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The coronary arteries and the myocardium in healed "rheumatic hearts"

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MYOCARDIUM IN 'HEALED' RHEUMATIC HEARTS

DAVID H. FULMER


1963

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THE CORONARY ARTERIES AND THE MYOCARDIUM
IN 'HEALED' RHEUMATIC HEARTS

David H. Fulmer

A Thesis

Presented to the Faculty of the School of Medicine

Yale University

In Partial Fulfillment of the Requirement

for the Degree of

Doctor of Medicine

Department of Pathology

1963



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To

Levin L. Waters, M.D.

whose knowledgeable guidance, many hours of personal assistance and stimulating enthusiasm made this paper possible.

To Messrs. Edward Iannucci and Peter Integlia whose experienced aid was available for the asking.

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THE CORONARY ARTERIES AND THE MYOCARDIUM
IN 'HEALED' RHEUMATIC HEARTS

Introduction

"Rheumatic heart disease ranks with coronary and hypertensive heart disease as one of the most common and serious types of cardiac disorder. Its special importance is in that it is a disease of youth, killing and crippling many children and young adults." This statement from Gould's "Pathology of the Heart" characterizes the special emphasis that has been placed on the pathology of the acute phase and of the chronic valvular lesions of rheumatic heart disease.

This study is a clinico-pathologic investigation of patients who have survived for long periods after the acute phase of rheumatic heart disease with particular regard to the state of their coronary arteries and myocardium at the time of death. Information for this was obtained from the clinical histories and necropsy material of patients who died some time after the disease had resolved or become quiescent. The central question to be considered is whether or not acute rheumatic fever accelerates or otherwise alters the usual process of arteriosclerosis of the coronary arteries and the associated ischemic heart disease.

Review of the Literature

The earliest recognition of the disease entity now known as rheumatic heart disease came in 1788-89 when Pitcairn (1) and Jenner (2) commented on the association of rheumatic joint disease and organic lesions in the heart. Adams (3) in 1827, was the first to discuss the myocarditis found with this disease. In 1835 Bouillard (4) emphasized the frequency with which pericarditis and endocarditis are found in rheumatic fever. The cellular proliferation near cardiac blood vessels and between myocardial fasciculi was described by Goodhart (5) in 1879 and six years later Vaisse (6) observed myocardial necrosis and scarring in active rheumatic fever. Krehl (7), in 1890, was the first to comment on the arteritis of small and medium sized myocardial vessels in which damaged and proliferative and medial elements often narrowed the lumen. He ascribed the angina-like precordial pain of rheumatic fever to the ischemic effect on the myocardium of this narrowing. In elaboration of Krehl's observations, Rhomberg (8) described diffuse hyaline thrombosis of the smaller arteries and also periarteritis involving the middle size coronaries. According to Rabe (9), the arterial lesions in acute rheumatic fever had been described earlier by DeMussy (1872), Legroux (1884), and Martin (1891).

In 1904, Aschoff (10) described the characteristic nodular lesions of rheumatic myocarditis, emphasizing their proximity to small and medium sized arteries. In 1926, Von Glahn and Pappenheimer (11) emphasized the apparent specificity of the

lesions to small and medium sized myocardial vessels but they also pointed out similar lesions which occur in peripheral arterioles, capillaries of the lung, and in other organ systems. The swelling and splaying of elastic tissue which these authors described was present in the acute phase of the disease. Geipel (12) described endothelial and collagenous hyperplasia in the intima, fibrin deposition in subintimal connective tissue, destruction of the elastica interna and marked narrowing of the lumen. Intimal fibrosis was also noted by Klotz (13) who examined the aortas in acute rheumatic fever. Klinge (14) described fibrinoid degeneration of the ground substance, lymphocytic and leukocytic infiltration and palisade arrangement of cells in the arterial walls. These changes are more pronounced than the associated hypertrophy and proliferation of connective tissue cells. He also believed that the fibrinoid degeneration which he saw in the media and intima is not specific and may be seen in diseases other than rheumatic fever. He also stated that in the chronic, 'healed' phase the hyaline, collagenous material both in arterial walls and in the center of Aschoff bodies disappears. Klinge did believe that the fibrinoid and infiltrative lesions that he saw in the media and intima evolve into fibrosis and granulomata within the arterial wall, often narrowing the lumen. In addition to describing necrotic lesions in the skeletal muscles of patients who died with acute rheumatic fever, Geipel (15) pointed out that Aschoff bodies are also seen in myocardial tissue at some distance from vessels. MacCallum (16) distinguished the arterial

lesions from those of periarteritis by showing that Aschoff nodules are never within and only rarely intimately surrounding the vessels. Von Glahn and Pappenheimer (11) remarked on the superficial resemblance of the lung arteriolar lesions to those of periarteritis nodosa but without thrombosis or aneurysms. Other investigators have also remarked on this similarity to periarteritis nodosa (14)(17)(18).

Both Swift (19) and MacCallum (16) felt that the proximity of Aschoff nodules to coronary arteries does cause compression and narrowing of the lumina. To the contrary, Karsen and Bayless (17) stated that Aschoff nodules rarely narrow the vascular lumen and never occlude it. They believed that coronary occlusion by whatever mechanism is an infrequent complication of rheumatic carditis. Nutrition of myocardial tissue is compromised, according to Swift (20), by endarteritis and thrombosis of small cardiac blood vessels. Acute swelling of the endothelium and intimal fibrosis of cardiac arterioles and capillaries may also lead to appreciable narrowing and even small, scattered areas of muscle necrosis (21)(22)(23)(24)(25). However, the supposition that emboli are sufficiently frequent to account for the widespread intimal lesions observed is not in accord with the actual incidence of embolization seen in rheumatic fever (17). A rare and peculiar occlusive lesion which has been seen in acute rheumatic fever is a verrucous endarteritis in which acidophilic, proliferative and necrotic vegetative-like endothelial elements project into the lumen of affected vessels (26)(27).

The frequency with which the coronary arteries are involved in rheumatic carditis is subject to many differences of opinion. Klotz (28) and Coombs (29) believed that the finer ramifications of the coronary arteries are invariably affected but MacCallum (71) regarded this as a complication only in severe cases. Perry (91) examined the large coronaries of nine patients who died with acute rheumatic fever and found involvement in all cases with swollen intima infiltrated with lymphocytes, intimal fibrosis and a variable amount of splaying and destruction of the elastica interna. He also found variable fibrosis in the media and adventitia. Zeek (30) stated that rheumatic heart disease was invariably accompanied by atheromatous changes in the aorta, pulmonary arteries or coronary arteries, as seen in her series of 1070 autopsies on individuals under 30 years of age. Gross et al. (21) found moderate scarring and elastification of the media of the main coronary arteries in about one-third of cases of inactive rheumatic heart disease and more frequently in patients with active rheumatic carditis. It was pointed out by Karsen and Bayless (17) that a high percentage of controls with no clinical history or pathological evidence of rheumatic heart disease have coronary arterial lesions similar to those described by Gross and Zeek including edema, necrosis, fibrinoid and elastica alterations and lymphocytic infiltration. This observation was confirmed by Hall and Anderson (31). These authors as well as Murphy (23) agree that Aschoff nodules can be seen in the hearts of patients who have never had

rheumatic fever; moreover, the hearts of patients with a good history of rheumatic carditis plus the pathological evidence of the characteristic valvular lesions may be free of Aschoff bodies. Gould (32) states that the presence of Aschoff nodules in the myocardium is neither definite proof of active rheumatic carditis nor evidence that an active phase of the disease has recently occurred. The lesions are found in about 69% of rheumatic hearts.

There remains much debate over the specific relationship of rheumatic heart disease to the development of arteriosclerosis. MacCallum (16) believed that there was insufficient evidence to assume such a relationship. Lloyd (33) expressed the opinion that a number of infectious diseases including rheumatic fever predispose the coronary arteries to sclerosis. MacLean (34), Giraldi (35) and Zeek (30) all shared the opinion that the coronary artery lesions of rheumatic heart disease result in early development of atheromatous changes which are progressive and may go on to calcify. Gross et al. (21) felt that rheumatic carditis induces in the walls of the main coronary arteries a series of prococious evolutionary metamorphoses which cannot be differentiated from those occurring normally as a result of age alone. These changes, they believed, are widespread, permanent vascular damage which lead to early sclerotic alteration and ischemic changes in the heart. However, these authors also point out that the primary arterial lesions in the acute, active phase involve the smaller vessels whereas

the main coronary arteries are affected in the inactive cases. Gould (32), in general agreement with Gross et al., stated that fibrosis of the coronary arteries occurs more frequently, more extensively and considerably earlier than in nonrheumatic control cases. Kaunitz (36) noted that many chronic disease processes, e.g.; tuberculosis, uterine fibroids, nephrotic kidneys and thyroid tumors, are associated with cholesterol deposition. He suggested that chronic rheumatic inflammation in the coronary arteries may likewise be accompanied by a local derangement of lipid metabolism. Waters (37) believed that any factor which damages the arterial wall, whether that factor is infectious or chemical inflammation, increased intraluminal pressure or direct trauma, predisposes the coronaries to arteriosclerosis.

In conflict with these opinions, Waterman and Hellerstein (38) found that in a study of 2000 autopsies the incidence of coronary artery disease in patients with known rheumatic heart disease, active and healed, is about the same as the incidence in the nonrheumatic group. Kaufman and Poliskoff (30) found significant coronary artery disease in only 30% of 23 males with rheumatic heart disease who came to autopsy. In their series of 500 autopsies, Roberts et al. (40) found no evidence to suggest that acute rheumatic carditis influences the severity or the extent of subsequent arteriosclerosis. Sprague (24) was of the same opinion.

The question as to whether or not the coronary arterial

lesions cause the myocardial damage seen in rheumatic carditis has been widely discussed. Krehl (7), Rhomberg (8) and Swift (20) all considered that much of the myocardial alteration is directly the result of impaired coronary artery function. Klotz (41) and Slater (42) attributed myocardial scarring to both the vascular lesions and to direct inflammatory destruction of muscle tissues. Aschoff (10) doubted the relationship of arterial changes to myocardial damage. Gross et al. (21) described narrowing of the coronary arteries and occlusion by granular plugs made up of sloughed necrotic elements together with platelets. They also saw wide bands of adventitial fibrosis surrounding the arteries in the healed, inactive state. They felt that these changes could lead to widespread myocardial necrosis in regions supplied by arteries so involved. Tedeschi (43) believed that "rheumatic coronary disease definitely interferes with the nutrition of the myocardium and causes ischemic muscular damage and weakness".

Gould (32) agreed that severe myocardial injury is probably associated with the changes seen in the coronaries though he felt that it remains to be clearly demonstrated that the arterial lesions are a direct result of the acute inflammatory process. Karsen and Bayless (17) state that the relation of the acute changes in the arteries to myocardial damage has not been positively established. The acute inflammatory myocarditis may go on to the chronic scarring seen in healed rheumatic hearts. Hall and Anderson (31) felt that the myocardial fibrosis seen in 'healed' rheumatic hearts cannot be

distinguished from the scarring which results from arteriosclerotic changes seen in nonrheumatic hearts. In her series of 1000 autopsies in which significant myocardial fibrosis was found in 110 cases, Brown (44) concluded that there is no evidence that infectious disease or toxicity gives rise to myocardial fibrosis. In her series, the rheumatic hearts showed the least fibrosis and the least coronary arteriosclerosis.

Much indirect evidence has been cited to show that the coronary arteries are significantly affected in rheumatic heart disease. Krehl (7) was the first to ascribe the angina-like precordial pain of rheumatic fever to the ischemic effect on the myocardium of coronary artery narrowing. Karsen and Bayless (17) also concluded that coronary adventitial and perivascular lesions which they described resulted in an ischemic type of pain. Sprague (24) felt that the angina which often accompanies chronic rheumatic heart disease signifies disturbance of coronary circulation which is not occlusive in nature but rather is secondary to inadequate perfusion resulting from aortic stenosis and/or aortic insufficiency. He noted, however, that the coronary ostia may be involved in the rheumatic process. Sir Thomas Lewis (45) and Gould (32) pointed out that poor coronary perfusion may also result from the mitral stenosis which so often accompanies chronic rheumatic carditis. Gould denies that there is morphological evidence of myocardial ischemia secondary to the rheumatic process alone. He also

notes that the amount of coronary arteriosclerosis varies inversely with the degree of aortic stenosis. Gross et al. (21) remarked on the high frequency of involvement of the arteries supplying the interventricular system with the destructive lesions of rheumatic carditis. They ascribed the frequent arrhythmias seen in rheumatic heart disease to ischemic damage of the A-V conduction system. They pointed out that the same vascular and conduction alterations are part of the evolutionary changes seen in nonrheumatic hearts but they claimed that these changes are earlier and more widespread in patients with rheumatic heart disease. The electrocardiographic changes seen in rheumatic heart disease include prolongation of the P-R interval (suggestive a conduction defect) and inversion of T waves in AVF and left ventricular epicardial leads (suggesting an ischemic process) (46). These changes usually revert to normal after the acute phase of the disease subsides and may be seen in any other form of myocarditis. Inflammatory lesions involving the conduction system alone and not the adjacent coronary arteries could account for the electrocardiographic abnormalities (32).

Myocardial infarction is also indirect presumptive evidence of coronary artery disease. In a hospital autopsy series of 2000 cases (ages 0-90, males and females) Waterman and Hellerstein (38) found that the incidence of myocardial infarction in the entire group was 9.2% while the incidence among the 120 with rheumatic heart disease was only 2.5%. (All of the rheumatics were over age 35 and 43% were over the age of 45). They also

stated that the incidence of coronary artery disease found in the rheumatic hearts was about the same as that found in nonrheumatic hearts. Kaufman and Poliakoff (39) found one case with myocardial infarction among a series of autopsies on 23 males (ages 40-81) who had rheumatic heart disease. Soloff and Zatuchini (47) noted that the average age of death of all rheumatic individuals in the United States in 1950 was 55 years of age and that myocardial infarction was not a significant cause of death. Yater et al. (48) in a series of 950 autopsies showed that coronary artery disease is a more serious threat to life the younger the individual who acquires it. This observation and the statements cited above do not correlate with the opinion of Gross et al. (21) and Karsen and Bayless (17) that rheumatic carditis induces in the coronary arteries early and widespread permanent sclerotic damage.

There remains considerable debate as to what lesions are characteristic of and specific to rheumatic heart disease. The Aschoff bodies are the most characteristic lesions though they may be seen in only about 69% of rheumatic hearts as well as in hearts where there is no evidence or history of rheumatic heart disease (op.cit.). They have been identified in the hearts of patients who died with tuberculosis, scarlet fever, polyarteritis nodosa and disseminate lupus erythematosus (23). Aschoff nodules are often seen in the active or acute phase of rheumatic carditis but as healing proceeds they contract, lose their characteristic hyaline center and polynucleated

basophils and become nondescript fibrous scars (31)(44). The cardiac histiocyte described in rheumatic heart disease by Clawson (49) is even less specific and has been identified in a number of infectious processes.

The lesions seen on the valves of rheumatic hearts are also nonspecific (23). Myocardial Aschoff bodies do not always accompany the vegetative valvular lesions nor is the converse true. Rich has shown that valvular, interstitial and verrucous endocardial lesions entirely similar to those of rheumatic fever may be found in disseminated lupus erythematosus. The valvular deformities result from protracted or repeated attacks rather than from simple healing and scarring of the initial lesion (23)(32). Calcification adds to the valvular damage. Gould feels that most valvular deformities are rheumatic in origin.

In their detailed description of the histopathology of the coronary arteries in rheumatic heart disease, Gross et al. (21) concluded that there are a number of specific lesions which are rarely or never seen in normal controls. In the small coronary arteries in the acute disease they found medial edema and hypertrophy with increase in number and size of smooth muscle cells irregularly arranged (metallaxis), intimal musculo-elastic hyperplasia and fibroblastic proliferation, fibrinous and granular vascular plugs with occasional frank thrombosis, occasional verrucal endarteritis and Aschoff bodies closely associated with vessels. In the inactive phase of rheumatic heart disease they described intimal and medial

elastification in one third of the main coronary arteries. They distinguished these changes from the evolutionary changes seen in normal control cases. Karsen and Bayless (17) in their study of active rheumatic carditis described some of the same lesions, but also pointed out that no fatty change can be found until the process becomes chronic. They noted that edema and necrosis were found in some part of the coronary tree of all of their controls and that fibrinoid and elastica alterations were found in 50% of normal controls. The older the patient at the time of onset the more severe are the destructive lesions. Hall and Anderson (31) found the stigmata described above (arteritis, fibrinoid changes, elastic tissue alterations, Aschoff bodies, lymphocytic infiltration) abundantly present in nonrheumatic hearts. Lowe and Wartman (25) denied that there was any vascular lesion characteristic of rheumatic heart disease except, perhaps, for the occasional Aschoff nodule. Gould (32) concurred in this opinion. The lack of specificity of the histopathological lesions described in rheumatic carditis had led many observers to speculate on the possibility that the etiology and nature of these lesions is similar to those found in any of the collagen group of diseases in which antigen-antibody mechanisms are postulated (18)(19)(51).

The natural history of rheumatic heart disease provides inferential evidence about the significance and permanency of the vascular lesions. Among the causes of death in adults with rheumatic heart disease, Friedberg lists arteriosclerotic

coronary occlusion with myocardial infarction (52). Soloff and Zatuchini (47) analyzed the causes of death in 114 patients (male and female, ages 12 to 83) who had clinical and autopsy findings of rheumatic heart disease. In none of these was coronary artery disease cited as a significant factor. Wallach et al. (53) stated that with increasing age rheumatic heart disease is more often a relatively inactive, incidental lesion and its role as a cause of death becomes less significant. The chronic valvular lesions are a significant cause of death in the middle age group while active rheumatic heart disease is usually significant only in the early decades of life. Cohn and Lingg (54) found that the earlier the age of onset, the poorer the prognosis and the greater the chance of recurrence. The work of Wilson and Lubschez (55) confirmed this. Jones and Bland (56) and Ash (57) agreed that in about 30% of long term follow-ups, the physical signs of valvular disease had decreased or disappeared. Rothschild et al. (58) found that heart failure, the major cause of death in rheumatic heart disease (47)(53), is attributable to active infection and unrelated to the severity of valvular defects. Rogers and Robbins (59) reached the same conclusion. In the fifth, sixth and seventh decades the disease becomes quiescent and myocardial failure is attributable to the usual expected causes occurring at that time of life, viz., hypertension, systemic, pulmonary or coronary atherosclerosis, thrombosis, and myocardial degeneration. Although the initial lesions of rheumatic fever may occur at any age, they are usually first seen

between the ages of 4 and 10 years (32). Factors other than age at onset which influence the natural history of rheumatic heart disease include sex, race, heredity, number of recurrences, extent and degree of valvular damage and concomitant disease states such as bacterial endocarditis, congenital heart abnormalities, hypertension, diabetes and hypercholesterolemia (22)(47)(60)(61)(62)(63).

In summary, no invariably present nor absolutely diagnostic pathological lesions have been demonstrated in rheumatic hearts, although the Aschoff body is generally considered to be the most characteristic finding in this disease. The lesions which are often seen in the hearts of patients with rheumatic fever are nonspecific and resolve during the recovery phase to disappear completely or to become nondescript scars. Nor is it widely accepted that the myocardium or the coronary arteries of patients who survive the acute disease contain characteristic stigmata or have a higher than normal incidence of degenerative changes. Statistics cited to delineate the natural history of rheumatic heart disease vary considerably but probably 50% of patients survive for 20 or more years after the onset of the illness. In the fifth, sixth and seventh decades of life the physical signs of the disease become static or quiescent in increasingly more patients and myocardial failure is attributable to the usual changes of aging, unrelated to rheumatic infection. Only in this group is myocardial infarction seen in a significant number of

patients but its incidence is generally thought to be no higher than that of the remainder of the population. However, the question of the meaningfulness of any of the earlier studies is raised by Feinstein (64) who points out that improved understanding of the mechanisms and components of rheumatic fever coupled with new methods for diagnosis have created a need for reappraisal of clinical characteristics of this disease.

Experimental

DESIGN and METHODS

Between the years of 1940 and 1963 approximately 12,500 autopsies were performed in the Yale University Department of Pathology. Three groups of 50 cases each were selected from this series. All of the patients were white males 37 years and older who had complete, detailed postmortem examinations. The first group consisted of patients who had a good clinical history and/or abundant pathological evidence of rheumatic heart disease. The second group was made up of men who had died from acute myocardial infarction in which coronary artery disease was the primary etiological factor. The third group was comprised of cases of suicide, poisoning or traumatic death. Group I includes males with rheumatic heart disease within the selected age range who came to autopsy between 1940 and 1963. Groups II and III were selected so that the range of ages and the dates of autopsy would be roughly comparable to the cases in group I. In each case, the clinical history and necropsy protocol were reviewed and the microscopic sections of the heart and coronary arteries were examined by two observers. A particularly careful search was made for histopathological elements which might distinguish the myocardium and coronary arteries of the rheumatic hearts from those of the other two groups.

A second phase of the investigation was directed toward the comparison of incidence of myocardial infarction in rheumatic hearts with the incidence of infarction in the entire

autopsy population of white males 37 years and older. Each rheumatic heart was scrutinized for evidence of old or recent myocardial necrosis. For comparison, the incidence of myocardial infarction in men 37 years and older dying of all causes between 1940 and 1963 was analyzed. In order to spread these figures equally over the 23 year period, the following sampling was used: first 230 autopsies done in 1940 plus first 230 autopsies done in 1950 plus first 230 autopsies done in 1960 giving a total of 690 autopsies done on white males 37 years and older dying of all causes.

Tabulation of Data

All cases are white males age 37 years or older who died between January 1940 and January 1963 and who were autopsied in the Department of Pathology, Grace-New Haven Community Hospital.

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Key to Abbreviations:

R.F. - Acute rheumatic fever

C.H.F. - Congestive heart failure

Sclerosis: 1+ - slight

2+ - moderate

3+ - marked

D.O.A. - Dead on arrival

C.V.A. - Cerebral vascular accident

M.I. - Myocardial infarction

R.B.B.B. - Right bundle branch block

B.P. - Blood pressure

Max. occ. - Maximum occlusion

TABLE I 'Healed' Rheumatic Heart Disease

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		B.P.	Sclerotic	Coronaries		Weight in gms.	Infarct	Myocardium			Valves		
			Max. Occ.	Ather-			Scarring	Mitral			Aortic	Other				
16458 6/62	Infarction of bowel	59	R.F. ages 7-14 with murmur Digitalized for C.H.F. 4 yrs. ago		170 100	3/	70%	Yes	625	No	Perivascular fibrosis Focal scars	Sclerosis 2/ Incompe- tent Calcified	0	0		
15971 10/61	C.H.F.	58	R.F. ages 5, 17 Digitalized for C.H.F. 2 yrs. ago		135 70	1/	20%	No	880	No	Perivascular fibrosis Sl. diffuse fibrosis	Sclerosis 1/ Sclerosis 3/ Stenosis 3/ Incompe- tent	0	0		
15904 9/61	C.H.F.	49	R.F. age 12 Obese		160 110	2/	50%	No	735	No	Perivascular fibrosis Focal scars	Stenosis 3/ Calcified	0	0		
15892 8/61	C.H.F.	53	R.F. age 18 Dyspnea for 5 yrs.		110 60	1/	5%	No	625	No	Perivascular fibrosis	Sclerosis 3/ Stenosis 3/ Calcified	0	0		
15666 5/61	C.H.F.	54	R.F. age 13 Digitalized for C.H.F. 2 yrs. ago		130 80	3/	80%	Yes	500	No	Large, old scar Perivascular fibrosis Diffuse fibrosis	Stenosis 3/ Calcified	0	0		

TABLE I (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		B.P.	Sclerosis	Coronaries		Weight in gms.	Myocardium		Valves		
							Max. Occ.	Atheroma		Infarct	Scarring	Mitral	Aortic	Other
15807 7/61	D.C.A.	67	Mitral valvulotomy 17 days ago Chronic congestion of viscera		$\frac{160}{100}$	3/4	70%	Yes	625	No	Perivascular fibrosis Diffuse fibrosis	Stenosis 3/4 Calcified	Sclerosis 2/4	0
15643 5/61	Lobar pneumonia Acute M.I.	58	Congestive failure for 4 yrs.		$\frac{120}{80}$	3/4	100%	Yes	553	Recent infarct only	Perivascular fibrosis Focal scars	Sclerosis 2/4 Stenosis 2/4 Calcified	0	0
15480 2/61	C.H.F.	78	Generalized arterio- sclerosis		$\frac{110}{85}$	3/4	90%	Yes	290	Old infarct only	Perivascular fibrosis Focal scars	Stenosis 3/4 Calcified	Stenosis 3/4 Calcified	0
15321 12/60	C.H.F.	45	R.F. age 7 Chronic dyspnea and congestion of viscera		$\frac{120}{85}$	1/4	10%	No	430	No	No scars	Stenosis 3/4 Calcified	0	0
15256 11/60	C.H.F.	74	R.F. age 12 Generalized arterio- sclerosis Diabetes for 1 yr.		$\frac{120}{70}$	3/4	80%	No	550	No	Sl. peri- vascular fibrosis Focal scars	Stenosis 3/4	Stenosis 2/4 Calcified	0

TABLE I (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Sclerosis	Coronaries		Weight in gms.	Myocardium			Valves		
			B.P.			Max. Oc.	Atheroma		Infarct	Scarring	Mitral	Aortic	Other	
14863 6/60	D.O.A.	47	R.F. age 10 Mitral valvulotomy 1 yr. ago Generalized arteriosclerosis	?	3+	100%	Yes	425	No	Perivascular fibrosis	Stenosis 3+	0	0	
14657 2/60	Died 3 days post aortic valvulotomy	51	R.F. age 8 Chronic dyspnea	$\frac{140}{85}$	2+	40%	No	915	Recent infarct only	Focal scars Traumatic infarction	0	Stenosis 3+	0	
14650 2/60	Died 4 hrs. post mitral valvulotomy	42	R.F. age 22 Chronic dyspnea	$\frac{130}{80}$	0	0	No	?	No	Focal scars Diffuse fibrosis	Stenosis 3+	Stenosis 3+	0	
14597 1/60	S.B.E.	54	R.F. age 7 Chronic dyspnea and congestion of viscera	$\frac{110}{70}$	1+	10%	No	430	No	Perivascular fibrosis Diffuse fibrosis	Stenosis 3+	0	0	
14562 1/60	D.O.A.	55	R.F. ages 8, 17, 35 40 Chronic congestion of viscera Alcoholism	?	1+	10%	No	650	No	Diffuse fibrosis	Stenosis 3+	Stenosis 3+	0	

TABLE I (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		B.P.	Coronaries		Weight in gms.	Myocardium			Valves				
						Sclerosis	Max. occ.		Atheroma	Infarct	Scarring	Mitral	Aortic	Other		
14472 12/59	Died at aortic valvulotomy	57	R.F. probable in childhood Murmur for 12 yrs. Generalized arteriosclerosis		$\frac{125}{75}$	2/	100%	Yes	No	Extensive diffuse fibrosis	0	Stenosis 3/	Sclerosis 3/	Calcified	0	
14451 11/59	Died 5 days post mitral valvulotomy	41	Enlarged heart for 26 yrs. Mitral valvulotomies 5 yrs. & 2 yrs. ago		$\frac{110}{75}$	2/	30%	No	No	Perivascular fibrosis	Stenosis 3/	Calcified	Incomplete		0	
14115 6/59	C.H.F.	47	C.H.F. for 2 yrs.		$\frac{125}{70}$	1/	5%	No	No	Diffuse fibrosis	Stenosis 2/		Stenosis 3/	Calcified	Incomplete	0
13750 1/59	C.H.F.	49	R.F. ages 16,33 C.H.F. for 3 mos.		$\frac{160}{60}$	1/	10%	No	No	Marked focal fibrosis Diffuse fibrosis	Stenosis 2/	Calcified	Stenosis 3/	Calcified		0
13326 6/58	C.H.F.	68	R.F. age 14		$\frac{150}{90}$	2/	40%	No	No	Perivascular fibrosis Diffuse fibrosis	Sclerosis 3/	Stenosis 3/	Sclerosis 2/			0

TABLE I (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Sclerosis	Coronaries		Weight in gms.	Myocardium			Valves		
			B.P.			Max. Occ.	Ather.		Infarct	Scarring	Mitral	Aortic	Other	
13206 4/58	C.V.A.	72	135 80	Chronic dyspnea Congestive failure 3 mos. ago	1+	10%	No	725	No	Perivascular fibrosis Sl. focal scars	Stenosis 2+ Calcified	Stenosis 3+	0	
12914 1/58	Cardiac arrest	60	120 50	R.F. age 40 C.H.F. for 15 yrs.	3+	70%	Yes	710	No	Focal scars	Stenosis 3+ Calcified	Stenosis 3+	0	
12724 10/57	Died 1 day post mitral valvulotomy	42	120 90	R.F. age 12 C.H.F. for 2 yrs.	1+	10%	No	?	No	Perivascular fibrosis	Stenosis 3+ Calcified Incomplete	0	0	
12613 8/57	C.H.F.	41	150 60	R.F. ages 8, 12, 24 37. Chronic dyspnea and congestion of viscera	2+	50%	No	780	No	Perivascular fibrosis Focal scars	Stenosis 3+ Calcified Incomplete	Stenosis 3+ Calcified Incomplete	Tricuspid incomplete	
12436 5/57	C.H.F.	49	106 80	R.F. probable in childhood. Chronic dyspnea and congestion of viscera	1+	30%	No	725	No	Perivascular fibrosis Diffuse fibrosis	Stenosis 1+	Stenosis 2+ Calcified Incomplete	0	

TABLE I (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death Age	Clinical History		Coronaries		Weight in gms.	Myocardium		Valves			
		B.P.	Sclerosis	Max. Occ.	Atheroma		Inferct	Scarring	Mitral	Aortic	Other	
12073 11/56	Acute bacterial endocarditis 68	160 100	2/	50%	Yes	540	No	Perivascular fibrosis	Stenosis 3/	Stenosis 0	Vegetations	0
12040 11/56	C.H.F. 42	130 100	1/	20%	No	995	No	Perivascular fibrosis Diffuse fibrosis Focal scars	Stenosis 3/	Stenosis 3/	Calcified Incompetent	0
12002 10/56	C.H.F. 56	?	3/	80%	Yes	645	No	Focal scars	Stenosis 3/	Stenosis 0	Calcified Incompetent	0
11294 9/55	C.H.F. 70	140 110	2/	50%	No	590	No	Large, old scar Focal fibrosis	Stenosis 1/	Stenosis 3/	Sclerosis 2/	Tricuspid sclerosis
11265 8/55	C.H.F. 57	100 70	3/	80%	No	520	No	Diffuse fibrosis Focal scars	Stenosis 1/	Stenosis 3/	Sclerosis 3/	Calcified Incompetent

TABLE I (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		B.P.	Sclerosis	Coronaries		Weight in gms.	Myocardium			Valves		
							Max. Occ.	Atheroma		Infarct	Scarring	Mitral	Aortic	Other	
11106 5/55	Died 3 days post mitral valvulotomy	43	R.F. age 5 Chronic dyspnea for 5 yrs.		$\frac{160}{80}$	1+	5%	No	710	No	Sl. Perivascular fibrosis Focal scars	Stenosis 3+	Stenosis 2+	0	
10571 5/54	D.O.A.	38	R.F. age 8 Angina		?	1+	10%	No	550	No	Perivascular fibrosis Focal scars	Stenosis 1+	Stenosis 3+	0	
10347 12/53	C.H.F.	61	R.F. age 21 C.H.F. for 3 yrs.		?	2+	40%	No	640	No	Sl. perivascular fibrosis. Diffuse fibrosis	0	Stenosis 3+	0	
10232 10/53	Pulmonary embolus	53	R.F. age 14 Generalized arteriosclerosis		$\frac{110}{70}$	3+	100%	Yes	320	Old infarct only	Diffuse fibrosis	Stenosis 3+	0	0	
9886 3/53	Cardiac arrest	52	R.F. age 15 C.H.F. for 3 yrs.		$\frac{150}{40}$	2+	40%	Yes	885	Old infarct only	Focal scars Diffuse fibrosis	Stenosis 3+	Stenosis 3+	0	
9841 2/53	C.H.F.	37	R.F. age 15 C.V.A. 2 yrs. ago Angina and dyspnea		$\frac{130}{90}$	1+	10%	No	620	No	Focal scars	Stenosis 3+	0	0	

TABLE I (cont)

Date & Number of Autopsy	Terminal event or Cause of Death	Age	Clinical History		Coronaries		Weight in gms.	Myocardium			Valves		
			B.P.	Sclerosis	Max. occ. Atheroma	Infarct		Scarring	Mitral	Aortic	Other		
9131 5/51	Died at mitral valvulotomy	41	105 70	R.F. age 10 Cardiac enlargement for 9 yrs.	50% Yes	No	470	Focal scars	Stenosis 3/ Calcified	Stenosis 2/ 0	0	0	
8858 9/50	C.H.F.	53	120 75	C.H.F. for 1 yr. Obese	50% Yes	No	675	Perivascular fibrosis Focal scars	Stenosis 3/ Calcified	0	Tricuspid sclerosis 2/ 0	0	
8417 6/49	C.H.F. S.B.E.	48	180 105	Generalized arteriosclerosis Hypertension for 3 yrs.	60% Yes	No	1250	Focal scars Diffuse fibrosis	Stenosis 3/ Calcified	Stenosis 2/ Incompetent Vegetations	0	0	
7575 5/47	C.V.A.	57	160 100	Generalized arteriosclerosis C.H.F. for 1 yr. Alcoholism	20% No	Old and recent infarcts	500	Focal scars Diffuse fibrosis	Stenosis 2/ Calcified	0	0	0	
7026 12/45	Pulmonary emboli	37	110 85	M.F. age 16 Chronic dyspnea and congestion of viscera	10% No	No	627	Perivascular fibrosis Focal scars	Stenosis 3/ 0	0	0	0	
7010 11/45	Cardiac arrest	77	?	Chronic dyspnea and congestion of viscera	80% Yes	Old infarct only	533	Perivascular fibrosis Focal scar	Stenosis 3/ Calcified	Stenosis 3/ Calcified	0	0	

TABLE I (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		B.P.	Sclerosis	Coronaries			Myocardium			Valves		
							Max. occ.	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
6921 8/45	T.B. pneumonia	43	Chronic and active rheumatic carditis		$\frac{130}{80}$	1+	5%	No	No	435	No	Perivascular fibrosis Diffuse fibrosis	Stenosis 3+ Calcified	0	0
6881 6/45	Cardiac arrest	37	R.F. ages 23, 33		$\frac{165}{60}$	1+	20%	No	No	1000	No	Perivascular fibrosis Diffuse fibrosis Focal scars	Stenosis 3+ Incompetent	0	0
6567 6/44	C.H.F.	66	R.F. age 34 C.H.F. for 2 yrs.		$\frac{160}{90}$	1+	15%	No	No	495	No	Perivascular fibrosis Focal scars	Stenosis 3+ Incompetent	0	0
6532 4/44	C.V.A.	42	R.F. age 15 C.H.F. one yr. ago		$\frac{150}{90}$	3+	70%	No	No	450	No	Perivascular fibrosis Focal scars	Stenosis 3+ Calcified Incompetent	0	0
5833 7/42	Azotemia	55	R.F. ages 20, 30, 40 Angina and Dyspnea Glomerulonephritis		$\frac{145}{80}$	2+	50%	No	No	785	No	No scars	Stenosis 3+ Calcified Vegetations	0	0

TABLE I (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
			B.P.	Sclerosis	Max. Occ.	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
5206 1/41	C.H.F.	48	150 <u>120</u>	2/	50%	Yes	370	No	Perivascular fibrosis Focal scars	Stenosis 3/4 Calcified	0	0	
5181 12/40	C.H.F.	52	165 <u>120</u>	1/	5%	No	750	No	Perivascular fibrosis Diffuse fibrosis	Stenosis 3/4 Calcified Incompetent	Stenosis 3/4 Calcified	Tricuspid sclerosis 2/4	
5074 9/40	C.H.F.	42	180 <u>72</u>	2/	60%	No	870	Old infarct only	Focal scars Diffuse fibrosis	Stenosis 3/4	Stenosis 3/4 Incompetent	0	

Year	1900	1901	1902	1903	1904	1905	1906	1907	1908	1909	1910	1911	1912	1913	1914	1915	1916	1917	1918	1919	1920	1921	1922	1923	1924	1925	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	1946	1947	1948	1949	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024																																																								
Population	100	105	110	115	120	125	130	135	140	145	150	155	160	165	170	175	180	185	190	195	200	205	210	215	220	225	230	235	240	245	250	255	260	265	270	275	280	285	290	295	300	305	310	315	320	325	330	335	340	345	350	355	360	365	370	375	380	385	390	395	400	405	410	415	420	425	430	435	440	445	450	455	460	465	470	475	480	485	490	495	500	505	510	515	520	525	530	535	540	545	550	555	560	565	570	575	580	585	590	595	600	605	610	615	620	625	630	635	640	645	650	655	660	665	670	675	680	685	690	695	700	705	710	715	720	725	730	735	740	745	750	755	760	765	770	775	780	785	790	795	800	805	810	815	820	825	830	835	840	845	850	855	860	865	870	875	880	885	890	895	900	905	910	915	920	925	930	935	940	945	950	955	960	965	970	975	980	985	990	995	1000

1900-2024

TABLE II Control Group: Traumatic Death, Suicide, Poisoning

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
16767 11/62	Fall 15 ft.	83	140 90	37	100%	Yes	340	Old infarct only	Focal scars Diffuse fibrosis	Sclerosis 17	0	0	
16753 11/62	Auto accident D.O.A.	59	?	37	80%	Yes	355	No	Perivascular fibrosis Focal scars	0	0	0	
16752 11/62	Electrical burns	58	115 85	17	10%	No	389	No	Perivascular fibrosis	0	0	0	
16747 11/62	Struck by auto	81	160 100	27	65%	No	390	No	No scars	0	0	0	
16416 5/62	Auto accident	52	160 90	27	50%	No	424	No	No scars	Sclerosis 17	Sclerosis 27	0	
16397 5/62	Struck by auto	42	130 90	27	40%	No	370	No	Focal scars	0	0	0	
16296 3/62	Barbiturate	58	120 80	17	20%	No	380	No	Sl. diffuse fibrosis	Sclerosis 27	Sclerosis 27	0	

TABLE II (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death (Age)	Clinical History	Coronaries			Weight in gms.	Myocardium			Valves		
			Sclerosis	Maximum Occlusion	Atheroma		Infarct	Scarring	Mitral	Aortic	Other	
16264 3/62	Severe beating	Generalized arteriosclerosis Obese	17	15%	No	450	No	No scars	0	0	0	
16210 2/62	Struck by truck	Good health	17	10%	No	650	No	Focal scars	0	0	0	
16201 1/62	Ammonia water ingestion	Good health Psychiatric history	17	10%	No	360	No	Sl. perivascular fibrosis	Sclerosis 17	Sclerosis 17	0	
16174 1/62	Fracture with pulmonary fat embolism	Alcoholism Pulmonary emphysema	37	75%	Yes	230	No	Sl. perivascular fibrosis	Sclerosis 17	Sclerosis 17	0	
15932 11/61	Struck by auto	Asthma	17	10%	No	445	No	Sl. perivascular fibrosis	0	0	0	
15269 9/61	Barbiturate poisoning D.O.A.	Generalized arteriosclerosis	27	35%	No	385	No	Focal scars	0	0	0	

TABLE II (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
15042 11/60	Carbon monoxide poisoning	61	130 80	2+	50%	No	480	No	Perivascular fibrosis	0	0	0	
13361 7/58	Bullet wound in head	41	180 80	2+	65%	No	420	No	No scars	0	0	0	
13346 7/58	Heat stroke	48	?	1+	30%	No	460	No	Focal scars	0	0	0	
12964 1/58	Fracture with pulmonary fat embolism	85	?	2+	50%	No	350	No	Focal scars	Sclerosis 2+	0	0	
12929 1/58	Strangulation D.O.A.	43	?	1+	20%	No	340	No	No scars	0	0	0	
12423 5/57	Multiple bullet wounds D.C.A.	49	?	2+	50%	No	365	No	No scars	0	0	0	
12244 2/57	Auto accident D.O.A.	71	?	3+	85%	Yes	380	No	Sl. perivascular fibrosis	0	0	0	

TABLE II (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries		Myocardium			Valves		
				B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in grams	Infarct	Scarring	Mitral	Aortic
11975 10/56	Severe beating	43	No history	$\frac{180}{110}$	1/	10%	No	No	No scars	0	0	0
11764 6/56	Fall down stairs	82	Alcoholism Generalized arteriosclerosis Obese	?	1/	15%	No	No	No scars	0	0	0
11181 8/55	Fall from 14 ft.	62	Hypertension Alcoholism	$\frac{140}{70}$	2/	30%	No	No	No scars	0	0	0
10877 12/54	Third degree burns	79	Generalized arteriosclerosis Obese	$\frac{135}{75}$	3/	80%	Yes	No	SI. perivascular fibrosis Focal scars	Sclerosis 1/	Sclerosis 2/ Calcified	0
10876 12/54	Struck by auto D.O.A.	62	Hypertension	?	2/	50%	Yes	No	Perivascular fibrosis Diffuse fibrosis	0	0	0
10579 5/54	Paraldehyde poisoning D.O.A.	37	Paraldehyde adict	?	1/	10%	No	No	No scars	0	0	C

TABLE II (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
10521 4/54	Lye ingestion	48	120 80	1+	10%	No	340	No	Focal scars	0	0	0	
10336 12/53	Struck by auto	63	130 80	2+	40%	No	350	No	No scars	0	0	0	
9380 12/51	Bullet wound in head D.O.A.	47	?	1+	10%	No	250	No	No scars	0	0	0	
9337 11/51	Struck by auto D.O.A.	42	?	1+	5%	No	280	No	No scars	0	0	0	
9310 10/51	Cleaning fluid ingestion D.O.A.	55	?	2+	50%	No	315	No	Focal scars	0	0	0	
8619 1/50	Struck by auto	62	140 85	1+	5%	No	350	No	No scars	Sclerosis 2+	0	0	
8414 6/49	Fall from 20 feet	57	130 70	1+	10%	No	450	No	Sl. perivascular fibrosis Focal scars	0	0	0	

TABLE II (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries		Myocardium		Valves				
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
8282 2/49	Bullet wound in head D.O.A.	40	?	Psychiatric history	1+	20%	No	340	No	No scars	0	0	0
8077 8/48	Struck by auto D.O.A.	50	?	No history	1+	10%	No	320	No	No scars	Sclerosis 1+	0	0
7823 1/48	Fall down stairs	73	$\frac{220}{90}$	Obese Good health	3+	70%	Yes	430	No	Perivascular fibrosis Diffuse fibrosis	0	0	0
7683 8/47	Auto accident D.O.A.	56	?	Very obese Generalized arteriosclerosis	3+	90%	Yes	600	No	Sl. perivascular Diffuse fibrosis	Sclerosis 2+	Sclerosis 2+	Tricuspid sclerosis 2+
7402 12/46	Struck by auto	44	$\frac{140}{80}$	No history	1+	5%	No	290	No	Diffuse fibrosis	0	0	0
6964 10/45	Severe beating D.O.A.	53	?	Generalized arteriosclerosis	2+	30%	No	400	No	Perivascular fibrosis	Sclerosis 1+	0	0
6705 12/44	Struck by auto	82	$\frac{140}{70}$	Adenoma of rectum	1+	20%	No	350	No	Diffuse fibrosis	Sclerosis	0	0

TABLE II (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death Age	Clinical History	B.P.	Coronaries			Myocardium			Valves		
				Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other
6380 12/43	Third degree burns 76	Generalized arteriosclerosis	$\frac{195}{120}$	2/	60%	No	450	Old infarct only	Focal scars	Sclerosis 2/	Sclerosis 2/ Calcified	0
6113 3/43	Third degree burns 80	Generalized arteriosclerosis	?	2/	50%	No	570	No	Focal scars	Sclerosis 1/	Sclerosis 2/	Tricuspid sclerosis 1/
6011 1/43	Auto accident 63	Ulcerative colitis	?	1/	15%	No	375	No	No scars	0	0	0
5821 7/42	Multiple skull fractures 52	Alcoholism	$\frac{180}{}$	1/	5%	No	300	No	No scars	0	0	0
5584 11/41	Struck by auto D.O.A. 51	No history	?	1/	10%	No	400	No	No scars	Sclerosis 1/	0	0
5563 11/41	Auto accident D.O.A. 75	Generalized arteriosclerosis Pulmonary emphysema	?	2/	30%	No	325	No	Diffuse fibrosis	0	0	0
5553 11/41	Alcoholic poisoning D.O.A. 64	Alcoholism	?	1/	5%	No	390	No	No scars	Sclerosis 2/	Sclerosis 2/	0

TABLE II (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
				B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other
5526 10/41	Struck by auto	52	Good health	$\frac{160}{80}$	1/	5%	No	400	No	Focal scars	0	Sclerosis 1/	0
5127 10/40	Struck by auto	48	Obese No history	$\frac{120}{80}$	1/	10%	No	375	No	No scars	0	Sclerosis 1/	0
5105 10/40	Struck by auto	77	Generalized arteriosclerosis	$\frac{160}{75}$	2/	30%	No	375	No	Perivascular fibrosis Focal scars	Sclerosis 1/	0	Tricuspid sclerosis 2/

TABLE III Control Group: Myocardial Infarction

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
15054 8/60	Acute M.I.	87		160 100	34	80%	Yes	410	Old infarcts only	Sl. perivascular fibrosis Focal scars Diffuse fibrosis	0	0	0
15338 12/60	Acute M.I.	52		180 100	34	100%	Yes	450	Recent infarct only	Sl. perivascular fibrosis Focal scars	0	0	0
14534 1/60	C.V.A.	54		100 70	27	40%	No	350	Old infarct only	Perivascular fibrosis	0	0	0
14373 10/59	Cardiac arrest	52		120 90	34	90%	No	410	Recent and old infarcts	Diffuse fibrosis Focal scars	0	0	0
14242 8/59	Acute M.I.	43		130 90	27	100%	Yes	355	Recent infarct only	Focal scars	0	0	0

TABLE III (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries		Myocardium			Valves		
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other
14234 8/59	D.O.A.	53	?	3/4	60%	No	460	No	Diffuse fibrosis Focal scars	0	0	0
14147 7/59	Cardiac arrest	46	160 110	3/4	100%	Yes	405	Old infarct only	Perivascular fibrosis Diffuse fibrosis	0	0	0
14123 6/59	Uremia	51	260 160	3/4	80%	Yes	765	Old infarct only	Perivascular fibrosis Diffuse fibrosis	0	Sclerosis 1/4	0
14047 5/59	Cardiac arrest	51	120 80	3/4	90%	Yes	350	Old infarct only	Perivascular fibrosis Diffuse fibrosis	Sclerosis 1/4 Calcified Vegetation	Vegetations	0
13940 5/59	C.V.A. D.O.A.	48	?	3/4	95%	Yes	600	Old infarct only	Focal scars Diffuse fibrosis	0	0	0
13567 10/58	Acute M.I.	54	140 90	3/4	95%	Yes	?	Recent and old infarcts	Focal scars	0	0	0

TABLE III (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves	
			B.P.	Sclerosits	Maximum Occlusion	Atheroma	Weight in grams	Infarct	Scarring	Mitral	Aortic	Other
13551 10/58	Acute M.I.	54	?	3/	90%	Yes	320	Old infarct only	Focal scars	0	0	0
13449 8/58	Acute M.I. D.O.A.	43	?	3/	100%	Yes	475	Recent and old infarcts	Focal scars	0	0	0
12010 10/56	Acute M.I.	71	$\frac{190}{100}$	3/	60%	Yes	400	Recent and old infarcts	Sl. perivas-fibrosis Focal scars	0	0	0
11967 10/56	Acute M.I. D.O.A.	68	?	3/	100%	No	475	Old infarct only	Perivascular fibrosis Focal scars	Sclerosits 1/	0	0
11753 6/56	Acute M.I.	66	$\frac{130}{90}$	3/	100%	Yes	450	Recent and old infarcts	Focal scars	0	0	0
11491 1/56	Acute M.I.	67	$\frac{130}{90}$	3/	100%	No	550	Recent and old infarcts	Focal scars	0	Sclerosits 2/	0

TABLE III (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
11297 9/55	Acute M.I.	74	Angina for 10 yrs. Previous M.I. 2 yrs. ago	120 70	2+	70%	Yes	370	Old infarct only	Focal scars	0	0	0
11080 4/55	Acute M.I.	59	Chronic dyspnea Generalized arteriosclerosis Azotemia	140 80	3+	80%	No	950	Old infarct only	Focal scars	0	0	0
10725 8/54	Cardiac arrest D.O.A.	42	Angina Chronic congestion of viscera	?	3+	80%	Yes	375	Old infarct only	Sl. perivascular fibrosis	0	0	0
10538 4/54	Acute M.I.	42	Obese Angina for 2 yrs. Chronic congestion	120 80	2+	80%	Yes	475	Recent infarct only	Perivascular fibrosis Focal scars	0	0	0
10382 1/54	Acute M.I.	47	Labile hypertension Angina for 3 mos. Chronic congestion of viscera	190	3+	100%	No	600	Recent infarct only	Focal scars	0	0	0
10170 9/53	Acute M.I.	46	Hypertension angina Previous M.I. 3 yrs. ago	150 105	3+	100%	No	470	Recent and old infarcts	Diffuse fibrosis	0	0	0

TABLE III (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
9781 12/52	Acute M.I.	53	120 80	2/	50%	Yes	300	Recent infarct only	Focal scars	0	0	0	
9266 9/51	Acute M.I.	58	110 90	3/	90%	Yes	400	Recent infarct only	No scars	0	0	0	
8843 9/50	Acute M.I.	42	160 85	2/	100%	Yes	550	Recent infarct only	Sl. perivascular fibrosis Diffuse fibrosis	0	0	0	
8642	Acute M.I.	57	120 80	3/	100%	Yes	830	Recent and old infarcts	Focal scars	0	0	0	
8422 6/49	Acute M.I.	57	120 70	3/	95%	Yes	375	Recent infarct only	No scars	Sclerosis 1/	0	0	
8218 12/48	Acute M.I.	47	108 70	3/	100%	Yes	375	Recent and old infarct	Focal scars Diffuse fibrosis	0	Sclerosis 1/	0	

Angina
Previous M.I. 2 yrs.
ago
Chronic congestion
of viscera

TABLE III (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
8006 6/48	Acute M.I.	50	Diabetes 13 yrs. Previous M.I. 9 yrs. ago Generalized arteriosclerosis	150 110	37	90%	Yes	420	Recent and old infarcts	Focal scars	0	0	0
7853 1/48	Acute M.I. D.O.A.	73	Angina 15 yrs. Generalized arteriosclerosis	120 80	37	100%	Yes	475	Recent and old infarcts	Perivascular fibrosis Diffuse fibrosis	0	0	0
7689 8/47	Acute M.I.	45	Angina 4 yrs. Generalized arteriosclerosis	115 70	37	100%	Yes	360	Recent infarct only	No scars	0	0	0
7413 12/46	Acute M.I.	52	Hypertension 7 yrs. Obese Angina	170 120	37	100%	No	475	Recent and old infarcts	Diffuse fibrosis	Sclerosis 27	Sclerosis 27	0
7166 4/46	Acute M.I.	68	Arteriosclerosis obliterans	100 70	37	80%	Yes	630	Recent and old infarcts	Diffuse fibrosis	0	0	0
6995 12/45	Acute M.I.	46	Previous M.I. 6,1 yrs. ago Angina	110 80	37	100%	Yes	495	Recent and old infarcts	Perivascular fibrosis Diffuse fibrosis	0	0	0

TABLE III (cont)

Date & Number of Autopsy	Terminal Event or Cause of Death Age	Clinical History		Coronaries			Myocardium				Valves	
		B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
6746 2/45	Acute M.I. 64	Generalized arteriosclerosis	140 70	27	100% Yes	550	Recent and old infarcts	Diffuse fibrosis	0	0	0	
6535 5/44	Acute M.I. 82	Generalized arteriosclerosis Angina 15 yrs.	?	37	100% No	480	Recent infarct only	Sl. perivascular fibrosis	0	0	0	
6435 1/44	Acute M.I. 69	Generalized arteriosclerosis Angina	120 62	37	100% Yes	410	Recent and old infarcts	Sl. perivascular fibrosis Focal scars	0	0	0	
6316 10/43	Acute M.I. 49	Generalized arteriosclerosis Hypertension 3 yrs. Angina	180 125	37	80% Yes	480	Recent and old infarcts	Diffuse fibrosis	0	0	0	
6008 12/42	Acute M.I. 63	Previous M.I. 9 mos. ago Generalized arteriosclerosis	120 80	37	100% Yes	450	Recent and old infarcts	Diffuse fibrosis	0	Sclerosis 27	0	
5691 3/42	Acute M.I. 55	Previous M.I. 8 mos. ago C.H.F. 1 yr. ago	130 80	37	100% Yes	625	Recent and old infarct	Diffuse fibrosis	Sclerosis	0	0	

TABLE III (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight In gms.	Infarct	Scarring	Mitral	Aortic	Other	
5668 2/42	Acute M.I.	58	205 130	2/	100%	Yes	700	Recent and old infarcts	Diffuse fibrosis	0	0	0	
5468 8/41	Acute M.I.	45	125 90	3/	90%	Yes	665	Recent and old infarcts	Diffuse fibrosis	0	0	0	
5384 5/41	Acute M.I.	75	140 90	3/	100%	Yes	760	Recent and old infarcts	Perivascular fibrosis Diffuse fibrosis	0	0	0	
5216 1/41	Acute M.I.	67	220 130	3/	100%	Yes	570	Recent and old infarcts	Perivascular fibrosis Diffuse fibrosis	0	0	0	
5111 10/40	Acute M.I.	57	150 90	2/	100%	Yes	570	Recent and old infarcts	Perivascular fibrosis Diffuse fibrosis	Sclerosis 2/	0	0	
5052 8/40	Acute M.I.	69	?	3/	100%	Yes	380	Recent and old infarcts	Focal scars Diffuse fibrosis	Sclerosis 1/	0	0	

TABLE III (con't)

Date & Number of Autopsy	Terminal Event or Cause of Death	Age	Clinical History		Coronaries			Myocardium			Valves		
			B.P.	Sclerosis	Maximum Occlusion	Atheroma	Weight in gms.	Infarct	Scarring	Mitral	Aortic	Other	
5014 7/40	Acute M.I.	69	?	3/4	100%	Yes	380	Recent and old infarcts	Focal scars Diffuse fibrosis	0	0	0	
4923 1/40	Acute M.I.	50	110 80	2/4	80%	No	690	Recent and old infarcts	Focal scars Diffuse fibrosis	Sclerosis 2/4	0	0	
4807 1/40	Acute M.I.	66	170 120	2/4	80%	No	?	Recent and old infarcts	Focal scars Diffuse fibrosis	Sclerosis 1/4	0	0	

TABLE IV Summary of Data by Age Groups

Rheumatic Hearts

Age at death	37-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80 up	Totals
No. of cases	14*	8	8	9	2	4	3	2	0	50
Coronary	14	10	4	3	3	0	1	0	0	21
Sclerosis	24	3	2	3	2	1	2	2	0	15
	34	1	2	2	4	1	1	1	2	14
100% occlusion	0	0	1	0	3	0	1	0	0	5
Recent M.I.	0	0	0	0	2	0	0	0	0	2
Old M.I.	1	0	0	2	1	0	0	0	2	6
Perivascular scars	9	5	5	5	3	1	4	2	2	31
Valve damage										
Mitral	13	8	7	7	8	2	4	2	3	47
Aortic	10	5	5	5	5	1	3	2	3	34
Tricusp.	1	0	0	2	0	0	0	1	0	4
C.H.F.	4	6	4	4	3	1	2	2	1	23
Years since R.F.	5-38	21-38	35-49	35-47	20,40	32-54	45-62	?	-	-

Average age at death: 53 years

Average heart weight: 647 grams

Bacterial Endocarditis as cause of death: 3 cases, ages 48, 54, 68

* In 37-44 age group, 5 patients died within 72 hours following valvulotomy

TABLE IV (con't)

Hearts of patients with traumatic causes of death

Age at death		37-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80 Up	Totals
No. of cases		8	6	8	7	7	1	2	4	7	50
Coronary sclerosis	1/	6	3	6	4	3	1	0	0	3	26
	2/	2	2	2	1	4	0	0	3	3	17
	3/	0	1	0	2	0	0	2	1	1	7
Perivascular scars		0	1	2	3	2	0	2	2	1	13
Valve damage	Mitral	0	1	6	2	2	0	0	4	3	18
	Aortic	0	2	3	2	1	0	0	3	0	11
	Tricusp.	0	0	0	1	0	0	0	2	0	3

Average age at death: 58 years
 Average heart weight: 397 grams
 Myocardial Infarction: 2 cases (both old M.I.), ages 76, 59
 100% occlusion: 1 case, age 83

Hearts of patients with myocardial infarction

Age at Death		37-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80 up	Totals
No. of cases		5	8	13	7	2	8	4	1	2	50
Coronary sclerosis	1/	0	0	0	0	0	0	0	0	0	0
	2/	3	0	3	2	1	1	1	0	0	11
	3/	2	8	10	5	1	7	3	1	2	39
100% occlusion		3	6	3	4	2	5	2	1	1	27
Recent M.I.		4	6	8	6	2	6	3	1	1	37
Old M.I.		2	6	9	5	2	7	4	1	1	37
Perivascular scars		3	2	4	1	0	4	2	1	2	19
Valve damage	Mitral	0	0	3	2	1	3	1	0	0	9
	Aortic	0	1	3	0	1	1	0	0	0	6
	Tricusp.	0	0	0	0	0	0	0	0	0	0

Average age at death: 55 years
 Average heart weight: 490 grams

RESULTS

Table I lists the data on 50 cases with 'healed' rheumatic heart disease. Table II gives the data on the control group in which the cause of death was trauma, suicide or poisoning. Table III includes information on the control group of males with clinical and/or pathological evidence of myocardial infarction, recent and/or healed. In each table listed under clinical history is information pertinent to the individuals' cardiac status including any history of rheumatic fever, myocardial infarction, congestive failure, angina, hypertension, arteriosclerosis, diabetes, obesity, alcoholism and the blood pressure. There is little or no history available on patients that were dead on arrival at the hospital or who died shortly thereafter. Scant clinical history was available on a number of patients. Many were seen for the first time in the hospital when they presented in the emergency room. Often they were in a state of shock when seen so that data on blood pressure may not represent the normal blood pressure for these patients. In the tables, the information on the coronary arteries, the myocardium and the cardiac valves is derived from a combination of the gross description in the original autopsy protocols and of findings from careful microscopic examination of the tissue sections.

Table IV is a summary of the data from the other three tables broken down by age groups. The ages at death of the cases with evidence of rheumatic heart disease ranged between 37 and 78 years with 53 years of age as the average. The two

control groups were selected so that the ages at death would be comparable to those in the rheumatic group. The age range in the series of traumatic deaths was from 37 to 87 years with the average 58 years of age. In the group with evidence of myocardial infarction, the average age of death was 55 years ranging from 37 to 87 years. Congestive heart failure accounted for death in 23 cases in the rheumatic group. Bacterial endocarditis played a final role in another three instances while acute myocardial infarction (not attributable to surgical trauma) was found in two cases. In the age group 37 to 44 years, five patients out of the total of 14 died within 72 hours after undergoing surgical procedures to correct valvular stenosis.

The average weight of the hearts in each group were as follows: rheumatic hearts: 647 grams; hearts in traumatic death: 397 grams; hearts in the myocardial infarction group: 490 grams. No correlation was found in this study between heart size and elevated blood pressure or age but in general the patients who died in congestive heart failure had the largest hearts and had the greatest amount of valvular damage.

As anticipated, the greatest amount of coronary arteriosclerosis was found in the group dying with myocardial infarction. The incidence of atheromatous deposition and of total arterial occlusion was also greatest in this group. In all groups the prevalence of these changes increased with age. It was also found that 'healed' rheumatic hearts contained more arteriosclerotic changes in the coronary arteries than did

the hearts in the series of traumatic deaths and this was paralleled by a greater number of myocardial infarctions. These differences were most striking when comparing the age groups below 60 years. In the rheumatic group six of the eight myocardial infarctions and four of the five complete coronary occlusions were found in cases younger than 60 years of age. The only two instances of myocardial infarction in the group of traumatic deaths were found in patients 59 and 76 years of age respectively. Despite the fact the average age at death was 5 years greater in the series of traumatic deaths, comparison of the total figures revealed more advanced coronary artery alteration in the rheumatic hearts. The changes seen in the coronary arteries of the rheumatic hearts consisted of focal and eccentric intimal thickening and hyaline change with varying amounts of lipid and calcium deposition. The elastica interna was frequently disrupted and splayed beneath the zones of fatty deposition. In some cases fibrous and hyaline changes were seen in the underlying media. The changes of acute inflammation, i.e.; polymorphonuclear and lymphocytic infiltration, edema, and hemorrhage were rarely seen. Intimal fibrous proliferation was infrequently present. Aschoff nodules and other giant cell lesions were not identified within or about the coronary arteries of the rheumatic hearts. The qualitative changes seen in these arteries could not be distinguished from the alterations seen in the coronary trees of the other two groups. As pointed out earlier, there were obvious quantitative differences.

The presence of perivascular fibrosis was noted most often in the group of rheumatic hearts and least frequently in the cases of traumatic death. In all groups, the amount of perivascular scarring increased with age but no direct correlation between perivascular scarring and either heart size or amount of arteriosclerosis in the coronaries could be demonstrated. Because of the unreliability of information about blood pressures (as discussed above) no comment may be made concerning the relationships between hypertension and either arteriosclerosis or myocardial perivascular fibrosis. The association of perivascular scarring with hypertensive heart disease is well recognized. In the group of rheumatic hearts there was no consistent difference in the appearance or distribution of perivascular scarring from that seen in the hearts of the control groups. The large, fibrous scars seen in the myocardium of the rheumatic hearts were often more patchy and scattered than the compact, well circumscribed scars generally attributed to healed zones of myocardial infarction. There was much less frank necrosis in the myocardium of the rheumatic hearts than in the hearts of the myocardial infarction group but none of these differences served to distinguish consistently between the hearts of the two groups. A careful search for Aschoff bodies in this study was unrewarding. No granulomatous lesions which could be unequivocally identified as Aschoff nodules were discovered.

As one would expect, by far the greatest amount of valvular

damage was seen in the rheumatic group. The amount of valvular stenosis, incompetence, sclerosis and calcification, thickening and rolling of edges and vegetation formation was much less in the other two groups. The incidence of valve alteration was least in the myocardial infarction group. In all groups, the mitral valve was most frequently damaged followed by the aortic valve and then the tricuspid valve. No pulmonary valve damage was noted. In the rheumatic group, aortic valve alterations were almost always accompanied by mitral valve damage while the incidence of aortic valve alteration alone was more frequent in the other two groups. Where tricuspid valve damage was seen it was always accompanied by changes in one or both of the other valves. In all 150 cases the frequency and extent of valve alteration increased with age.

A subsidiary phase of this investigation involved a review of 690 autopsies on white males 37 years of age and above who died from all causes between the years of 1940 and 1963. Acute myocardial infarction accounted for 94 of these deaths or about 14%. The average age at death in this group of acute infarctions was 67 years. The average age at death in the 150 cases selected for detailed study was about 55 years or about 12 years below the age of peak incidence of fatal acute myocardial infarction. Therefore, one would expect a lower incidence of fatal myocardial infarction in both the group of rheumatic hearts and the group of traumatic deaths than in the total population of males who come to autopsy.

Discussion

In this investigation, the coronary arteries in 50 hearts in which there was evidence of rheumatic carditis at some time in the past were more frequently and more widely involved with arteriosclerosis than were the coronary arteries in 50 hearts of men in the same age group who died as the result of trauma or poisoning. If it is assumed that this latter group is representative of the population at large, it appears that acute rheumatic carditis predisposes the coronary arteries to a greater than normal incidence of arteriosclerosis. This finding bears out the assumption of Gross et al. (21) and of Karsen and Bayless (17) that acute rheumatic fever predisposes the coronary arteries to early and extensive arteriosclerotic changes. However, the lesions that these authors described as distinctive and characteristic of healed rheumatic arteritis could not be verified in this study. Nothing resembling the fibrous endarteritis that follows acute rheumatic carditis was seen in this series nor were any other signs of active inflammation present. The changes observed in the coronary arteries were indistinguishable from the arteriosclerotic lesions in the nonrheumatic group. The variation in the extent of the coronary artery lesions in the rheumatic group may be accounted for by the age of the patient and the number of years since recovery from the acute disease. It may also reflect the severity of the initial attack or the number of recurrences of the disease. Just as there are a number of cases of rheumatic fever in which

such commonly involved sites as the heart valves, the aorta and the joints are spared so there must be instances in which the coronary arteries are not involved by the disease. The process of acute inflammation in the walls of the coronaries (which has been frequently described in rheumatic carditis) is followed by scarring and, later, the development of sclerotic changes, lipid retention and calcification. This is analogous to the morphological sequences in the heart valves and aorta of post-rheumatic individuals. There is little morphological evidence that these changes result only from chronic, continuing inflammation of allergic or infectious etiology. Allergy or infection may initiate this process as described by Waters (65). It is postulated that once the vessel wall is damaged and has become fibrotic, atheromatous changes can be progressively superimposed. The mechanism of atheroma formation is not clearly understood, but it involves further alterations in the vessel wall together with factors that influence the retention of plasma lipids and the deposition of calcium salts.

The advanced coronary arteriosclerosis of 'healed' rheumatic hearts is reflected in the higher incidence of complete coronary occlusion and of myocardial infarction than was found in the hearts of group of traumatic deaths. This difference might have been more striking if the average age of the traumatic group had not been five years greater than the average age at which the rheumatic patients died. It should be remembered that the patient must live at least 24 to 36

hours after a complete coronary occlusion for there to be identifiable necrosis and evidence of infarction in the heart muscle. Because of their severely compromised cardiac status, the patients with rheumatic heart disease would not be expected to survive many hours after a major coronary closure. Among the 23 rheumatic cases in which congestive heart failure was listed as the cause of death a number of complete coronary occlusions may have gone undetected. With the apparent cause of death so obvious, few prosectors would undertake a diligent survey of the coronary arteries. Acute myocardial infarction was found to have played a role in only 2 cases or 4% of the rheumatic group. In the sample of 690 males from the entire autopsy population, the incidence of fatal, acute myocardial infarction was about 14%. However, the average age at death of this group was 67 years while that of the rheumatic group was 51. Many patients whose hearts are damaged by rheumatic carditis succumb to congestive heart failure, recurrence of rheumatic myocarditis, bacterial endocarditis and embolization before the extent of their coronary artery disease is sufficient to result in fatal myocardial infarction.

Another factor to be considered in assessing the cardiac status of patients who have survived acute rheumatic fever is the limitations placed on their physical activity. Many are cardiac cripples, either because of limited cardiorespiratory reserve or because of the admonitions of their physicians. According to the belief that regular exercise is important for the development of coronary collateral circulation and

of myocardial resistance to anoxia, many years of inactivity have left these patients highly vulnerable to functionally disastrous coronary occlusion, and they are candidates for sudden cardiac failure. The clinical impression that myocardial infarction is rare in patients with 'healed' rheumatic carditis reflects both the early age at which these individuals die from other causes and the abrupt demise following complete coronary occlusion. This impression should not be construed as evidence for the lack of coronary arteriosclerosis.

Though no unique or distinctive lesions could be demonstrated in the 'healed' rheumatic hearts, these hearts could be characterized as larger and as containing more valvular damage and more perivascular fibrosis than the nonrheumatic hearts. The increased size was primarily hypertrophy (increased weight) but some degree of dilatation of the chambers was a common finding. The myocardial hypertrophy in most cases appeared to be secondary to valvular stenosis and/or insufficiency although hypertension and active myocarditis could not always be rule out. The failing ischemic heart also tends to hypertrophy as well as dilate. This phenomenon may account for the fact that the average heart weight was greater in the group dying with myocardial infarction than it was in the series of traumatic deaths. This was contrary to expectations when it is noted that more than twice as much cardiac valvular damage was observed in the group of traumatic deaths. One explanation for this apparent contradiction might be in the tendency for prosectors to describe more minutely

the valves in a heart that otherwise presents as unremarkable. When either mitral or aortic stenosis is present, there is experimental evidence to suggest that amount of arteriosclerosis in the ascending aorta and in the coronaries is less than normal (32). Less arterial wall damage because of reduced systolic pressure has been given as the explanation for this observation. This protective mechanism would work to the advantage of the patients with chronic rheumatic valvulitis. The valvular changes are often considered to be the most characteristic gross lesion found in the 'healed' rheumatic heart. As pointed out earlier, similar valve alterations are seen in a number of other disease entities, especially those of the collagen group of disorders. The view of some authors that all valvular lesions are of rheumatic origin remains to be proved.

The Aschoff body was once considered to be the hallmark of rheumatic carditis. Fewer investigators today accept this view. In this study no lesions were seen which could be unquestionably identified as Aschoff nodules. Perhaps these lesions could have been found if more sections had been taken from the posterior ventricular wall, the interventricular septum or the auricular appendage. It is to be expected, however, that in 'healed' rheumatic hearts the inflammatory granulomata of the acute phase would have evolved into small, nondescript fibrous scars. The presence of Aschoff lesions would suggest the recurrence of rheumatic fever or the presence of some other inflammatory process but would not necessarily

be diagnostic. Similar nodules have been described in other forms of myocarditis.

An attempt was made to correlate the number of years of survival after the initial rheumatic onset with the extent of valvular damage and the amount of coronary arteriosclerosis. Assuming that the only contributions of rheumatic fever to these changes are the initial, acute inflammatory changes within the valve and artery tissues, one would expect the sclerotic lesions to appear early and widespread and to progress with age. When the onset of the disease is late, i.e., in the third and fourth decades of life, the acute inflammatory process is said to be more destructive. In this study no relationship could be demonstrated between either years of survival after the initial attack or the age at which the attack occurred and the age of death or the extent of the lesions at the time of death. There are several reasons which would account for the absence of such correlations. The initial attack may be subclinical or may not be accurately diagnosed, the residual heart murmurs being discovered at some later date. The patient's memory of the dates and events surrounding his childhood illness are often faulty. Recurrent attacks which add to the scarring sometimes go unrecognized or, for lack of clinical history, may be interpreted as initial bouts of rheumatic fever. The term 'healed' rheumatic heart disease must be used advisedly. These patients usually have some degree of permanent damage to their heart valves, myocardium and coronary arteries and are subject to recurrences

of acute myocarditis and valvulitis.

In light of this study, an additional deadly potential in the natural history of rheumatic heart disease should be emphasized. Many children who survive the life-threatening acute myocarditis at the onset of this disease live on with progressively more sclerotic heart valves and succumb in middle adulthood to congestive heart failure. (According to Rogers and Robbins (113) congestive failure is frequently the result of latent rheumatic myocarditis rather than secondary to valvular compromise.) At some time after the initial damage to the valves, about 10% of these patients develop bacterial endocarditis with a fatal outcome. Another 25% (approximately) of patients survive into middle age and escape the first three deadly potentials of rheumatic heart disease. But they carry the stigma of their rheumatic carditis as advanced coronary arteriosclerosis and concomitant ischemic heart disease.

The material in the Grace-New Haven Hospital autopsy series is unusually complete, containing long and detailed descriptions of the clinical history and of the gross and microscopic findings at each autopsy. Tissue sections taken from the major organs and from sites of pathology are on file for each case. Despite the overall superiority of this series, clinical details and myocardial and coronary artery slides were absent for a few of the cases included in this investigation. In addition, the interpretation of data must be cautiously approached because of biases and errors which are

inherent in any autopsy series (66). One such built-in sampling error results from the fact that the composition of a hospital population does not reflect the composition of the population at large. This is less true at Grace-New Haven which is a community hospital than it is at a private diagnostic center where the patients are from an upper socio-economic group and to which patients may have come from distant communities in order to take advantage of a speciality of the hospital. The population that comes to autopsy is further altered from the population at large by factors such as racial and religious practices which lead relatives to refuse permission for postmortem examination. This bias is avoided to some extent in the group of traumatic deaths because a number of these are coroner's cases. The selection of only adult white males for inclusion in this study also partially avoids this sampling bias. Secular changes, i.e.; changes occurring with the passage of time, further becloud the interpretation of results from a study such as this one which encompasses a 22 year period. Population shifts and variations in rates of disease prevalence as well as changes in the knowledge and procedures that go into a postmortem examination have occurred within the period under consideration. The prejudices and variable skills of many prosecutors is an integral part of any autopsy series. In some of the cases included in this study, the initial episode of acute rheumatic fever was diagnosed over 50 years ago. In light of subsequent knowledge, the diagnoses in these cases might be very different

today.

Berkson (67) has pointed out several fallacies frequently encountered in the interpretation of hospital data. The presence of two diseases in the same person, e.g.; rheumatic heart disease and coronary arteriosclerosis, may increase the probability of his admission to the autopsy population. Also, if two diseases have different fatality rates then one disease process may bring the patient to autopsy before the other disease entity has had time to express itself. This factor operates in the comparison of the fatality rate of rheumatic heart disease and with that of coronary arteriosclerosis. With so great a latitude for errors in the data, detailed statistical analysis is inappropriate for an autopsy survey.

Summary and Conclusions

A comparison was made of the clinical history and necropsy material of 50 men with evidence of 'healed' rheumatic carditis, 50 men with evidence of myocardial infarction and 50 men who died as the result of trauma. A greater amount of arteriosclerosis is present in the coronary arteries of the patients who had survived acute rheumatic carditis than is found in the coronary arteries of the nonrheumatic hearts. The advanced coronary arteriosclerosis is paralleled by a higher incidence of narrowing and complete occlusion of the coronaries and of myocardial infarction in the hearts of post-rheumatic patients. Except for quantitative variations, the histological appearance and distribution of the coronary arteriosclerosis of 'healed' rheumatic hearts is no different from that seen in nonrheumatic hearts. There are no specific alterations nor characteristic lesions which clearly differentiate the myocardium, or the coronary arteries of a 'healed' rheumatic heart from those of a heart which has never undergone the changes of acute rheumatic carditis. In general, the rheumatic hearts are heavier, they have more perivascular fibrosis and widely distributed myocardial scarring and they have more valvular damage than the hearts of persons dying acutely of trauma or of persons dying of coronary heart disease.

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