of the men and 2 per cent of the women had evidence of coronary disease; the corresponding figures for peripheral artery disease were 4 per cent in men and 1 per cent in women; those for cerebrovascular disease were 0.6 per cent in men and 0.4 per cent in women. As many as 26 per cent of the men and 23 per cent of the women demonstrated aortic calcification on the roentgen film. In the men 19 per cent of the calcifications were in the thoracic aorta, 62 per cent were in the abdominal aorta, and 19 per cent were in both sites. For women the corresponding figures were 14 per cent, 67 per cent and 19 per cent.

Eighteen of the 35 men with coronary artery disease had this as the sole atherosclerotic lesion. Four of 9 with peripheral atherosclerosis had this alone, and 71 of a total of 89 men with aortic atherosclerosis had it as the