

ACKNOWLEDGMENTS

The acknowledgments I must make are many, and it is a pleasure to record them. First and foremost, I would express my thanks to Dr. A. Rae Gilchrist under whom I have had the privilege of working and whose cases I have investigated and treated for 3 years. He also gave me the opportunity to assemble the facts presented. I would thank,

MYOCARDIAL INFARCTION

A Clinical Study of the Aetiology and Prognosis, with special reference to The influence of Anti-coagulant Therapy on Prognosis.

A Thesis submitted for the Degree of Doctor of Medicine of the University of Edinburgh

by

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April 1950.



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Cardiac disease stands supreme and unopposed as a cause of death. A small but ever increasing proportion of these cardiac deaths is due to disease of the coronary arteries. Coronary artery disease was recognized in the 17th century, but the clinical features of occlusion of such a diseased artery have been appreciated only during the past 40 years. Although a new entity to the clinician, coronary artery occlusion with myocardial infarction was far from being a new disease. Pathologically myocardial infarction had long been recognized in both the acute and healed stages. Cardiac aneurysm formation was also well known to the pathologist. In 1749 De Senac had referred to thin walled parietal aneurysms of the left ventricle. Cardiac rupture was also recorded and no doubt was associated with myocardial infarction. Even a King of England was not spared - George II. died of a ruptured heart. Why then did the clinical features, so dramatic, and sudden in their onset, pass unrecognized or wrongly interpreted?

Once established, "coronary thrombosis" was diagnosed with increasing frequency, and the anterior descending branch of the left coronary artery soon vied with the lenticulo-striate artery, as "the artery of sudden death". There is little doubt that the incidence of "coronary thrombosis" has increased remarkably /

II.

remarkably over the past 3 decades. Both sexes and all ages may be affected, but the basic lesion - arteriosclerotic change in the coronary arteries - is commonly not well established until middle life. The victims are frequently men in the prime of their lives, in their most productive years, whom the community and the family can ill spare. Many an economic or social problem follows in the wake of a "coronary thrombosis".

Aetiology, treatment, and prognosis are therefore of the utmost importance, not only to the individual, but to society. A study of these problems has prompted submission of this thesis.

A historical review of myocardial infarction is first presented (section II.). The material is arranged in the sequence - early history, aetiology, clinical features, course and complications, treatment, prognosis - immediate and remote, pathology, electrocardiography, and roentgenkymography. The incidence of "coronary thrombosis" as the certified cause of death has been determined by a study of the annual reports of the Registrar-General for Scotland between the years 1937 and 47 (Section III.). Aetiology is stressed again in section IV. and the results of a clinical approach to the problem are presented. Embolic coronary artery occlusion is discussed /

III.

discussed separately (Section XV.) and the incidence of this complication in subacute bacterial endocarditis is noted.

Two series of cases are then presented for comparison. The first comprises 100 cases of myocardial infarction treated conservatively, and the second, 70 cases who received anti-coagulant therapy during the first 3 weeks, but who were otherwise similarly treated. In sections V. to XII. the two series are analysed in detail and compared both at the time of the myocardial infarct and during the succeeding months and years. The features important in determining the immediate and ultimate prognosis in the conservatively treated series, and the complications which may follow myocardial infarction, are discussed. They provide a standard with which the series treated with anti-coagulants may be compared. The advantages, or otherwise, of anti-coagulant therapy during the first 3 weeks are thereby assessed. Section XIII. deals with the changes observed in blood clotting after myocardial infarction, and indicates a rational basis for anti-coagulant therapy. The most recent advance in treatment - specific anti-shock therapy - is briefly summarised in section XIV. The electrocardiographic features of 65 cases are presented and analysed in section XVI. This section is not intended /

intended as a comprehensive study of electrocardiography in myocardial infarction, but records the incidence of the various diagnostic features, in these 65 cases. Finally, after the conclusions (XVII.) and summary (XVIII.) the clinical details of 35 cases are presented. (section XIX.)

Diagnosis and differential diagnosis, and the established methods of treatment are not discussed.

Reber (1772) was the first to describe a symptom complex due to disorder of the heart, but even he did not recognize that disease of the coronary arteries was the primary factor. This was left to Jenner and Parry (1799) who considered that calcification of the coronary arteries was the essential lesion.

Infarction of the myocardium due to coronary artery obstruction was originally considered to be incompatible with life and to be the cause of the sudden death in those afflicted with angina pectoris. Osler (1910), in discussing his extensive autopsy of cases of angina pectoris states that "obstruction of a (coronary) branch with a fresh thrombus is the cause of sudden death in angina pectoris." Osler (1910) also states "Coronary occlusion has been considered an episode in the progress of angina pectoris, a narrowing episode it is true, and yet but the greater ending of an interesting and varied clinical story."

Pathologically myocardial infarction was recognized

II. HISTORICAL REVIEW OF MYOCARDIAL INFARCTION.(a) Early History :

The belief that the heart was the ruler over all other organs and as such was immune from disease was handed down from the time of Hippocrates (quoted from Herrick, "Diseases of Coronary Arteries and Cardiac Pain" 1936.) Physicians were slow to recognize that no immunity hedged in this king. Heberden (1772) was the first to describe a symptom complex due to disorder of the heart, but even he did not recognize that disease of the coronary arteries was the primary factor. This was left to Jenner and Parry (1799) who considered that calcification of the coronary arteries was the essential lesion.

Infarction of the myocardium due to coronary artery occlusion was originally considered to be incompatible with life and to be the cause of the sudden death so common in those afflicted with angina pectoris. Osler (1910), in discussing his seventeen autopsies of cases of angina pectoris states that "Blocking of a (coronary) branch with a fresh thrombus is very common in cases of sudden death in angina." Hamman (1926) also states "Coronary occlusion has been considered an episode in the progress of angina pectoris, a harrowing episode it is true, and yet but the dramatic ending of an interesting and varied clinical story."

Pathologically myocardial infarction was recognized /

recognized during the latter half of the 19th century (Weigert 1880, Ziegler 1881, Cohnheim 1881, Huber 1882 and Leyden 1883-84,) but clinically it was not established as a condition which could be diagnosed during life until the early part of the present century. The first tentative diagnosis during life was made by Hammer in 1876. Commenting on the case, he writes "I thought that only a sudden progressively increasing disturbance to the nutrition of the heart itself such as cutting off the supply of nourishment could produce such changes as this case showed, and that such obstruction could be produced only by a thrombotic occlusion of at least one of the coronary arteries. From lack of ground for any other satisfactory explanation I was carried away by this thought."

Autopsy confirmed his suspicions. It showed a thrombus occupying the right sinus of Valsalva and occluding the mouth of the right coronary artery.

In 1890 Huchard published autopsy records of 185 cases of coronary sclerosis, in which can be found all the clinical and pathological features of coronary occlusion. René Marie, in his thesis "L'Infarctus du Myocarde et ses Consequences." (1896) described the pathology of both myocardial infarction and cardiac aneurysm, but did not co-relate the clinical and pathological findings. Krehl's monograph (1901) upon diseases of the heart muscle shows a much clearer /

clearer interpretation of the clinical records and pathological findings. (These original articles have not been referred to personally.)

Dock (1896) was the first to report cases of myocardial infarction diagnosed ante-mortem and proved at autopsy. His fourth case merits recording in some detail. - The patient, an elderly male, had experienced exertional dyspnoea for 3 months. One week before death he had a very severe pain in the heart region and fainted, becoming pulseless and very dyspnoeic. Evidence of left ventricular failure developed. Pericardial friction could be heard at the apex. Death occurred suddenly while he was straining at stool. At autopsy, the coronary arteries were very arteriosclerotic, and the anterior descending branch of the left artery, and a branch of the circumflex artery were both blocked by thrombus. The myocardium was infarcted, with an apical pericarditis and a thin layer of endocardial thrombus formation.

Commenting on the case Dock states "In this case the relation of the coronary sclerosis to the gradually developing dyspnoea, and of the infarction to the acute attack a week before death is clear. The case also illustrates the fact that a heart extensively necrosed may continue to act for some time fairly well, if exposed to no sudden strain, thus explaining the early stages of these cases in which large fibrous areas are found post mortem in the heart. It is also /

also a fine example of atheroma limited almost entirely to the coronary vessels."

It is probable that, in establishing the clinical entity of coronary thrombosis, and in suggesting that it is not immediately fatal, Dock has received less credit than is his due.

In 1910, Obrastzow and Strascheska described the clinical features in detail, emphasising the triad of retro-sternal pain, dyspnoea and orthopnoea, and epigastric pain. They drew attention to many features now considered important, - a gallop rhythm, pericardial friction, faint heart sounds, Cheyne-Stokes breathing, etc.. However they believed that infarction led to an early death.

Herrick (1912) drew attention to the fact that obstruction of a coronary artery was a recognizable clinical condition, and that it was not necessarily fatal - "But there are reasons for believing that even large branches of the coronary arteries may be occluded - at times acutely occluded - without resulting death, at least without death in the immediate future. Even the main trunk may at times be obstructed and the patient live." In support of his statement he reported 5 cases living for 3, 7, 12, 12, and 20 days after the onset of their symptoms and also made extensive reference to the literature both clinical and pathological. His clinical grouping of cases is still applicable today and will be referred to later in /

in this review. After a lapse of six years (1918, published 1919) he enlarged on his original observations, and on this occasion had a more receptive audience. In the same year, Levine and Tranter (1918), quite independently of Herrick, reported on two cases. Libman was also aware of the condition, having discussed Herrick's 1912 communication, and in 1919 he published his own observations. Corroborative evidence was soon supplied by Fred Smith (1918, 1920 and 1923) by reason of his experimental work on dogs. Electrocardiographic changes were recognized in the dogs, and also by Pardee (1920) in human beings. Coronary thrombosis had become firmly established as a recognizable clinical entity.

In 1926 Hamman gave a brief review of the development of knowledge of this condition, and described the symptoms in considerable detail, dividing them into four groups:-

1. The immediate symptoms associated with the occlusion: the anginal seizure.
2. The symptoms associated with the myocardial damage: myocardial insufficiency.
3. The symptoms associated with the myocardial infarct.
4. Additional symptoms - chiefly gastro-intestinal and vaso-motor.

He emphasised how embolic phenomena may assist diagnosis, and, in a discussion of the pathological anatomy, drew attention to the importance of coronary arteriosclerosis.

Levine and Brown (1928) were the first to report on a large series of cases - 145 - and to analyse in detail the various clinical features. Since then many papers have appeared, and all manifestations of the disease and its treatment have been discussed. Mention might be made of those by Conner and Holt (1930), Meakins and Eakin (1932), Cooksey (1935), Willius (1936(a)), Blumer (1937), Bean (1937 & 38 (a) & (b)), Mallory, White, and Salcedo-Salgar (1939), Bland and White (1941), Levine and Rosenbaum (1941 (a) & (b)), Rathe (1942), Wood and Barnes (1942), Nay and Barnes (1945), Hellerstein and Martin (1947), and Katz and Mintz (1947).

In Britain, knowledge of this new condition lagged, and when Sir James MacKenzie published his monograph on angina pectoris in 1923, he included a number of cases of coronary thrombosis. Without doubt eighteen cases had sustained a myocardial infarct and in 2 and other cases, the clinical records suggest/^{such}an upset. Forty cases died suddenly or were found dead in bed, in whom a coronary thrombosis may have been the terminal event. Gibson (1925) and McNee (1925-26) were the first to report cases in the British literature, but soon Parkinson and Bedford (1928 (a)) published a series of 100 cases. Coombs (1927), Gilchrist (1929-30), Bramwell (1930) Parkinson (1932), Hay (1935), Bedford (1935) Cowan (1936) and Palmer (1937) added to the literature.

(b) Aetiology /

(b) Aetiology :

All reported series indicate that males are more prone to develop coronary thrombosis than are females. The sex ratio varies from the 2.2:1 reported by Katz and Mintz (1947) and by Bean (1937) to the 13.3:1 of Parkinson and Bedford (1928). Details are given in Table I.

TABLE I. Sex incidence of coronary thrombosis reported by various authors.

Authors.	Sex Ratio.		Number of Cases.
	Male	: Female	
Levine & Brown(1928)	3.26	: 1	145
Parkinson & Bedford(1928a)	13.3	: 1	100
Conner & Holt (1930)	5.5	: 1	287
Willius (1936a)	7	: 1	370
Bean (1937)	2.2	: 1	300
Master et al. (1939b)	3.4	: 1	500
Katz & Mintz (1947)	2.2	: 1	572
Master (14 series) (1939b)	4.6	: 1	2803
Average of 20 series	3.6	: 1	4857

The six series added to the 14 analysed by Master in 1939 are those of Rosenbaum and Levine (1941a), Rathe (1942), Smith(1942), Chamberlain (1946) Katz and Mintz (1947) and Wright (1948).

Myocardial infarction has always been considered to be a disease of the middle-aged and elderly.

Master (1939b) analysed 12 series comprising 1761 cases and /

and found the maximum incidence in the 6th decade (35%), but only a slightly lower incidence in the 7th decade (32%). Five out of the twelve series had their maximum incidence in the 7th decade. Katz and Mintz (1947) found the incidence in these two decades practically equal - 32.7% and 33.6% respectively.

When the sexes are considered separately, there is a striking disparity in their respective age incidence. Males invariably show a maximum incidence in the 6th decade. Table II. A, records incidence in the 6th and 7th decades, and the percentage in the under 60 years and over 60 years groups, among males.

TABLE II. Age distribution of cases of coronary thrombosis among (A) Males, & (B) Females.

Authors.	%Incidence in each Age Group.			
	6th Decade	Under 60 yrs.	Over 60 yrs.	7th Decade
A Males				
Conner & Holt (1930)	41	76.5	23.5	18.5
Willius (1936a)	41.7	62.1	37.9	30.6
Master et al. (1939b)	35.9	66.4	33.6	26.6
Rathe (1942)	31	46	54	37
Katz & Mintz (1947)	32.2	56.6	43.4	29.3
B Females.				
Conner & Holt (1930)	46	65	35	22
Willius (1936a)	28.3	34.8	65.2	41.3
Master et al. (1939b)	34.9	58	42	34
Rathe (1942)	24	41	59	36
Katz & Mintz (1947)	31.1	40.5	59.5	42.8

The average age of males varied from the 54.7 years of Master (1939b) to the 58.4 years of Katz and Mintz (1947).

Females on the other hand generally show a maximum incidence in the 7th decade, and it is uncommon for cases to occur in patients under the age of 50 years.

Table II. B, gives details of the age incidence of females. Conner and Holt (1930) and Master (1939b) do not bear out the maximum incidence in the 7th decade. 65% of Conner and Holt's 44 cases were under 60 years, but the maximum incidence was in the 56 - 60 year group. Master (1939b) reporting on 112 females, found the incidence in the 6th and 7th decades to be practically equal - 34.9% & 34% respectively and the average age was 56 years.

In the early literature, isolated cases occurring in young adults were periodically recorded. (Smith and Bartels 1932, Cullinan and Graham 1934, Durant 1937, Blazé 1937, Smith and Hinshaw 1937, White, Glendy, and Gustafson 1937, Miller and Wood 1943). In recent years large series of cases have been reported by Glendy, Levine and White (1937), French and Dock (1944), Newman (1946), Poe (1947) and Yater et al. (1948). The grouping of men in the armed forces has facilitated this work. The most recent series by Yater and his associates comprises 866 cases which occurred in the United States armed forces during the recent war. All cases were between the ages of 18 and 39.

Myocardial infarction occurring during adolescence /

adolescence is very uncommon. Apart from those reported by Yater (1948) 13 cases have been recorded. (Zacks 1943, Jukl and Greenstein 1944, Evans and Graybiel 1948, Shivelhood 1948, and McDougall 1949). Only two were female.

Even infancy and childhood are not exempt from this disease. Myocardial infarction has been reported in an infant dying 10 $\frac{1}{2}$ hours after delivery and in another dying 66 hours after delivery. In this latter case, the coronary arteries showed a generalized medial sclerosis. This was most marked in the region of the infarct and the vessels were occluded by thrombus (Ravich and Rosenblatt 1947). Other cases have been recorded in older infants - one died at 7 weeks (Hughes and Perry 1929), one at 4 months (Ramsay and Cumrine 1931), a third at 9 months (Ellis 1935), and a fourth at 11 months (Scott and Miller 1946). Ellis' case showed cardiac aneurysm formation. The exact state of the vessel wall in the thrombosed segment is not clear from all reports, but in one case, the changes suggested thromboarteritis obliterans. In no case was there arteriosclerotic change. Stryker (1946) discusses occlusive coronary artery disease in infancy and childhood, and quotes eight aetiological factors. These are (1) medial calcification with fibroblastic proliferation of the intima; (2) Polyarteritis nodosa; (3) Arteriosclerosis; (4) Syphilitic arteritis; (5) Embolism; (6) Congenital abnormalities; (7) Rheumatic arteritis; (8) Hypertension.

The incidence of previous hypertension is variously reported - 28% by Howard (1934) and 74% by Chamberlain (1946). This variation is in part due to different criteria for hypertension adopted by some authors. Most accept a diastolic level of 90 mm. Hg. or over but some require a level of 100 mm. Hg.. Details of the incidence of hypertension are given in Table III. and of the sex distribution in Table IV.

TABLE III. Incidence of hypertension preceding myocardial infarction.

Author.	% incidence of Hypertension	Number of cases.
* Levine & Brown (1928)	40	145.
Conner & Holt (1930)	33.9	287.
Howard (1934)	28	165.
Bean (1937)	49.3	300.
Master (1939b)	62.4	500.
White & Bland (1941)	34	200.
Levine & Rosenbaum (1941)	57	208.
Master (1943)	69	538.
Chamberlain (1946)	74	100.
Katz & Mintz (1947)	35.9	572.
Yater (1948)	19.1	866.

* Only cases showing a diastolic pressure of over 100 mm. Hg. are included.

TABLE IV. /

TABLE IV. Incidence of hypertension preceding myocardial infarction in the two sexes.

Author	% Incidence of Hypertension.	
	Male	Female
Master (1939b)	56.5	80.
Levine & Rosenbaum (1941)	44	86.
Katz & Mintz (1947)	29.7	49.4

Levine and Brown (1928) state that hypertension is probably the most common aetiological factor.

Master (1943) found an incidence of 69% in 538 cases analysed. He considers that hypertension plays a paramount role in increasing the incidence of coronary occlusion (1939b). In his series, hypertension was present in 28 per cent. of the males and 25 per cent. of the females under the age of 35 years. This percentage increased with age, reaching 80 per cent. in men over 75 years and 90-100 per cent. in women over 45 years. To emphasise the importance of hypertension in the aetiology of coronary thrombosis, he analysed 14 reports totalling 42,000 cases, dealing with blood pressure levels in the general population. These indicate that for both sexes, 5 per cent. of those under 25 years, 26 per cent. under 55 years, and 45 per cent. under 65 years have hypertension. At all ages the incidence is less than among those sustaining a coronary thrombosis. Also, the incidence of coronary thrombosis among the hypertensive male population is much greater at all ages /

ages than among the normotensive males. In both groups it increases with age, up to 64 years, and then falls away slightly. Hypertension was more common in those sustaining recurrent or multiple infarcts - 64% of men and 80% of women, but Master (1943) considered that the height of the blood pressure after the attack did not significantly influence the future course of the patient with regard to subsequent angina pectoris, heart failure, coronary occlusion or death.

All reports indicate that in the younger age groups, hypertension is less common. Glendy, Levine, and White (1937) report an incidence of 16.6%, but their criteria for diagnosis were a systolic blood pressure of 160 mm. Hg. or over, and a diastolic level of 110 mm. Hg. or over. Yater (1948) reported that 19.1% of his series had a diastolic level of over 89 mm. Hg.. This compares unfavourably with his control figure of 3.8% for a similar age group.

Paterson (1939 and 1941) considers hypertension, either sustained or temporary, of extreme importance in aetiology.

Pre-existing angina pectoris has been reported in from 22.4% (Willius 1936a) to 72.9% (Katz & Mintz 1947) of cases. The incidence varies, depending on the completeness of the case histories. Table V. gives details of a number of reported series.

TABLE V. Incidence of angina pectoris preceding myocardial infarction.

Author.	Incidence of Angina Pectoris.
Parkinson & Bedford (1928a)	62%
Conner & Holt (1930)	26.1%
Willius (1936)	22.4%
Bean (1937)	33.6%
Rosenbaum & Levine (1941)	72%
Bland & White (1941)	62.5%
Katz & Mintz (1947)	72.9%

The incidence in the two sexes is approximately equal.

Diabetes is common, being reported in most series of cases. The incidence varies from 8% (Smith et al. 1942) to 23.7% (Levine and Brown 1928). Conner and Holt (1930) found the majority of their cases with diabetes to be in the 50-60 year age group, but Master (1939b) considered that diabetes is more common in the older patients - it was present in 17% of their cases over the age of 60 years, and in only 4.8% of those under 50 years. It is definitely more common among females - 26% as against 6.7% for males (Master et al. 1939). Katz and Mintz (1947) found diabetes in 36 males (9.18%) and 49 females (27.22%).

Levine and Brown (1928) consider that increased body weight is of some importance in aetiology /

aetiology and quote insurance company statistics to prove their point. They state that "The body weight of patients is of some importance in considering aetiological factors. It has been quite striking to us that coronary thrombosis does not commonly occur in the thin individual. After the age of 40 years it is now well known that vascular disease of one kind or another is the most frequent cause of death, and in this connection, disease of the coronary arteries plays no insignificant role. Recently it has been shown by statistics compiled by insurance companies that those who are accepted as normal risks at the ages of 40 years or over, who are 20 to 40% overweight, have an increased mortality of 30 to 80% respectively in the following decades". Bean (1937) could find no characteristic build or weight. Goldsmith and Willius (1937) in a particular study on this subject found that individuals who had hypertension tended to be more overweight than did those who had a normal blood pressure. Yater (1948) considered that obesity was not a factor in the young adult.

Heredity is of considerable importance. Goldsmith and Willius (1937) found that out of 300 cases 165 (55%) had a family history of cardio-vascular renal disease. Levine and Brown (1928) state "Heredity is of considerable importance in the aetiology of this disease. A large number of the patients /

patients here discussed have family histories indicating great susceptibility of the vascular system to degenerative disease. The typical patient is a well set person some-what overweight, often of considerable physical strength, who enjoyed unusual good health."

"No accurate figures were obtained in this study as to the exact frequency of a family history of coronary or vascular disease. Suffice it to note that after a considerable experience with this condition, it is amazing how frequently one finds various members of the same family suffering from early vascular hypertension or coronary disease." 48% of Rathe's series (1942) gave a family history of vascular disease. Both authors found that, in

Syphilis is considered to be of very minor importance, although Warthin (1930) reported that arteriosclerosis of the coronary arteries is more common in the latent syphilitic than in the non-syphilitic. Only Conner and Holt (1930) found a high incidence of syphilis in their cases - 14.2%. Katz and Mintz (1947) found 4 out of 572 cases. Other arterial diseases - peri-arteritis nodosa and thromboangiitis obliterans - are equally rare. (Logue and Mullins 1946, Samuels and Feinberg 1930, Fathree and Hines 1938, and Greenfield 1941). Polycythaemia is occasionally reported (Boyd 1933, Miller 1939).

Tobacco and alcohol have been shown to be of no aetiological importance (White and Shaber 1934, Master,

Dack and Jaffe 1937b). Recently it has been shown that inhalation of nicotine in cigarette smoke causes the liberation into the blood of the anti-diuretic hormone of the posterior lobe of the pituitary gland. (Bulbring et al. 1949). The anti-diuretic principle also causes vaso-constriction, but the reduction in coronary blood flow is likely to be considerable only in sensitive individuals who smoke heavily. These observations in no way cast doubt on the above conclusions of White and Master.

That there is a seasonal incidence in onset of coronary thrombosis is suggested by Bean and Mills (1938) and Hoxie (1940). Both authors found that, in the northern temperate region of America - Philadelphia, Pittsburgh, New York, Boston and Cincinnati - and in the subtropical climate of Los Angeles, acute attacks of coronary occlusion are definitely more frequent in winter and early spring than in the late summer and early autumn.

Levine and Brown (1928) draw attention to two other factors in aetiology :-

(1) The infrequency with which coronary thrombosis is encountered in cases of established auricular fibrillation.

(2) The rarity with which it occurs in subjects who have rheumatic heart disease.

Karsner and Bayless (1934) believed that
rheumatic /

rheumatic fever predisposed to the premature development of coronary arteriosclerosis, but the reverse view was later proposed by Gross and Oppenheimer (1936). These latter authors considered that the occurrence of rheumatic fever and coronary thrombosis in the one subject was fortuitous. Ten of the 866 cases reported by Yater (1948) had rheumatic valvular disease.

Embolism of a coronary artery is a rare event except in bacterial endocarditis. Saphir (1932) and later Hamman (1941) have reviewed the literature and reported their own cases. Hamman discusses 40 cases and gives six possible sites of origin of the embolus. These are (1) a thrombus or atheromatous material in a coronary artery; (2) a thrombus covering an arteriosclerotic plaque at the root of the aorta; (3) bacterial vegetations on the mitral or aortic valve (the most common cause); (4) intra-cardiac mural thrombi; (5) thrombi in pulmonary veins; (6) paradoxical embolism. He considers that the two outstanding features of coronary embolism are that (1) in most cases death is very sudden, or indeed instantaneous. This is due to the absence of disease of the coronary arteries, the heart being quite unprepared by the gradual development of an efficient collateral circulation, to withstand the effects of occlusion of a large branch; (2) Although the immediate prognosis is poor, should the patient survive, then the ultimate prognosis is good, there being no vessel disease.

The work of Manning and his associates (1939) on reflex coronary artery spasm following sudden occlusion of other branches, may have some bearing on the frequency with which sudden death occurs in these cases of coronary embolism.

They compared the mortality rate following sudden occlusion of a major coronary artery in anaesthetised and non-anaesthetised dogs. Occlusion of the anterior descending branch of the left coronary artery caused death in less than 10% of the anaesthetised dogs, but in 40% of the conscious dogs. For the circumflex branch, the figures were 25% and 75% respectively. They considered that the great increase in mortality of the conscious dogs may be the result of reflex spasm of collateral arterioles and small arteries, producing additional areas of ischaemia. All the animals dying suddenly in the conscious state showed the sequence of ventricular extra-systoles, tachycardia, and fibrillation. Opdyke and Selkurt (1948), observed reflex spasm of the coronary tree after coronary occlusion in only 2 out of 10 anaesthetised dogs. Electrocardiograms taken from the "non-ischaemic" areas of the ventricular muscle did not show changes suggestive of ischaemia.

Premonitory symptoms of acute coronary occlusion have been reported since 1926 onwards. (Kahn 1926, /

1926, Willius 1936b, Watzkin 1944). Hay (1933) was aware of these symptoms. Feil (1937) and Sampson and Eliaser (1937) also drew attention to them. Master (1941) recorded their presence in 44.2% of 260 cases. The most common symptom was substernal or praecardial pain or discomfort, but other symptoms recorded were fatigue, weakness, gastric distress, dyspnoea, palpitation, nervousness, and dizziness. The praecardial pain consisted of (1) sudden appearance of typical angina pectoris; (2) sudden accentuation of a previously existing angina, or (3) attack of anginal pain occurring at rest. Such symptoms usually appeared in the 24 hours prior to the attack, but in some cases preceded it by 2-3 weeks. The anatomical basis for these symptoms was presumed to be a gradual occlusion of the lumen of the coronary artery by progressive or recurrent intramural haemorrhage, or by primary thrombosis on a plaque, which might take hours or days for completion. The initiation and progression of the coronary artery occlusion occurs irrespective of physical activity or lack of it, but during the process, effort may induce myocardial ischaemia with production of pain.

Master and his associates (1937^b and 1939^a) believe that the time of onset of the clinical picture of myocardial infarction is fortuitous. In 1939 they investigated the activities of 1440 cases of coronary /

coronary occlusion, and decided that :

- (1) Occupation and social status do not influence the incidence of coronary thrombosis.
- (2) Physical activity and excitement are not factors in the onset - 60 of their cases had been bedridden for weeks or months because of some chronic illness.
- (3) Operation may have some influence in precipitating attacks.
- (4) The attacks are well distributed throughout all hours of the day and night, with peaks at 2 a.m. and 10 p.m. - also indicating that activity is not an aetiological factor.
- (5) There is no evidence that physical effort or excitement produced intimal haemorrhage. It was found at necropsy as frequently in patients who had been bedridden prior to the occlusion, as in those who had been physically active.

In sharp contrast to the findings of Master as to the importance of occupation and social status are the views expressed by Ryle and Russell (1949). Studying the statistics available in the Registrar-Generals Occupational Supplement for 1930-32, they reported that the mortality rate from angina pectoris (coronary thrombosis was not classified as a separate disease in 1930-32) for both men and wives, decreased with descent in the social grading. For males in class /

class I. (professional workers) the mortality is 137% in excess of the average for all males aged 20-65 years; in class III. (skilled artisans) it is 4% in defect of the average; while in class V. (unskilled workers) the mortality is 33% below the expected or normal value. Wives show a similar trend but the extremes are less - +55% for class I. and -18% for class V. A separate study of the occupations comprising the various social orders is even more instructive. Among males, physicians and surgeons show the highest standardized mortality rates from coronary vessel disease - 368. Proprietors of whole-sale businesses; judges, barristers and solicitors; come in at a much lower level - 235 and 227. By way of contrast, agricultural and gardener's labourers show a standardised mortality of 32, while workers in chemical processes are even lower at 20. The mortality ratio of male professional workers to male manual workers is far higher than that of men to women. Geographically also Ryle and Russell demonstrated a definite zoning of mortality from coronary vessel disease, the highest levels being found in the densely populated areas and the lowest levels in the rural areas.

In a separate paper Master (1938) reports 35 cases of coronary thrombosis occurring post-operatively, half the cases developing within the first 3 days after operation. All were proved either at autopsy or /

or by classical electrocardiographic changes. 66% died but in only 8 cases was death attributable directly to the occlusion. The factors possibly leading to the occlusion were considered to include surgical shock attended by a diminution in blood volume and a drop in blood pressure, tachycardia, dehydration, and infection. Bed rest was not a factor.

Winternitz and his colleagues (1938) in their investigation of the development of arteriosclerosis subjected coronary arteries to intra-luminal pressures of 500 and 1000 mm. Hg. without precipitating capillary rupture in the arteriosclerotic plaques. The observations of Master (1937b and 1939a) and of Winternitz are not, however, universally accepted. Paterson (1939 and 41) is the proponent of the theory stressing relationship of exertion to the onset of coronary thrombosis. He, it was, who first demonstrated the continuity of the intimal capillary haemorrhage in the arteriosclerotic plaque with the thrombus in the lumen. (1936). He considers (1941) that:

- (1) The pressure of the blood within the arterial lumen,
 - (2) the strength and elasticity of the capillary wall, and
 - (3) the rigidity of the supporting tissues of the plaque,
- are the three factors governing the integrity of the capillary wall. A raised blood pressure, either permanent /

permanent or temporary as in effort, may therefore precipitate rupture of the capillary and initiate the process of thrombotic occlusion of the vessel. Boas (1939 and 1942) and Blumgart (1945) also consider that effort is of aetiological importance. The capillaries growing from the lumen of the coronary artery into the arteriosclerotic plaques are peculiar in that they have no shock absorbing arteriole to protect them from the arterial blood pressure. They are exposed to a continuously high pressure and to periodic fluctuations in pressure, which, Paterson believes, may facilitate or precipitate their rupture.

(c) Clinical Features:

The classical clinical features have been admirably described by Herrick (1912 and 1919), Hamman (1926), Levine and Brown (1928), Gilchrist (1929-30), Parkinson (1932), and many others. The patient is seized with sudden severe substernal pain which rapidly increases in intensity. His chest feels tight as if gripped in a vice; he is short of breath, sweats profusely and may feel sick. He is restless and cannot find a comfortable position. It is the worst pain he has ever had and may radiate to the shoulders, arms, neck, jaw or epigastrium. Nitrites have no effect on the pain and morphine is required for its relief. He may feel that he is about to die. Such is the classical picture, but by no /

no means all cases present in this manner. The atypical and mild cases deserve close attention. Hamman states "In patients presenting the cardiac symptoms of arteriosclerotic heart disease, any sudden aggravation of the symptoms should arouse suspicion" and "In patients past middle life, without valvular disease, the abrupt onset of myocardial insufficiency should stimulate a careful search for other symptoms of coronary occlusion." As an aid to diagnosis fever and leucocytosis are important. A progressive increase in the blood sedimentation rate during the first 1-2 weeks and the behaviour of the blood pressure during the same period are probably of greater significance.

Mild cases are discussed by Levy (1931). He was impressed by (1) the relative youth of his 8 cases (all of whom were under 50 years) and (2) the rapid rate of recovery, both subjective and objective. The atypical case may present in a variety of ways - (1) mild indigestion; (2) peripheral site of pain - wrist, jaw etc., with no chest pain (Bramwell 1930); (3) chest pain in an unusual site - in the back between the shoulderblades, beneath the clavicles, in the axilla, etc.; (4) the pain may be entirely abdominal in situation, and may simulate that produced by an acute abdominal emergency (Levine and Tranter 1918, Mohler 1933, Hay 1933, Connell 1939); or (5) there may be no pain and some other symptom such as dyspnoea, weakness, /

weakness, fainting or palpitation takes its place (Hay 1933, Cookson 1942). Post-operatively pain may not be a prominent feature (Master et al. 1938). Bedford and Parkinson (1928a) state that when infarction supervenes in a case with pre-existing signs and symptoms of heart disease, the clinical picture may be less distinctive. Pain is not a prominent symptom; it is either absent, or quite overshadowed by dyspnoea. A sudden exacerbation of the signs of failure may be the only evidence of infarction. Many painless infarcts have been reported. (Stroud and Wagner 1941, Davis 1932, a & b, Babey 1939, Kennedy 1937). Bean (1938a) found sudden dyspnoea or rapidly developing left ventricular failure; sudden weakness; syncope; sudden onset of palpitation; as the substitution symptoms for pain. These were present in 28% of his 300 cases. Chamberlain (1946) reported no pain in 21% of his 100 cases. Hay's figure was higher - 38% (1933). Gorham and Martin (1938) in a study of the clinical history of 100 necropsy cases of myocardial infarction reported that 42 had experienced no pain. These patients were mainly among the older age groups, and fewer were hypertensive or had suffered previous effort pain, than in the group experiencing pain at the time of infarction. In their series there were 29 cases of old healed infarcts and it is in this group that a history of pain is most commonly absent. Twelve of the painless cases /

cases were in a group of 17 showing fibrotic narrowing of the coronary arteries without actual thrombosis, and old infarction without pericarditis. Acute infarcts causing death tend to be accompanied by pain. Kennedy (1937) considered that the frequency of painless infarcts had been overstressed. In a study of 152 cases, he reported that in 91% of recent, and in 64% of old infarcts, there was classical coronary pain.

The acute stage of the myocardial infarction may be completely overlooked, and a diagnosis be made in retrospect when a complication, particularly an embolic episode or sudden death from rupture of the infarct occurs (Jetter and White 1944, Friedman and White 1944). The former has been stressed by Levine and Brown (1928) and others (Hay 1933 and Dozzi 1939).

(d) Course and Complications:

The clinical course pursued varies widely. In 1912, Herrick divided his cases into four groups. (1) Cases in which death is sudden, seemingly instantaneous; (2) Cases in which the attack is anginal, the pain severe, the shock profound, and death follows in a few minutes or several hours at the most; (3) Non-fatal cases with mild symptoms, difficult and almost impossible to recognize; (4) Cases /

Cases in which the symptoms are severe and distinctive enough to be recognized, in which the accident is usually fatal, but not immediately and not necessarily so.

Levy and Bruenn (1936) considered that (1) in 12% of the fatal cases of coronary sclerosis, death occurred suddenly; also (2) 91% of cases of sudden death from natural causes, resulted from disease of the cardio-vascular system; and (3) of the deaths from sudden heart failure, 65% were due to disorder of the coronary arteries.

Cases which survive the critical first few days may have an entirely uneventful convalescence or this may be marred by a number of complications, particularly heart failure, arrhythmias, or an embolic or thrombotic episode or episodes. Death may occur at any time, and from a variety of causes.

Master and his associates (1937a) found evidence of heart failure in 93 out of 140 consecutive cases (66.4%). Rosenbaum and Levine (1941a) considered that 75% of their 208 cases showed some objective evidence of failure. Katz and Mintz (1947) reported a lesser incidence - 121 cases out of 572 (21.1%). In many cases, the failure progresses steadily in spite of treatment, and death is inevitable. On the other hand, improvement may occur and the patient survive, usually for a few months, but in some instances /

instances for a number of years. Master (1937a) considers that heart failure is least common after first infarcts, but that the incidence increases with each successive infarct.

	Heart failure	Mortality
1st infarcts	53%	11%
3rd infarct	88%	50%

Embolie and thrombotic episodes have been reported by all authors. These may adversely influence prognosis, greatly handicapping a recovering patient, or, they may prove fatal. Such episodes comprise (1) the sudden occlusion of a systemic artery, in the brain, kidney, spleen, mesentery, or extremities; (2) development of a fresh coronary thrombosis; (3) pulmonary infarction and (4) peripheral phlebothrombosis, notably in the calf veins. Hellerstein and Martin (1947) have recently reviewed the literature and reported their own series of 160 autopsy cases of myocardial infarction. Analysing the autopsy reports of 8 authors comprising 924 cases - Table VI. - they found endocardial mural thrombus in 44% of cases.

TABLE VI. /

TABLE VI. Incidence of mural thrombi found at autopsy in cases of myocardial infarction.

Authors.	Number of Autopsies	Cases with Mural Thrombi
Wolff & White (1926)	23	7
Parkinson & Bedford (1928)	83	14
Levine & Brown (1928)	46	38
Lisa & Ring (1932)	100	34
Meakins & Eakin (1932)	62	29
Appelbaum & Nicholson (1935)	150	81
Bean (1938)	300	142
Hellerstein & Martin (1947)	160	65
	---	---
	Total 924	410 = 44%
	===	===

However sudden arterial occlusion is not necessarily embolic in nature. In their own series, Hellerstein and Martin found 54 such episodes in 65 cases with mural thrombus and 57 episodes in 95 cases without mural thrombus. The 111 thrombo-embolic episodes occurred in 73 cases i.e. 45.6% of the series. This figure indicates that the clinical recognition of such episodes in no way parallels their incidence. Analysing the clinical reports of eleven authors - Table VII. - they found peripheral emboli or infarcts in only 11.5% of 1,605 cases.

TABLE VII. /

TABLE VII. Incidence of thrombo-embolic complications in clinical series of myocardial infarction.

Authors.	No. of cases.	Number with Peripheral Emboli or Infarcts.
Gordinier (1924)	13	3.
Anderson (1928)	9	1.
Parkinson & Bedford(1928)	100	8.
Levine (1929)	145	17.
Conner & Holt (1930)	287	42.
Hyman & Parsonnet (1932)	51	17.
Howard (1934)	165	17.
Blumer (1937)	175	27.
Master et al. (1939b)	500	29.
Nay & Barnes (1945)	100	14.
Peters et al. (1946)	$\frac{60}{1605}$	$\frac{10}{185} = 11.5\%$
Total	<u>1605</u>	<u>185</u>

Foot note to table: From the series of Nay and Barnes 14 patients are included as having embolic phenomena. All thrombotic lesions have been excluded, three apparently on autopsy findings - two cerebral and one femoral. Clinically it is probable that these episodes were considered embolic, making the number of patients affected 17.

Autopsy Analysis of the distribution of the peripheral arterial occlusions shows that the kidneys, spleen, brain, extremities and mesentery are involved in that order of frequency. Table VIII. records the findings of 8 authors (page 31.)

TABLE VIII. /

TABLE VIII. Incidence of systemic arterial occlusions found at autopsy in cases of myocardial infarction	Authors.	Number of		Site of Occlusion.					Mesenteric	
		Autopsies	Arterial Occlusions	Brain	Kidney	Spleen	Extremities	Carotid or Aorta		
	Wolf & White (1926)	19	11	2	6	2	0	0	0	1
	Parkinson & Bedford(1928)	83	24	1	9	8	2	1	1	3
	Meakins & Eakin (1932)	62	40	4	14	9	11	2	2	0
	Bean (1938)	300	73	15	29	17	8	1	1	3
	Wood & Barnes (1941)	60	10	9	0	0	1	0	0	0
	Garvin (1942)	133	83	18	32	19	11	0	0	3
	Nay & Barnes (1945)	11	9	4	2	0	3	0	0	0
	Hellerstein & Martin(1947)	160	78	14	28	17	13	0	0	6
	Totals	828	328	67	120	72	49	4	4	16

Involvement of the brain, mesentery, and limbs were the most serious.

Turning aside from peripheral arterial occlusion, pulmonary infarction and a recurrence of coronary thrombosis are more common and are potentially more serious. Pulmonary infarction may arise in three ways: (1) embolism from mural thrombus in the right ventricle or right auricle; (2) embolism from a peripheral vein, and (3) a local thrombosis.

Analysing 10 series comprising 1,146 autopsied cases, Hellerstein and Martin record an incidence of pulmonary infarction of 23.5%. Massive pulmonary infarction causes or contributes to death more commonly than do peripheral arterial episodes. Nay and Barnes (1945) in a detailed clinical study of 100 cases report 15 cases of recurrence of myocardial infarction. This was more common in those previously normotensive than in those previously hypertensive. Wright (1948) in his control series of 368 cases records extension of the original thrombosis in 9% and a fresh thrombosis in 6.5%. Peripheral phlebothrombosis occurs in about 6% of cases (Hellerstein and Martin 1947).

The advent of anti-coagulant therapy has stimulated search for all forms of thrombo-embolic complications and the incidence reported in recent control series is higher than in earlier reports.

TABLE IX. Incidence of thrombo-embolic complications after myocardial infarction: recent clinical series.

Author.	No. of cases.	Number with Thrombo-embolic Episodes.	% Incidence.
Nay & Barnes (1945)	100	37.	
Peters et al. (1946)	60	10.	
Glueck et al. (1948)	44	27.	
Greisman & Marcus (1948)	100	21.	
Wright et al. (1948)	<u>368</u>	<u>92</u>	
	Total <u>672</u> ===	<u>187</u> ===	27.8%.

All such episodes are most common in the first few weeks after myocardial infarction. Nay and Barnes report that 87% occur between the 4th and 20th days. Phlebothrombosis is most common between the 10th and 16th days.

The effect of digitalis therapy in increasing the number of embolic complications has been stressed by Askey and Neurath (1945a).

Arrhythmias occur mainly during the first few days and are transient. They are more common in severely ill patients who have previous cardiac damage resulting from hypertension or previous myocardial infarction. They are more prone to develop in women and their frequency increases with age (Katz and /

and Mintz 1947, Master et al. 1937-38). Persistence of arrhythmia may be followed by heart failure. Master reports 46 instances of arrhythmia, excluding extra-systoles, occurring in 42 out of 300 patients - an incidence of 14%. In an analysis of 800 reported cases he finds an incidence of 17%. Table X. gives details of a few series.

TABLE X. Incidence of arrhythmias following myocardial infarction.

	Number of Cases showing Arrhythmia.	Total Cases.	% Incidence of Arrhythmia.
Levine & Brown(1928)	51	145	35
Parkinson & Bedford (1928a)	14	100	14
Master (1937-38)	42	300	14
Katz & Mintz (1947)	94	572	16.4

Master (1937a) considers that the arrhythmias may arise in three ways -

(1) reflexly from the functional derangement attendant on the acute injury to the heart, or directly from an irritable focus in the damaged area.

(2) in coronary thrombosis a strain is placed on the auricles which may account for the initiation of auricular flutter or fibrillation. In addition, the right coronary artery may be thrombosed and the blood supply to the right auricle interfered with.

(3) /

(3) the conducting system may be the site of injury, particularly in thrombosis of the right coronary artery which, in 62% of cases, supplies the sino-auricular node, and in 92% supplies the auriculo-ventricular node, and the posterior part of the inter-ventricular septum. These percentages are obtained from Gross (1921).

Any type of arrhythmia may occur and more than one type may occur at differing times in the one patient. Auricular fibrillation is the most common, occurring in 33 of the 51 cases recorded by Levine and Brown (1928), and in 22 of the 46 cases recorded by Master (1937-38). Askey and Neurath (1945^a) report on 84 cases of auricular fibrillation - 29 transient and 55 persistent - occurring in 1247 cases of coronary thrombosis. In 40 of the 55 cases of persistent fibrillation the arrhythmia coincided with the onset of the myocardial infarct whereas in 27 of the 29 transient cases the arrhythmia developed some time after the onset. Evidence of preceding cardio-vascular disease favoured persistence of the arrhythmia. Prognosis was definitely worsened by persistence of the fibrillation, the mortality being 89.4% in the persistent cases and 58.6% in the transient cases. Embolic phenomena were also more common in the group with the persistent fibrillation, than in the transient group; and in both groups than in the cases with normal rhythm. Administration of digitalis favoured persistence /

persistence of the arrhythmia whereas quinidine alone favoured its disappearance.

Heart block - either partial or complete - is probably the next most common arrhythmia. Nine cases occurred in Master's series (1937-38). Salcedo-Salgar and White (1935) found heart block in 13.1% of 328 cases of coronary thrombosis - 3.6% auriculo-ventricular block, 8.9% inter-ventricular block, and 0.6% both forms combined - but the cases were not studied during the acute stage. Kerr (1937) reviews the literature and gives an overall incidence of auriculo-ventricular block, partial and complete, as 7.4% in 1436 published cases of coronary thrombosis. He states that although the prognosis in coronary thrombosis in general is adversely affected by the complication of heart block, clinical recovery and disappearance of the block is by no means unknown. Conner and Holt (1930) consider that patients with evidence of arborisation and bundle branch block do poorly. Stokes-Adams attacks are rarely encountered.

The combined incidence of the various tachycardias is only slightly less than that of heart block. Ventricular tachycardia is probably the most common type. Levine and Brown (1928) encountered 6 cases. They discuss the clinical diagnosis and treatment in some detail. Katz and Mintz (1947) report ventricular tachycardia in 5.3% of their arrhythmias, but Master /

Master (1937-38) found it only once in 46 arrhythmias. In his series, auricular tachycardia, and auricular flutter were more common, each occurring thrice. Table XI. (page 38) illustrates the incidence of the commoner arrhythmias in a number of series.

Sudden death may occur at any time during the early weeks after myocardial infarction. This may be due to -

(1) sudden arrhythmia, probably ventricular fibrillation or a Stokes-Adams attack. (2) recurrence of myocardial infarction; (3) a major embolic episode or (4) rupture of the infarcted area. This last event is recorded in most series, and has been reported in detail by White (Jetter and White 1944, Friedman and White 1944). He records an incidence of 3.7% in all infarcts, and states that rupture rarely occurs after the end of the second week. It is more common in the elderly patient. He also draws attention to the possible influence of exertion in causing rupture of the infarct. In an analysis of the cause of death in 115 consecutive cases of sudden deaths in inmates of a mental institution, he found 22 cases of recent myocardial infarction. Of these 22, 16 showed cardiac rupture at the site of the infarct. Myocardial infarction had not been recognized during life and in only 2 cases had there been a brief spell of bed rest prior to death.

Rarely /

TABLE XI. Incidence of the common types of arrhythmia following myocardial infarction.

	Auricular Fibrillation.	Auricular Flutter.	Supra-ventricular Tachycardia.	Ventricular Tachycardia.	Nodal Rhythm	Partial Heart Block (Dropped Beats)	Complete A.V. Block.	Total cases of Arrhythmia
Levine & Brown	33	1		6	-	9	2	51
Master (1937-38)	22	3	5	1	3	3	3	44
Katz & Mintz (1947)	47	4	3	5	7	11	5	94
Parkinson & Bedford (1928)	7	4	2	1	-	1	1	14
Rosenbaum & Levine (1941)	25	5	-	6	4	7*	5	-

* Including the 5 cases who had at one stage complete heart block.

Rarely perforation of an infarcted inter-ventricular septum occurs (Wood 1944). This is commonly followed by the development of congestive heart failure and early death, but one case is recorded that survived 4 years 10 months (Wood and Livezey 1942).

A rare complication which may occur is cardiac aneurysm formation. This is seldom recognized during the immediate convalescent period. It is more common after anterior infarcts than after posterior infarcts. Parkinson and his associates (Parkinson, Bedford and Thomson 1938) discuss the aetiology and clinical features in some detail. Such a complication is not necessarily associated with early death, and instances of long survival have been recorded (Codounis 1948).

Troublesome shoulder pain is frequently experienced - sometimes soon after the infarct, but more often during the first few months after discharge. (Edeiken and Wolferth 1934, Spillane and White 1940, Ernstene and Kinell 1940, Shott 1947). As a rule it is unilateral and felt on the side to which the coronary ischaemic pain radiated, or still radiates. There is considerable limitation of movement, particularly abduction, and external rotation. Associated with the shoulder pain, there may be pain, stiffness and tingling in the fingers and hand. (Askey 1941). The hand . /

hand and fingers may be swollen and the long flexor tendons of the finger may contract. The pain is very intractible and is not greatly influenced by analgesics, heat or massage. It is considered to be akin to causalgia.

(e) Mortality :

Reports of immediate mortality (i.e. within the first 6 weeks of onset) vary widely, from the 53% of Levine and Brown (1928) to the 16.2% of Conner and Holt (1930). These latter authors were only considering first attacks in which the prognosis is better than after subsequent attacks. Table XII. records some of the series.

TABLE XII. Immediate mortality rate after myocardial infarction.

Author.	No. of Cases	Mortality Rate.
Levine & Brown (1928)	145	53 %
Conner & Holt (1930)	284	16.2%
Master et al. (1936)	267	16.5%
" (1937a)	140	21 %
*Bland and White (1941)	200	19 %
Levine & Rosenbaum(1941)	208	33 %
Wood and Barnes (1941)	128	46.9%
Newman (1946)	50	78 %.
Katz & Mintz (1947)	572	21.8%
*Yater et al. (1948)	866	50.1%
Wright et al. (1948)	368	24 %

* In these series the mortality rate is calculated over the /

the first 4 weeks as opposed to the first 6 weeks in the remainder.

In the two series reporting myocardial infarction in young adults - those of Newman and Yater the great majority of deaths occurred within 24 hours of the onset. Thirty-three of Newman's 39 fatal cases were found dead or died almost immediately after a collapse. Three hundred and seventy-five of Yater's 434 deaths took place in the first 24 hours.

Death occurs most commonly in the first day, being either sudden or rapid in onset; or in the first few days when there is commonly a persistent severe degree of peripheral circulatory failure. Master (1935) states that if the first day is survived, then recovery is likely. In the subsequent weeks, death may be due to heart failure - either left ventricular failure or congestive heart failure; to the recurrence of the infarct, or some other major thrombo-embolic complication; to the occurrence of an arrhythmia, or to rupture of the infarct.

In a study of 140 consecutive cases, Master (1937a) reported a mortality rate of 30% in cases showing evidence of heart failure, and a rate of only 4% in cases showing no evidence of failure.

The major factors influencing the mortality rates are (1) Age of the patient; (2) Number of previous infarcts; (3) State of the patient at the time of the infarct. All have a bearing on the adequacy of the circulation /

circulation to the remaining myocardium, and on the efficiency of that myocardium. The high mortality rate in young adults is probably associated with the lack of an adequately developed system of inter-coronary anastomoses.

(f) Prognosis :

Prognosis is discussed by Levine and Rosenbaum (1941 a & b), Wood and Barnes (1942), Master et al. (1935 and 1937a), Bedford (1935), Conner and Holt (1930), Cowan, (1936), and many others. They are in general agreement. In a consideration of the immediate prognosis, Levine and Rosenbaum consider that a number of factors are associated with a poor outlook -

- (1) Severe and persistent pain;
- (2) Severe degree of shock;
- (3) Marked drop in Blood Pressure particularly to below 100 mm. Hg.;
- (4) Pulse pressure of 20 mm. Hg. or under;
- (5) Pulse rate of 100/min. or over;
- (6) Orthopnoea;
- (7) Cyanosis;
- (8) Detection of gallop rhythm or tic-tac rhythm;
- (9) Marked leucocytosis;
- (10) Fever of over 100°F. particularly if maintained for 4-5 days;
- (11) Development of evidence of heart failure;
- (12) Cardiac enlargement.

Development of arrhythmias, and the occurrence of thrombo-embolic complications add to the gravity of the condition. They conclude by stating that the immediate outlook is extremely difficult to predict.

There is practically no criterion that is infallible, but /

but weighing all the information available, together with the general appearance of the patient enables the physician to make a fair estimate.

The ultimate prognosis and life expectancy of the patient has been discussed by Hay (1934), Cooksey (1935), Willius (1936), Cowan (1936), Palmer (1937), Bland and White (1941), Levine and Rosenbaum (1941^b) and others.

Bland and White have followed 200 cases of coronary thrombosis during 10 years or more. Of the 162 who survived the initial attack, 50 were still alive at the end of 10 years, and the longest period of survival was 25 years. 112 died during the first 10 years, 30 in the first year, and 34 in the next 3 years. Consideration of the individual cases show that -

(1) 34% of the survivors made a complete recovery and of these 56% survived 10 years.

(2) 39% developed effort pain and of these only 30% survived 10 years.

(3) 27% developed exertional dyspnoea and all died within 10 years.

The majority of deaths were associated with coronary insufficiency or congestive heart failure. The three factors influencing the outcome were -

- (1) Sex - few women survived 10 years.
- (2) Age at onset - the younger patients had a better prognosis. Those surviving 10 years had an average age at the onset, of 51 years, and those not surviving /

surviving 10 years, 57 years.

(3) Hypertension - over the years it adds a burden on the heart, and few hypertensives survived 10 years.

Willius (1936^a), in a consideration of 370 cases, concluded that the cardiac death rate increased progressively with each recurrent occlusion. Conner and Holt (1930) have shown that liability to a second attack diminishes with time; 50% of all second attacks develop within 12 months of the first. Smith's figures (1942) show an even higher percentage of recurrences within the first year. Over a 3 year follow up 80% of recurrences of infarction took place in the first year.

Cooksey (1935) reports on 53 private cases with 32 survivors, 25 of whom have been restored to their previous occupations. He considers that a period of many weeks convalescence, with appropriate restriction for a full year following the acute episode, is of great importance in management.

Cowan (1936) states the case very aptly - "Prolongation of life for 2 years or more seems to indicate that the original lesion has healed and that danger lies in the underlying pathological state rather than in the past infarct; in the possibility of the recurrence of a fresh lesion rather than from progressive changes in the ancient one." Prognosis is improved if : (1) The patients are in the younger /

younger age groups; (2) the initial attack has been moderate in its severity; (3) the B.P. is not unduly high; (4) the heart is not appreciably enlarged; (5) the electrocardiogram is normal in character; (6) adequate care has been taken at the time of the acute attack; (7) the patient reacts favourably to his disability and is willing to cooperate.

Hay (1934) considers that two facts stand out in assessing prognosis and progress - (1) the frequency with which life is ended suddenly; (2) the ominous significance of a progressive tendency to dyspnoea and congestive heart failure.

A number of cases of long survival have been reported. White (1933 and 1937) records survival for $17\frac{1}{2}$ and $24\frac{1}{2}$ years, but the record is that of a man who survived for just under 40 years after his infarct, and was working to within 3 years of his death (Drake 1940).

(g) Treatment:

Treatment is relatively stereotyped and is adequately summarised by Hay (1935) - (1) Morphine, repeated as desired; (2) rest in bed for a month or more, the bed rest being complete during the first few weeks; (3) treatment of shock with heat both externally and internally, the head low position, /

position, and caffeine intravenously or 5 minims of adrenaline intra-muscularly; (4) treatment of abdominal distension by restriction of diet, enemata, and laxatives; (5) oxygen if there is cyanosis; (6) sedation, both during the day and at night; (7) morphine if nocturnal dyspnoea ensues and (8) treatment of the complications - persistent auricular fibrillation - digitalis; ventricular tachycardia - quinidine; heart block - ephedrine $\frac{1}{2}$ gr. orally or adrenaline 5 minims intra-muscularly. Levine and Brown (1928) state that "the treatment of coronary thrombosis is mostly concerned with the care of the complications which arise." They considered that if evidence of congestive heart failure developed, particularly in the presence of auricular fibrillation, digitalis should be given; apart from that digitalis is best avoided, as it is more likely to do harm than good. Fishberg (1934) considers that digitalis is contra-indicated as - (1) it increases the excitability of the heart muscles, predisposing to ventricular tachycardia or fibrillation; (2) it increases the force of contractions of the muscle, predisposing to rupture of the infarct; (3) it increases the liability to embolization; (4) it causes coronary artery vaso-constriction.

Askey and Neurath (1945^a) investigated 84 cases of auricular fibrillation occurring in coronary thrombosis. Forty-four were treated with digitalis alone, /

alone, and a further twelve with quinidine and digitalis. Eleven had quinidine alone. They found that exhibition of digitalis caused no increased liability to sudden death from ventricular fibrillation or cardiac rupture, but that there was a definite increase in the number of systemic emboli.

Forty-eight of the cases were in congestive heart failure - 32 received digitalis alone and 31 died, 13 from clinically recognised fatal embolism. Of the 16 other cases, 11 died and none had a fatal embolus. The authors concluded that digitalis administered alone for congestive heart failure with auricular fibrillation and myocardial infarction would seem contra-indicated.

De Takats (1944) has demonstrated another action of digitalis of possible importance in these cases - the production of an increased clotting tendency in the blood. This was confirmed by Massie (1944) but Sokoloff and Ferrer (1945) could find no effect of digitalis on the clotting time of whole blood. Recently Flinn (1948) has shown that there is no change in the Lee-White coagulation time or in the prothrombin time of whole or diluted plasma, in digitalized patients. However, digitalization had a definite effect in diminishing the anti-coagulant effect of heparin in human beings.

Prophylactic use of quinidine to prevent ventricular fibrillation has been suggested, but is not generally /

generally used as a routine measure. (Wood and Barnes 1941, Levine 1947).

The importance of oxygen was stressed by Baroch and Levy (1934) who considered that at times it might be life-saving. Others have used it with success. (Kilgore 1933, Hick 1934).

The first major innovation in treatment was that of Master (1935), when he introduced the low calorie diet. While confined to bed, patients were given a diet containing approximately 800 calories daily, and had a daily fluid intake of 1000-1200 c.c.. The diet was well balanced, and contained 80 Gms. of carbohydrate, 50 Gms. of protein, and 30 Gms. of fat. While the diet is being taken, the B.M.R. is reduced to -20% to -35%; there is some drop in body weight; the pulse rate and B.P. are reduced, and with these the work of the heart is reduced. Clinically it was observed that the patients lost their pain more quickly and there was less tendency to gastro-intestinal complaints. In 1935, 85 attacks occurring in 75 patients and, treated with this diet, were reported. The mortality rate was 9.5% for all attacks, and only 2% for first attacks. Such a restricted diet is not, however, universally used and is replaced by a light diet.

Narcosis during the first few days has been suggested /

suggested (Buchbinder 1944), particularly if the pain is very severe and the patient restless. Treatment is carried out with the patient in an oxygen tent. Hourly inhalations of carbon dioxide are given, and morphine 1/6th gr. and atropine 1/150 grs. are given subcutaneously, 4 hourly. Barbiturates are given intravenously as required. Three thousand c.c. of fluid are given daily either orally or subcutaneously, and calories totalling 1600 in 3 days are supplied by milk and eggs. This method of treatment results in a great reduction of metabolic activity by (1) relaxation of body musculature; (2) almost total deprivation of food, and (3) abolition of pain and apprehension.

Undoubtedly the most important advance in treatment has been the introduction of anti-coagulants. This form of treatment was suggested by Best in 1938. One year later, in conjunction with Solandt, he provided experimental evidence that myocardial infarction with thrombus formation in the coronary tree, and endocardial mural thrombus formation, could be prevented by the administration of heparin. Cost and difficulty of administration prevented its introduction into clinical use, and it was only when dicoumarol became available that the great theoretical possibilities of anti-coagulant therapy became a practical proposition.

The first reports of dicoumarol therapy appeared in 1945 and 46 (Wright 1945 and 46 a & b, Peters, Guyther, and Brambel 1946, Nichol and Page 1946). It was used during the first 4-6 weeks with the object of abolishing thrombo-embolic complications. Peters (1946) reported that in 50 treated cases, 2 died, and one instance of clinical embolism occurred; compared with a 20% mortality and 16% incidence of embolism in their 60 control cases. Wright(1946b) concluded that the thrombosing and embolic tendencies appeared to have been interrupted by dicoumarol. Such reports were very encouraging and dicoumarol therapy became adopted as a routine method of treatment in most centres. In 1946 a committee was set up in America to assess the value of anti-coagulant treatment in coronary thrombosis. Sixteen centres participated, all adopting the same routine of treatment. To provide an adequate control, only cases admitted on odd days received anti-coagulant therapy. The first 800 cases have been recently reported (Wright, Marple and Beck 1948). The control series (368 cases) and the treated series (432 cases) were roughly comparable. Of the treated series 81% received dicoumarol alone and 14% heparin plus dicoumarol 5% received no anti-coagulants. The death rates for the two series were :-

control series	24%
treated series	15%

The greatest improvement in the treated series was in the number who suffered one or more major thrombo-embolic complication before death - such deaths occurred in 10% of the control series and in 3% of the treated series. The greatest reduction in mortality was in the cases over 60 years. Under 50 years, the mortality rate was not appreciably altered, but the number of thrombo-embolic complications were greatly reduced. The actual incidence of these complications was -

control series 25%

treated series 11% of which 3.5%

occurred before treatment and 1.5% during the first 3 days of treatment, i.e. only 6% occurred while treatment was theoretically adequate.

The authors conclude that anti-coagulants should be used in all cases of coronary thrombosis unless a definite contra-indication exists. Treatment should be continued for 4 weeks or for at least 4 weeks after the last thrombo-embolic episode, and should be begun as late as the 2nd or 3rd week after the onset of the infarct. Tables XIII. and XIV. summarise the results of reported series. (pages 52. & 53).

TABLE /



TABLE XIII. Deaths in cases of myocardial infarction treated with anti-coagulants and in control cases.

Author	Anti-coag. Number Treated.	Cases. Deaths.	Control Number Treated.	Cases. Deaths.
Wright (1946)	76	15	-	-
Nichol (1947)	68	11	-	-
*Peters (1946)	50	2	60	13
Parker & Barker (1947)	50	5	-	-
*Greishman & Marcus (1948)	75	7	100	35
Glueck (1948)	44	9	44	20
Reich & Eisenmen- ger (1948)	24	4	-	-
*McCall (1948)	71	9	-	-
Wright (1948)	<u>432</u>	<u>65</u>	<u>368</u>	<u>88</u>
Total	890	127	572	156

Mortality Rate = 14.3%

= 27.3%

*Cases dying within 48 hours of admission are not included.

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TABLE XIV. /

TABLE XIV. Incidence of thrombo-embolic complications occurring in cases of myocardial infarction treated with anti-coagulants and in control cases.

Author	Anti-Coagulant Cases.		Control Cases.	
	Number Treated.	Number with Thrombo-Em-bolic Epi-sodes.	Number	Number with Thrombo-Em-bolic Epi-sodes.
Nichol (1947)	68	2	-	-
Peters (1946)	50	1	60	10
Parker & Barker(1947)	50	4	-	-
Greisman & Marcus(1948)	75	3	100	21
Glueck (1948)	44	3	44	12
McCall (1948)	71	2	-	-
Wright (1948)	<u>432</u>	<u>48*</u>	<u>368</u>	<u>92</u>
Total	790	63	572	135
Incidence		= 8%		= 23.6%

*22 of these complications occurred in patients not under the influence of anti-coagulants.

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Dicoumarol has also been used prophylactically to prevent a recurrence of coronary thrombosis. Cotlove and Vorzimer (1946) stated that dicoumarol was probably of no value in preventing or minimising coronary thrombosis, but this is not the general opinion. Nichol and Fassett (1947) have treated 5 cases of recurrent coronary thrombosis for 6 to 32 months. Four are alive and well, but one died of a recurrence at 21 months while lax with his treatment. Peters (1946) also considered prophylactic use of dicoumarol.

The possibility that dicoumarol might have a deleterious effect on the rate of healing of myocardial infarcts was investigated by Blumgart (1948) and Levy (1948). Using dogs, in whom experimental myocardial infarction was produced, Blumgart was able to show that dicoumarol did not influence the healing process.

Quite apart from the obvious clinical usefulness of anti-coagulants, their administration rests upon a sound experimental basis. Meyers and Poindexter (1946) have shown that after the acute phase of coronary occlusion there is a definite trend towards shortening of the prothrombin time of a 12½% dilution of plasma in saline, which continues for several weeks during the period of infarction. Ogura and his associates (1946) using the Waugh, Ruddick (1944) heparin retarded clotting test, have shown /

shown a marked clotting tendency developing about the 3rd day, reaching a maximum about the 12th day, and returning to normal on the average about the 17th day after the coronary thrombosis. There was some individual variation as to the speed of onset of this change and also as to its duration. The clotting tendency was appreciably more marked than that shown by (1) non-cardiac patients confined to bed, and (2) other cardiac cases confined to bed. This period of enhanced clotting coincides with the period shown by Nay and Barnes (1945) to be most important for the occurrence of thrombo-embolic episodes. Recently a marked increase in plasma fibrinogen (Meyers 1948) and also of serum muco-protein (Simkin, Bergman and Prinzmetal (1949) has been shown to occur after myocardial infarction.

It is strange that a method of treatment directed at maintaining the prothrombin content of the blood at 100% should be reported and considered helpful. Doles (1947) observed that following coronary occlusion the prothrombin content of the blood rapidly fell to 70% of normal or lower. By restoring the prothrombin content to normal with large doses of Vitamin K, and then maintaining it at a normal level he obtained very satisfactory results - relief of pain, restoration of the B.P. to its original level, and absence of recurrence of infarction. In recent years /

years he has had no need for digitalis or quinidine. A few cases showed a hypo-prothrombinaemia which could not be corrected by Vitamin K, and in these cases, recurrence of infarction and congestive heart failure were liable to occur. Out of 55 adequately treated cases, he had 2 deaths - a mortality rate of 3.6%. Embolic phenomena are not mentioned. The prothrombin estimations were done by the bedside method of Smith et al. (1940). The changes observed in the prothrombin content have not been confirmed by other observers. In view of this, and of the proved effectiveness of reduction of prothrombin by dicoumarol, the claims by Doles must await further investigation.

The most recent advance has been the treatment of shock by transfusion. Originally specific anti-shock therapy was discouraged (Gilbert 1944, Falk 1942). Hay (1935) considered that heat, both external and internal, the head low position, and the judicious use of adrenaline were the only measures that should be adopted. It is well recognized that shock is common (Master, Dock, and Jaffe 1937^a), and that it may of itself cause death. A systolic B.P. of 80 mm. Hg. or less is of grave significance, (Master et al. 1943), recovery being uncommon. Wiggers (1947) has shown that if hypotension induced experimentally in dogs by bleeding, persists for 135 minutes, /

minutes death results even though the blood volume be restored by transfusion. There is myocardial depression with progressive insufficiency of the heart.

Prinzmetal and his associates (Corday, Bergman, Schwartz, Spritzler and Prinzmetal 1949) have investigated experimentally the effect of shock on a myocardial infarct due to coronary artery occlusion. Normally the ischaemic area is supplied from collateral vessels. If shock is present - (1) the concentration of blood in the ischaemic area is markedly reduced, both in the endocardial and pericardial surface; (2) the quantity of blood in the normal myocardium is also markedly diminished, lowering the progressive gradient in the collateral vessels; (3) the ischaemic area becomes cyanosed and balloons during systole. Electrocardiographic changes could be recorded, demonstrating the ischaemia.

Treatment recommended is - (1) transfusion of whole blood, plasma or glucose saline; (2) pressor agents - adrenaline 3-4 minims every 15 minutes, caffeine, or coramine. Treatment should be instituted as soon as possible as the longer the hypotension exists, the more coronary insufficiency and myocardial damage will result. In many patients severely shocked after coronary occlusion, the organic damage to the heart is such that death is inevitable regardless of treatment; likewise others with mild shock will recover /

recover without specific treatment. Between these two extremes are the cases where treatment of shock is life-saving. The danger of treatment lies in that heart failure may be precipitated, but this is less likely to occur, the earlier treatment is instituted.

Schwartz (1947) records one case in profound shock, treated by transfusion with recovery and no evidence of failure. Levine (1947) also records one case. Katz (1947) recommends this type of shock treatment.

(h) Pathology:

Pathologically it has been repeatedly demonstrated that apart from embolism of a coronary artery or the rare involvement of a coronary artery by periarteritis nodosa, or thrombo-angiitis obliterans, myocardial infarction only occurs in the presence of marked coronary arteriosclerosis. Horn and Finkelstein (1940) state "Arteriosclerosis was observed in every instance in which a partial or complete arterial occlusion was found. In not a single instance had a thrombus developed in a normal artery. Judging from the morphological analysis, coronary artery occlusion is an incident in arteriosclerosis". The rate of development of the arteriosclerotic process is the fundamental factor determining when a clinical coronary thrombosis will occur. Coronary artery disease without tibial, cerebral or aortic lesions - an exceptional/

exceptional finding after the 6th decade - is the rule in men under 40 years (French and Dock, 1944). Gross (1934) has demonstrated the remarkable thickness of the coronary intima compared with that of the radial, tibial, cerebral or visceral arteries, even in infants. He has also emphasised the increase in thickness with age, and the variability in depth of the intimal layer, from place to place in the same artery, and in different persons of the same age. Dock (1946) considered that the familial and sex differences in tendency to coronary disease might be related to inborn variations in the thickness of the coronary intima. He studied twelve infants of each sex, dying within 24 hours of birth, taking sections of the right coronary artery, and of the circumflex and anterior descending branches of the left coronary artery, and was able to demonstrate a definite sex difference in thickness of the intima. Sixty-one per cent. of the females, but only 32 per cent. of the males, had no trace of intimal thickening. Among the males, the intima was on the average 26,5 per cent. the thickness of the media, whereas the average figure for the females was only 8.2 per cent.. Males therefore begin life with three times as much coronary intima as females. Dock also stated that, from a study of a small number of cases, this sex difference is no less at maturity than at birth. He considers that the anatomy of the coronary artery plays a decisive part in preparing the way for arteriosclerosis, and /

and accounts for the difference in the incidence of myocardial infarction among the sexes. The females born with a thick coronary intima are the potential victims of coronary thrombosis. This work awaits confirmation.

As previously stated, Paterson (1936) was the first to demonstrate how intimal haemorrhage in an arteriosclerotic plaque could initiate thrombus formation in the lumen. This has been confirmed by Wartman (1938) Winternitz et al. (1938), Horn and Finkelstein (1940) and Nelson (1941). Wartman also showed that intimal haemorrhage could cause haematoma formation in the plaque and block the lumen without secondary thrombosis.

Saphir (1935) and later Blumgart (1940) and his associates have shown that before uncomplicated angina pectoris or myocardial infarction occurs, at least one major coronary vessel has been occluded. Using the injection and dissection technique of outlining the coronary arteries described by Schlesinger (1938) and with roentgenograms of the unrolled injected heart, Blumgart studied the coronary circulation in 125 consecutive autopsy cases. Thirty cases had shown definite clinical evidence of angina pectoris, congestive heart failure, or myocardial infarction. His investigations permitted the following conclusions:

(1) functional inter-coronary anastomotic channels develop only when and where required. Their development /

development is not related to age; (2) such anastomotic circulation may so well compensate for occlusion, or marked narrowing of a major coronary artery that the blood supply to the heart remains adequate for the ordinary activities of life. Coronary occlusion per se may be quite symptomless; (3) in twelve cases of uncomplicated angina pectoris 25 occlusions of main coronary arteries were found. In 3 cases, all three main coronary arteries had been occluded, and in only 2 cases was only one main artery occluded; (4) in angina pectoris complicated by antecedent or co-incident congestive heart failure or valvular disease, there were relatively few occluded coronary arteries - only one old occlusion; (5) recent or old coronary artery occlusions were found in the absence of angina pectoris in 13 cases, but only 12 main coronary arteries had been occluded prior to the final illness in these cases, - as opposed to the 25 main occlusions in the 12 cases with angina; (6) the site of infarction in the heart bears no necessarily constant or immediately obvious relationship to the location of an occlusion or occlusions in the coronary arteries - a fresh occlusion of the right coronary artery may produce an infarct in the left ventricle i.e. "infarction at a distance"; (7) the clinical consequence of occlusion of the coronary arteries are significantly influenced by the original pattern of the coronary arteries in any given heart.

Much earlier Gross (1921) had stated that inter-coronary anastomoses developed as coronary arteriosclerosis progressed, and that coronary artery occlusion might occur without interfering with the blood supply to the myocardium. He considered that the heart of a man at 60 years was better prepared to withstand the effects of coronary artery occlusion, than the heart of a man at 20 years.

The extent of infarction which follows coronary artery occlusion depends upon the following factors - (1) the size and location of the vessel or vessels occluded; (2) the rapidity with which occlusion occurs; (3) the condition of the general circulation and the coronary circulation; (4) the age of the patient.

The pathology of the infarct and its speed of healing have been studied by Mallory, White and Salcedo-Salgar (1939). The rate at which healing occurs is in part dependent on the size and position of the infarct, and in part on the state of the remaining vessels. Small infarcts are almost completely healed after 5 weeks, whereas large infarcts are healed or undergo no further discernible change after 2 months. Rupture of the infarct is most common during the first week, and may occur during the second week, but is rare thereafter. Endocardial mural thrombus may be present as early as the 5th day and organization has commenced by the 9th day.

Cushing (1942) draws attention to infarction of the auricular muscle. He reviews the literature and reports 31 cases in 182 cases of myocardial infarction occurring in 2704 consecutive autopsies. Twenty-three of the cases had been electrocardiographed and 17 showed evidence of disturbed auricular activity. Twenty-six (80)% showed mural thrombus formation. Gross occlusion of an atrial artery was demonstrated in only one case. Hellerstein (1948) also draws attention to atrial infarction with its diagnostic electrocardiographic findings. Pulmonary thrombo-embolization frequently occurs. Rupture of the atrial infarct has been reported (Clowe et al. 1934).

A novel concept in the localization of the area of infarction is that of Robb and Robb (1935 and 1939 a & b) who consider that the muscle bundles of the ventricular muscle, or parts of these bundles, are the units infarcted by occlusion of a vessel. Electrocardiographically they recognize four types of infarct; (1) infarction of the superficial bulbo-spiral muscle - depression of the R - T segment in standard lead I., and its elevation in lead III.; (2) infarction of the superficial sino-spiral muscle - elevation of the R - T segment in both lead I. and lead III.; (3) infarction of the deep bulbo-spiral muscle - take off of the R - T segment from the peak of the R wave, or from near the peak, in all leads, especially /

especially in the presence of low voltage initial deflections; (4) infarction of the deep sino-spiral muscle - depression of the R-T segment in lead III. and its elevation in lead I. They considered that superficial muscle injury resulted in severe pain, and, if anteriorly placed, in the development of pericardial friction. A moderate fall in blood pressure takes place over a few days. Deep muscle injury on the other hand, is associated with variegated and atypical pain and there is an abrupt, profound fall in blood pressure. Superficial muscles may be infarcted repeatedly and the prognosis remain good. Deep muscle infarction is serious and the prognosis grave, deep bulbo-spiral involvement being frequently associated with sudden death. The pathological and electrocardiographic grouping is over-simplified however as they state that mixed lesions are common. Lowe and Wartman (1944) also consider that muscle bundle infarction is a definite entity.

Finally from a pathological study of a number of clinical cases of myocardial infarction, it became apparent that infarction could occur without coronary vessel occlusion, and at times without coronary vessel disease (Gross and Sternberg 1939, Friedberg and Horn 1939, Price and Jones 1943, Pirani and Schlichter 1946). Such infarcts were subendocardial in position and widespread in distribution. From this there arose the concept that prolonged /

prolonged insufficiency of the coronary circulation without occlusion of a vessel could cause muscle damage and even extensive necrosis. The third clinical syndrome of "coronary insufficiency" or "coronary failure" was thus evolved. Acute coronary insufficiency has been described in detail by Master and his associates (1941 and 1944) and by Freedberg (1948). It exists whenever there is a disproportion between the coronary blood flow and the oxygen demands of the heart, and is provoked by factors which increase the work of the heart, e.g., exercise, emotion, tachycardia; or which reduce the coronary blood flow, e.g. aortic stenosis or incompetence. If the inadequacy of blood flow is of sufficient degree or duration, the ischaemia results in irreversible changes in the myocardium, the parts furthest from the blood supply being most affected, particularly the papillary muscles and interventricular septum. The infarction is subendocardial in position, and on occasions is extensive.

The clinical picture is commonly less severe than when coronary thrombosis has occurred. Most cases show evidence of previous heart disease - hypertension, cardiac enlargement, severe coronary sclerosis, long standing aortic valvular disease, etc.. Recovery is more rapid and complete, and complications are less common than in myocardial infarction due to coronary artery occlusion. Electrocardiographically /

Electrocardiographically the changes are generally of short duration and involve only the S T segments and T waves.

(i) Electrocardiography:

Electrocardiography is essential in an investigation of coronary vessel disease, particularly when myocardial infarction has occurred. In the doubtful or atypical clinical case it may be of diagnostic importance. Herrick (1919) was the first to observe the characteristic changes after myocardial infarction obtaining his record on May 3rd, 1917, 41 days after the acute episode. At the end of his article he suggests "May it perhaps be possible to localize a lesion in the coronary system with an accuracy comparable to that with which we locate obstructive lesions in the cerebral arteries?" Had he said "localize a lesion in the ventricular muscle" it would be correct to say that the hope so expressed is now frequently realized. By the use of multiple unipolar praecordial leads, the area of infarction can be accurately mapped out in many cases.

Smith (1918, 1920, and 1923) carried out extensive experimental work on dogs and reported alterations of the T wave and of the R - T segment occurring more or less constantly after ligation of the branches of the left coronary artery. Pardee (1920) observed a similar change in man and designated this the /

the "coronary T wave". Five years later he amplified his observations, and stated that the characteristics of the electrocardiogram in myocardial infarction were the presence in one or more leads, usually only in one, of a downward, sharply peaked T wave with an upward convexity of the S-T or R-T interval; the T wave did not start from the zero level, turned away quickly from its starting point in a sharp curve, and ended in a sharply peaked T wave somewhat larger than normal. When the change in the T wave occurred in lead III. only however, he considered that this was not significant. An associated T in lead II. was required, before T inversion in lead III. signified myocardial infarction.

Parkinson and Bedford (1928b) found, as had Pardee, that the R-T segment arose above or below the iso-electric line in leads I. and III. and that it occurred "constantly in opposite directions in these two leads, thus R-T elevation in lead I. is associated with an S-T depression in lead III. and vice versa." Moreover they showed that R-T deviation might occur not only in a single lead, but simultaneously in leads I. and II., or II. and III., in which case the deviation was in the same direction in the two leads. They recognised various contours of the R-T interval, and emphasised that when R-T deviation was marked. T waves, strictly speaking, were not evident. Disappearance of the R-T deviation took place /

place before the negativity of the T wave was well developed. Not only did they demonstrate the progressive characteristic changes in the R T segment and T waves but they drew attention to the QRS changes, and to the low voltage of the initial deflections.

Although they (Parkinson and Bedford) divided the curves into two types - T₁ and T₃ according to whether the T waves were inverted in lead I. or lead III., they did not associate either type with infarction of a particular area of ventricular muscle. The first broad electrocardiographic localization of infarction into T₁ or anterior and apical infarction, and T₃ or posterior and basal infarction resulted from the work of Barnes and Whitten (1930) at the Mayo Clinic. Wilson, and his associates (1933) confirmed this finding and stressed the associated Q wave changes. Much of the experimental work on myocardial infarction was carried out in Wilson's laboratory (1933-34, 1935 (a) (b) (c), 1938), and the fact that multiple unipolar praecordial leads were used from 1930 onwards added to the value of their periodic communications.

The use of praecordial leads in the diagnosis of myocardial infarction in man was first suggested by Wilson in 1930. Two years later Wolferth and Wood reported on lead IV. - a chest lead taken with the electrodes on the front and back of the chest. This gave positive results in some cases showing no change /

change in the standard leads. In 1933 they amplified their preliminary report (Wood et al 1933), and a year later drew attention to the huge T waves sometimes found in the praecordial leads in infarction. Katz and Kassim (1933) have also reported on lead IV. It was recognized however (Wood and Wolfarth 1933) that a small proportion of undoubted infarcts could give a normal electrocardiogram. In 1925 Pardee had suggested that a certain minimal area of myocardium had to be involved to affect the electrocardiogram, while a lesser area might still cause pain.

Further clinical reports have appeared from Bohrung and Katz (1938), Kossman and de la Chapelle (1938, and 1939 a & b), Cutts et al. (1941), Dressler (1943) Baer and Frankel (1944), and Burton (1945.). Praecordial leads were standardised in 1938 (report by the committee established by the American Heart Association and by the committee representing the Cardiac Society of Great Britain and Ireland) and in 1944 Wilson reported in detail the use of the unipolar type of lead. Unipolar limb leads had also been described by Goldberger (1943). With this increase in the number of leads available and their standardisation, electrocardiographic diagnosis of myocardial infarction became more accurate, and localization of the infarct more exact. Myers and his associates (1948 a & b, and 1949, a,b,c,d) now classify infarcts into /

into seven groups pathologically and are in the process of demonstrating the electrocardiographic changes associated with each location. These groups are (1) antero-septal (2) large antero-lateral (3) antero-posterior, (4) septal (5) posterior (6) postero-lateral (7) lateral. Considerable overlapping of the groups occurs. High lateral infarction has been discussed by Wilson and his associates (Rosenbaum, Wilson and Johnston 1946). Infarction is suggested by the left arm unipolar lead in the absence of diagnostic signs in the routine praecordial leads. Exploration of the praecordium at higher levels above V_3 , V_4 , V_5 and V_6 demonstrates the infarct.

In 1948 Dressler amplified his original report (1943) on the diagnostic importance of T_1 being lower than T_3 . This pattern is observed in both the earliest stage of myocardial infarction and as a late sign. It may persist for years after the acute coronary episode, but is no more specific for myocardial infarction or coronary vessel disease than is inversion of the T wave. Dressler also suggests that this finding may indicate infarction, in the absence of changes in the routine praecordial leads, and further exploration of the praecordium may reveal a high infarct. Clinically, cases showing this change, are usually mild.

The association of cardiac infarction and bundle branch block is not uncommon. When left bundle branch /

branch block is present it may be impossible to make a diagnosis of cardiac infarction. Wilson (1944) has shown that when the infarct includes the ventricular septum, leads facing the left ventricle show the Q waves characteristic of infarction. In the absence of septal involvement, such leads show an initial positive deflection. Right bundle branch block on the other hand, does not as a rule obscure signs of infarction. Recently Somerville and Wood (1949) have analysed 60 cases of myocardial infarction, 41 showing left bundle branch block, and 19 right bundle branch block. 48% of the cases of left bundle branch block and 93% of the cases of right bundle branch block showed evidence of infarction. In the presence of left bundle branch block, anterior infarction was revealed as frequently with standard leads as with multiple chest leads and unipolar limb leads, but in the presence of right bundle branch block signs of anterior infarction were sometimes seen only in the chest leads. The signs of posterior infarction were practically confined to the standard limb leads and the left leg unipolar lead whether the block was in the right or left bundle branch.

Occasionally there occur anomalous changes, such as the temporary return to normality of the electrocardiogram in cases of proved infarction. This has been commented on by Master (1947) but his paper has not been accessible for reference.

Changes associated with the presence of a cardiac aneurysm have been reported. Eliaser and Konigsberg (1939) recorded three varieties of curves.

(1) A downward directed major deflection in lead I, with inversion of the T wave and upright P wave; upright ventricular complex in lead III. This was present in 27.3% of their cases, and they considered that its presence was presumptive evidence of a cardiac aneurysm; (2) the ventricular complexes in leads II. and III. are directed downwards, while in lead I. the major deflection is upright, and may or may not be of low voltage. This was present in 36.4% of their cases; (3) left bundle branch block - present in 18.2%. Crawford (1943) could not confirm these findings. Nordenfelt (1939) stated that probably there were no electrocardiographic changes which are so typical of cardiac aneurysm that they allow of direct diagnosis, but he described a combination of changes, which if they remained unchanged for a long period in a patient with a previous history of acute myocardial infarction might suggest chronic aneurysm or extensive fibrosis on the anterior wall of the left ventricle. The changes were (1) a relatively low R_1 , and deep S_2 and S_3 ; (2) elevated S T segment in all leads; (3) negative T_1 and positive T_2 and T_3 ; (4) often there is a clear Q_1 . (5) in lead IV. R is absent and S deep, S T is elevated, and T is upright.

Auricular infarction is commonly evidenced electrocardiographically - as clinically - by disturbance of auricular activity. In Cushing's series (1942) the following changes were recorded - auricular fibrillation 9 cases; auricular flutter 2 cases; auricular extra-systoles 4 cases; wandering pace maker 1 case; sinus arrest 1 case. Depression of the P Q interval occurred in only 5 cases. Six cases showed no evidence of auricular damage.

Hellerstein's case (1948) showed a changing auricular mechanism with coarse auricular fibrillation, varying degrees of A-V block, and elevation of the P - TA (P R) segment in leads II. and III.

Acute coronary "insufficiency" is characterised by depression of the S T segment in two or more leads and possibly the development of T wave inversion in those leads. Q wave changes do not occur. Within a few days or weeks these changes retrogress and disappear (Master 1944, Master et al. 1944, Freedberg et al. 1948).

Master (1942) in a follow up study of 202 cases of myocardial infarction reported that in 21% of cases the electrocardiogram had returned to within normal limits within 1 year of the acute attack. In other cases the T waves had become normal but abnormal Q waves persisted. Not infrequently the only remaining sign of infarction in these 21% of cases was an abnormality of ventricular contraction which could be /

be observed fluoroscopically or with the roentgenkymogram.

(j) Roentgenkymography:

In 1939 Gubner and Crawford reported on their observations with the roentgenkymogram in 45 convalescent cases of coronary thrombosis, while a year later Sussman and his associates (1940) discussed their findings in 200 cases of typical coronary artery occlusion. The characteristic abnormalities in left ventricular pulsation so recorded are (1) localised diminution or absence of pulsation; (2) complete systolic expansion or paradoxical pulsation; (3) partial systolic expansion indicated by expansion early in systole or a delay in the completion of systole; (4) marked diastolic splintering. These changes were found in 75% of Sussman's cases. They are likely to be permanent, being found in both recent and old infarction, but progression and regression of the changes have been noted. A persistently normal kymogram does not exclude the possibility of myocardial infarction. In most cases, abnormalities appear within 3 weeks of the attack, if they appear at all, but occasionally characteristic changes do not appear for several months. Gubner and Crawford (1939) state that it is difficult to explain why in one case the pulsation is absent and in another, paradoxical pulsation occurs; also why both types /

types may occur in different segments in the same patient. A possible explanation lies in the varying degree of endocardial lamination of the infarct with mural thrombus; in cases in which pulsation is absent there may be dense mural thrombus, whereas paradoxical pulsations are more likely to occur when there is no mural thrombus and the thinned area of infarction can be distended with the systolic rise of intra-ventricular pressure.

Dack (1940) has correlated the clinical course, electrocardiographic changes, and roentgenkymographic observations in the same 200 cases, and was able to report that (1) the kymogram is usually normal when the attack is mild and the recovery good. Regression or complete disappearance of kymographic abnormalities is a good prognostic sign. The kymographic abnormalities are usually marked when the attack is severe and the recovery incomplete; (2) the kymogram not infrequently presents abnormalities characteristic of myocardial infarction when the electrocardiogram is normal or atypical. On the other hand, the kymogram may remain normal or return to normal, while typical electrocardiographic abnormalities persist. These two methods of examination therefore supplement each other; (3) posterior infarction produced abnormalities in the postero-anterior kymogram as often as did anterior infarction. In only a minority of cases of either anterior or posterior infarction were abnormalities /

abnormalities visualized better in the left oblique position than in the postero-anterior position.

When multiple infarcts were present, or one infarct involving both surfaces of the left ventricle, the frequency and degree of kymographic abnormalities increased; (4) at post mortem examination, systolic expansion in four cases could be correlated with a large area of infarction or thinning of the left ventricle. Diminution of pulsation occurred in one case in which there was a small posterior infarct, and in another in which there was diffuse fibrosis. Dack considers that the roentgenkymogram should prove to be of most diagnostic value during the acute stage, when the clinical course and electrocardiogram are not typical of coronary artery occlusion, and following recovery, when the characteristic signs of infarction have disappeared. In these cases of bundle branch block reported by Gubner and Crawford (1939) the kymogram showed an area of infarction.

Fluoroscopic examination of the heart in a group of 80 cases with cardiac infarcts revealed abnormalities which corresponded closely with those observed in the roentgenkymograms. (Master et al. 1940).

III. THE ANALYSIS OF THE IMPORTANCE OF MYOCARDIAL INFARCTION AS A CAUSE OF DEATH.

The increasing incidence of deaths from coronary thrombosis has been commented on by Master(1947) in America, and Ryle and Russell (1949) in this country. Master calculated that, at a conservative estimate, 120,000 deaths occurring in the U.S.A. in 1942 were due to coronary thrombosis, and assuming that the death rate was 15%., the total number of attacks was in the region of 800,000. If the sex ratio were 3:1 in favour of males, then 1 male in 38, and 1 female in 115, over the age of 40 years, sustained a coronary thrombosis in that year. Master attributed the increase in incidence of the disease since it was first described to (a) lengthening of the span of life; (b) ageing of the population; (c) improved diagnosis and treatment, and (d) accuracy in terminology. In his opinion there was no significant incidence of coronary thrombosis in any social class or occupation.

As the title of their article "The Natural History of Coronary Disease. A clinical and epidemiological study" suggests, Ryle and Russell have studied both angina pectoris and coronary thrombosis. The statistical section of their paper comprises an analysis of the Reports of the Registrar General for England and Wales during the period 1921-45. The statistical patterns shown by the two sexes are similar /

similar. Each 5 year age group between the ages of 40 and 75 years showed an increase of approximately 250% in the mortality due to coronary vessel disease in 1931-39 as compared with 1921-30. The increase continued and in 1940-45 amounted to approximately 450%. In middle-life - between 40 and 55 years - the male death rate had increased more rapidly than that for females, whereas in old age, the position was reversed. In 1940-45, the male death rate at age 40-50 years was more than 5 times greater than that for females; at 55-60 years the ratio dropped to 4.0, and at 75 years it was less than 2. After allowing for changing fashions in diagnosis, amendments to the international classification of causes of death, and the lengthening span of life, Ryle and Russell concluded that the increase in deaths due to coronary thrombosis was real. Although the increase was striking they considered that it was now less rapid than in the period before the war (1939-45).

Prior to the appearance of Ryle's paper, it had been decided to study the reports of the Registrar General for Scotland and compare the years 1937 and 1947. This period was chosen for two reasons, (a) by 1937 coronary thrombosis would probably be recognized as an entity by practitioners generally throughout the country, and (b) accuracy in diagnosis would probably not have increased greatly during the decade following 1937. Prior to 1941, the International /

International classification used in death certification did not distinguish between coronary thrombosis and angina pectoris, the two being grouped as "Diseases of the coronary arteries, angina pectoris". In 1941 the present classification came into force separating the two diseases. It then became the practice for the Registrar General to return to the certifier every death certified as due to angina pectoris, enquiring if it were due to "disease of the coronary arteries." The result was that practically every death had to be reclassified to coronary thrombosis (personal communication from office of Registrar General for Scotland 1949). Since 1946 the Medical Superintendent of Statistics has combined the two causes as "Diseases of coronary arteries, and angina pectoris." Consequently deaths in 1937 classified as "Diseases of coronary arteries, angina pectoris", may be compared with those classified as "Diseases of Coronary arteries, and Angina Pectoris", in 1947.

In the 10 years from 1937, the population of Scotland has increased by 2.87% - males 3.08%, and females 2.67%. - but the increase is not spread evenly over the decades. Between the ages of 5 and 34 years there were fewer males and females alive in 1947 than in 1937, but from 35 years onwards the population has increased (with the exception of males between 55 and 64 years, who show a very /

very slight decrease). This change is shown diagrammatically in figure 1. It is most marked over the age of 75 years, i.e. ageing of the population is taking place. This increase in the population over the age of 35 years provides more candidates for coronary thrombosis, and will in part explain any increase in incidence of the disease.

As shown in Table XV., the increase in deaths classed as due to coronary artery disease has been striking.

TABLE XV. Comparison of deaths due to disease of the coronary arteries, (and) angina pectoris in 1937 and 1947.

Year	Male	Female.
1937	1142	614
1947	2989	1834
Increase	1747	1222
% Increase	162%	199%

Figure 2 shows that the increase has been spread evenly over the intervening years. It is also relatively evenly spread over the age groups except among the young and the very old. (Table XVI.)

TABLE XVI. /

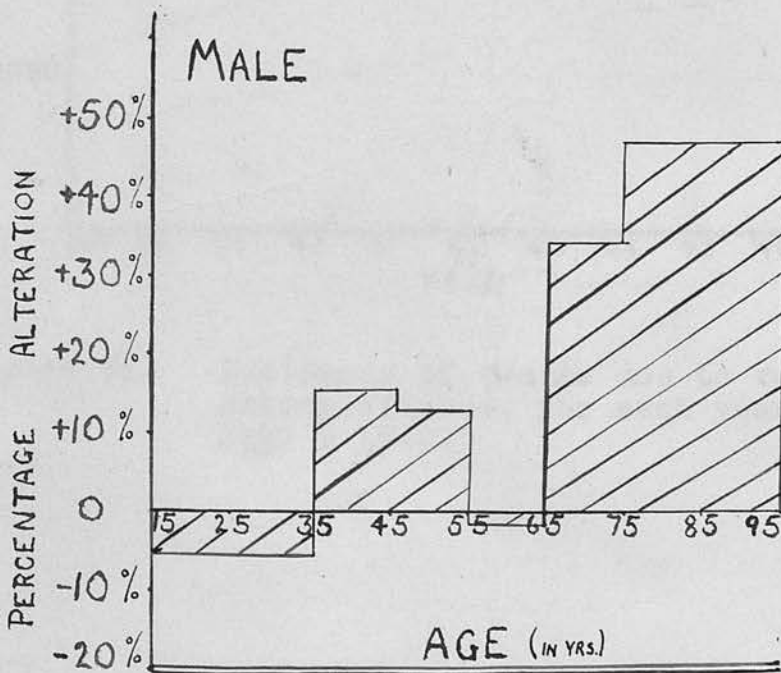
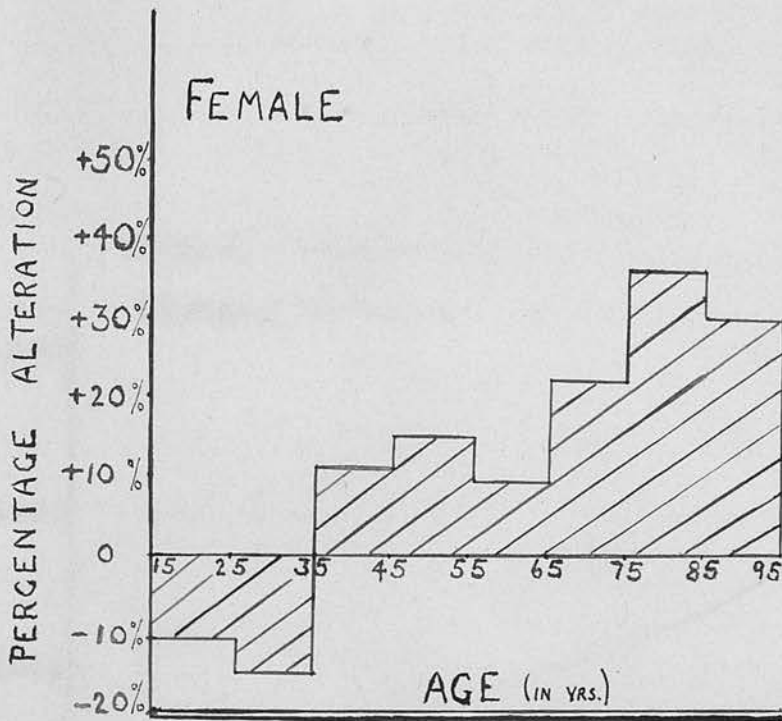


Figure I. The percentage alteration in the population of Scotland between 1937 & 1947.

TABLE 3VI. Increase in deaths from coronary artery disease between 1937 and 1947 as shown by each 10 year age group.

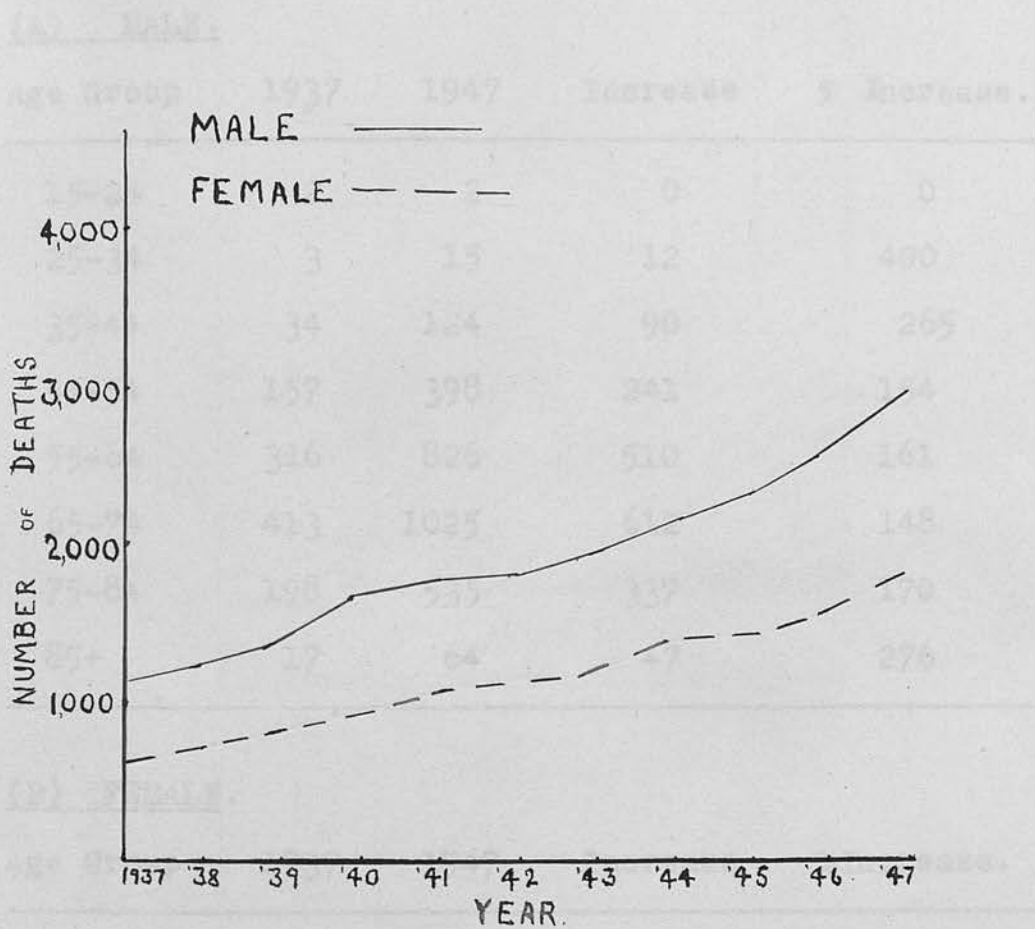


Figure II. Incidence of deaths due to coronary artery disease, for each year between 1937 & 1947.

Figure 3 illustrates how little part the change in the population in each age group has played in the increase in deaths due to coronary artery disease.

TABLE XVI. Increase in deaths from coronary artery disease between 1937 and 1947 as shown by each 10 year age group.

(A) MALE.

Age Group	1937	1947	Increase	% Increase.
15-24	2	2	0	0
25-34	3	15	12	400
35-44	34	124	90	265
45-54	157	398	241	154
55-64	316	826	510	161
65-74	413	1025	612	148
75-84	198	535	337	170
85+	17	64	47	276

(B) FEMALE.

Age Group	1937	1947	Increase	% Increase.
15-24	1	0	-1	-
25-34	4	6	2	50
35-44	6	17	11	183
45-54	37	104	67	181
55-64	158	412	254	160
65-74	269	755	486	181
75-84	125	454	329	263
85+	13	88	75	577

Figure 3 illustrates how little part the change in the population in each age group has played in the increase in deaths due to coronary artery disease.

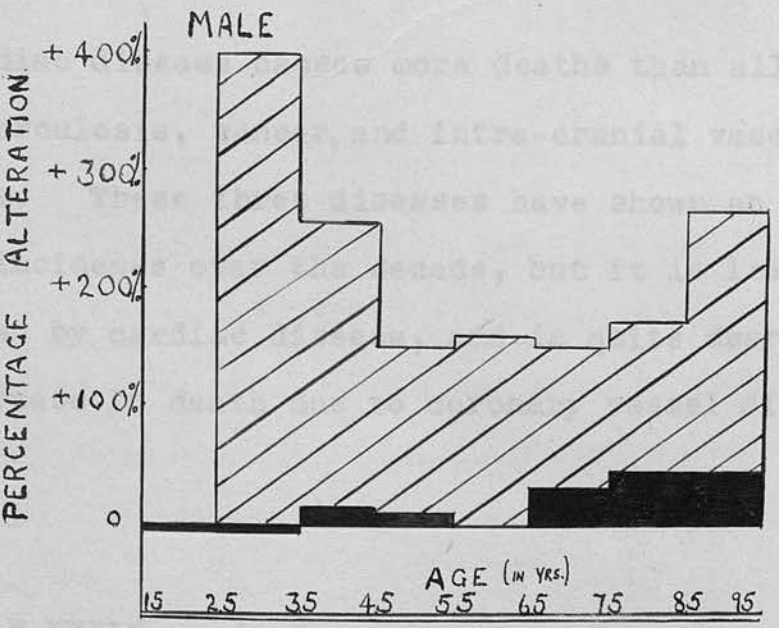
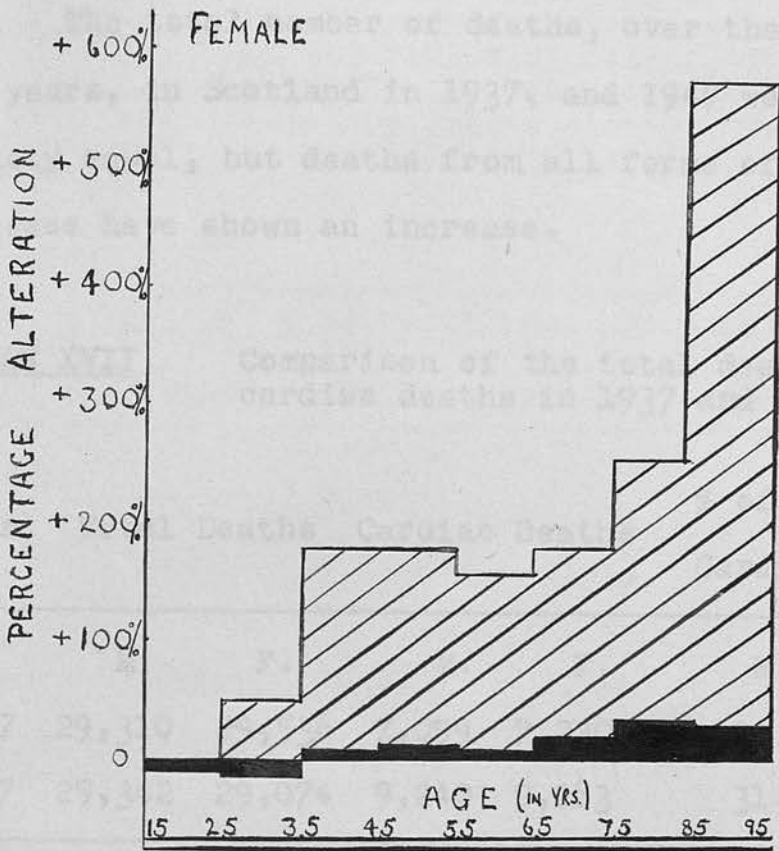


Figure III. Comparison of (1) the change in the population and (2) the increase in the number of deaths due to coronary artery disease, between 1937 & 1947.

POPULATION.
 CORONARY ARTERY DISEASE.

The total number of deaths, over the age of 10 years, in Scotland in 1937, and 1947 were approximately equal, but deaths from all forms of cardiac disease have shown an increase.

TABLE XVII. Comparison of the total deaths, and cardiac deaths in 1937 and 1947.

Year	Total Deaths		Cardiac Deaths		% of Total Deaths due to Cardiac Disease.	
	M.	F.	M.	F.	M.	F.
1937	29,310	29,536	7,099	7,230	24	24.4
1947	29,342	29,074	9,240	9,283	31.4	31.9

Cardiac disease causes more deaths than all forms of tuberculosis, cancer, and intra-cranial vascular lesions. These three diseases have shown an increase in incidence over the decade, but it is less than that shown by cardiac disease, and is quite dwarfed by the increase in death due to coronary vessel disease.

TABLE XVIII. /

TABLE XVIII. Comparison of the relative importance of tuberculosis, cancer, intra-cranial vascular lesions, cardiac disease, and coronary artery disease, as a cause of death in 1937 and 1947.

Disease	1937		1947		% Increase over decade.
	No. of deaths	% of Total deaths	No. of deaths	% of Total deaths	
Tuberculosis	3262	5.54	3,659	6.26	12
Cancer	7791	13.23	9,049	15.99	16
Intra-cranial	6394	10.86	7,918	13.55	23
Vascular Lesions					
Cardiac Disease	14,329	24.35	18,526	31.71	27
Coronary Disease	1,756	2.98	4,823	8.22	177

Among both males and females, the proportion of the total deaths which is due to cardiac disease increases with age. This increase in cardiac deaths between 1937 and 1947 is evenly spread over the age groups. On the other hand, the proportion of total deaths which is due to coronary artery disease shows a different curve. Among males, the highest proportionate incidence is reached in the 6th and 7th decade, while among females, the peak is in the 7th decade. (Figures 4 & 5). The percentage of cardiac deaths which are due to coronary artery disease is also shown in figures 4 & 5. Proportionately coronary /

MALE

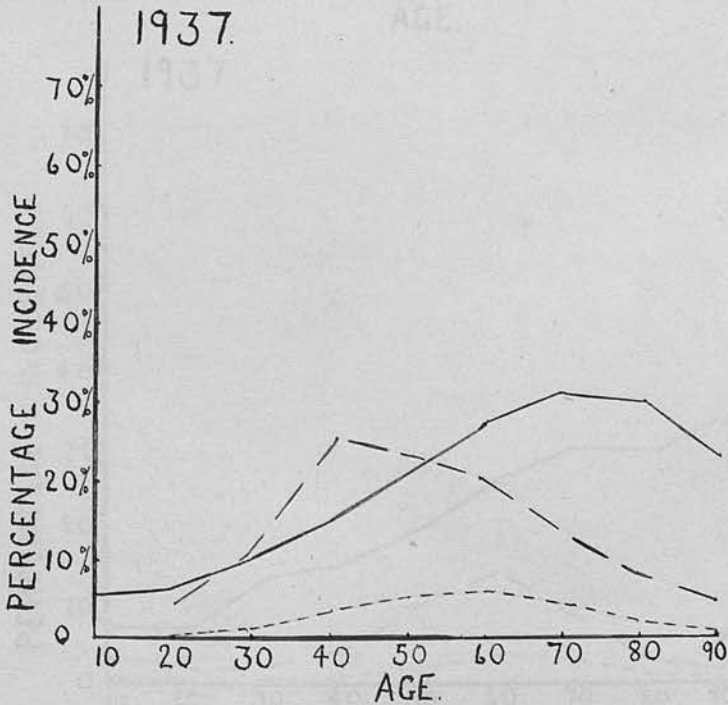
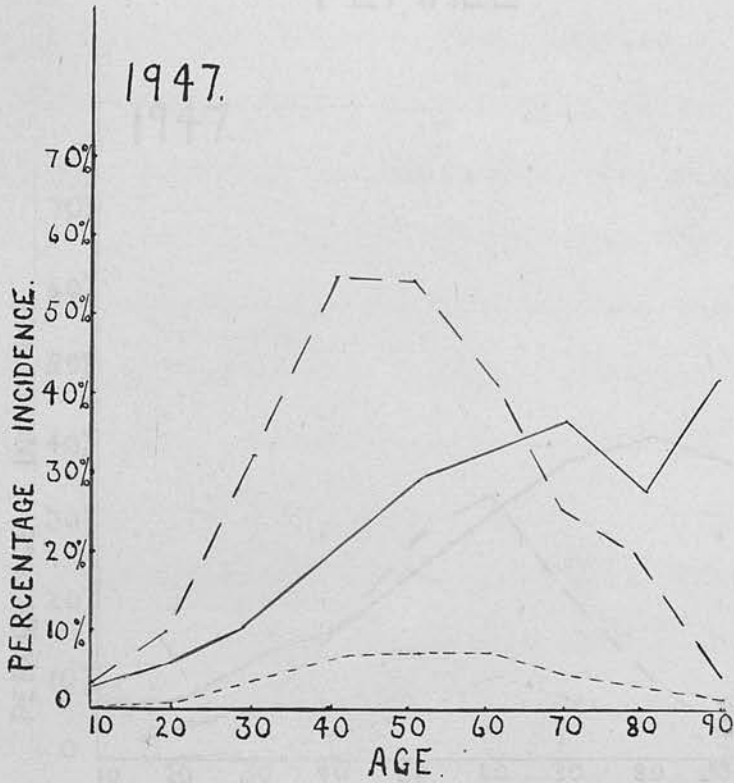


Figure IV. The proportion of the total deaths in each 10 year age group, due to (1) cardiac disease (—), and (2) coronary artery disease (-----) in both 1937 & 1947 are illustrated. The proportion of the cardiac deaths which are due to coronary artery disease (— — —) is also shown.

FEMALE

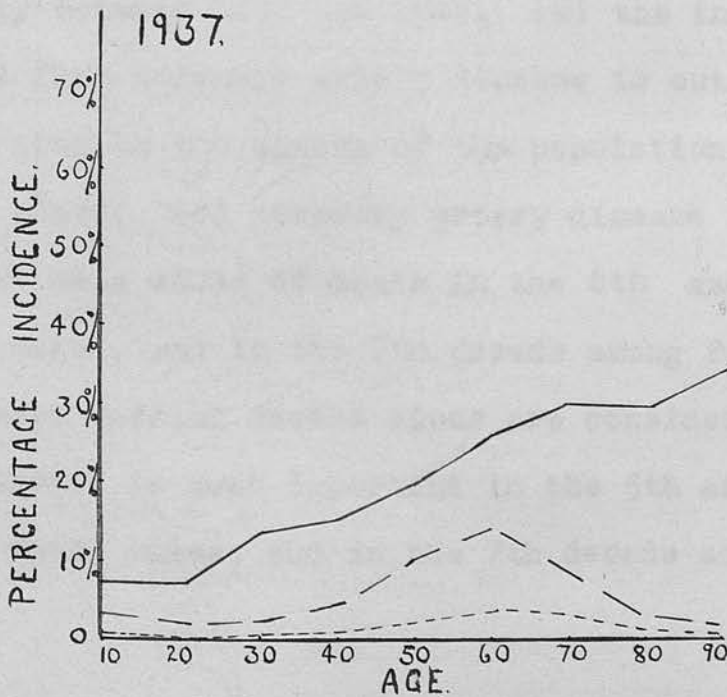
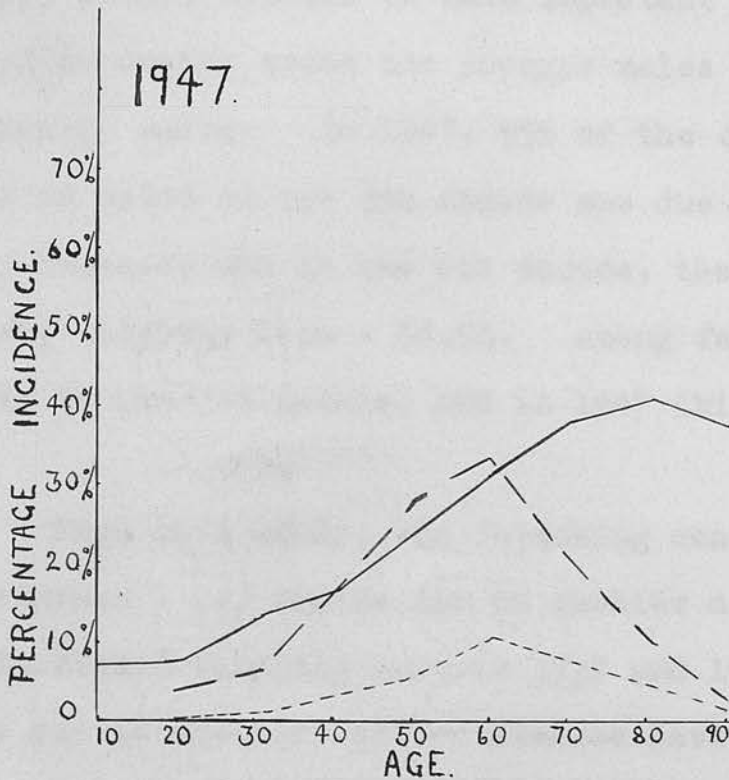


Figure V. The proportion of the total deaths in each 10 year age group, due to (1) cardiac disease (—————), and (2) coronary artery disease (-----) in both 1937 & 1947 are illustrated. The proportion of the cardiac deaths which are due to coronary artery disease (— — — — —) is also shown.

coronary artery disease is more important as a cause of cardiac deaths among the younger males than among the elderly males. In 1947, 55% of the cardiac deaths in males in the 5th decade was due to coronary artery disease, and in the 6th decade, the proportion was only slightly less - 54.5%. Among females the peak is in the 7th decade, and in 1947 this reached 33%.

From this study, the following conclusions may be drawn - (a) deaths due to cardiac disease have increased slightly between 1937 and 1947; (b) deaths due to coronary artery disease have increased greatly between 1937 and 1947; (c) the increase in deaths from coronary artery disease is out of all proportion to the ageing of the population which has taken place; (d) coronary artery disease is most important as a cause of death in the 6th and 7th decade among males, and in the 7th decade among females; (e) when cardiac deaths alone are considered, coronary disease is most important in the 5th and 6th decades among males, and in the 7th decade among females.

IV. /

IV. AETIOLOGY.

In view of the increasing toll of lives exacted by coronary artery thrombosis with myocardial infarction, the problem as to aetiology of the condition is of paramount importance. In the following pages, the main factors known to play some part are summarised; our own experience regarding these factors is briefly stated; and two additional aspects which have been investigated are reported in some detail.

(a) Factors of Known Importance.

(I.) Disease of the Coronary Arteries.

This is the primary factor as thrombosis does not occur in a healthy artery. With the rare exception of peri-arteritis nodosa and thromboangiitis obliterans, arteriosclerosis is the fundamental lesion. The rate of development of the arteriosclerotic process is the factor determining when a clinical "coronary thrombosis" will occur. Coronary artery disease without tibial cerebral or aortic lesions - an exceptional finding after the 6th decade - is the rule in men under 40 years (French and Dock 1944). The degree of arteriosclerotic change varies in each artery and in different sections of the same artery. Commonly the anterior descending branch of the left coronary artery is the most affected. Thrombotic occlusion of a coronary artery follows a capillary haemorrhage in /

in one of the arteriosclerotic plaques (Paterson 1936), but as the arteriosclerotic arteries are not end arteries, such an occlusion is not necessarily followed by muscle infarction. Commonly two or more sites of arterial occlusion can be demonstrated in each case of myocardial infarction (Blumgart et al 1940).

Although of primary importance, the aetiology of arteriosclerosis does not come within the scope of this thesis, and will not be discussed.

(II.) Sex. Males are affected about four times as frequently as females. (Dock 1946) suggests that this sex difference is due to an inborne difference in thickness of the intima of the coronary arteries (as stated in the historical review, page 59).

(III.) Age. "Coronary thrombosis" is a disease mainly of the middle aged and elderly. Males are affected at a younger age than females.

(IV.) Hypertension. This is present prior to myocardial infarction in over 50% of cases. Master (1939b) considers it to be of paramount importance in increasing the incidence of coronary artery occlusion.

(V.) Angina Pectoris. Commonly about 40% of cases have complained of effort pain prior to their infarct.

(VI.) Family History of Vascular Disease. Levine and Brown (1928) were impressed by the frequency with which this was found. Goldsmith and Willius (1936a) reported its presence in 55% of their cases.

(VII.) /

(VII.) Diabetes. This is not frequently present, but is most common in the elderly female.

(VIII.) Body Weight. Probably this is of little or no importance.

(IX.) Social Status and Occupation. Master (1947) considers that no social grade and no occupation render a person more liable to myocardial infarction than any other. "Acute coronary artery occlusion is no respecter of persons; the rich, the poor, the labourer, the executive, or the ordinary man at the desk are all possible victims." Ryle and Russell (1949) however, believe that occupation and social status are of great importance particularly among males, the middle aged professional man being the candidate par excellence.

(X.) Established Auricular Fibrillation
 () These
 (XI.) Rheumatic Heart Disease)

would appear to have some protective influence, coronary thrombosis with myocardial infarction being uncommon in both conditions.

(b) Data derived from analysis of 170 cases.

(I.) Pathology. Fortysix autopsies were carried out on cases dying soon after a myocardial infarct. With one exception all showed well marked arteriosclerosis of the coronary arteries. This one exception was the sole case of embolism of a coronary artery encountered in the cases analysed. The patient was a woman aged 63 years with mitral stenosis, auricular /

auricular fibrillation and congestive heart failure. Her coronary arteries were healthy.

(II.) Sex. In the two series, there were 116 males and 54 females, the sex ratio being 2.15:1.

This ratio is artificial as twice the number of beds were available for female cases as for male cases.

(III.) Age. Of the 116 males, 89 (76.7%) were 50 years or over and of these 70 (60%) were in the 50-65 years age group. The average age was 55.7 years. Among the 54 women only 9 (16.6%) were under 60 years. The average age was 64.4 years.

(IV.) Hypertension. Fifty (43%) of the 116 males, and 33 (61%) of the 54 women were known to have been hypertensive, but in 42 male cases (37%) and 15 female cases (28%) the level of the blood pressure prior to the myocardial infarct was not known. Only 24 males (20%) and 6 females (11%) had been normotensive.

(V.) Angina Pectoris. Fiftyfour males (46.5%) and 29 females (53.7%) had suffered effort pain.

(VI.) Family History. In only 50 cases, recorded mainly in the past 2½ years, are there adequate details for analysis. Twenty-two (44%) had a family history of vascular disease, (shock, sudden death, or heart attack). A positive history was more common among the females than among the males. Twelve of 32 males (37.5%) gave a family history of vascular disease, as against 10 of 18 females (55%). This high familial /

familial incidence of the various forms of vascular disease becomes significant only when the incidence of vascular disease among families in the general population is known. As a rough guide, two series of 100 consecutive cases (excluding cases of myocardial infarction) admitted to Wards 25 and 26 of the Royal Infirmary Edinburgh during the summers of 1947 and 1948 have been analysed. In a number of cases, details of family history were incomplete, only facts relevant to the patient's illness (e.g. tuberculosis) being recorded. In the first series 18 cases, and in the second 17 cases, gave a history of illness among parents, brothers or sisters, which could be attributed to vascular disease. Probably this is a minimum figure and greater attention to detail in recording family history would show a higher incidence.

However these investigations would suggest that 1 in every 2 victims of myocardial infarction will give a family history of vascular disease, as opposed to 1 in 5 of the general population.

(VII.) Diabetes. Only two males (1.7%) and four females (7.4%) had diabetes.

(VIII.) Body Weight. Thirtynine males (33.6%) and 31 females (57.4%) were overweight.

(IX.) Social Status and Occupation. In this small series these two factors have not been investigated.

(X.) Established Auricular Fibrillation. Only one case had auricular fibrillation prior to the myocardial /

myocardial infarct. This was the elderly female with rheumatic heart disease who sustained an embolic occlusion of a coronary artery. Hypertension is commonly the factor associated with auricular fibrillation in the elderly. During the past 10 years 662 cases of hypertension have been admitted to Wards 25 and 26 in the Royal Infirmary Edinburgh. Of these, 21 (12 males and 9 females) had associated auricular fibrillation - all were elderly; none had a valvular lesion; not one had sustained a myocardial infarct. On the other hand 107 of the remaining 641 hypertensive cases had sustained a myocardial infarct, either at the time of admission or prior to admission, i.e. 1 in 6 of the hypertensive cases in normal rhythm had at one time a myocardial infarct. Although the number of cases with co-existing hypertension and auricular fibrillation is small, it is significant that none suffered myocardial infarction.

(XI.) Rheumatic Heart Disease. Apart from the elderly female already mentioned, there were no cases of rheumatic heart disease.

In view of the fundamental importance of arteriosclerosis of the coronary arteries in the development of coronary thrombosis and myocardial infarction, the relative immunity enjoyed by elderly subjects with rheumatic heart disease might be due to the absence of marked arteriosclerotic changes. During the past 10 years, there have come to autopsy from wards 25 and 26 Royal /

Royal Infirmary Edinburgh, ten patients with rheumatic heart disease who were 40 years of age or over. Five were male and five female. Four were over 60 years, two being hypertensive. (Only two (20%) showed naked eye atheroma of the coronary arteries - one female aged 60 years, and one male aged 45 years. In both cases the changes were slight - in the male, a section of the anterior descending branch of the left coronary artery, one inch below its origin showed atheromatous thickening, whereas in the female one branch of the circumflex artery was affected. The other vessels were normal. The female is of interest in that the area of muscle supplied by the affected vessel was infarcted, although no thrombus was found in the vessel; the remaining myocardium was healthy. This female is not included in the series of cases of myocardial infarction on which this thesis is based, as she was admitted in congestive heart failure, 8 weeks after the infarct and died from a pulmonary embolus.

A random selection from the ward records of thirty autopsy cases (16 female and 14 male) in patients over 40 years - none of whom had sustained a myocardial infarct - showed arteriosclerosis of the coronary arteries in 19 cases (63.33 per cent.). Of the 16 females, eight had arteriosclerosis and eight had healthy vessels, whereas only three males had healthy vessels. The average age of the two groups /

groups of females was the same but the males with arteriosclerosis averaged 6 years older than those without. Twelve of the thirty cases had hypertension and only two of these did not have arteriosclerotic coronary arteries.

This incidence of coronary arteriosclerosis in the 10 elderly patients with rheumatic heart disease is less than that shown by a random series of 30 elderly patients. This would suggest that coronary arteriosclerosis is less common in cases who have had rheumatic fever and would afford an explanation of the rarity of coronary thrombosis with myocardial infarction in the presence of rheumatic heart disease. It must be emphasised, however, that no firm conclusion may be drawn from such a small number of cases.

(c) Factors of Possible Importance in Aetiology :

Two factors of possible importance have been investigated clinically and are herewith reported. They are (1) the resistance of the skin capillaries on the patient's admission and during the subsequent weeks, and (2) the changes in blood coagulation found on admission.

(I). Capillary Resistance. This was determined by the negative pressure method described by Scarborough (1941). The minimum negative pressure in mm. of mercury, which, when applied to three separate /

separate areas of skin on the right forearm for 30 seconds, will produce 1, 2 or 3 petechial haemorrhages is accepted as the capillary resistance. Three standard areas are used. (1) on the outer side of the mid-line of the forearm, 4 cms. below the flexure of the elbow (area I), (2) on the inner side of the mid-line at the same level (area III), and (3) in the mid-line of the forearm, 2 cms. above the flexure of the wrist (area V). It is conventional to record the results as a fraction, the numerator indicating the negative pressure, and the denominator the number of petechiae produced e.g. $\frac{220}{2}$ $\frac{550}{1}$ $\frac{400}{1}$. Area V

is recorded beneath areas I. and III. Area I. is commonly the most fragile. Details of the normal range of capillary strength using this method are given on page 101.

Fifty patients were investigated as soon as possible after their infarct. This varied from a few hours to a few days. Thirty-five (70 per cent.) had a low capillary resistance. All had been receiving a good general diet. The degree of fragility was in no way related to age or state of shock, but was more common in the hypertensive than in the non-hypertensive patients. Twenty-four of these cases had a raised blood pressure; in six the previous level was unknown, and in five it had been within normal limits. Of the 15 cases who had a satisfactory capillary /

capillary resistance, only six were definitely hypertensive (40 per cent.); in six the previous level of the blood pressure was unknown, and in three it had been normal. Although the figures for the capillary resistance of these patients were in the range commonly accepted as normal, it is quite possible that they were below the accustomed level of these patients.

During recovery and convalescence, several cases showed little change in capillary strength, this being maintained at a low level during the 6 weeks of observation. (Figure 6). Others showed a definite steady increase in resistance during the first week after the infarct, and with minor fluctuations, this new level was maintained. (Figure 7). It is possible that this fragility of the skin capillaries indicates a generalised weakness of the capillaries throughout the body. Rupture of a poorly supported intimal capillary in an arteriosclerotic plaque may well be facilitated by this weakness.

The capillary resistance shown by two patients who have sustained/^arecurrence of myocardial infarction is of interest. One male had a recurrence 5 weeks after the first infarct, and 10 days after going to a convalescent home. Nine hours after the first infarct his skin capillaries were fragile - $\frac{160}{1}$ $\frac{440}{2}$ $\frac{220}{1}$,

and in five days this had improved, the capillary strength /

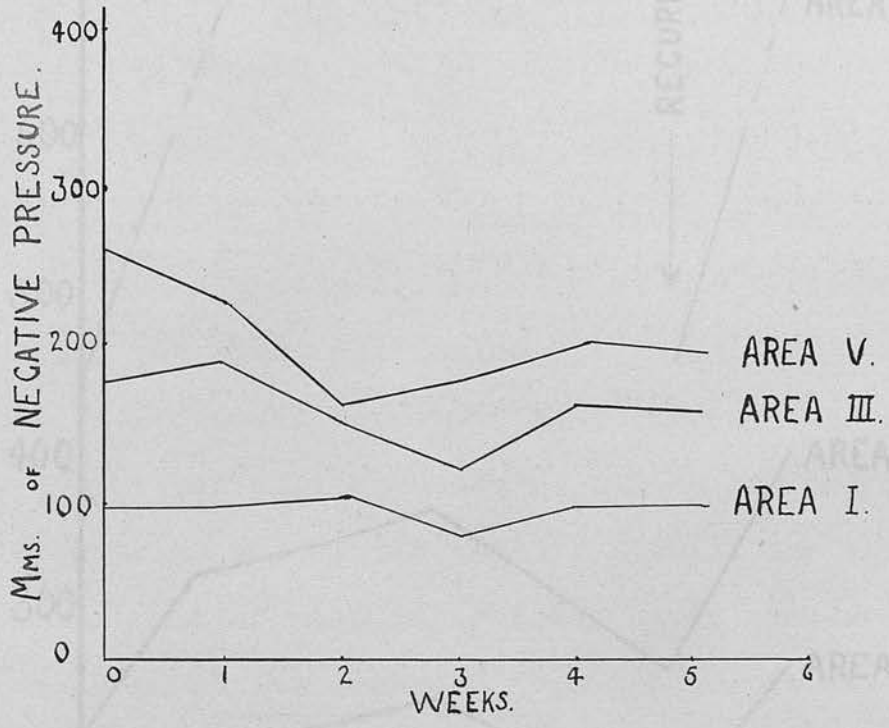


Figure VI. Case showing fragile skin capillaries during the weeks after myocardial infarction. The patient was an elderly diabetic

Figure VII. Variation in the resistance of the skin capillaries at the time of, and following myocardial infarction; and also at the time of a recurrence of infarction in the 5th week.

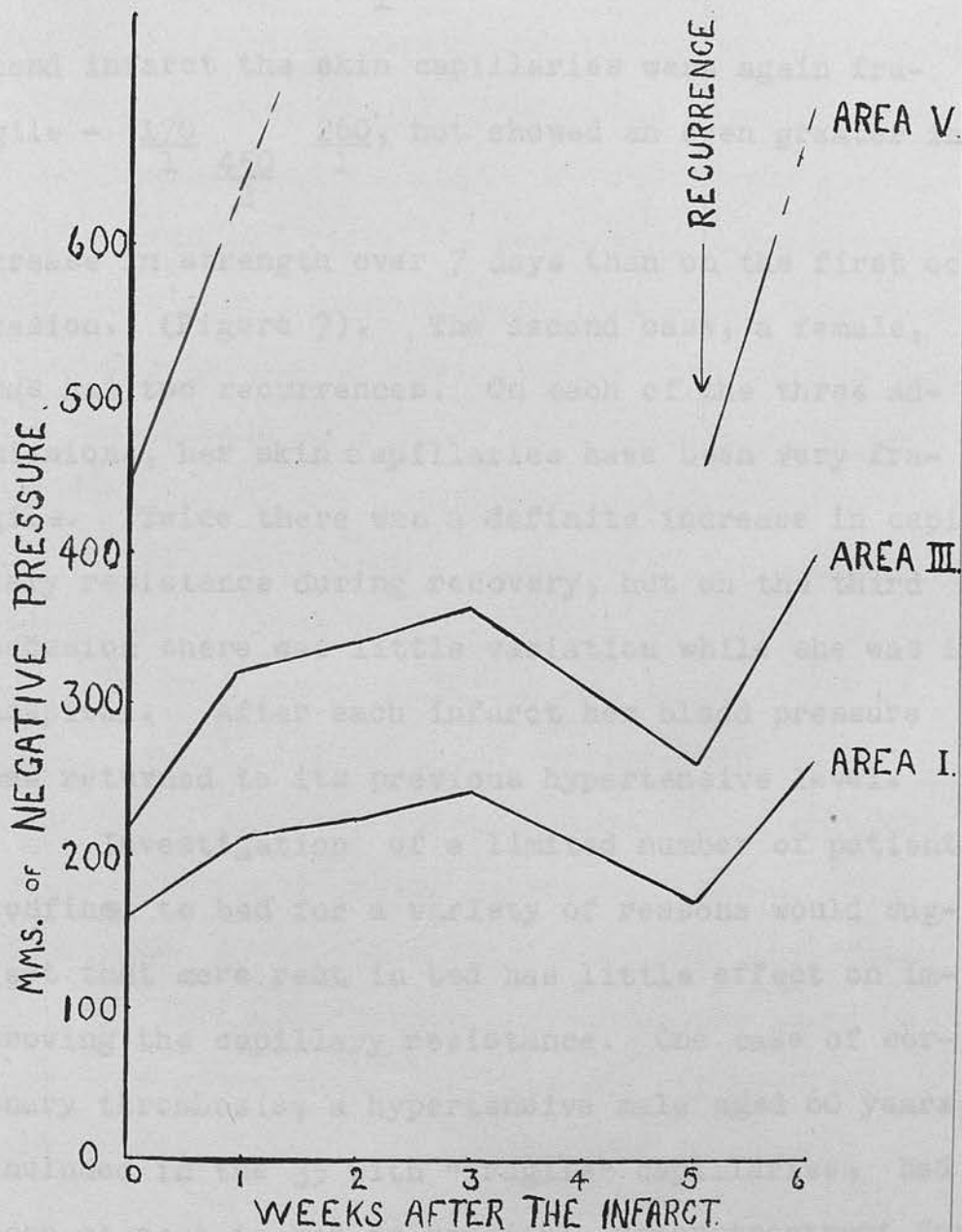


Figure VII. Variation in the resistance of the skin capillaries at the time of, and following myocardial infarction; and also at the time of a recurrence of infarction in the 5th week.

strength being $\frac{250}{1}$ $\frac{530}{1}$ $\frac{335}{2}$. One day after the se-

cond infarct the skin capillaries were again fra-
gile - $\frac{170}{1}$ $\frac{450}{2}$ $\frac{260}{1}$, but showed an even greater in-

crease in strength over 7 days than on the first oc-
casion. (Figure 7). The second case, a female,
has had two recurrences. On each of the three ad-
missions, her skin capillaries have been very fra-
gile. Twice there was a definite increase in capil-
lary resistance during recovery, but on the third
occasion there was little variation while she was in
hospital. After each infarct her blood pressure
has returned to its previous hypertensive level.

Investigation of a limited number of patients
confined to bed for a variety of reasons would sug-
gest that mere rest in bed has little effect on im-
proving the capillary resistance. One case of cor-
onary thrombosis, a hypertensive male aged 60 years,
included in the 35 with "fragile" capillaries, had
been at rest in bed in hospital, under treatment for
left ventricular failure, for 4 weeks prior to his
infarct. During the succeeding week, his capillary
strength rose to within the normal range..

The study would suggest that (1) the capil-
lary resistance is frequently low at the time of on-
set of a coronary thrombosis; (2) the fragility of
the /

the capillaries is not related to the degree of shock or to age; (3) hypertensive patients show fragile capillaries more commonly than do non-hypertensive patients; (4) following the coronary thrombosis, increase in the capillary resistance may occur. Also the two cases sustaining a recurrence of infarction show a suggestive relationship between onset of the infarct and fragility of the capillaries. That both should show a normal capillary strength some weeks after the infarct would suggest that there is a cyclical variation in capillary strength and that coronary thrombosis is liable to occur during the phase when the capillaries are fragile.

Schweppe, Lindberg and Barker (1948) have stated that capillary strength does show a cyclical variation in hypertensive patients. Beaser, Rudy and Seligman (1944) have shown that capillary fragility is more common in the hypertensive than the non-hypertensive case, and that the maximum incidence of fragility is found in cases in the 6th and 7th decades. Diabetics show an even higher incidence of capillary fragility than do the hypertensive cases.

This factor of increased capillary fragility may partly explain the importance of hypertension and diabetes in the aetiology of coronary thrombosis, and may also be responsible for the high incidence of this disease in the 6th and 7th decades.

Were it possible to produce a permanent increase in capillary strength, it is conceivable that, if capillary fragility plays a part in aetiology, the incidence of coronary thrombosis might be lessened. A large number of factors influence capillary resistance. Rutin has been claimed to restore capillary strength in hypertensive patients showing a low resistance (Griffiths, Couch and Lindauer, 1944, Shanno, 1946). However this improvement may occur in only 50 per cent. of cases, (Schweppe, Lindberg and Barker, (1948). The effect of Rutin on an individual case can not be predicted. Nevertheless, a long term investigation of a series of selected hypertensive patients who respond to its administration would be of considerable interest, particularly with reference to the incidence of coronary thrombosis. This may point the way to one method of prophylaxis of coronary thrombosis. Such a method however would still be dependent on the rate of development of the arteriosclerotic process.

II. Changes in Blood Coagulation : The second method of clinical approach to the problem of aetiology has been an investigation of the clotting changes shown by the blood. Using the Waugh Ruddick (1944) heparin retarded clotting test, fifteen cases have been investigated during the first 24 hours after the onset. Eight showed normal clotting. Six showed /

showed definitely enhanced clotting, and the fifteenth gave a result in the lower limits of normal. Only two cases, one with normal clotting, and the one at the lower limit of normal, had a normal capillary resistance. All the others had fragile capillaries. In this test, blood is added to solutions of heparin in saline of strengths of 1/10th unit to 7/10ths unit heparin / $\frac{1}{2}$ c.c. saline. Nine tubes, - one empty, one with $\frac{1}{2}$ c.c. saline, and seven with $\frac{1}{2}$ c.c. of the seven strengths of heparin solution are set up and 1 c.c. of blood is added to each, after a clean vene-puncture. The clotting time of each tube is then determined at a room temperature of 18-20°C. Normally tube 9 (7/10ths unit heparin) clots last in about 60 minutes, but if enhanced clotting be present all the tubes will be clotted in about 30 minutes or less. (Figure 8).

As a general rule, an enhanced clotting tendency develops about the 3rd or 4th day after a myocardial infarct, but may be delayed until several days later, or occasionally may not develop. In the 6 cases mentioned above, who showed this change on the first day, it is possible that the enhanced clotting preceded the coronary artery thrombosis and was responsible for its development. Fullerton(1949) has suggested that the lipaemia following a fatty meal may be associated with accelerated clotting and induction of thrombosis in the coronary arteries. Post-operatively the /

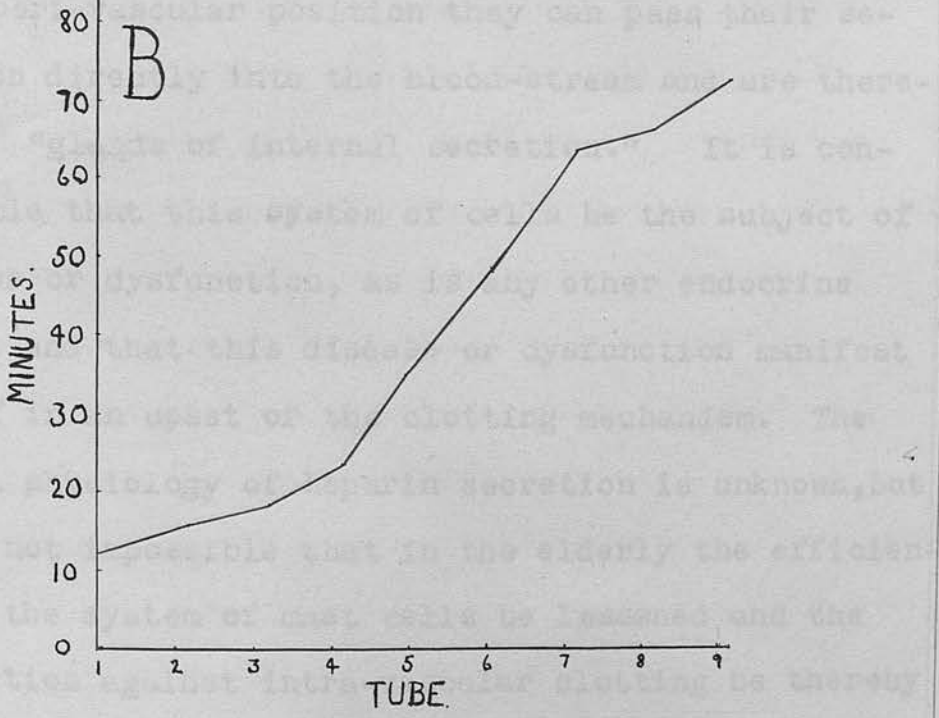
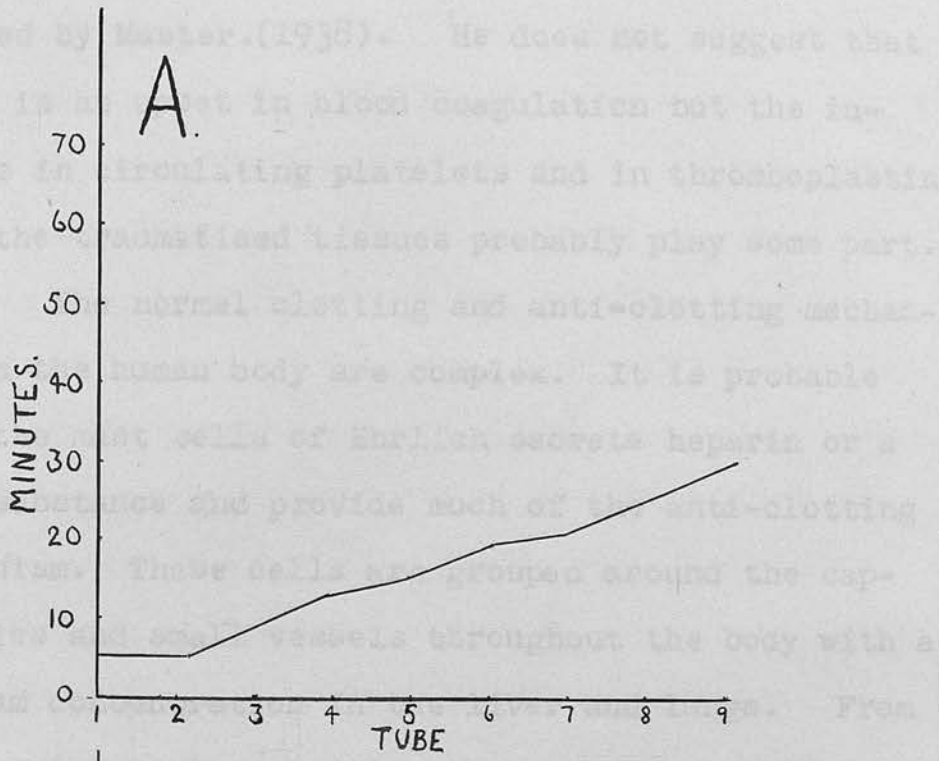


Figure VIII. Graphs illustrating (A) enhanced clotting, (B) normal clotting as demonstrated by the Waugh-Ruddick heparin retarded clotting test.

the occurrence of coronary thrombosis has been described by Master.(1938). He does not suggest that there is an upset in blood coagulation but the increase in circulating platelets and in thromboplastin from the traumatised tissues probably play some part.

The normal clotting and anti-clotting mechanism in the human body are complex. It is probable that the mast cells of Ehrlich secrete heparin or a like substance and provide much of the anti-clotting mechanism. These cells are grouped around the capillaries and small vessels throughout the body with a maximum concentration in the liver and lungs. From this peri-vascular position they can pass their secretion directly into the blood-stream and are therefore "glands of internal secretion." It is conceivable that this system of cells be the subject of disease or dysfunction, as is any other endocrine gland, and that this disease or dysfunction manifest itself in an upset of the clotting mechanism. The normal physiology of heparin secretion is unknown, but it is not impossible that in the elderly the efficiency of the system of mast cells be lessened and the protection against intra-vascular clotting be thereby reduced. Spontaneous clotting would probably not occur but any breach in endothelial continuity would tend to be followed by superimposed thrombus formation.

Whether or not an upset in the clotting mechanism be responsible for a coronary thrombosis, there /

there is little doubt that recurrence of infarction tends to occur during the first two or three weeks after the onset while the blood shows a marked clotting tendency. Four cases investigated had a recurrence while greatly enhanced clotting was present. Figures 9 and 10 illustrate two of these cases. One other case is of interest, although not seen until 1 month after the onset - Mrs E.T. aged 36 years, previously perfectly fit, had a myocardial infarct the day after the birth of her baby. The labour had not been prolonged and there had not been an excessive loss of blood. She was not hypertensive, but had arteriosclerotic peripheral and retinal arteries. The coronary arteries were probably also affected. Trauma to the tissues during labour had possibly liberated sufficient thromboplastin to upset the normal "clotting - anti-clotting" balance and initiate thrombosis in a diseased coronary artery.

Although an enhanced clotting tendency may be important, myocardial infarction may also occur even though the blood be rendered relatively incoagulable with dicoumarol. One middle-aged male was admitted ten days after a myocardial infarct and had a recurrence after eleven days on dicoumarol. His blood showed a prothrombin time in the middle of the therapeutic range. His capillary resistance was increasing and was almost within the normal range. His peripheral vessels were extremely arteriosclerotic and /

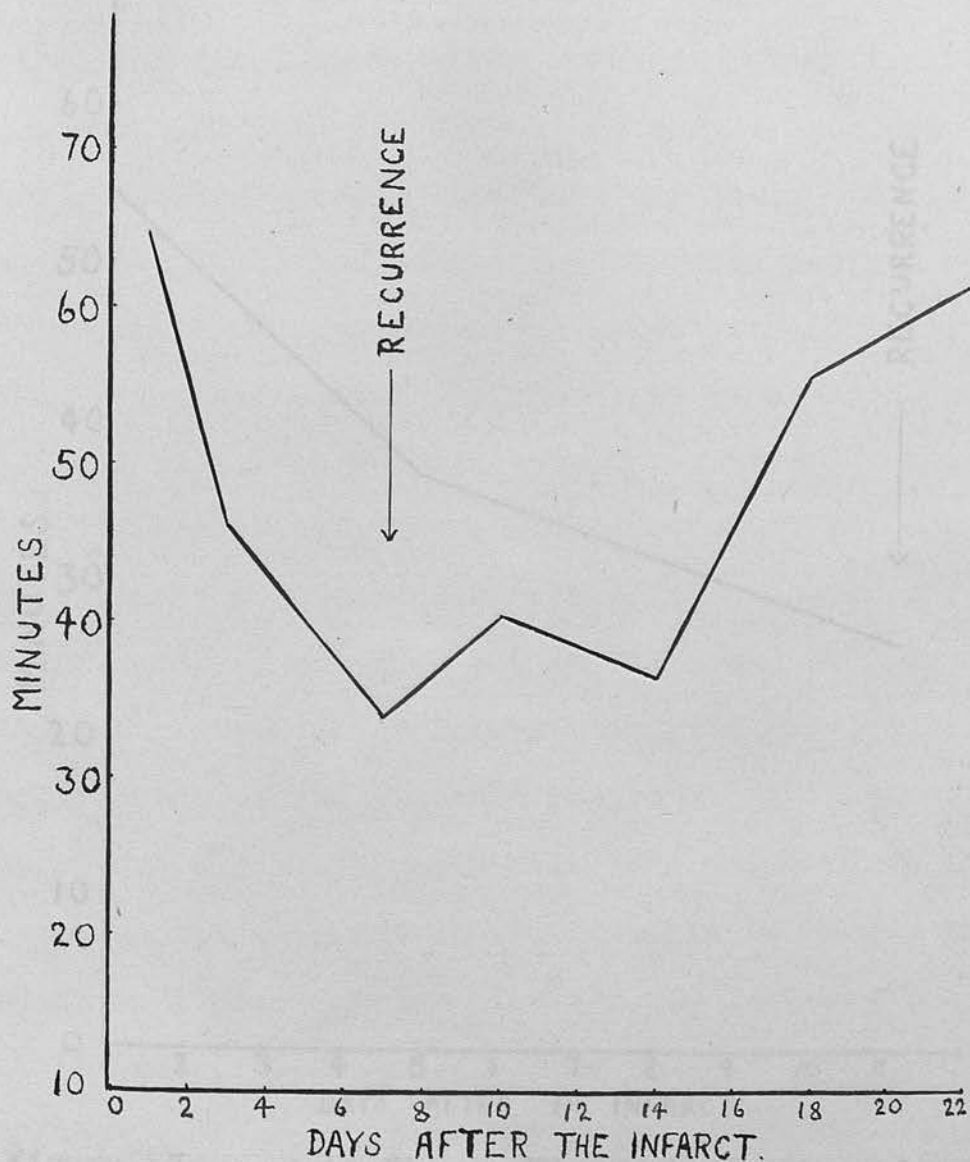


Figure IX. The graph records the clotting time of tube 9 (7/10ths unit of heparin / $\frac{1}{2}$ c.c. saline) of the Waugh-Ruddick heparin retarded clotting test, at intervals of a few days, after myocardial infarction, and demonstrates the development of a clotting tendency. A recurrence of myocardial infarction occurred while the enhanced clotting was present.

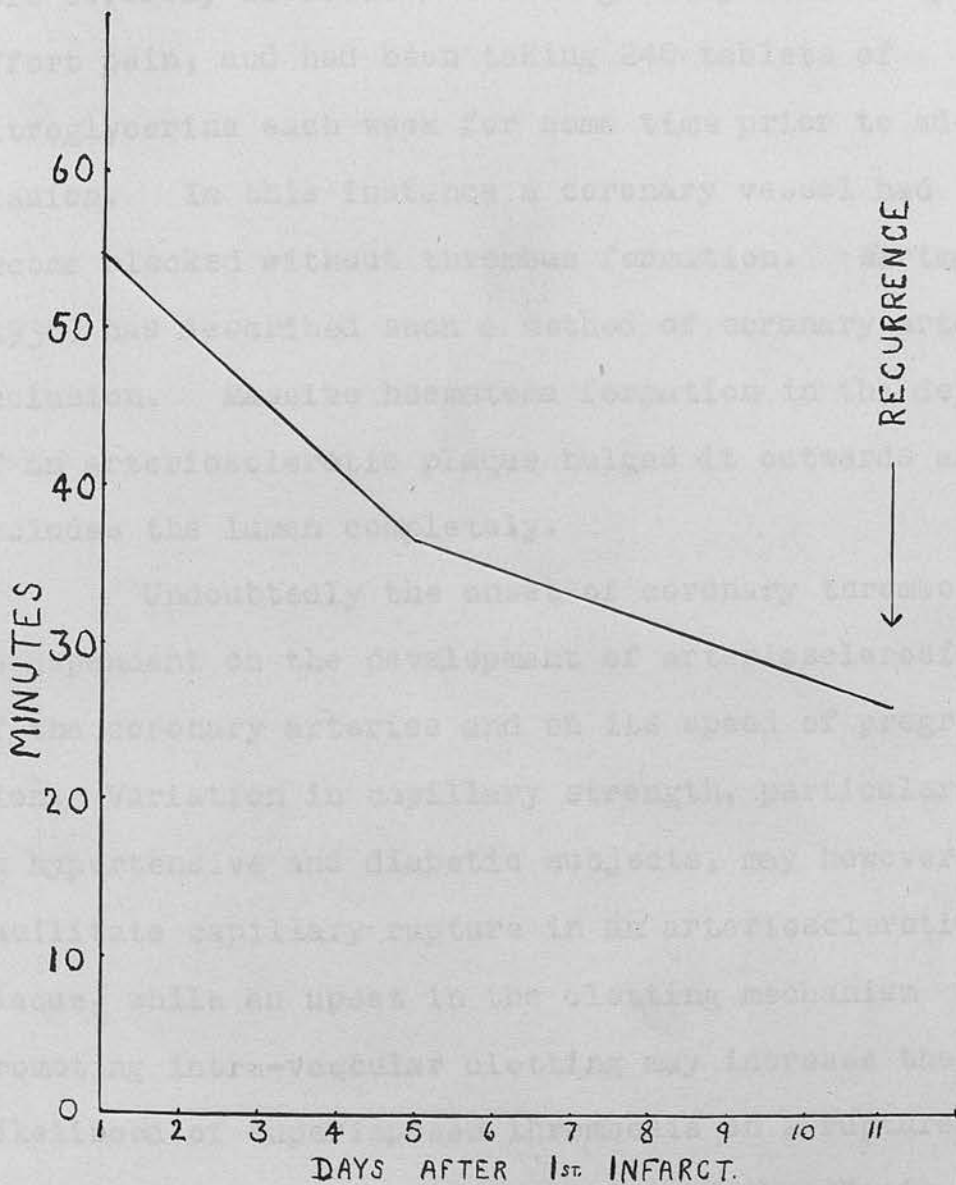


Figure X. As in Figure IX, the clotting times of tube 9 are recorded, and the development of a clotting tendency is demonstrated. A recurrence of myocardial infarction with death occurred while enhanced clotting was present.

and the history suggested that his coronary vessels were severely affected - he was greatly limited by effort pain, and had been taking 240 tablets of nitroglycerine each week for some time prior to admission. In this instance a coronary vessel had become blocked without thrombus formation. (Wartman (1938) has described such a method of coronary artery occlusion. Massive haematoma formation in the depths of an arteriosclerotic plaque bulges it outwards and occludes the lumen completely.

Undoubtedly the onset of coronary thrombosis is dependent on the development of arteriosclerosis of the coronary arteries and on its speed of progression. Variation in capillary strength, particularly in hypertensive and diabetic subjects, may however facilitate capillary rupture in an arteriosclerotic plaque, while an upset in the clotting mechanism promoting intra-vascular clotting may increase the likelihood of superimposed thrombosis on a ruptured capillary, or may conceivably initiate thrombosis in an arteriosclerotic vessel, even in the absence of capillary rupture.

In a personal communication (1950) Dr Scarborough states that in healthy, young and middle-aged people the normal capillary resistance in the three standard areas on the right forearm is -

Area /

101A.

Area I. 250-400 mm. Hg. negative pressure

" III. 300-450 "

" V. 350-500 "

There is no doubt however that in the elderly, normal figures may be considerably lower and it is not correct to accept the above standard as applicable to healthy persons over the age of 60 years.

The age distribution of the cases is shown in Table XVIII. The average age of the entire series was 53 years being 54.5 years for males and 55 years for females.

TABLE XVIII. Age and sex distribution of 100 cases of acute myocardial infarction.

Age	Total		Died within 6 wks.		Survivors	
	Male	Female	Male	Female	Male	Female
30	1	-	-	-	1	-
37	4	-	2	-	2	-
40	6	-	1	-	5	-
45	9	-	3	-	6	2
50	8	1	3	-	5	1
55	24	3	7	1	7	2
60	16	7	8	5	8	2
65	4	10	3	9	3	5
70	3	6	2	4	1	2
V. /		1	2	1	1	-
Total	70	30	30	16	40	14

V. ANALYSIS of 100 CASES of ACUTE MYOCARDIAL
INFARCTION TREATED CONSERVATIVELY.

(a) Clinical Details :

(1) Age and Sex.

Seventy infarcts occurred in males and thirty in females, giving a sex ratio of 2.33:1.

(As previously explained, page 88, this ratio is artificial and is probably about half the true ratio.)

The Age distribution of the cases is shown in Table XVIII. The average age of the entire series was 58 years being 54.5 years for males and 65 years for females.

TABLE XVIII. Age and sex distribution of 100 cases of acute myocardial infarction.

Age	Total		Died within 6 wks.		Survivors	
	Male	Female	Male	Female	Male	Female.
30	1	-	-	-	1	-
35	4	-	2	-	2	-
40	6	-	1	-	5	-
45	9	2	3	-	6	2
50	8	1	2	-	6	1
55	14	3	7	1	7	2
60	16	7	8	5	8	2
65	6	10	3	5	3	5
70	3	6	2	4	1	2
75	3	1	2	1	1	-
Total	70	30	30	16	40	14

(2) Immediate mortality.

Forty-six cases - 30 males and 16 females died within 6 weeks of the onset of the infarct. This mortality rate is high. It is lower among males (43%) than among females (53%). The average age of those dying was only slightly greater than the total average for each sex - males 55 years, and females 66 years. Twelve males died during the first 24 hours after the onset. Their average age was 52 years.

(3) Blood pressure level prior to the infarct.

Twenty-seven males (38.5%) and fourteen females (47%) were known to have been hypertensive before their myocardial infarct. A diastolic blood pressure of 90 mm. Hg. or more was taken as evidence of hypertension. In a further 41 cases - 30 males and 11 females - the previous blood pressure level was not known, while only fourteen males (20%) and five females (17%) were known to have had a normal pressure. Table XIX. records the age distribution of the patients in the three groups.

TABLE XIX. Blood pressure level prior to myocardial infarct in 100 cases.

Age	Male			Female		
	Hyper- tensive	Normo- tensive	Unknown	Hyper- tensive	Normo- tensive	Unknown
30	-	-	1	-	-	-
35	3	-	1	-	-	-
40	-	3	3	-	-	-
45	2	3	4	1	-	1
50	4	-	4	1	-	-
55	4	4	6	2	1	-
60	8	2	7	3	-	4
65	3	1	1	6	1	3
70	2	-	1	1	3	1
75	1	-	2	-	-	2
Total	27	13	30	14	5	11

The hypertensive males were older than the average for the series - they averaged 59 years, whereas the normotensive males were younger than the average - 53 years. In spite of this the same proportion of the normotensive and hypertensive males died in the first 6 weeks - 40%. Table XX. records the numbers dying in each group.

TABLE XX. /

TABLE XX. Mortality rate in the first 6 weeks according to the blood pressure level prior to the myocardial infarct.

	Male		Female	
	Total	Deaths	Total	Deaths
Hypertensive	27	11 (41%)	14	6 (43%)
Normotensive	13	5 (38%)	5	2 (40%)
B.P. unknown	30	14 (47%)	11	8 (73%)

(2) Angina Pectoris prior to the Infarct.

Thirty-four males (48.5%) and fourteen females (47%) had complained of effort pain prior to the myocardial infarct. Their average ages were similar to those of the whole series (56 years and 65 years, respectively.) Ten males and five females died. They averaged 62 years and 69 years respectively. Mortality was higher, however, among those giving no history of previous effort pain.

% Mortality.

	Male	Female.
Effort pain	29%	36%
No effort pain...	55%	69%

Those with no history of effort pain died at a younger age than those who had suffered effort pain -

		Male	Female
Average age of) (a) with effort pain		62 yrs.	69 yrs.
those dying) (b) no effort pain		57 yrs.	65 yrs.

Premonitory symptoms are not included in this analysis of effort pain.

(5) Body Weight.

Twenty males (28.5%) and thirteen females (43%) were overweight. Nine males and five females died; five of these males were under 60 years, whereas all the females were over 60 years. The obese males died at an earlier age than the non-obese - 57 years as against 60.5 years.

(6) Diabetes etc.

One male and one female had diabetes. Both survived. Two males and one female had syphilis. All three had aortic incompetence and all three died. One female had rheumatic heart disease, - mitral stenosis with auricular fibrillation and congestive heart failure. Her myocardial infarct was embolic in origin. One other female had myxoedema.

(7) First, second, and third infarct.

Seventy cases were admitted with their first myocardial infarct; twenty-five with their second infarct and five with their third infarct.

TABLE /

	Male	Female
1st infarct	35%	43%
2nd infarct	25%	25%
3rd infarct	5%	10%

TABLE XXI. Age and sex distribution for 1st, 2nd and 3rd myocardial infarct.

Age	Male			Female		
	1st	2nd	3rd	1st	2nd	3rd
30	1	-	-	-	-	-
35	3	-	1	-	-	-
40	4	1	1	-	-	-
45	5	4	-	1	1	-
50	6	2	-	1	-	-
55	10	4	-	2	1	-
60	12	4	-	5	2	-
65	4	1	1	8	2	-
70	1	1	1	3	2	1
75	3	-	-	1	-	-
Total	49	17	4	21	8	1

The mortality rate within the first 6 weeks of the onset increased after each successive infarct.

This is shown in Table XXII.

Table XXII. Mortality rate following 1st, 2nd and 3rd infarct.

	% Mortality.	
	Male	Female
1st infarct	35%	43%
2nd infarct	65%	75%
3rd infarct*	50%	100%

* The number of cases is too small to give accurate figures for comparison with the 1st and 2nd infarcts.

(8) Cardiac Grade prior to the Infarct.

Using the method of estimating cardiac function suggested by the American Heart Association the patients were grouped according to their cardiac grade prior to the infarct. Symptoms appearing for the first time within 2 weeks of the infarct were not considered, as it is probably that these were premonitory in nature. Eighteen cases were entirely symptom free but the great majority - 60 cases - had some slight limitation of their activities. Thirteen were severely limited, and seven were in congestive heart failure.

TABLE XXIII. Cardiac grade prior to the myocardial infarct.

Age	Male				Female *			
	I	IIA	IIB	III	I	IIA	IIB	III
30	1	-	-	-	-	-	-	-
35	1	1	-	2	-	-	-	-
40	3	3	-	-	-	-	-	-
45	3	3	2	1	1	1	-	-
50	1	8	-	1	-	1	-	-
55	2	7	2	2	-	1	1	-
60	3	11	2	-	-	2	3	1
65	1	5	-	-	2	7	1	-
70	-	2	1	-	-	4	1	1
75	-	3	-	-	-	1	-	-
Total	15	43	7	5	3	17	6	2

* In the case of two females, the previous cardiac grade is unknown.

The grade I males averaged 51 years of age, whereas the grade IIA males averaged 59 years, and the grade IIB, 58 years. The grade III males averaged only 47 years. Females did not show any striking variation in the average age of the four groups. The mortality rate increased with each descent in cardiac grade, reaching 100% in grade III.

TABLE XXIV. Immediate mortality after myocardial infarction according to the cardiac grade prior to the infarct.

	Grade I		Grade IIA		Grade IIB		Grade III	
	M	F	M	F	M	F	M	F.
Total Number	15	3	43	17	7	6	5	2
Mortality Rate	13%	33%	42%	41%	71%	83%	100%	100%

(9) Time of onset :

The time of the symptoms of myocardial infarction was accurately known in only 51 cases. Twenty-five began between 8 a.m. and 8 p.m., and twenty-six between 8 p.m. and 8 a.m.. The early morning and the early afternoon were the two peak periods. Nine cases began between 2 a.m. and 4 a.m., and ten between 1 p.m. and 3 p.m..

(10) /

10. Presenting Symptom :

Pain was the predominant symptom, being present in 82 cases - 55 males and 27 females. The substitution symptoms or features were -

- (1) sudden dyspnoea - 5 cases.
- (2) tight feeling in chest and dyspnoea - 2 cases.
- (3) weakness, tightness in chest and dyspnoea - 1 case.
- (4) collapse. 2 cases.
- (5) sudden unconsciousness . . . 3 cases.
- (6) worsening of congestive heart failure - 3 cases.
- (7) sudden death 2 cases.

Thirteen of the 18 painless cases died, a mortality rate of 72%.

In 66 cases the pain was described as being either substernal or across the front of the chest with the point of maximum severity beneath the sternum. Thirty-four cases had pain in the arms - in the left arm only, 18 cases; in the right arm only 1 case; in both arms 15 cases. Other sites in which pain was experienced were (a) the inter-scapular region 10 cases; (b) both sides of the neck, 6 cases; (c) left side of neck only, 2 cases; (d) Jaw 4 cases; (e) epigastrium 4 cases; (f) beneath the left breast, 4 cases; (g) left shoulder 3 cases; (h) left side of chest 2 cases; (i) right side of chest, inferior angle of right scapula, back of left side of chest, both shoulders, root of neck, left upper abdomen, and left ante-cubital fossa to wrist, 1 case each.

Sixteen/

Sixteen cases experienced pain in a site
 other than across the front of the chest/^{or}in the mid
 line beneath the sternum. Nine had pain on other
 parts of the chest. In three it was epigastric in
 position, while in the four remaining cases pain was
 felt (a) at the root of the neck; (b) at the left
 shoulder; (c) from the left ante-cubital fossa to
 the wrist and (d) in the left upper abdomen.

(11) Electrocardiography :

In 85 cases, one or more electrocardio-
 grams were obtained. The chest leads in 73 cases
 were of the CF type, and in the great majority of
 cases only leads C2F and IVF were recorded. In the
 12 remaining cases, unipolar chest and limb leads
 were recorded in addition to the standard limb leads.
 The records in this series will therefore not be
 analysed in detail. The location of the myocardial
 infarct as indicated by the electrocardiographic
 pattern is shown in Table XXV.

TABLE XXV. Electrocardiographic localization of
 the site of myocardial infarction in 85
 cases, and mortality rate for each
 group.

	Male			Female.		
	Anter- ior.	Poster- ior.	Atyp- ical.	Anter- ior.	Poster- ior.	Atyp- ical.
Total Num- ber.	25	19	11	14	7	4
% Mortal- ity	36%	31.5%	27%	28.5%	57%	75%

In addition 3 cases showed evidence of bundle branch block without other evidence of infarction; one case showed both anterior and posterior infarction; and in one other the record was entirely normal. This last case, a male aged 64 years, had an otherwise typical myocardial infarct both as regards history and clinical course. The average age of the males in the three main groups is of interest. Those with an atypical electrocardiogram averaged 51 years, those with an anterior infarct, 55 years, and those with a posterior infarct 61 years. In both the "anterior" and "posterior" groups, the elderly tended to die and the young to survive, - those dying averaged 61.5 years and 66 years respectively.

(12) Degree of shock at the onset:

The severity of the shock present at the time of the onset of the infarct could be estimated in all but 6 cases. It was graded as being (1) marked, (2) mild, or (3) absent, by a study of (a) the general appearance of the patient, particularly the colour of the skin and mucous membranes, (b) the profuseness of sweating, if present, (c) the sensation of weakness or exhaustion experienced by the patient, (d) the character of the pulse and its rate; (e) the blood pressure and pulse pressure, and (f) the rate and type of respirations. In 30 cases, the shock /

shock was marked, in 27 it was mild, and 37 cases were not shocked. As shown in Table XXVI., a severe degree of shock is associated with a high mortality. The duration of the shock is also important as in four females, its persistence was the major factor in causing death.

TABLE XXVI. Correlation of mortality rate and severity of shock at the onset in 94 cases of myocardial infarction.

Degree of Shock.	Male			Female.		
	Marked	Slight	Absent	Marked	Slight	Absent.
Number	21	20	25	9	7	12
Mortality	81%	25%	24%	66%	57%	50%

Among the males, and to a less extent among the females, those who had a severe degree of shock and died were of the average age for the series, but the deaths, among those showing a mild degree of shock, or no shock at all, were among the elderly.

(13) Heart Sounds :

The character of the heart sounds heard during the first few days after the infarct are listed in Table XXVII.

TABLE XXVII. /

TABLE XXVII. Character of heart sounds in 100 cases of myocardial infarction.

Type of Heart Sound.	Total		Died in Ward.	
	M.	F.	M.	F.
Gallop	3	3	3	2
Tic-Tac	3	3	3	2
Faint	31	9	9	6
Poor Quality	12	5	5	4
Inaudible	4	-	4	-
Normal	15	8	2	2
Not Recorded	2	2	1	-

Most commonly the heart sounds were normal but faint. Gallop rhythm and tic-tac rhythm were not frequently heard, nor was it common for no heart sounds to be detected. This was fortunate as such findings are associated with a high mortality. Among those having faint or normal heart sounds, the elderly tended to die, and the young to survive.

(14) Blood pressure after the infarct.

Blood pressure records are available for analysis in 90 cases. Five of the remaining ten cases died before the pressure was estimated, and in the other five, no pressure could be recorded. These also died. Table XXVIII. groups the lowest systolic blood pressure levels recorded in the days following the infarct.

TABLE XXVIII. /

TABLE XXVIII.

Lowest systolic blood pressure recorded after myocardial infarction in 90 cases.

	Total		Died in Ward	
	M	F	M	F
B.P. above 100 mm. Hg.	45	21	14	9
B.P. below 100 mm. Hg.	16	8	8	6

The mortality rate was considerably increased when the systolic blood pressure fell to under 100 mm. Hg.. In each group, except that of females with a systolic pressure of under 100 mm. Hg., the deaths occurred among the elderly. This was most noticeable among males with a systolic pressure greater than 100 mm. Hg.; those dying averaged 61 years, and those surviving 53.5 years.

(15) Pulse pressure after the infarct:

The pulse pressure records were divided into (a) 30 mm. Hg. or more, (b) 20-30 mm. Hg. and (c) under 20 mm. Hg. Table XXIX. shows the distribution in these groups.

TABLE XXIX. Pulse pressure records in 86 cases of myocardial infarction.

	Total		Died in Ward.	
	M.	F.	M.	F.
Over 30 mm. Hg.	44	22	11	10
20-30 mm. Hg.	12	3	6	1
Under 20 mm. Hg.	2	3	1	3

In 4 cases, no diastolic level could be recorded. All four died. The mortality rate increased as the pulse pressure fell - 31% over 30% mm. Hg., 47%, 20-30 mm. Hg., and 80% under 20 mm. Hg. When the pulse pressure was over 30 mm. Hg., age was of importance in prognosis - the elderly in both sexes died. On the other hand, when the pulse pressure fell to under 30 mm. Hg., age was not important.

(16) Pulse rate after the infarct:

Records of pulse rate are available in all cases. These were grouped, according to the most rapid rate at any stage after the infarct, into (a) over 120/min., (b) 100-120/min., and (c) under 100/min.

Table XXX. Most rapid pulse rate in 100 cases of myocardial infarction.

	Total		Died in Ward.	
	M.	F.	M.	F.
Over 120/min.	6	6	6	4
100 - 120/min.	26	11	15	6
Under 100/min	38	13	9*	6

* Seven died in the first 24 hours.

Mortality rate increased as the pulse rate increased. In cases showing a rate of under 100/min., or over 120/min., age was of little consequence in determining the /

the outcome. With pulse rates of between 100 and 120/min., however, age was of extreme importance -

	Male	Female
Average age of (a) those dying	63 yrs.	70 yrs.
(b) those surviving	54 yrs.	59 yrs.

In 43 of the 49 cases with a pulse rate of 100/min. or more, the most rapid rate was recorded within the first week after the infarct. Twenty-seven of these 43 cases (63%) died. Of the six cases having a pulse rate of over 100/min. at some time after the first week, four (66%) died.

(17) Heart size:

Heart size was determined in 93 cases, clinically or by XRay examination of the chest, or in some cases only by autopsy examination. Seventy cases had enlarged hearts, while 23 had no detectable enlargement.

TABLE XXXI. Heart size in 93 cases of myocardial infarction.

	Total		Died in Ward	
	M.	F.	M,	F.
Cardiac Enlargement	49	21	26	11
No Enlargement	18	5	2	1

The mortality rate was higher when cardiac enlargement was present than when there was no enlargement. The males showing a heart of normal size were on the average /

average $5\frac{1}{2}$ years younger than those with a large heart. The two female groups were of the same age. Correlation of the heart size with the cardiac grade present prior to the infarct is of interest.

<u>Males</u>	Grade I.		Grade IIA.	
	Total	Died	Total	Died
No Cardiac Enlargement	5	-	13	2
Cardial Enlargment	9	2	28	14

The combination of cardiac enlargement and a grade IIA functional capacity was associated with a high mortality. No male in grade IIB or III had a heart of normal size. The findings among the females were essentially similar except that one female in grade IIB had a heart of normal size. She survived.

(18) Degree of leucocytosis:

Records of the leucocyte count done in the days following the infarct are available in 74 cases. These have been grouped as (a) above 10,000 /c.m. and (b) under 10,000/c.m..

TABLE XXXII. Highest leucocyte count recorded after 74 cases of myocardial infarction.

	Total		Died in Ward.	
	M.	F.	M.	F.
Over 10,000/c.m.	22	13	9	5
Under 10,000/c.m.	31	8	8	3

A fatal outcome was more common in the cases developing a leucocyte count of over 10,000/c.m., than in those with a count of under 10,000/c.m.. In each group, both male and female, the average age of the fatal cases was greater than that of the survivors. e.g. Cases with a count of under 10,000/c.m.. -

M. F.

Average age of (a) those dying 63 yrs. 72 yrs.
(b) those surviving 54.5 yrs. 60 yrs.

(19) Blood Sedimentation Rate:

In only 45 cases was the blood sedimentation rate estimated. Twenty-three cases had a maximum reading of over 25 mm/hr. and of these eight died. Twenty-two had a maximum reading of under 25 mm/hr. and of these five died. In several of the cases, however, only one or two estimations were made, and the true maximum was undoubtedly missed.

(20) Body temperature :

Records of body temperature are available for analysis in all the cases. The maximum recordings have been grouped as (a) over 100°F (b) up to 100°F. and (c) normal.

TABLE XXXIII. Maximum temperature recorded after 100 cases of myocardial infarction.

	Total		Died in Ward	
	M.	F.	M.	F.
Over 100°F	11	6	4	2
Up to 100°F	26	8	8	6
Normal	33	16	18	8 2

1. Nine died in the first day. 2. one died within 30 hours.

The elderly of both sexes tended to develop a high temperature. Among males with a temperature of over 100°F., those who died averaged 65.5 yrs. of age as against the 55.5 yrs. of the survivors. In the group with no rise of temperature, age was of no importance in prognosis.

(b) Treatment:

A routine system of treatment was adopted for the entire series. The measures consisted of (a) rest in bed in the most comfortable position - generally flat with 2 pillows. (b) No activity on the part of the patient for 3 weeks and then a very gradual return to activity. (c) Morphine for relief of pain, (d) sedation with phenobarbitone during the day and a quicker acting sedative at night. (e) Light diet. (f) Attention to the bowels, with enemata if required. (g) Graduated exercises for the limbs and breathing exercises, under a physiotherapist from the 4th week onwards. (h) Treatment of the complications as they arose - digitalis mercurial diuretics, oxygen and morphine as needed for heart failure, quinidine for ventricular tachycardia etc.. At the end of the 5th week, or during the 6th week the patient was allowed up, and after a few days was discharged home to convalesce.

(c) Course after myocardial infarction:

(1) Complications. Only 48 of the 100 cases had /

had an uneventful convalescence, complications occurring in 33 males and 19 females. Fifteen males and fourteen females showed more than one complication. Table XXXIV, (page 122) lists the various complications. Heart failure was the most common, occurring in 31 cases - eighteen of congestive heart failure and thirteen of left ventricular failure. Only four of the 31 cases survived. Thromboembolic complications occurring during the first 6 weeks are listed in Table XXXV. (page 123). Thirty episodes took place in 24 patients - 13 males and 11 females. Recurrence of myocardial infarction was the most common event, occurring twelve times in ten cases. Apart from one case of pulmonary infarction, and another of thrombo-phlebitis, all episodes in males over 60 years occurred in males who died. Recurrence of myocardial infarction occurred in four elderly males all of whom died, and in four young males, all of whom survived. Age was of less importance among the females, as only one case under 60 years suffered any embolic complication.

The various forms of arrhythmia encountered are listed in Table XXXVI. (page 124). Nineteen arrhythmias occurred in fourteen cases - ten males and four females. Ten cases died. Apart from two males aged 50 years and 59 years, all the cases were 60 years or over. Auricular fibrillation and paroxysmal /

TABLE XXXIV.

Complications occurring in the first 6 weeks after myocardial infarction in 100 conservatively treated cases.

	10	7	5	10	5	8	1	1	1	1	1	1
C.H.F. L.V.F. Pericardial Friction												
Arrythmia												
Thrombotic Complications												
Embolism												
Myocardial Infarction												
Recurrence of Myocardial Infarction												
Anginal Pain												
Cardiac Aneurysm												
Rupture of I.V. septum												
Uraemia												
Diphtheria												
Urinary Infection												
Total	10	7	5	10	5	8	1	1	1	1	1	1
Died in Ward	8	6	3	7	3	4	-	-	-	-	-	-
Total	8	6	2	4	10	2	-	-	1	2	-	-
Died in Ward	8	5	2	3	4	1	-	-	1	-	-	-

C.H.F. = Congestive Heart Failure. L.V.F. = Left Ventricular failure.
I.V. Septum = Inter-ventricular septum.

1. Excluding recurrence of myocardial infarction.
2. This was a clinical diagnosis only as autopsy examination was refused.

TABLE XXXV. Thrombo-embolic complications occurring in the first 6 weeks after myocardial infarction.

		Cere- bral Embo- lism.	Pulmon- ary In- farct.	Thrombo- Phlebi- tis.	Recur- rence of Myo- cardial Infarc- tion.	Periph- eral Em- bolism.	Mesen- teric Embol- ism.
Male	Total	2	1	1	8 ¹	1	-
	Died in Ward	2	-	-	4	1	-
Female	Total	1	5 ²	3	2	2	1
	Died in Ward	-	3	-	1	1	-

1 In two cases each sustained two recurrences of myocardial infarction. One died.

2 One case had two pulmonary infarcts. She died.

TABLE XXXVI. /

TABLE XXXVI.

Incidence of arrhythmias recorded after 100 myocardial infarcts.

	Auricular Fibrillation.	Auricular Flutter.	Auricular Tachycardia. dia.	Paroxysmal Auricular Tachycardia. dia.	Paroxysmal Auricular Tachycardia. 2:1 A.V. Block.	Wenchebach Periods.	Com-plete Heart Block.	Auricular Standstill. of Sinus Rhythm.	Disturbance of Sinus Rhythm.	Paroxysmal Ventricular Tachycardia
Male	4	-	2	2	2	1	2	1	-	-
Total died in Ward.	3	-	2	2	1	-	1	-	-	-
Female	1	1*	1	-	1*	-	-	-	-	1
Total died in Ward.	-	1	1	-	1	-	-	-	-	1

* Clinical diagnosis only. In one the ventricular rate periodically doubled or halved its rate, while in the other the ventricular rate was regular at 40/min..

paroxysmal auricular tachycardia were the most common, occurring five times each. On two occasions the auricular tachycardia was associated with a 2:1 auriculo-ventricular block. One male who survived showed three forms of disturbance of auricular activity - auricular fibrillation, auricular standstill, and a marked disturbance of the sinus rhythm. The other three survivors showed (1) complete heart block which later disappeared, (2) Wenchebach periods and (3) auricular fibrillation.

(2) Cause of death:

Death occurred most commonly on the first day or within the first two weeks. Twelve males (40%) died on the first day, and 21 (70%) in the first two weeks; no female died on the first day, but 13 (81%) died during the first 2 weeks.

Table XXXVII. (page 126) lists the causes of death

In several cases, more than one factor played a part, but only the main factor is listed. Heart failure was the most common cause, accounting for 50% of the /deaths after the first day. Left ventricular failure and

congestive heart failure were equally common among the males, but in the majority of the female cases, peripheral congestion had developed prior to death.

In 5 cases, death occurred suddenly and for no apparent reason. Rupture of the infarct was found at autopsy in two of these cases. Six other cases died suddenly /

TABLE XXXVII. Cause of death in 46 cases of myocardial infarction.

	First 24 hrs.	C.H.F.	L.V.F.	Recur- rence.	Persis- tent Shock.	Arryth- mia.	Hemi- pleg- ia.	Sud- den.	Urae- mia.
Male	12	5	5	2	-	1	1	3	1
Female	-	7	1	1	4	1	-	2	-
Total	12	12	6	3	4	2	1	5	1

suddenly - five were in congestive heart failure and were being treated with digitalis, while the 6th had a recurrence of myocardial infarction. Only one death could be attributed directly to an embolic episode. This was a cerebral embolus which caused a complete hemiplegia. In four women, persistence of a severe degree of shock for several days after the onset was the major factor in causing death.

(3) Digitalis Therapy:

Digitalis was used to treat 16 cases - twelve in congestive heart failure, three in left ventricular failure, and one male with paroxysmal auricular tachycardia. This male had become unconscious and was in fact uraemic. Four cases recovered - two males in congestive heart failure with paroxysmal arrhythmias (one complete heart block and one auricular fibrillation); and two cases (one male one female) in left ventricular failure. One other male responded well /

well to digitalis and was recovering, but died of a fresh myocardial infarct, four weeks after the digitalis was stopped.

Only one thrombotic episode - a case of thrombo-phlebitis - occurred while digitalis was being given. Two other episodes - one a recurrence of myocardial infarction, and the second a case of thrombo-phlebitis - occurred 5 days after a course of digitalis had been stopped. No embolic phenomena occurred. Of the eleven cases who died while receiving digitalis, or in the gap of the few days between digitalis courses, six died suddenly. In one, death was associated with a recurrence of myocardial infarction, but in the other 5 cases, no cause of death was established. These five cases comprise nearly half the cases of sudden death in the entire series (11 cases).

Mercurial diuretics were used in 6 cases of congestive heart failure to supplement digitalis therapy. Quinidine was used twice - once to treat paroxysmal ventricular tachycardia, and once for paroxysmal supra-ventricular tachycardia. Both cases died.

(b) Pathology:

Thirty-five of the 46 cases dying in the first 6 weeks came to autopsy. In all but one - the case of rheumatic heart disease - the coronary arteries /

arteries were the seat of arteriosclerosis of moderate or marked degree. In eleven cases a recent thrombus was found blocking an artery. The blocked arteries were (a) anterior descending branch of left coronary artery, 7 cases, (b) circumflex branch of left coronary artery, 2 cases, (c) main left coronary artery 2 cases, (d) right coronary artery 1 case. In one case two recent arterial thromboses were found. This incidence of fresh thrombosis in the coronary arteries may be low, as in 9 cases no specific mention of a search for a thrombus was made in the autopsy report. Endocardial mural thrombus had formed in 17 cases. In one there was thrombus formation in both ventricles, while in one other the right auricle contained a thrombus. Sixteen of the eighteen cases without mural thrombus died in the first week, seven in the first day. Those with mural thrombus formation died at intervals of from 1 day to 5 weeks after the onset. Three of these cases dying on the first and second days showed mural thrombus which was probably associated with an earlier myocardial infarct, and not with the infarct causing death. If cases dying during the first week be excluded, the incidence of mural thrombus formation becomes much higher - 13 out of 15 cases (87%) were affected. Ten of these 13 cases showed peripheral and pulmonary infarcts - 6 in the kidneys, 5 in the lungs, and 3 in the spleen. Only four of these episodes had been diagnosed clinically. In /

In one case in which both lungs were involved, the condition was a local thrombosis. Only one case without mural thrombus showed a peripheral infarct - in the spleen. In neither case in which rupture of the infarcted area occurred was there mural thrombus formation.

The weight of the heart was known in 31 cases. It ranged from 300 Gms. to 750 Gms.. All but three were over 400 Gms., with the majority weighing between 400 Gms. and 500 Gms.. In 20 cases the infarcted area was described as "large", "massive" or "extensive", while in the remaining 15 cases it was of moderate size or was small. The finding of a massive infarct at autopsy was not associated with the constant presence of any particular clinical feature or group of features during life. Of the 20 cases, three had been in cardiac grade I. prior to their infarct, 13 were in grade IIA, 1 in grade IIB, and 2 in grade III. One was not classified. Shock was marked in only 8 cases at the time of onset, and in only 5 did the systolic blood pressure fall to under 100 mm. Hg.. Six cases had a pulse pressure of under 30 mm. Hg.. The most common finding was a rapid heart rate - 14 cases had a pulse rate of over 100/min., and of the remaining 6 cases, one had complete heart block, and another auricular tachycardia with 2:1 A.V. block. The character of the heart sounds was known in all but one case. 7 had faint heart sounds, 6 had /

had poor quality sounds, 2 had gallop rhythm, and two had tic-tac rhythm, while in the remaining 2 cases the heart sounds were of normal character and intensity. Congestive heart failure supervened in 10 cases. The cause of death varied. Two died on the third day and 2 others on the 4th and 5th days from persistence of a severe degree of shock. One developed a hemiplegia and died, while another became uraemic. Two died of left ventricular failure, and two of congestive heart failure. Nine deaths occurred suddenly. Two were associated with rupture of the infarcted area and one with a fresh myocardial infarct; three others had been receiving digitalis.

VI. THE IMMEDIATE PROGNOSIS in MYOCARDIAL
INFARCTION.

The 100 cases reported in section V. have been analysed with the object of assessing the relative value of the various clinical features in determining the immediate prognosis. "Immediate" is used to signify the first 6 weeks after the myocardial infarction, while the patient is in bed in hospital. No single feature determines the outcome in any case and it is only by a consideration of the composite picture presented by all the features in each case that the immediate prognosis may be estimated.

The three factors of major importance are (1) the cardiac grade prior to the myocardial infarct, (2) the age of the patient, and (3) the size of the heart. These provide information as to the state of the myocardium prior to the infarct and form the foundation on which a prognosis is to be based.

If a patient is in cardiac grade III when myocardial infarction occurs, death is inevitable and may be very rapid. (Figure 11). Grade IIB is only slightly less serious. If death does not occur quickly, there is, with rare exceptions, a progressive increase in the degree of cardiac failure. In these rare cases which recover, the myocardial infarct is presumably small, and rest in bed, possible with the aid of digitalis, enables the patient to compensate for /

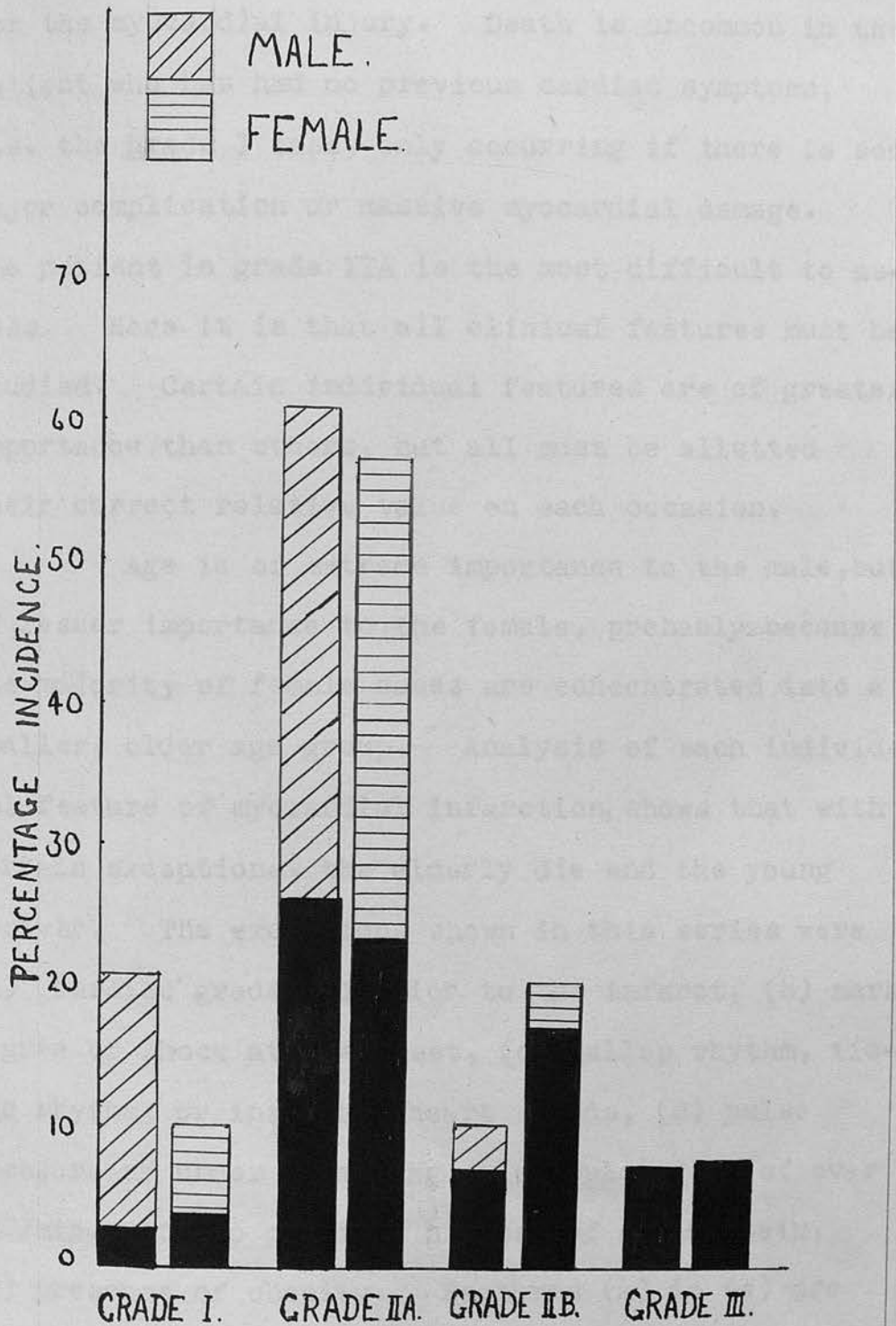


Figure XI. The distribution of the conservatively treated cases in the cardiac grades prior to myocardial infarction is illustrated. The proportion of cases dying in each grade is shown in black.

for the myocardial injury. Death is uncommon in the patient who has had no previous cardiac symptoms, i.e. the grade I case, only occurring if there is some major complication or massive myocardial damage.

The patient in grade IIA is the most difficult to assess. Here it is that all clinical features must be studied. Certain individual features are of greater importance than others, but all must be allotted their correct relative value on each occasion.

Age is of extreme importance to the male, but of lesser importance to the female, probably because the majority of female cases are concentrated into a smaller, older age group. Analysis of each individual feature of myocardial infarction, shows that with certain exceptions, the elderly die and the young recover. The exceptions shown in this series were (a) cardiac grade III prior to the infarct, (b) marked degree of shock at the onset, (c) gallop rhythm, tic-tac rhythm, or inaudible heart sounds, (d) pulse pressure of under 30 mm. Hg., (e) pulse rate of over 120/min., (f) no previous history of effort pain, (g) presence of obesity. Features (a) to (e) are only found in the seriously or gravely ill and are associated with a poor prognosis at any age. By way of contrast, analysis of the cases showing (a) good quality heart sounds, (b) a systolic blood pressure of over 100 mm. Hg., (c) a mild degree of shock at the /

the onset, and (d) a pulse rate of 100-120/min., all bring out the importance of age. (Figure 12). The males who had good quality heart sounds but died averaged 60 years of age, while those who survived averaged 52 years. The corresponding ages for the females were 65 years and 61 years.

Heart size is closely associated with age and cardiac grade. A heart of normal size is commonly found among the young, and it is with increasing age that enlargement occurs. Similarly patients in cardiac grade I commonly have a heart of normal size, but in grade IIA cardiac enlargement is frequent, and in grades IIB and III it is the rule rather than the exception. In grade IIB only one case, a female, had a heart of normal size.

Grade IIA males with a heart of normal size seldom die if the first day is survived. Even a recurrence of myocardial infarction (twice in one patient) did not seriously retard convalescence in two cases. In the presence of cardiac enlargement however, the grade IIA male is in much greater danger of death. Of the 28 males in this group, 14 died. The average ages of those dying and those surviving were closely similar (61 years and 60 years respectively). Three died on the first day, and one died in uraemia. Of the remaining ten, three developed heart failure which proved fatal, and in seven, deterioration and death were due to some complication - rupture /

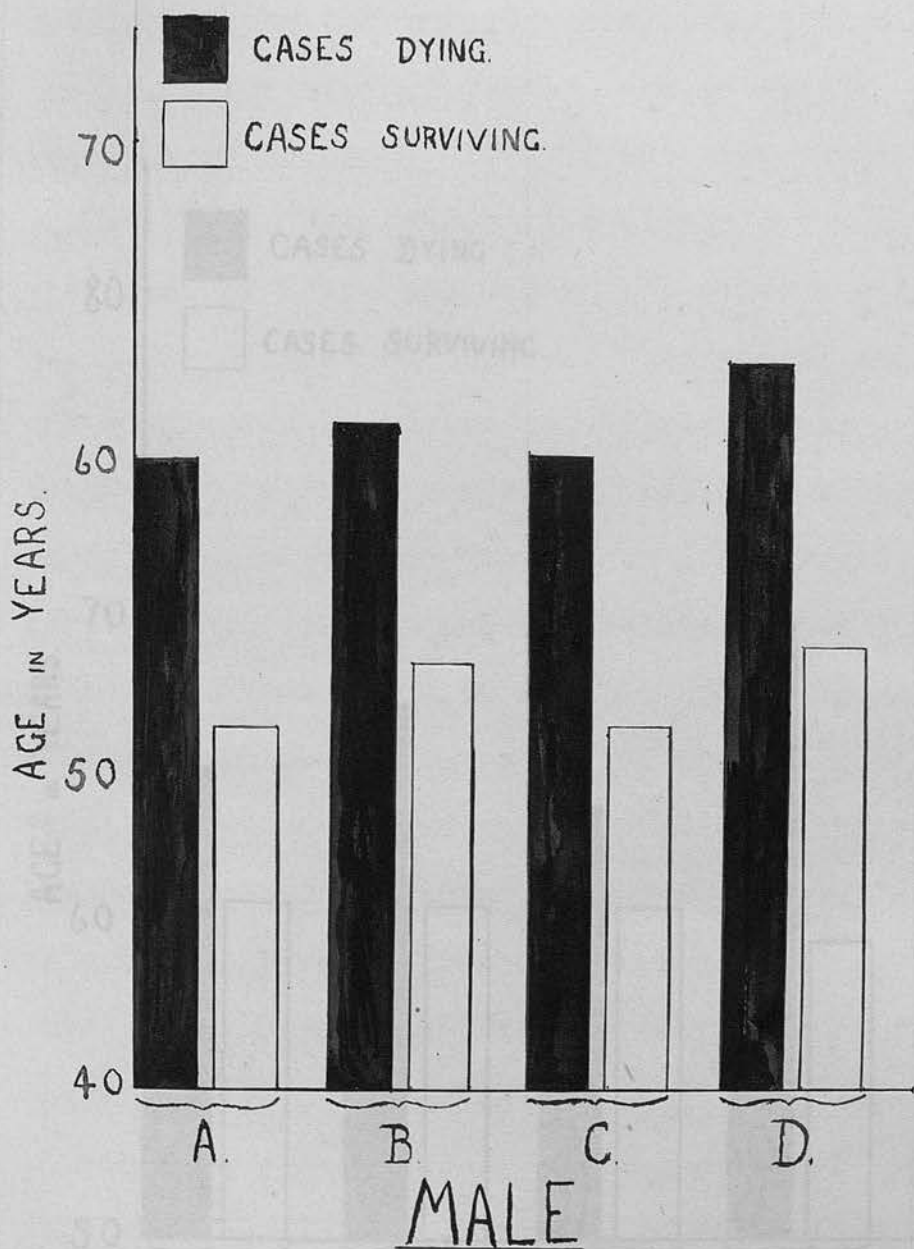


Figure XIIA. The disparity in ages of (a) those dying & (b) those surviving myocardial infarction treated along conservative lines, is illustrated, as occurring among the cases showing (A) good quality heart sounds, (B) systolic B.P. over 100 mm. Hg., (C) mild degree of shock at the onset, (D) pulse rate 100-120/min..

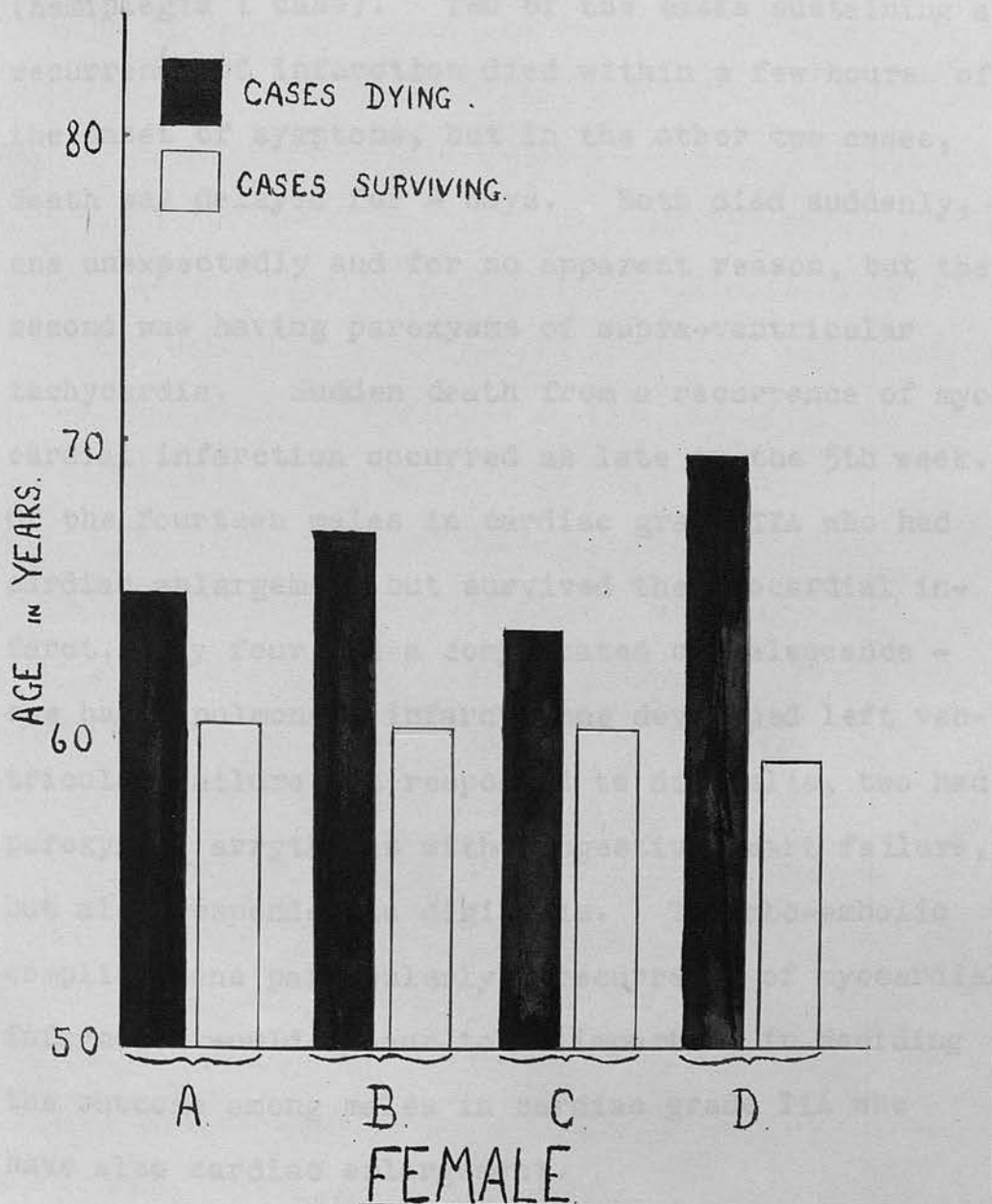


Figure XIIB. The disparity in ages of (a) those dying & (b) those surviving myocardial infarction treated along conservative lines, is illustrated, as occurring among the cases showing (A) good quality heart sounds, (B) systolic B.P. over 100 mm. Hg., (C) mild degree of shock at the onset, (D) pulse rate 100-120/ min..

rupture of the infarct (2 cases), recurrence of myocardial infarction (4 cases), and an embolic episode (hemiplegia 1 case). Two of the cases sustaining a recurrence of infarction died within a few hours of the onset of symptoms, but in the other two cases, death was delayed for 4 days. Both died suddenly, one unexpectedly and for no apparent reason, but the second was having paroxysms of supra-ventricular tachycardia. Sudden death from a recurrence of myocardial infarction occurred as late as the 5th week. Of the fourteen males in cardiac grade IIA who had cardiac enlargement but survived the myocardial infarct, only four had a complicated convalescence - one had a pulmonary infarct, one developed left ventricular failure but responded to digitalis, two had paroxysmal arrhythmias with congestive heart failure, but also responded to digitalis. Thrombo-embolic complications particularly a recurrence of myocardial infarction would appear to be important in deciding the outcome among males in cardiac grade IIA who have also cardiac enlargement.

Of the females in cardiac grade IIA who died (7 cases) only one was known to have a heart of normal size. She died 30 hours after the onset of her symptoms. Three had large hearts; one died on the first day, and the two other cases died from heart failure. Three other females in grade IIA died whose heart size /

size was unknown- two from persistent shock, and one from a recurrence of myocardial infarction. Ten females in cardiac grade IIA survived. Seven were known to have enlarged hearts, and of these only two showed complications - one had a pulmonary infarct, and the other developed left ventricular failure which was relieved by digitalis. Complications of a thrombo-embolic nature would therefore not appear to be important in influencing the course of the grade IIA female - at least in this small series.

Sex is of minor importance in prognosis compared with age, cardiac grade, and heart size. Over the age of 60 years proportionately more females died than did males - 15 out of 24 females (62.5%) as against 15 out of 28 males (53.5%).

The presence of effort pain prior to a myocardial infarct carries with it a slightly lower mortality rate than when there has been no such complaint. (Figure 13.) This may be due to the greater development of a collateral circulation in those with effort pain. Similarly the absence of pain at the time of the myocardial infarct is associated with a much higher mortality than when pain is present - in this series 72% of those with painless infarcts died while only 40% of those with pain died.

A history of previous myocardial infarction, particularly if recent also worsens the prognosis -
37% /

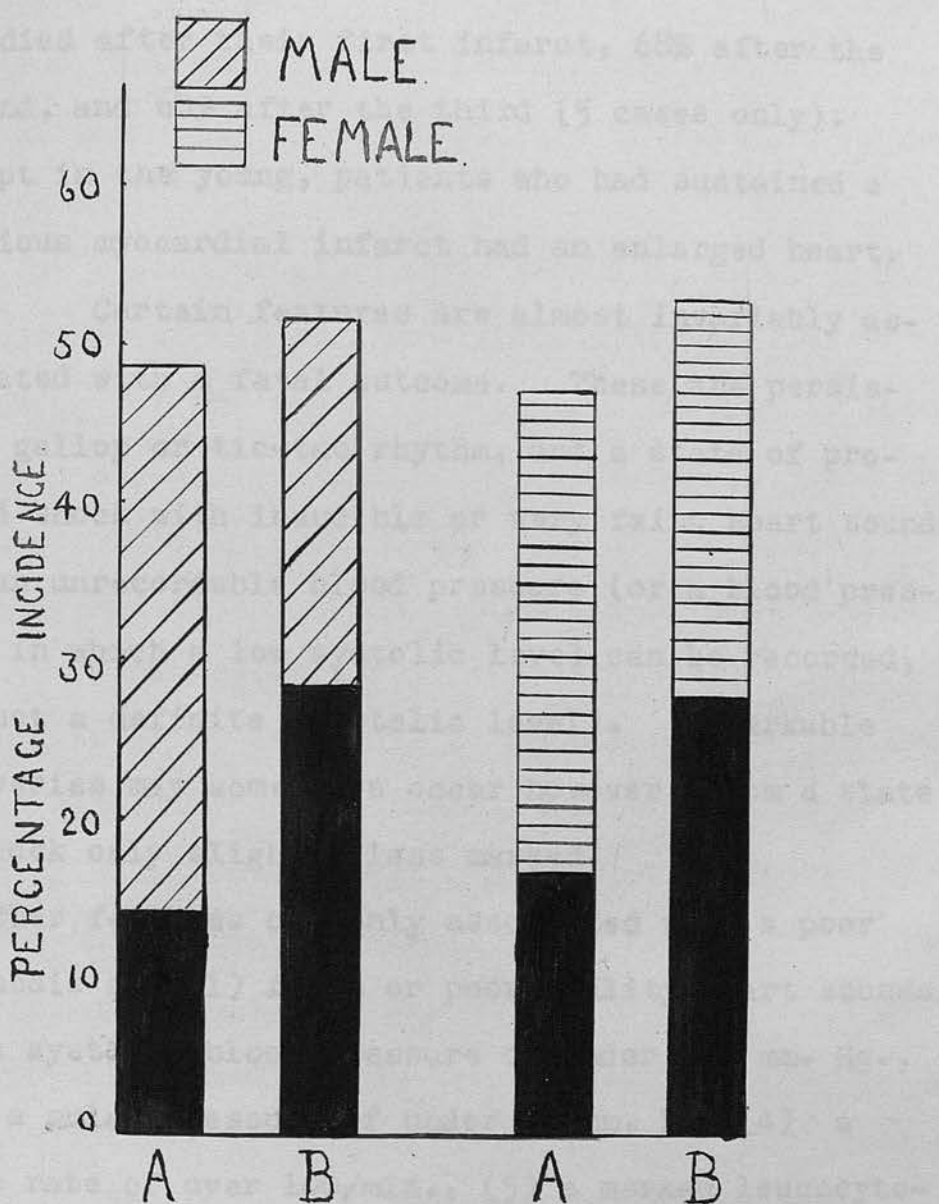


Figure XIII. The percentage of cases experiencing effort pain prior to the myocardial infarct (A), and (B) no effort pain prior to the infarct is illustrated. The proportion of cases dying is shown in black.

37% died after their first infarct, 68% after the second, and 60% after the third (5 cases only).

Except in the young, patients who had sustained a previous myocardial infarct had an enlarged heart.

Certain features are almost invariably associated with a fatal outcome. These are persistent gallop or tic-tac rhythm, and a state of profound shock with inaudible or very faint heart sounds and an unrecordable blood pressure (or a blood pressure in which a low systolic level can be recorded, but not a definite diastolic level). Remarkable recoveries may sometimes occur however, from a state of shock only slightly less marked.

Other features commonly associated with a poor prognosis are (1) faint or poor quality heart sounds, (2) a systolic blood pressure of under 100 mm. Hg., (3) a pulse pressure of under 30 mm. Hg., (4) a pulse rate of over 100/min., (5) a marked leucocytosis, and (6) a high blood sedimentation rate. Of these, the pulse rate, pulse pressure, and the systolic blood pressure, are the most important, but all acquire an increased significance when several, or all, occur together in the one person. In the elderly, the importance attached to each feature is greater than in the young. As isolated findings, faint heart sounds, a marked leucocytosis, and a high blood sedimentation rate, have little adverse influence on prognosis. /

on prognosis. It is in the setting of the individual case that each feature becomes important, producing the composite clinical picture of recovery or deterioration.

A good prognosis can generally be given in the absence of the features already listed i.e. if the shock, at the onset is slight or absent, if the systolic blood pressure is over 100 mm. Hg., and the pulse pressure is over 30 mm. Hg., if the heart rate is slow, and if the heart sounds are of good quality.

Convalescence may be interrupted at any stage however by a variety of complications. In this series 24% suffered a thrombo-embolic complication, and arrhythmias occurred in a partly overlapping 14%. Thrombo-embolic complications may gravely disable the recovering patient, and may at times cause, or contribute largely to, death. As previously stated, the grade IIA males with cardiac enlargement constitute the group in whom prognosis is most seriously influenced by such complications. Arrhythmias, particularly if persistent, may be responsible for the development of myocardial insufficiency with evidence of heart failure, while certain forms of arrhythmia may cause sudden death. Heart failure occurred in 31 cases and of these 27 (87%) died. In only 18 cases however was heart failure the main or sole factor responsible for death. Digitalis was used in treatment on 16 occasions, five times with benefit. Of the /

the eleven who died while receiving digitalis, six died suddenly, a very high proportion of the sudden deaths in the entire series (11 cases). Thrombo-embolic complications reputed to occur frequently while digitalis is being given were conspicuous by their absence - only one case of thrombo-phlebitis occurred. Digitalis therapy of heart failure developing after myocardial infarction carries with it, therefore, the risk of sudden death. Quite apart from digitalis therapy sudden death may occur at any stage, but is most common in the first two weeks. Rupture of the infarct, an arrhythmia, recurrence of myocardial infarction, or a major embolic episode, may all be responsible.

To summarise, the immediate prognosis in acute myocardial infarction is based on a consideration of (a) the age of the patient, (b) the cardiac grade prior to the infarct, (c) the size of the heart, (d) the degree of shock which develops at the onset, (e) the character and audibility of the heart sounds, (f) the degree of fall of the systolic blood pressure (g) the pulse pressure, (h) the pulse rate, and (i) the occurrence of complications particularly heart failure, thrombo-embolic episodes, and arrhythmias.

VII. FOLLOW UP of 50 SURVIVORS of ACUTE
MYOCARDIAL INFARCTION.

Fifty of the 54 cases surviving the acute myocardial infarct have been traced (37 males and 13 females). Twenty-six are still alive and 24 have died. Twenty-eight have been seen again during the months and years after their infarct and two have reported by letter. Twenty of those dying were not seen again. Information as to their clinical course, and the date and cause of their death has been supplied by the general practitioner concerned, in 15 instances, while the Registrar-General for Scotland has supplied the date and cause of death in the remaining 5 cases. The clinical details of the follow up are therefore incomplete and the figures in the following pages are minimum.

(1) Age at onset.

The age at the time of the myocardial infarct is shown in Table XXXVIII.

TABLE /

(2) Period of follow-up.

The period over which the cases have been followed ranges from 2 months to 10 years 7 months. 39 cases still alive has been observed for less than

TABLE XXXVIII. Age distribution of 50 cases surviving acute myocardial infarction, subdivided to show (a) subsequent fatal cases and (b) survivors.

	Male.		Female.	
	Died Subsequently	Still Alive	Died Subsequently	Still Alive
30	-	1	-	-
35	1	1	-	-
40	1	4	-	-
45	3	2	-	2
50	3	3	1	-
55	2	3	1	1
60	1	7	2	-
65	2	1	3	1
70	1	-	2	-
75	1	-	-	-
Total	15	22	9	4

The average age at the time of the myocardial infarct of those dying subsequently was 56 years for the males and 64 years for the females, in contrast to the 53 years and 52 years respectively of the survivors.

(2) Period of follow up:

The period over which the cases have been followed ranges from 2 months to 10 years 7 months. No case still alive has been observed for less than 8 /

8 months. The average duration of survival of the 37 male cases is 3 years $6\frac{1}{2}$ months, and for the 13 females, 3 years $\frac{1}{2}$ month.

TABLE XXXVIII A. Duration of survival after myocardial infarction.

	Male.		Female.	
	Died Subsequently	Still Alive	Died Subsequently	Still Alive
0 - $\frac{6}{12}$ yr.	5	-	-	-
$\frac{6}{12}$ - 1 yr.	2	1	3	-
1 - $1\frac{1}{2}$ yr.	1	2	1	-
$1\frac{1}{2}$ - 2 yrs.	-	1	2	-
2 - $2\frac{1}{2}$ yrs.	-	1	-	2
$2\frac{1}{2}$ - 3 yrs.	-	2	-	-
3 - $3\frac{1}{2}$ yrs.	2	5	-	1
$3\frac{1}{2}$ - 4 yrs.	-	2	-	-
4 - $4\frac{1}{2}$ yrs.	1	2	1	-
$4\frac{1}{2}$ - 5 yrs.	1	-	-	-
5 - 6 yrs.	1	1	1	-
6 - 7 yrs.	1	2	-	-
7 - 8 yrs.	-	-	-	1
8 - 9 yrs.	2	1	1	-
9 - 10 yrs.	-	-	-	-
10 - 11 yrs.	-	2	-	-

(3) Subsequent Deaths :

The deaths took place between 2 months and 8 years 9 months after the infarct. Duration of survival and cause of death are listed in Table XXXIX.

TABLE XXXIX. Duration of survival of 24 cases dying after myocardial infarction and cause of death.

Duration of Survival		Cause of Death.
Male	Female	As certified by the General Practitioner.
$\frac{2}{12}$ (56)		Angina Pectoris ¹ .
$\frac{10}{52}$ (75)		Coronary Thrombosis.
$\frac{11}{52}$ (67)		Diphtheria.
$\frac{4}{12}$ (57)		Coronary Thrombosis ¹ .
$\frac{6}{12}$ (46)		Coronary Thrombosis.
	$\frac{29}{52}$ (70)	Gangrene of the leg following femoral artery thrombosis.
	$\frac{7}{12}$ (68)	Congestive heart failure.
$\frac{8}{12}$ (68)		Coronary Thrombosis.
	$\frac{9}{12}$ (67)	Coronary Thrombosis.
$\frac{42}{52}$ (37)		Coronary Thrombosis.
$\frac{13}{12}$ (50)		Coronary Thrombosis.
	$\frac{13}{12}$ (63)	Coronary Thrombosis.
	$\frac{19}{12}$ (52)	Coronary Thrombosis.
	$\frac{20}{12}$ (63)	Cerebral Thrombosis.
3 years (54)	/	

TABLE XXXIX. (Continued)

Duration of Survival		Cause of Death.
Male	Female	as certified by the General Practitioner.
3 yrs.	(54)	Coronary Thrombosis.
3 yrs.	(60)	Bronchiectasis.
4 yrs.	(44)	Coronary Thrombosis.
	4 $\frac{1}{3}$ yrs (59)	Coronary Thrombosis ¹ .
5 $\frac{3}{4}$ yrs	(49)	Angina Pectoris.
	5 $\frac{10}{12}$ yrs(66)	Coronary Thrombosis.
6 $\frac{1}{2}$ yrs	(48)	Coronary Thrombosis.
8 yrs	(73)	Left ventricular failure.
	8 $\frac{1}{2}$ yrs(70)	Coal gas poisoning ¹ .
8 $\frac{3}{4}$ yrs	(51)	Angina Pectoris.

Age at the onset of the myocardial infarct treated in hospital is given in brackets. ¹. Information supplied by the Registrar General for Scotland.

Five males died in the first 6 months and 8 in the first 13 months. No females died within 6 months of the onset, but 4 died during the first 13 months, i.e. 50% of the deaths to date, took place within 13 months of the acute myocardial infarct. Of the total deaths, five resulted from conditions unrelated to the heart - cerebral thrombosis, femoral artery thrombosis with peripheral gangrene in a paralysed /

paralysed leg, coal gas poisoning, diphtheria, and profuse haemoptysis from bronchiectasis. The remaining 19 cases, however, all died a cardiac death. Six of the eight males dying during the first 13 months died of a recurrence of myocardial infarction and one died of angina pectoris; two of the four female deaths during the same period were due to a recurrence of myocardial infarction. Of the remaining 7 male deaths 3 were certified as being due to a fresh myocardial infarct and 2 to angina pectoris; while 3 of the 5 remaining female deaths were also due to a fresh myocardial infarct. In the first 13 months 9 of the 12 deaths were due to myocardial infarction, or angina pectoris, while in the succeeding years, 8 of the 12 deaths had a similar cause. Only two cases died from progressive heart failure.

(4) Cardiac Grade after Myocardial Infarction.

The cardiac grade after the myocardial infarct is known in 42 cases (32 males and 10 females) and is listed in Table XXXX.

TABLE XXXX. Lowest cardiac grade after myocardial infarction in 42 cases.

	Died after Discharge.		Still Alive.	
	M.	F.	M.	F.
Grade I.	-	-	4	-
II A	6	3	16	4
II B	4	2	2	-
III	-	1	-	-

Twelve males and four females had to be regraded after the infarct, their functional capacity being reduced - seven males passed from grade I to grade IIA, and five from grade IIA to grade IIB; two females also passed from grade I to IIA, one from grade IIA to IIB, and one from grade IIA to III. The cardiac grade in which the patient is classed after the myocardial infarct is of considerable importance. Those remaining in grade I have all survived. Of the 29 in grade IIA twenty are still alive, but of the 8 in grade IIB, six are dead. The only case in grade III has died, i.e.

grade I	100% survival.
IIA	69% survival.
IIB	25% survival.
III	100% death.

(5) Ability to return to work :

The four males still in grade I were aged 31 years, 36 years, 60 years and 64 years, at the time of their myocardial infarct. Three are still at work, while the fourth, aged 64 years has retired. The patient aged 60 years actually does more strenuous work than he did before his infarct; while the one aged 36 years thinks nothing of going for a day's shooting on the hills. Of the 37 males surviving the myocardial infarct, 21 are known to have returned to some form of work. Only 4 of the 15 cases dying subsequently /

subsequently were known to have worked again, and in no case was the work strenuous. On the other hand 17 of the 22 males still surviving have returned to work, and in 5 cases, the work may be classed as strenuous. Of the women, 2 of the 4 survivors are fit for their housework, but the other 2 do not do much. Only 4 of the 9 females dying were fit for much housework. Two did none at all.

(6) Complications after myocardial infarction:

Complications are common during the months and years following the myocardial infarct. Among the 15 males dying subsequently, the clinical course of 3 is completely unknown, but 11 of the remaining 12 cases had one or more complications prior to death. The twelfth died only 2 months after his infarct. Among those still alive, complications are equally common, occurring in 20 of the 22 male survivors.

TABLE XXXXI. Complications arising after myocardial infarction in 34 males.

	Died Subsequently	Still Alive	Total.
Angina Pectoris	7	8	15
Recurrence of Myocardial Infarct)	2	-	2
Hypertension	3	10	13
Left Ventricular Failure	2	2	4
Congestive Heart Failure (Mild)	-	2	2
Arrhythmia	2	2	4
Cardiac Aneurysm	-	1	1
Cardiac Neurosis	1	-	1

Eleven of the fifteen males suffering effort pain after the myocardial infarct, had also experienced pain prior to the infarct; (six are dead and 5 still alive). In the remaining 4 cases with effort pain the disability caused is slight and all are still alive. Five who had suffered effort pain prior to their infarct, were free of pain thereafter (2 died subsequently but 3 are still alive). Seven of the thirteen cases who developed hypertension had been hypertensive prior to the myocardial infarct (six are still alive); one had a normal blood pressure (he is dead); and in five cases the previous level of the blood pressure was unknown (4 are still alive). At least 3 cases who had been hypertensive prior to the infarct had no return of hypertension thereafter. The arrhythmias recorded were, auricular fibrillation 1 case, (dead); ventricular tachycardia 2 cases (one still alive one dead); nodal rhythm 1 case (still alive). The ventricular tachycardia was only proved by electrocardiography in one case. In the second case, short paroxysms were suspected on clinical examination, but only fairly frequent ventricular extra-systoles were recorded electrocardiographically. This male died 10 days after the examination, death being certified as due to angina pectoris.

Among the females the complications have been of a similar nature. The clinical details of 2 cases who have died are unknown.

TABLE XXXXII. Complications occurring in 11 females after myocardial infarction.

	Died subsequently	Still Alive	Total
Angina Pectoris) & Coronary Insufficiency)	3	1	4
Recurrence of) Myocardial Infarction)	1	-	1
Hypertension	1	2	3
Left Ventricular Failure	1	-	1
Congestive Heart Failure	1	-	1
Cardiac Aneurysm	-	1	1
Hemiplegia & Femoral) Artery Thrombosis)	1	-	1
Severe Arthritis	1	-	1
Diabetes		1	1

All four cases with anginal pain after the infarct had previously experienced such pain. Only one case whose activities were moderately unrestricted after the infarct was free of the effort pain which had formerly limited her activities. The three cases developing hypertension had all been hypertensive prior to the infarct. Three others known to have been hypertensive had no return of hypertension.

(7) Electro-cardiographic changes:

In 27 cases, the electrocardiogram has been repeated at intervals after the myocardial infarct.

Thirteen /

Thirteen records are still diagnostic of infarction (9 "anterior" infarcts and 4 "posterior"). In another, evidence of left bundle branch block persists. Four records though not quite within normal limits are no longer diagnostic of myocardial infarction (3 "posterior", one "atypical"). Eight records have returned to within normal limits (3 anterior, 3 posterior, 2 atypical). One has been normal throughout. Return of the record to normality is not associated with freedom of symptoms however. One male who died, and whose record was perfectly normal, was extremely disabled by effort pain.

X-Ray examination has been carried out in a number of cases but the technique for estimation of heart size was not used. The films have therefore not been analysed for change in heart size over the years after the myocardial infarction. The two cases of cardiac aneurysm show up well on X-Ray examination. One is on the posterior surface of the heart and was only detected on routine X-Ray examination.

(8) After care :

Management of the cases observed during the follow up has comprised (1) advice as to the type of work to be undertaken and when it should be begun, (2) provision of adequate rest and sleep by sedation when necessary, (3) reduction in weight of the obese, (4) /

(4) prescription of nitroglycerine or a longer acting drug e.g. erythrol tetra-nitrate, for the relief of effort pain, (5) treatment of anaemia if present, (6) digitalis (and mercurial diuretics) for heart failure, (7) lastly, but by no means of least importance, maintenance of the patient's morale. Proper management can do much to improve the lot of the patient who has had a myocardial infarct. It is advisable to allow as much activity as is consistent with good judgment, letting the patient enjoy all that he can of life within the limits of his handicap.

to the myocardial infarct, (a) during the period in hospital, and (b) during the months and years after the infarct, in an attempt to indicate the features of importance in estimating the ultimate prognosis.

(a) Sex and Age:

The first striking feature is the importance of sex. Only 15 of 17 males (40.5%) have died, whereas 9 of 13 females (69%) are dead. This sex difference is undoubtedly bound up with the older age of the female victims of myocardial infarction, but age is not the only factor. Of 13 males who were 50 years or more at the time of the infarct, only 5

VIII. / died, whereas of 6 females 50 years or over only one is still alive. The thirteen females

VIII. THE ULTIMATE PROGNOSIS IN MYOCARDIAL
INFARCTION.

In the convalescent stage after acute myocardial infarction, the patient looks to the future. What does it hold in store for him? Will he be fit to work and support his family? Will he be fit for his old job? What are the chances of a return of the same trouble? These are the vital questions. The 50 cases reported in section VII. have been analysed according to the clinical features shown (a) prior to the myocardial infarct, (b) during the period in hospital, and (c) during the months and years after the infarct, in an attempt to indicate the features of importance in estimating the ultimate prognosis.

(a) Sex and Age :

The first striking feature is the importance of sex. Only 15 of 37 males (40.5%) have died, whereas 9 of 13 females (69%) are dead. This sex difference is undoubtedly bound up with the older age of the female victims of myocardial infarction, but age is not the only factor. Of 13 males who were 60 years or more at the time of the infarct, only 5 have since died, whereas of 8 females 60 years or over only one is still alive. The thirteen females had /

had an average age of 61 years at the time of their infarct, in contrast to the 54 years of the males. The nine females who died averaged 64 years and the four survivors 52 years. This disparity in the average ages of those dying subsequently and those still alive is also apparent, though to a less marked degree when the various features determining male prognosis are studied. The 15 males who died averaged 56 years at the time of their infarct as opposed to the 53 years of the survivors.

As the number of female cases studied is small, subdivision provides two groups which are too small for accurate determination of the factors favouring survival or subsequent death after myocardial infarction. The male cases alone will be analysed in detail.

(b) Factors present prior to the myocardial infarct:

The following factors have been associated with survival after the infarct rather than with subsequent death.

(1) Absence of effort pain prior to the infarct:

Of 16 males who had not experienced effort pain prior to the infarct, only 3 have died ; whereas of 21 who did complain of effort pain, 12 have died. These twelve averaged 57 years at the time of their infarct as against the 51 years of the nine survivors. Males with no effort pain prior to a myocardial infarct are more likely to survive subsequently /

subsequently than those with effort pain; while of those with effort pain, the young tend to survive and the elderly to die.

(2) No history of previous myocardial infarction.

Twenty-nine were admitted with their first myocardial infarct and of these 19 are still alive, - their average age is 53.5 years, while that of the 10 who died is 56 years. Six gave a history of one previous infarct - three have died and three are still alive. The average age of the two groups is the same viz. 51 years. Two had suffered two infarcts prior to admission. Both are dead. Subsequent survival is more common after first infarct than after second or third infarcts.

(3) Body weight within normal limits. Only 9 cases were obese prior to their infarct, but of these 7 have died. Twenty-eight were not obese and of these 20 are still alive; they are younger than the non-obese who have died, - 52.5 years as against 55.5 years. Obesity prior to myocardial infarction is associated with subsequent death, and absence of obesity with survival.

(4) Cardiac grade I prior to myocardial infarction. Of the twelve males in grade I prior to their infarct only one aged 57 years has died. The eleven survivors averaged 48 years. Twenty-three males were in grade IIA. Twelve have died and 11 are still alive, the average ages of the two /

two groups being similar. Two males in grade IIB have both died. Males in cardiac grade I tend to survive after myocardial infarction while those in grade IIA have only a 50% chance of subsequent survival.

(5) Hypertension prior to the myocardial infarct.

Only 15 males were known to have had hypertension prior to the infarct but of these 10 are still alive. Surprisingly the dead averaged 53 years as against the 60 years of the survivors. Nine were known to have had a normal blood pressure prior to the infarct, and of these 5 are dead. None were elderly but the younger cases have survived. In 13 cases the previous level of the blood pressure was unknown. Eight are still alive and again the young have survived and the elderly have died. Those previously hypertensive have a better chance of surviving subsequently than those with a normal blood pressure or in whom the blood pressure is unknown prior to the infarct.

(c) Factors arising immediately after the myocardial infarct :

The following factors have been associated with survival rather than death after the myocardial infarct. Other factors have had little bearing on the ultimate prognosis.

(1) Absence of shock at the onset: Of 18 cases showing no evidence of shock 12 are still alive, whereas /

whereas of the 14 showing a mild degree of shock, seven have died. These seven were slightly older than the seven survivors - 54 years as against 50 years.

(2) Good quality heart sounds: Twelve had heart sounds of normal character and intensity; only four have died. But of 6 with poor quality heart sounds only 2 have died. Eighteen had faint heart sounds and of these only 10 are still alive. These ten survivors are much younger than the eight who died - 52 years as against 59 years. Those in whom the heart sounds remain of normal character and intensity at the time of the infarct tend to survive subsequently more often than do those in whom the heart sounds are altered in character or intensity.

(3) Systolic blood pressure above 100 mm. Hg.: Twenty-eight cases had a systolic blood pressure of over 100 mm. Hg. and of these 18 are still alive. The 10 who died were elderly, averaging 57 years as against the 51 years of the survivors. Nine had a systolic blood pressure of under 100 mm Hg. and of these 5 have died. Those with a systolic blood pressure persistently above 100 mm. Hg. tend to survive subsequently more often than do those in whom the pressure falls to under 100 mm. Hg., at any stage.

(4) Pulse rate of under 100/min. Twenty-seven cases had a pulse rate of less than 100/min., and /

and of these 17 are still alive. Their ages average 52.5 years as against the 58 years of the 10 dying. Ten had a pulse rate between 100-120/min. and of these 5 have died. Those with a pulse rate of under 100/min. tend to survive subsequently more commonly than do those in whom the pulse rate rises above 100/min..

The various factors which are important in immediate prognosis but have not proved important in ultimate prognosis are (1) Heart size - twenty-one had enlarged hearts and of these 12 (57%) are still alive. Fifteen had no cardiac enlargement and of these 9 (60%) are still alive. These latter 9 are younger than the 6 without cardiac enlargement who have died - 50 years as against 55.5 years. (2) Pulse pressure during the acute phase, the degree of leucocytosis, the degree of fever, and the rise in the blood sedimentation rate have all proved of little consequence. (3) Complications occurring in hospital have played little part. One third of those dying subsequently suffered one or more complications while in hospital, whereas almost half of those still alive also had one or more complications. The type of electrocardiogram too, has no bearing on the final outcome.

(d) Factors developing after the myocardial infarction:

The following factors have been associated with survival.

(1) Cardiac grade I or IIA after the infarct:

Of these still in grade I (4 cases), all are still alive. Twenty-two were grouped in grade IIA and only 6 have died, whereas of 6 in Grade IIB, only 2 are still alive.

(2) Freedom from recurrence of myocardial infarction :

This is the crucial factor governing prognosis. Not a single survivor has had a recurrence. Seventeen of the 24 deaths were due to a recurrence, and 3 of these 17 cases had earlier had another non-fatal recurrence.

(3) Freedom from effort pain after the infarct:

Seven of the 15 males dying subsequently had effort pain whereas this was present in only 8 of the 22 survivors, and in 4 cases was very slight.

(4) Development of hypertension after the infarct:

Ten of the survivors are known to have become hypertensive, whereas only three of those dying were hypertensive. This latter figure is a minimum one as the blood pressure readings were not known in all the cases who died. Probably this factor is not important in determining recovery, but is more an expression of myocardial recovery.

(5) Regression of the electrocardiographic signs of myocardial infarction:

As only 4 records were obtained in those dying the true importance of a return to normality of the electrocardiographic /

electrocardiographic picture cannot be assessed. In 2 of these 4 cases, the record was within normal limits, while in 6 of the survivors, the record had also returned to normal. Such a change is not however associated with freedom from symptoms.

(e) Discussion:

It would therefore appear that the ultimate prognosis after myocardial infarction may be estimated with reasonable accuracy. The sex and age of the patient and the efficiency of the myocardium are the factors of primary importance. In the natural course of events, myocardial efficiency decreases with age. After a myocardial infarct, this natural process is likely to be hastened. The elderly therefore tend to die after a myocardial infarct more readily than the young. This would serve to explain in part, the sex difference in subsequent survival after myocardial infarction, as relatively few females are affected before the 7th decade of life. Myocardial efficiency is good if (1) the following factors were present prior to the infarct (a) no effort pain, (b) no previous myocardial infarcts, (c) the patient was in cardiac grade I; and (2) if the degree of injury sustained at the time of infarction was slight as suggested by (a) absence of shock, (b) good quality heart sounds (c) systolic blood pressure of over 100 mm. Hg., and (d) a pulse rate of under /

under 100/min.. In the subsequent course after the infarct corroborative evidence of a good prognosis is provided if (a) the patient remains in cardiac grade I or IIA, (b) he does not develop effort pain or does so only to a mild degree, (c) hypertension develops. Absence of obesity both before and after the infarct is important, in that no avoidable burden is imposed upon the myocardium.

By way of contrast, the ultimate prognosis is poor if (a) the patient has suffered effort pain prior to the infarct, (b) if he has had one or more previous infarcts, (c) he is obese (d) he is in grade IIA or worse grade IIB prior to the infarct, (e) the extent of myocardial damage at the time of infarction is extensive, and (f) he shows evidence of heart failure after the infarct.

No matter how carefully the pros. and cons. are weighed in each individual case, there remains the one unknown factor, which in a moment, and at any stage, may upset all predictions. This "sword of Damocles" is a recurrence of myocardial infarction. In this series 17 of the 24 deaths were probably due to a recurrence of infarction. In all, 20 recurrences took place and 17 were fatal. No case still surviving has had a recurrence. Commonly 50% of all recurrences take place within a year of the onset (13 months in this series) but there is no time limit after which a recurrence will not take place.

In a comparison of the factors important in immediate and ultimate prognosis, it is interesting that the presence of effort pain prior to the infarct should be a favourable sign in estimation of immediate prognosis and an unfavourable sign in estimation of ultimate prognosis. This is understandable, and even to be expected, as (1) the presence of effort pain would suggest that a collateral circulation is already partly established and (2) that the efficiency of the myocardium is impaired.

Age Yrs.	Total		Died in Ward		Survivors	
	Male	Female	Male	Female	Male	Female
35-	1	-	-	-	1	-
40-	2	-	-	-	2	-
45-	4	-	-	-	4	-
50-	11	2	1	2	10	-
55-	8	1	1	-	7	1
60-	13	10	3	2	10	8
65-	3	9	1	3	2	6
70-	4	2	1	-	3	2
IX.						
Total	46	24	7	9	39	15

(1) - Immediate mortality: Sixteen cases - 7 male and 9 female - died during the first 5 weeks after the infarct, a mortality rate of 23%. The male mortality rate was much lower than the female mortality rate -

IX. ANALYSIS of 70 CASES of ACUTE MYOCARDIAL
INFARCTION TREATED WITH ANTI-COAGULANTS.

(a) Clinical Details:

(1) Age and Sex: Fortysix cases were male and 24 were female. Age distribution is shown in Table XXXXIII.

TABLE XXXXIII: Age and sex distribution of 70 cases of acute myocardial infarction treated with anti-coagulants.

Age. Yrs.	Total.		Died in Ward.		Survivors.	
	Male	Female	Male	Female	Male	Female
35-	1	-	-	-	1	-
40-	2	-	-	-	2	-
45-	4	-	-	-	4	-
50-	11	2	1	2	10	-
55-	8	1	1	-	7	1
60-	13	10	3	2	10	8
65-	3	9	1	5	2	4
70	4	2	1	-	3	2
Total	46	24	7	9	39	15

(2) Immediate mortality: Sixteen cases - 7 male and 9 female - died during the first 6 weeks after the infarct, a mortality rate of 23%. The male mortality rate was much lower than the female mortality rate - /

rate - 15% as against 37.5%. The average age of the 7 males dying was higher than the average of the series - 62 years as against 57 years, but the females dying had a lower average age than that of the series - 62 years as against 64 years. This was due to the two female deaths in the 50-54 year age group.

(3) Blood pressure level prior to the infarct:

This is shown in Table XXXIV.

TABLE XXXIV. Blood pressure level prior to myocardial infarction in 70 cases treated with anti-coagulants.

	Male		Female	
	Total	Deaths	Total	Deaths
Hypertensive	24	3(12.5%)	19	6.(31%)
Normotensive	10	2(20%)	1	-
Unknown	12	2(17%)	4	3(75%)

Fifty-two percent. of the males and 79% of the females had been hypertensive prior to the infarct. Their average ages are those of the general series.

(4) Angina Pectoris prior to the infarct:

Twenty males (43%) and fifteen females (62.5%) had complained of effort pain prior to the myocardial infarct. Again, the average ages were those of the general series. Only 4 males and 3 females died. They averaged 60 years and 58 years respectively.

Among /

Among those with no previous history of effort pain - 26 males and 9 females, - 3 males and 6 females died.

% Mortality.

	Male	Female
Effort pain	20%	20%
No effort pain	11%	67%

Those giving a history of effort pain died at a younger age than did those with no pain -

Male Female

Average age of) (a) with effort pain	60 yrs.	58 yrs.
those dying) (b) no effort pain	64 yrs.	64 yrs.

These two observations contrast with the finding in the series of 100 conservatively treated cases.

Premonitory symptoms were present in 27 cases - 18 males and 9 females. The male cases experiencing these symptoms were younger than those in whom the onset was sudden, averaging 54 years as against 59 years. The two groups of females were of the same age - 64 years. Only 5 cases experiencing premonitory symptoms died - 2 males and 3 females. Both the males were elderly. A fatal outcome was more common in those not experiencing premonitory symptoms.

% Mortality.

Males. Females.

Premonitory Symptoms	11%	33%
Sudden Onset	18%	40%

(5) Body Weight : Nineteen males (41%)

and eighteen females (75%) were overweight. Two males /

males and seven females died. These two obese males were younger than the five non-obese males who died - 60 years as against 62.5 years.

(6) Diabetes etc.: One male and two females had diabetes. All three were elderly but all survived the infarct. Three males had syphilis; one died.

(7) First, second, or third infarct: Forty-eight cases were admitted with their first infarct; thirteen with their second infarct; and six with their third. One male experienced his fourth infarct, and one remarkable female was admitted three times after her third, fourth and fifth infarcts.

Table XXXV. gives details of the mortality in each group.

TABLE XXXV. Mortality after 1st, 2nd, 3rd, 4th, and 5th Myocardial Infarcts.

	Male.		Female.	
	Total	Deaths	Total	Deaths.
1st Infarct	32	3	16	7
2nd "	10	3	3	1
3rd "	3	-	3	1
4th "	1	1	1	-
5th "	-	-	1	-

The /

The numbers are small except for those experiencing their first infarct, but the increase in mortality commonly found after each successive infarct has not taken place.

(8) Cardiac Grade prior to the infarct: As in the series of 100 cases, symptoms appearing for the first time in the 2 weeks prior to the infarct, were not considered in assessing the cardiac grade. Fourteen males had experienced no disability prior to their infarct; the activities of 23 had been slightly restricted; and only 6 had been severely restricted. One male was in heart failure prior to the infarct - his fourth. Seventeen females were in grade IIA; six were in grade IIB; and one was in grade III. Table XXXXVI. records the number dying in each grade.

TABLE XXXXVI. Cardiac grade prior to myocardial infarction in 70 cases treated with anti-coagulants with the deaths in each grade.

Grade	Male.		Female.	
	Total	Deaths	Total	Deaths.
I	14	2 (14%)	-	-
IIA	23	1 (4.3%)	17	8 (47%)
IIB	7	3 (43%)	6	-
III	1	1 (100%)	1	1 (100%)

There is no progressive increase in the mortality from grade I to grade III as observed in the series of 100 conservatively treated cases.

(9) Time of Onset : This was accurately known in 66 cases. In 33 cases symptoms began between 8 a.m. and 8 p.m., while the other 33 cases began between 8 p.m. and 8 a.m. Thirty-three patients were in bed at the time of onset.

(10) Presenting symptoms: Pain was present in 66 of the 70 cases, though in one case it had been slight and was overlooked, embolic phenomena being the presenting feature. Sudden dyspnoea; sudden weakness and dizziness; sudden weakness and sickness; and sudden loss of consciousness were the complaints in the four painless cases. Three died while in the ward.

In 60 cases the pain was described as being substernal in position or radiating across the front of the chest. Of the 6 other cases, four experienced pain only on the left side of their chest; in one it was entirely epigastric in situation; and in the 6th it was felt in the back between the shoulders. Radiation of pain to the arms was common - to both arms in 11 cases, the left arm alone, 11 cases, and the right arm alone 5 cases. In 4 cases pain did not radiate beyond the shoulders - left shoulder 3 cases, right shoulder 1 case. Eleven experienced pain in the throat, 4 on the left side only, and 2 had pain in the jaw. Only 3 cases had radiation into the epigastrium.

(11) /

(11) Electrocardiography: One or more recordings were obtained in all 70 cases. Localization of the infarct is shown in Table XXXVII.

TABLE XXXVII. Electrocardiographic localization of the site of myocardial infarction in 70 cases and treated with anti-coagulants, and the mortality rate in each group.

	Male.			Female.		
	Anterior.	Posterior.	Atypical.	Anterior.	Posterior.	Atypical.
Total Number	27	10	5	11	8	3
% Mortality	7.4%	20%	40%	36%	37.5%	33%

One female who died showed evidence of both anterior and posterior infarction. Two cases - one male and one female - had a high lateral infarct; one male showed left bundle branch block, and one male had a normal record. This last male had a typical history and clinical course and since the infarct has developed heart failure. Four cases - 3 male and 1 female - had a right bundle branch block, but also showed evidence of anterior infarction. All four died. The average ages of the three groups, anterior, posterior and atypical, were similar, in both sexes.

(12) Degree of Shock at the onset: The severity of the shock at the onset was estimated and graded in the manner described in section V. page 112. It could be assessed in 66 cases. Twenty-six cases showed /

showed a marked degree of shock, and of these 9 died. Sixteen showed a mild degree of shock and only one died; while of 24 with no evidence of shock 3 died. Table XXXXVIII. summarises the findings.

TABLE XXXXVIII. Degree of shock at the onset of myocardial infarction and mortality rate in each grade.

	Male.			Female.		
	Marked	Mild	Absent	Marked	Mild	Absent
Number	16	11	18	10	5	6
Mortality.	31%	9%	5.5%	40%	-	33%

Although the trend is similar to that shown in the conservatively treated cases, the mortality rates are lower. The average ages of the cases in each grade are similar, and the elderly have tended to die and the young to survive.

(13) Heart sounds: The varieties of heart sounds heard in the first few days after myocardial infarction are listed in Table XXXXIX.

TABLE XXXXIX. /

TABLE XXXIX. Character of heart sounds in 70 cases of myocardial infarction treated with anti-coagulants.

	Total		Died in Ward	
	Male	Female	Male	Female
Gallop	4	4	1	2
Tic-Tac	1	2	1	-
Faint	20	4	2	2
Poor Quality	3	6	2	4
Normal	17	8	-	-
Inaudible	1	-	1	-

In each group, among males, the cases who died were older than the average. Among the females on the other hand, age did not influence survival.

(14) Blood pressure after the infarct : The lowest systolic blood pressure recorded in the days following the infarct is analysed in Table L.

TABLE L. The lowest systolic blood pressure recorded in 70 cases of myocardial infarction treated with anti-coagulants.

	Total		Died in Ward	
	M.	F.	M.	F.
B.P. over 100 mm. Hg.	30	18	3	5
B.P. under 100 mm. Hg.	16	6	4	4

Among the males, those with a systolic blood pressure of /

of over 100 mm. Hg., were younger than those in whom the pressure fell below 100 mm. Hg. - 56 years as against 61.5 years. In each group however the young survived and the elderly died. Females showed no pattern according to age.

(15) Pulse pressure after the infarct: The majority of cases, 51 in all, had a good pulse pressure, but 10 died. The mortality increased with the fall in pulse pressure.

TABLE LI. Pulse pressure records in 70 cases of myocardial infarction treated with anti-coagulants.

	Total		Died in Ward.	
	Male	Female	Male	Female
Over 30 mm Hg.	30	21	4	6
20-30 mm. Hg.	13	2	2	2
Under 20 mm. Hg.	3	1	1	1

The average ages of the males in each group are similar - 55 years, 56 years, and 55 years, - and in each group the elderly died and the young survived.

16. Pulse rate after the infarct: The most rapid rate recorded after the infarct is subdivided into two groups in Table LII.

TABLE LII. /

The males with a heart of normal size were on the average 8 years younger than those with an enlarged heart - 50 years as against 58 years. The females too were younger when the heart was not enlarged - 60 years as against 64.5 years. Correlation of cardiac grade prior to the infarct and heart size show that of males with an enlarged heart and (a) in cardiac grade I, one of eight has died, (b) in cardiac grade IIA, one of eighteen has died, (c) in grade IIB three of six cases have died, and (d) in grade III the only case has died. These findings for males in grade IIA contrast markedly with the findings in the series of conservatively treated cases reported in section V. (page 118).

(18) Degree of leucocytosis: This was estimated in the days following the myocardial infarct in 67 cases.

TABLE LIV. Degree of leucocytosis after myocardial infarction in 67 cases treated with anti-coagulants.

	Total		Died in Ward	
	Male	Female	Male	Female
Over 10,000/c.m.	27	16	6	6
Under 10,000/c.m.	17	7	1	2

A fatal outcome is more common when the leucocytosis exceeds 10,000/c.m. than when it is under that figure.

The /

TABLE LII. Most rapid pulse rate after myocardial infarction in 70 cases.

	Total		Died in Ward	
	Male	Female	Male	Female.
Under 100/min.	12	8	6	5
Over 100/min.	34	16	1	4

Fifty percent. of the males and 62.5% of the females with a pulse rate of over 100/min. have died. These males were elderly compared with the survivors - averaging 61 years as against 57 years. The one male who had a pulse rate of under 100/min., but died was also elderly - 65 years. Of the 20 cases with a pulse rate of over 100/min., the most rapid rate was recorded within the first week after the infarct in 14 cases. Seven (50%) of these 14 cases died. Only six developed a pulse rate of over 100/min. after the first week, and of these 4 (66%) died. In one surviving case, the tachycardia was associated with toxæmia from incipient gangrene of a foot.

(17) Heart size: This was known in 64 cases.

TABLE LIII. Heart size in 64 cases of myocardial infarction treated with anti-coagulants.

	Total		Died in Ward	
	Male	Female	Male	Female
Cardiac Enlargement	34	18	6	6
No enlargement	8	4	-	2

The /

The two groups of males are of the same average age - 57 years, and in each the elderly died and the young survived.

(19) Blood Sedimentation Rate: This was estimated at intervals in 69 cases.

TABLE LV. Most rapid blood sedimentation rate following myocardial infarction in 69 cases treated with anti-coagulants.

	Total		Died in Ward	
	Male	Female	Male	Female
Over 25 mm./hr.	34	16	5	6
Under 25 mm./hr.	11	8	2	3

In 27 cases the highest reading was over 50 mm./hr.. The two groups of male cases averaged 57 years and 58 years respectively, and in each group those dying averaged 62 years.

(2) Body Temperature: This was known in all cases.

TABLE LVI. Maximum temperature recorded after myocardial infarction in 70 cases treated with anti-coagulants.

	Total		Died in Ward	
	Male	Female	Male	Female
Over 100°F.	11	7	-	4
Up to 100°F,	11	12	4	4
Normal	24	5	3	1

The /

The males and females having no fever were slightly older than those with a rise of temperature. Among males, those dying in each group were elderly and the survivors were young - e.g. of males with a temperature of under 100°F., those dying averaged 61.5 years, as against the 53 years of the survivors. As with most other features the females showed no such age pattern.

(b) Treatment:

The methods were those adopted in the conservatively treated series (listed on page 120) plus anti-coagulant therapy during the first 3 weeks after the myocardial infarct. Both heparin and dicoumarol were used in 64 cases, and dicoumarol alone in 6 cases. Apart from 2 cases, the heparin was given intravenously 8 hourly, and was continued until the dicoumarol was effective. The 2 exceptions received 6 hourly injections. In the first 7 cases treated, the unit dose of heparin varied between 5,000 international units and 8,000 units, but thereafter no injection of less than 10,000 units was given. Adequacy of heparin dosage was decided by estimation of the clotting time of whole blood, one hour after the injection. Using the Lee-White method, (1913) a time of 20 minutes or more was considered satisfactory*. Commonly 4-5 days elapsed before the

* The preparation of heparin used throughout the investigation was the Roche product "Liquemin". One hundred milligrams of this preparation is the equivalent of 13,000 international units.

dicoumarol became effective. It was then continued during the first 3 weeks after the myocardial infarct. In all cases 300 mgms. of dicoumarol were given on the first day and 200 mgms. on the second day. Commonly 200 mgms. were also given on the third day, but a number of cases received only 100 mgms., or rarely none at all. Thereafter the daily dose varied between 0 & 200 mgms.. Throughout the 3 weeks of treatment the daily dose was regulated by daily estimation of the prothrombin time. This was done by the Fullerton modification of the Quick method (1940) using venom as the source of thrombokinase. If the haemorrhagic complications of dicoumarol therapy are to be minimised, it is essential that all estimations of prothrombin time are done by the one person, that a standard technique is used, and that a normal control is done daily. In spite of these precautions, bleeding will occasionally occur, owing to individual variation in response to the drug. In this series of 70 cases, all prothrombin estimations were done by one person (myself), and at the same time each day - before breakfast. This last precaution was taken as Fullerton (1949) believes that variation in the blood lipoid content influences estimation of the prothrombin time when venom is used as the source of thrombokinase. During the first year of the investigation a prothrombin time of 18-20 seconds, from a normal person was /

was adopted as the standard. Thereafter it was found more suitable to have a control prothrombin time of about 25 seconds. At this level, the range of prothrombin times indicating that the desired reduction in prothrombin content of the blood has been achieved is wider, and dicoumarol dosage may therefore be more accurately assessed. In dicoumarol therapy the object is to reduce the prothrombin content of the blood to 20-30% of normal and to maintain it at that level. Such is a difficult task, and there is little margin for error, although bleeding complications are not likely to occur unless the prothrombin content is reduced to under 10% of normal.

A period of 3 weeks anti-coagulant therapy was decided upon for 3 reasons (1) the clotting tendency which develops in the blood after myocardial infarction (briefly mentioned in section IV. page 98 and to be discussed later in section XIII.) seldom persists for more than 3 weeks, (2) the majority of thrombo-embolic complications occur during the first 3 weeks, and (3) the action of dicoumarol persists for several days after administration of the drug has ceased. Only one case was treated for more than 3 weeks. In this man, dicoumarol was given continuously for 11 weeks (Case number 20 page 308).

(c) Course after Myocardial Infarction :

(1) Complications: Only thirty-four of the seventy cases had an uneventful convalescence. A total of /

of 69 complications occurred in the remaining 36 cases. Thirty-four complications occurred in the 16 patients who died and thirty-five in 21 survivors. Two or more complications occurred in 26 cases. Table LXVII. on page 177 lists the various complications. Heart failure was the most common complication, occurring in 13 of the 16 fatal cases and in 10 of the survivors. In these 10 survivors there was a good response to treatment.

Thrombo-embolic complications occurring during the first 6 weeks are listed in Table LVIII.

Eighteen episodes occurred in 12 cases, but of these 5 took place before anti-coagulant treatment was begun, and one, two weeks after treatment was completed, leaving twelve episodes in 9 patients while anti-coagulants were being given. One female who suffered 3 episodes - a recurrence of myocardial infarction, a pulmonary infarct, and a splenic infarct, received quite inadequate heparin dosage, and in fact only 9 episodes occurred in 8 patients (11% of the series) while the anti-coagulant therapy was theoretically adequate. The hemiplegia which developed in 2 males may have been haemorrhagic in origin as in both, the prothrombin time was high and one showed haematuria later in the day on which the hemiplegia developed. However these 2 cases must be included in the 8 experiencing thrombo-embolic episodes. None of the male cases developing a thrombo-embolic complication died, whereas /

TABLE LVII. Complications occurring after myocardial infarction in 70 cases treated with anti-coagulant

	C.H.F.	L.V.F.	Peri-cardial Friction.	Thrombo-Embolic Complications. 1.	Hemi-plegia. 2.	Arrythmia. Pain.	Anginal Shock.	Per-sisting Shock.	Pneumonia.	Brach-ial Neu-ritis.	Right Shoul-der pain.	Left Wrist pain
Male												
Total	8	5	6	6	2	3	3	1	1	1	1	-
Died in Ward	5	2	2	-	-	1	1	1	1	-	-	-
Female												
Total	5	5	2	3	-	4	-	1	-	-	-	1
Died in Ward	3	3	1	3	-	4	-	1	-	-	-	1

C.H.F. = Congestive Heart Failure - L.V.F. = Left ventricular failure.

1. Including recurrence of myocardial infarction.
2. Grouped apart from the thrombo-embolic episodes as they may have been haemorrhagic in origin.

In addition one male who died in the ward had evidence of mitral incompetence clinically and at autopsy, and one male survivor had very troublesome meteorism.

TABLE LVIII. Thrombo-embolic episodes occurring after myocardial infarction in 70 cases treated with anti-coagulants.

		Recur- rence.	Pulmon- ary Infarct	Cere- bral Em- bolus	Periph- eral Embolus	Splen- ic In- farct.	Hemiplegia ?Haemorrhagic.
Male	Total	2	2	1	3	-	2
	Died in Ward	-	-	-	-	-	-
Female	Total	1	3	1	2	1	-
	Died in Ward	1	3	1	2	1	†

whereas all the affected females died. Recurrence of myocardial infarction which was the most common event in the conservatively treated series, only occurred once while anti-coagulant therapy was adequate.

Seven patients - 3 male and 4 female - experienced one or more arrhythmias (Table LIX. page 180). Auricular fibrillation was the most common, occurring in 4 cases. In one, a male aged 63 years who was going into congestive heart failure, treatment with digoxin resulted in the superimposition of frequent paroxysms of ventricular tachycardia, but administration of quinidine brought about a reversion to normal rhythm. Three cases showed two varieties of arrhythmia - auricular fibrillation and auricular flutter, auricular fibrillation and partial heart block, auricular /

auricular fibrillation and ventricular tachycardia; while one case showed three varieties of arrhythmia - paroxysmal auricular tachycardia, Stokes-Adams attacks, and complete heart block. The four females affected all died, but only one male died. He showed the three varieties of arrhythmia on the morning of his death. All were elderly.

(2) Cause of death :

Eight of the 16 deaths were due to heart failure. In 5 the failure was of the left ventricle, and 3 were in congestive heart failure.

TABLE LX. Main cause of death in 16 cases of myocardial infarction treated with anti-coagulants.

	C.H.F .	L.V.F.	Sudden	Arrhythmia	Hemiplegia.
Male	2	3	1	1	-
Female	1	2	4	1	1
Total	3	5	5	2	1

(Only the main cause in each case is listed. Three dying suddenly and 1 dying of an arrhythmia were also in early congestive heart failure, one other dying suddenly had mild left ventricular failure).

Seven of the remaining 8 deaths occurred suddenly. Two were probably due to an arrhythmia - paroxysmal ventricular tachycardia, and a Stokes-Adams attack ; while one resulted from rupture of the myocardial infarct /

TABLE LIX.

Incidence of various arrhythmias after myocardial infarction in 70 cases treated with anti-coagulants.

	Auricular Fibrillation.	Auricular Flutter.	Paroxysmal Auricular Tachycardia.	Paroxysmal Ventricular Tachycardia.	Partial Heart Block.	Complete Heart Block	Stokes-Adams Attack.
Male							
Total	2	-	1*	1	-	1*	1*
Died in Ward	-	-	1	-	-	1	1
Female							
Total	2	1	-	1	2	-	-
Died in Ward	2	1	-	1	2	-	-

* One patient showed all three arrhythmias.

infarct. No cause was found in the other 4 cases. The sixteenth death took place a few days after a cerebral embolus which had caused a complete hemiplegia. Not a single death occurred on the first day. Five took place in the first week, seven in the second week, two in the third week, and two in the fourth week.

(3) Digitalis Therapy :

Digitalis was used to treat 16 cases, of whom 10 were in left ventricular failure, and 6 in congestive heart failure. One of the latter group was the male with auricular fibrillation previously mentioned. Death occurred in eight cases - five with left ventricular failure and three with congestive heart failure. Three of these cases, although deteriorating, died suddenly. Embolic phenomena occurred in two females while digitalis was being given. One had paroxysmal auricular fibrillation and auricular flutter, and was receiving inadequate dosage of heparin; the other had experienced embolic phenomena before starting on anti-coagulants and again before starting on digitalis.

Mercurial diuretics were used in 8 cases, six times to supplement digitalis therapy. Quinidine sulphate was given to the two cases exhibiting ventricular tachycardia. One died 2 hours after the /

the first dose, but in the other normal rhythm was restored.

(a) Pathology: Only 9 of the 16 cases came to autopsy. All had markedly arteriosclerotic coronary arteries and in 6 a fresh thrombus was found blocking an artery - five in the anterior descending branch of the left coronary artery, and one in the right coronary artery. Endocardial mural thrombus was present in only two hearts - one the inadequately treated female who had the paroxysmal arrhythmias and embolic phenomena; and the second, a female who had a very extensive myocardial infarct covered in one part by a thin layer of thrombus. She was in congestive heart failure at the time of death, having been admitted after her third infarct within 1 month. Peripheral infarcts in the spleen and kidneys were found in the inadequately treated female but in no other case. One case dying in congestive heart failure showed terminal thrombosis in one small pulmonary artery.

The hearts weighed from 250 Gms. to 530 Gms., only two weighing under 400 Gms.. In all cases, the infarcts were "large" or "extensive". Three died from congestive heart failure, and four from left ventricular failure. The two remaining cases died suddenly - one from rupture of the infarct and one from an arrhythmia.

X. COMPARISON of the IMMEDIATE PROGNOSIS in the CONSERVATIVELY TREATED SERIES and the SERIES RECEIVING ANTI-COAGULANT THERAPY.

(a) Composition of the two series: The two series comprise waiting day admissions to the Royal Infirmary Edinburgh and were unselected, with the exception of a few cases showing a contra-indication to anti-coagulant therapy. They differ in the detailed incidence of many features, as listed below. Some differences would favour a higher recovery rate in the control series, others in the treated series. However, when considered as a whole the two series are not dis-similar. As they were not observed over the same period of time they are not acceptable for statistical analysis. For convenience the conservatively treated series will be referred to in the text as the "control series" and the series receiving anti-coagulant therapy as the "treated series".

The two series differ in the following respects :

(1) Age: The males in the treated series averaged 57 years as against the 54.5 years of the control series. In the treated series there were fewer males under the age of 50 years than in the control series.

(2) Previous Hypertension: Was more common in the treated series than in the control series, occurring /

occurring in 52% of the males and 79% of the females as opposed to 38.5% (male) and 43% (female) in the control series.

(3) Previous Effort Pain: was more common among the females in the treated series (62.5%) than among those in the control series (47%).

(4) Obesity: was more common in both sexes of the treated series - 41% (male) and 75% (female), than in the control series - 28.5% (male) and 43% (female).

(5) Two cases in the treated series were admitted after their 4th myocardial infarct and one again after her fifth infarct.

(6) In the control series there were seven cases in cardiac grade III prior to their infarct, as opposed to 2 cases in the treated series.

(7) A higher proportion of the control series had painless infarcts - 18% as against 6% in the treated series.

(8) A severe degree of shock at the time of onset was more common in the treated series than in the control series - 37% as against 30%.

(9) A pulse rate of over 100/min. after the infarct was more common in the control series - occurring in 49% of cases as opposed to 30% in the treated series.

(10) A high leucocytosis, a rapid blood sedimentation rate, and a high temperature after the infarct /

infarct were all more common in the treated series than in the control series.

(11) Electro-cardiographically anterior infarcts were more common among the treated males and posterior infarcts in the treated females, than in the control series.

Probably the most important difference between the two series is in the incidence of a pulse rate of over 100/min. As discussed in section VI. this feature is important in assessing the immediate prognosis. The possibility that this lower incidence in the treated series may be the result of the anti-coagulant therapy will be commented on later.

(b) Mortality Rates: In the control series 30 males and 16 females died during the first 6 weeks after the myocardial infarct - the sex mortality rates being 43% and 53%. In marked contrast, only 7 males and 9 females in the treated series died during the same period, the sex mortality rates being 15% and 37.5% respectively. Were statistical methods of analysis applicable to the investigation the reduction in male mortality is highly significant (calculation of the χ^2 gives P as less than 0.01). On the other hand the reduction in the female mortality rate is not statistically significant. The duration of survival after the myocardial infarct differs in one important respect in the two series, namely that in the control series 12 males died, on the first day, whereas /

whereas in the treated series there were no deaths on the first day. If these 12 cases be excluded from the control series, the male mortality rate drops from 43% to 31%. This is still considerably in excess of the 15% male mortality in the treated series, (but the difference would no longer be of statistical significance P being between 0.05 and 0.1).

(c) Incidence of Thrombo-Embolic Complications:

One or more thrombo-embolic complications occurred in 24% of the control series. In the treated series only 11% experienced such an upset while anti-coagulant treatment was effective. This reduction is considerable but statistically it is within the bounds of a possible chance happening. More striking has been the fact that in the treated series none of the males involved died, although only two were under 60 years of age. In the control group, thrombo-embolic episodes in males over 60 years were associated with a fatal outcome in 7 of 9 cases (although the episodes were not necessarily directly responsible for death). The three females in the treated series who suffered thrombo-embolic complications, all had serious complications and all died. They were elderly being aged 65 years, 66 years and 67 years. In the control series on the other hand, 11 females suffered thrombo-embolic complications, and of these only 5 died.

In /

In the discussion on immediate prognosis after myocardial infarction in section VI. it was stated (page 134) that "thrombo-embolic complications, particularly a recurrence of myocardial infarction would appear to be important in deciding the outcome among males in cardiac grade IIA who have also cardiac enlargement". Of 28 males so classed, 14 died, 4 from a recurrence of myocardial infarction and one after a cerebral embolus. Only one episode - a pulmonary infarct - interrupted recovery in the 14 survivors. In no other group did the occurrence of thrombo-embolic complications so influence the outcome. In the treated series, eighteen out of 23 males in grade IIA had a large heart. Not one suffered a thrombo-embolic complication and only one died. In a comparison of the immediate mortality among the males in the four cardiac grades only males in grade IIA have shown an improvement with anti-coagulant therapy - (Figure 14). The over-all mortality rate of the grade IIA males (i.e. cases with no cardiac enlargement, plus those with cardiac enlargement) dropped from 42% in the control series to 4% in the treated series.

Among the females in the control series, thrombo-embolic complications were not important in influencing prognosis in any group. A marked reduction in female mortality as a result of a reduction in the frequency of thrombo-embolic episodes is therefore /

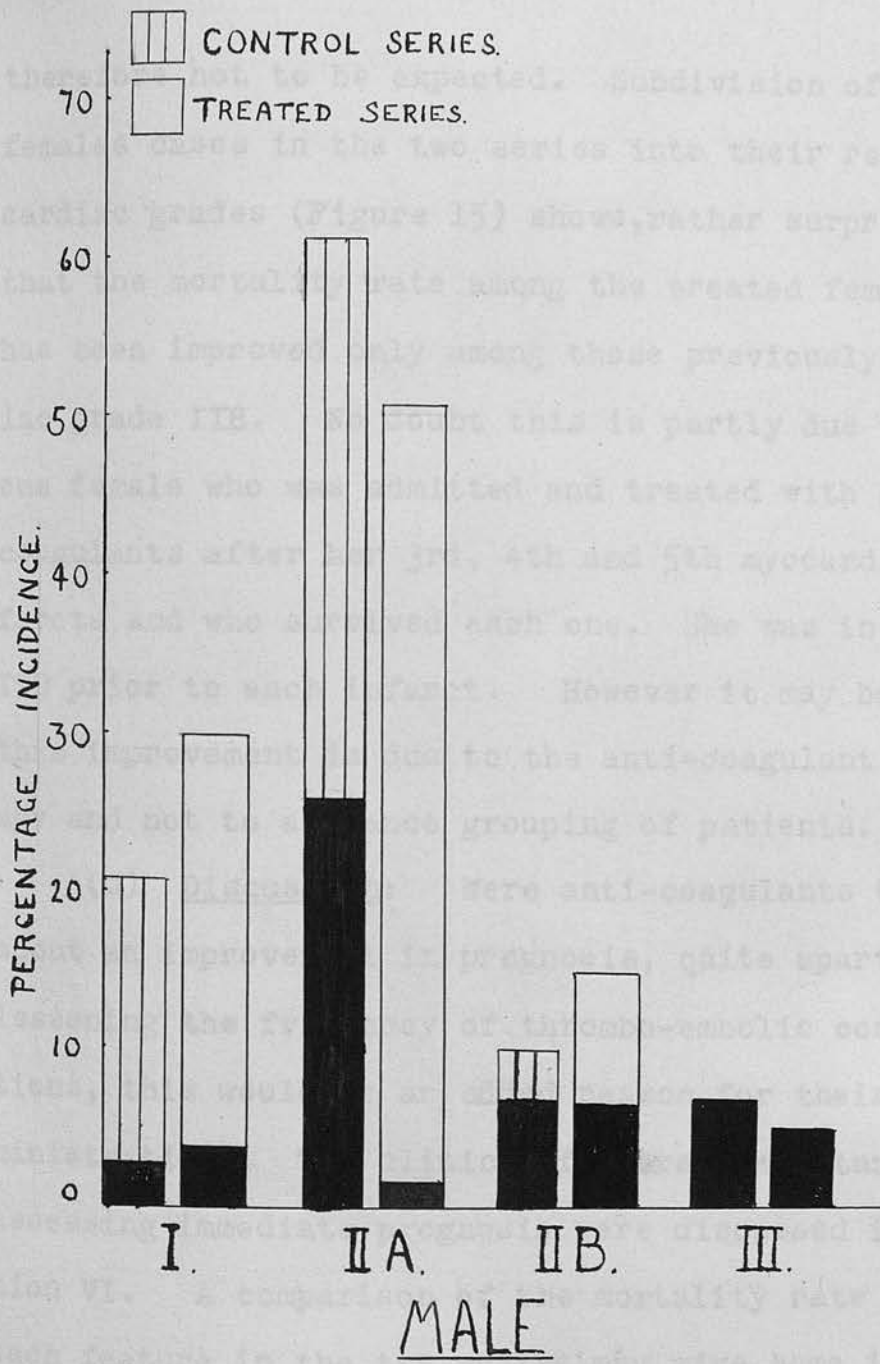


Figure XIV. The distribution of cases in the cardiac grades prior to the myocardial infarct is illustrated for both the control and treated series. The proportion of cases dying is shown in black.

therefore not to be expected. Subdivision of the females cases in the two series into their respective cardiac grades (Figure 15) shows, rather surprisingly, that the mortality rate among the treated females has been improved only among those previously in cardiac grade IIB. No doubt this is partly due to the one female who was admitted and treated with anti-coagulants after her 3rd, 4th and 5th myocardial infarcts and who survived each one. She was in grade IIB prior to each infarct. However it may be that this improvement is due to the anti-coagulant therapy and not to a chance grouping of patients.

(d) Discussion: Were anti-coagulants to bring about an improvement in prognosis, quite apart from lessening the frequency of thrombo-embolic complications, this would be an added reason for their administration. The clinical features important in assessing immediate prognosis were discussed in section VI. A comparison of the mortality rate for each feature in the two series may give some indication whether anti-coagulants do influence the prognosis, other than by reducing thrombo-embolic complications, or not. The feature invariably associated with a fatal outcome - persistent gallop or tic-tac rhythm, and a state of profound shock with inaudible or very faint heart sounds, and an unrecordable blood pressure - need not be discussed. It is inconceivable that anti-coagulant therapy could improve such cases.

The /

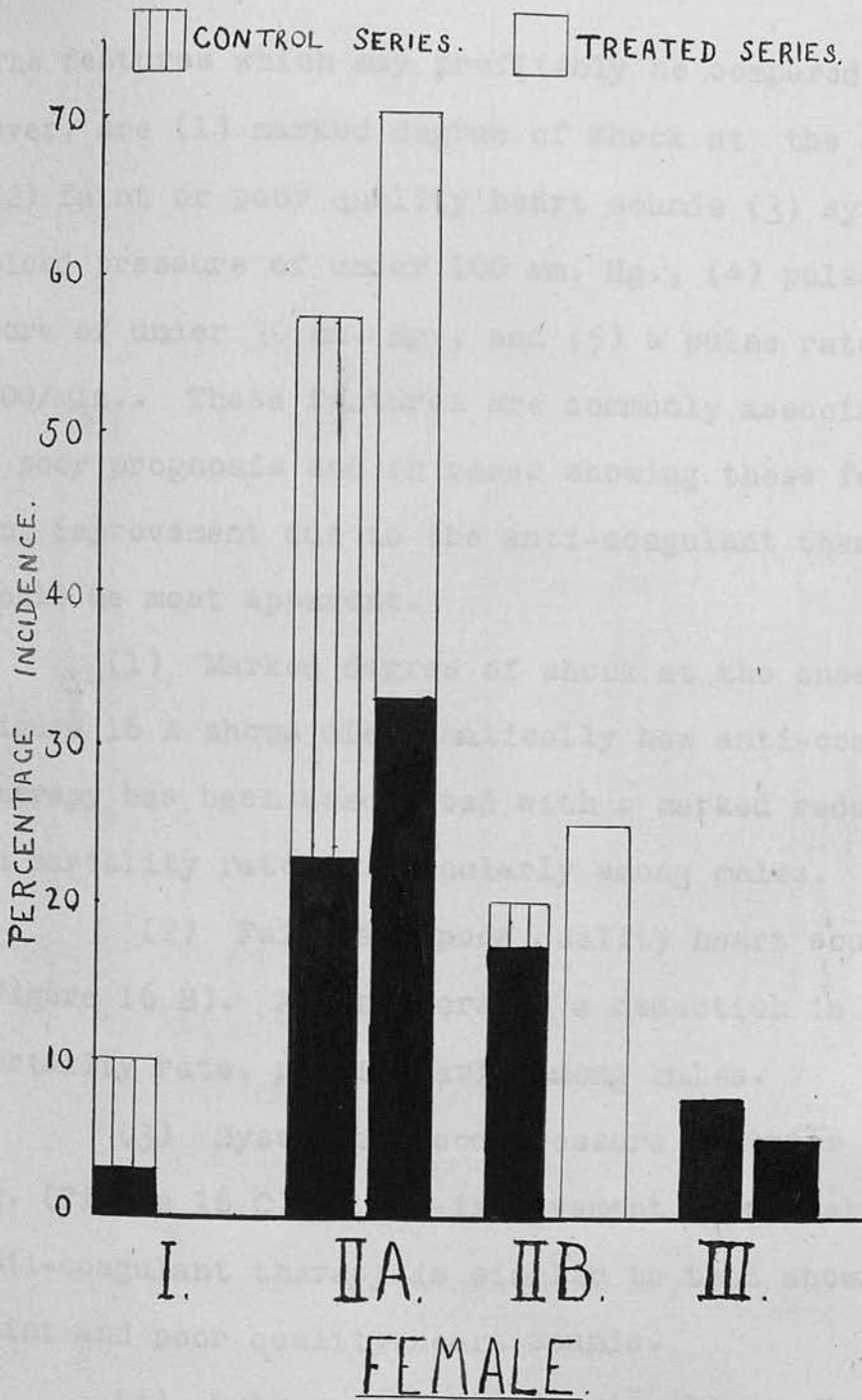


Figure XV. The distribution of cases in the cardiac grades prior to the myocardial infarct is illustrated for both the control and treated series. The proportion of cases dying is shown in black.

The features which may profitably be compared, however, are (1) marked degree of shock at the onset, (2) faint or poor quality heart sounds (3) systolic blood pressure of under 100 mm. Hg., (4) pulse pressure of under 30 mm. Hg., and (5) a pulse rate of over 100/min.. These features are commonly associated with a poor prognosis and in cases showing these features, any improvement due to the anti-coagulant therapy would be most apparent.

(1) Marked degree of shock at the onset.

Figure 16 A shows diagrammatically how anti-coagulant therapy has been associated with a marked reduction in mortality rate, particularly among males.

(2) Faint and poor quality heart sounds.

(Figure 16 B). Again there is a reduction in the mortality rate, particularly among males.

(3) Systolic blood pressure of under 100 mm. Hg. (Figure 16 C). The improvement in mortality with anti-coagulant therapy is similar to that shown for faint and poor quality heart sounds.

(4) Pulse pressure of under 30 mm. Hg..

(Figure 16 D). The improvement in male mortality has been striking, but in the small number of female cases in the anti-coagulant series, (3 cases) there has been a 100% mortality.

(5) Pulse rate of over 100/min. (Figure 16 E).

The improvement in male mortality associated with anti-coagulant therapy has been slight, while females have shown no improvement.

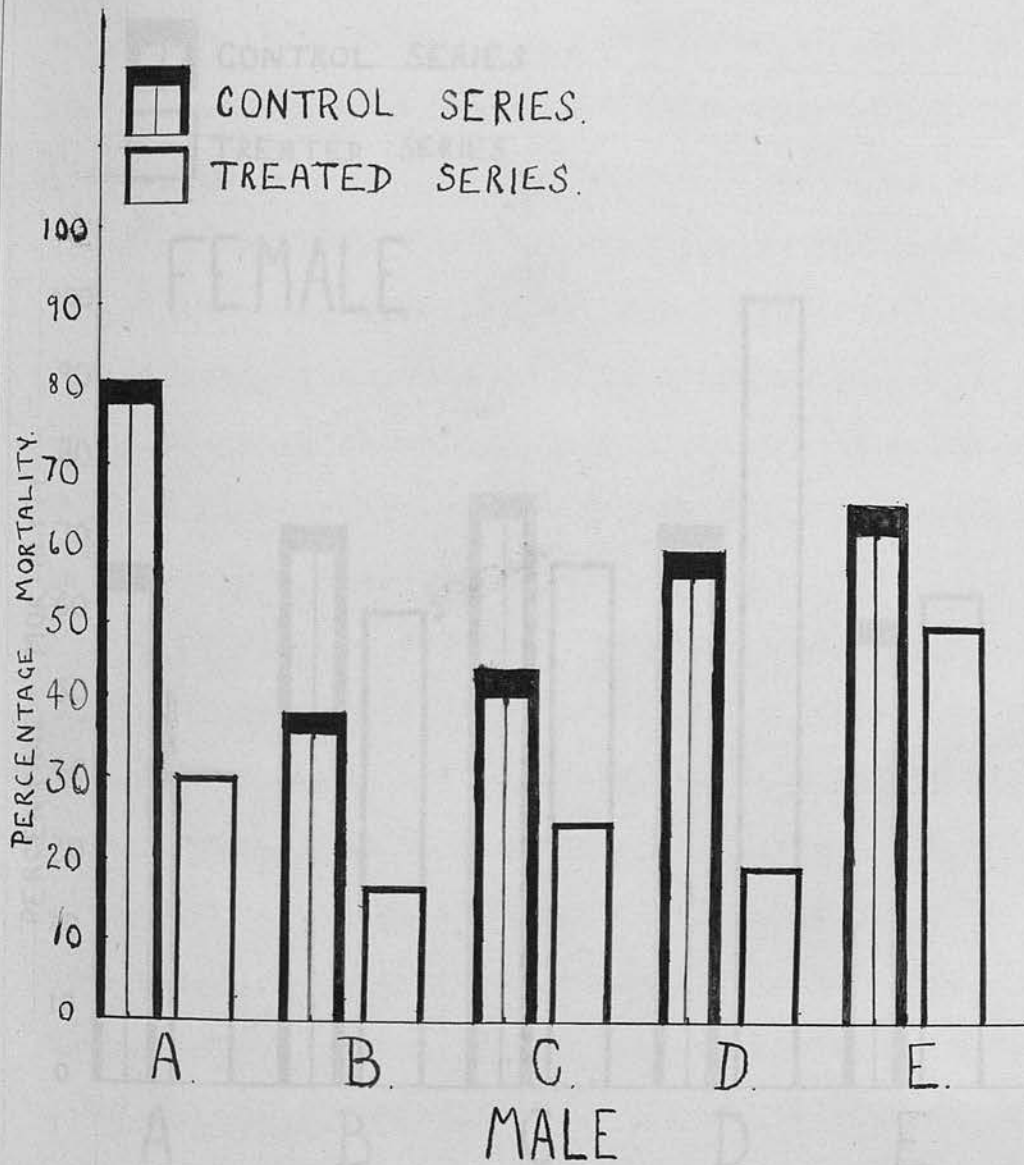


Figure XVI. The mortality rate in the control and treated series is compared, among cases showing (A) a marked degree of shock at the onset, (B) faint or poor quality heart sounds, (C) systolic B.P. under 100 mm. Hg., (D) pulse pressure under 30 mm. Hg., (E) pulse rate over 100/min..



CONTROL SERIES

TREATED SERIES

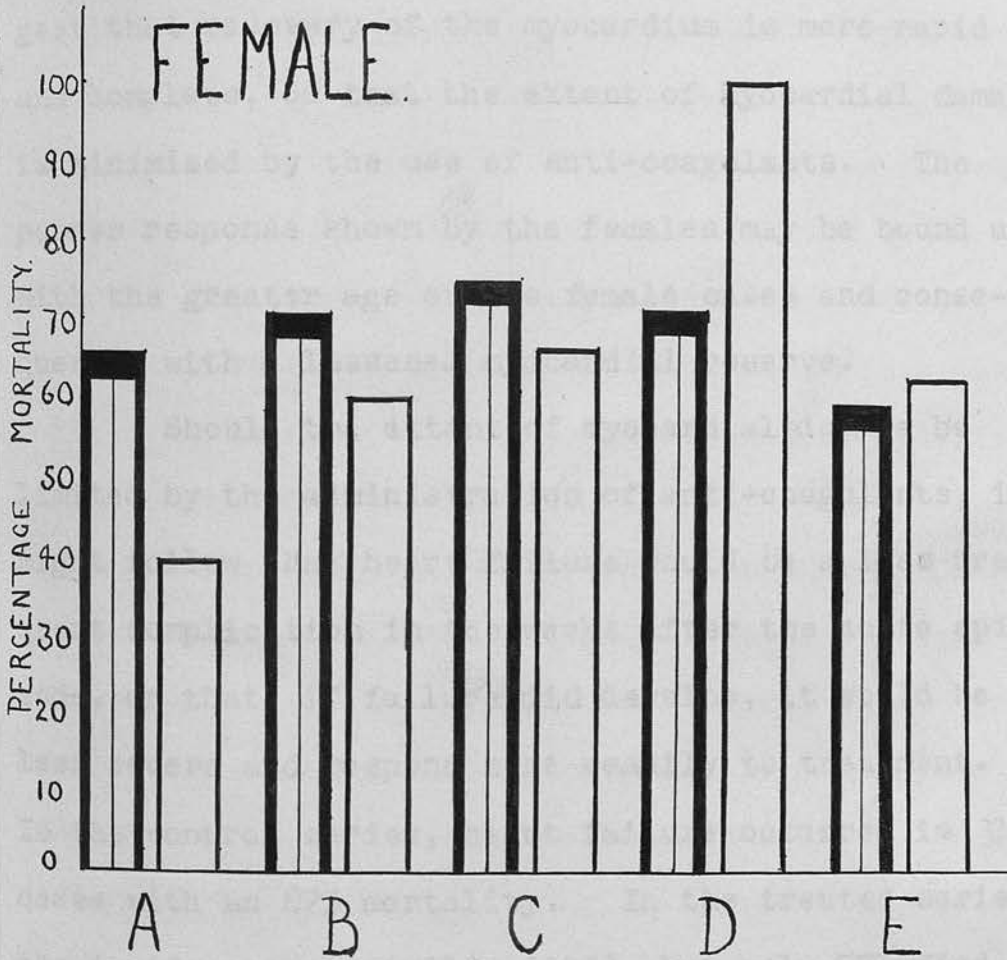


Figure XVI. The mortality rate in the control and treated series is compared, among cases showing (A) a marked degree of shock at the onset, (B) faint or poor quality heart sounds, (C) systolic B.P. under 100 mm. Hg., (D) pulse pressure under 30 mm. Hg., (E) pulse rate over 100/min..

The finding that a reduction in mortality has occurred among males receiving anti-coagulant therapy in each one of the features investigated might suggest that recovery of the myocardium is more rapid and complete, or that the extent of myocardial damage is minimised by the use of anti-coagulants. The poorer response shown by the females may be bound up with the greater age of the female cases and consequently with a lessened myocardial reserve.

Should the extent of myocardial damage be limited by the administration of anti-coagulants, it might follow that heart failure would be a less frequent complication in the weeks after the acute episode, or that, if failure did develop, it would be less severe and respond more readily to treatment. In the control series, heart failure occurred in 31 cases with an 87% mortality. In the treated series the incidence was similar (33%), but only 57% died. This would support the opinion advanced above that anti-coagulant therapy limits the extent of myocardial damage. The relative infrequency of a pulse rate of over 100/min. in the treated series, as compared with the control series and the improvement in mortality of the grade IIB female in the treated series may also have resulted from this effect.

The nine cases who died while receiving anti-coagulants and who came to autopsy all had "large" ~~xxxxxx~~ or "extensive" myocardial infarcts. In the control /

control series on the other hand only 21 of the 35 autopsied cases had "large" or "extensive" infarcts. In the remaining 14 cases the infarct was small or of moderate size, It is probable that prompt administration of anti-coagulants, particularly heparin, minimises or prevents thrombosis in the collateral vessels which must supply the infarcted area, thereby limiting or preventing any concentric enlargement of the infarct. The prognosis in a case with a small infarct or an infarct of moderate size might therefore be improved.

That adequate anti-coagulant therapy does prevent endocardial mural thrombus formation over the infarcted area is amply demonstrated in the autopsy cases. One case in congestive heart failure showed a very thin patch of thrombus over one part of a large infarct, but no other case showed any evidence of thrombus formation. Similarly no peripheral or pulmonary infarcts were demonstrated, although one man dying in congestive heart failure had a terminal thrombosis in one small pulmonary artery. But is this great efficiency of anti-coagulant therapy in preventing mural thrombus formation entirely without risk to the patient? Is not formation of this mass of endocardial mural thrombus, nature's method - albeit a dangerous method - of splinting, immobilizing, and strengthening the infarcted area, and, through subsequent organization of the thrombus, of /

of increasing the thickness and probably the strength of the resulting scar ? Does absence of this layer of thrombus weaken the infarcted area rendering it more liable to rupture or to bulge with cardiac aneurysm formation; or does the concomitant action of the anti-coagulants in limiting extension of the infarcted area and in improving the collateral blood supply minimise any such weakening of the ventricular wall ?

Clinically there has been no increase in the incidence of rupture of the area of infarction, only one case occurring in the 70 treated cases. Cardiac aneurysm formation will be discussed in the follow up investigation in section XI.

Only two points remain to be mentioned, the first a technical one. Eight hourly intravenous injections of heparin have proved adequate in all cases except when thrombo-embolic episodes have preceded treatment. In such cases mural thrombus is already present and injections should be given at least 6 hourly and preferably 4 hourly, and the transition from heparin plus dicoumarol to dicoumarol alone should not be abrupt. Over a few days, the frequency of heparin injections and the size of the dose should be gradually reduced, before being stopped completely. In 2 cases in this series, who had suffered embolic phenomena before treatment was begun, the heparin was stopped abruptly when the dicoumarol /

dicoumarol was apparently effective. Both cases sustained a further thrombo-embolic episode within 24 hours, and the heparin had to be restarted.

Lastly the 3 weeks duration of dicoumarol therapy proved adequate in all but one of the 70 treated cases. This one man had a recurrence of myocardial infarction in the fifth week after the onset. Such a single event does not justify the work, or the inconvenience and risk to the patient, involved in continuing dicoumarol therapy for a longer period. Moreover the changes in the clotting mechanism to be discussed in section XIII. seldom persist in marked degree beyond the third week. It is probable that dicoumarol should be continued beyond the end of the third week only if a major thrombo-embolic episode takes place during the second or third week of treatment.

XI. /

The average age at the time of the myocardial infarction of those dying subsequently was 55 years for

XI. FOLLOW UP of 54 SURVIVORS of ACUTE MYOCARDIAL
INFARCTION TREATED with ANTI-COAGULANTS.

The subsequent course of all 54 cases is known. Fortysix have been re-examined, many repeatedly. Two have reported by letter, while in the remaining 6 cases the general practitioners concerned have supplied certain clinical details.

(1) Age at onset: The age at the time of the myocardial infarct is shown in Table LXI.

TABLE LXI. Age distribution of 54 cases surviving acute myocardial infarction treated with anti-coagulants, subdivided to show (a) subsequent fatal cases, and (b) survivors.

	Male.		Female.	
	Died Subsequently	Still Alive	Died Subsequently	Still Alive
35-	-	1	-	-
40-	1	1	-	-
45-	1	3	-	-
50-	-	10	-	-
55-	1	6	1	-
60-	-	10	2	6
65-	-	2	-	4
70	1	2	-	2
Total *	4	35	3	12

The average age at the time of the myocardial infarct of those dying subsequently was 55 years for the /

the males and 61 years for the females, in comparison with the 56.5 years and 66 years respectively of those still alive.

(2) Period of follow up: The interval over which the cases have been followed varies between 3 months and 2 years 10 months. No case still alive has been followed for less than 6 months. The average duration of survival of the 39 male cases is 1 year $4\frac{1}{2}$ months, and of the 15 females, 1 year $\frac{1}{2}$ month.

TABLE LXI A. Duration of survival after myocardial infarction of 54 cases treated with anti-coagulants.

	Male.		Female.	
	Died Subsequently	Still Alive	Died Subsequently	Still Alive
0 - $\frac{1}{2}$ yrs.	1	1	2	1
$\frac{1}{2}$ - 1 yrs.	1	13	1	4
1 - $1\frac{1}{2}$ yrs.	1	8	-	2
$1\frac{1}{2}$ - 2 yrs.	-	3	-	5
2 - $2\frac{1}{2}$ yrs.	1	6	-	-
$2\frac{1}{2}$ - 3 yrs.	-	4	-	-

(3) Subsequent deaths: The deaths took place between 3 months and 2 years 5 months after the infarct. Duration of survival and cause of death are listed in Table LXII.

TABLE LXII. /

TABLE LXII. Duration of survival of 7 cases dying after a myocardial infarct treated with anti-coagulants, and cause of death.

Duration of Survival (Years)		Cause of Death.
Male	Female	
$\frac{3}{12}$ (48)		Sudden.
	$\frac{14}{52}$ (56)	Recurrence of myocardial infarction.
	$\frac{6}{12}$ (64)	Recurrence of myocardial infarction.
$\frac{7}{12}$ (71)		Hemiplegia.
	$\frac{9}{12}$ (62)	Recurrence of myocardial infarction.
$\frac{15}{12}$ (56)		Angina pectoris.
$\frac{29}{12}$ (44)		Pontine haemorrhage.

Age at the time of the myocardial infarct treated in hospital is given in brackets.

Five of the seven deaths took place within the first year. Only 2 deaths were from causes unrelated to the heart - a pontine haemorrhage, and a hemiplegia. All three females died within a few hours of a fresh myocardial infarct. In the case of the female aged 56 years this was her second infarct after discharge from hospital and her third in 4½ months. The male dying of angina pectoris was treated during his second myocardial infarct. He was extremely incapacitated by anginal pain both before and /

and after each infarct, and had developed early congestive heart failure before death. Lastly the male who died suddenly did so while removing his clothing preparatory to being examined. At autopsy no cause was found. He had given a history of momentary loss of consciousness while sitting in a barber's chair 2 weeks previously, and may have had a paroxysmal arrhythmia.

(4) Cardiac Grade after Myocardial Infarction:

This is known for 36 males and for all 15 females. Three males have not been reclassified - two were handicapped by a hemiplegia, and the third has had a mid-thigh amputation of a leg.

TABLE LXIII. Lowest cardiac grade after myocardial infarction in 51 cases treated with anti-coagulants.

	Died after Discharge		Still Alive	
	M.	F.	M.	F.
Grade I	-	-	1	-
IIA	1	3	23	4
IIB	3	-	8	8
III	-	-	-	-

Eighteen males and three females had to be regraded after the infarct, their functional capacity being reduced, - eleven males passed from grade I to grade IIA, and seven from grade IIA to grade IIB; three females passed from grade IIA to grade IIB. One male /

male and one female regraded as IIB have since regained their lost exercise tolerance (i.e. are now grade IIA). Among males, the subsequent mortality has increased as the functional capacity of the patient has decreased, but as yet, all the females in grade IIB have survived.

(5) Ability to return to work: Thirty of the 39 males who survived the myocardial infarct had been working prior to the onset. Twenty-four males who are still alive returned to some form of work. Four are doing work of a strenuous nature, while a fifth does heavy work; three had been in cardiac grade I prior to their infarct and two were in grade IIA. Three cases have had to give up work because of a deterioration in their effort tolerance. Only 2 of the males who died subsequently had previously been at work and neither had recommenced work prior to death. Of the 15 women who survived the myocardial infarct, only two are fit for all household duties. Three others - one of whom died after 9 months - found the heavier household tasks beyond their capabilities; while the 10 remaining cases - two of whom have since died - were fit for only the lightest of duties. In fact the 8 survivors, all of whom are in grade IIB, do virtually no work at all.

(6) Complications after myocardial infarction: Complications are common in the months and years following myocardial infarction. Forty-four of the

54 cases who survived the acute episode have since developed one or more complication.

TABLE LXIV. Complications arising in 39 males surviving myocardial infarction treated with anti-coagulants.

	Died Subsequently	Still Alive	Total
Angina Pectoris	2	13	15
Recurrence of Myocardial Infarction)	-	1	1
Hypertension	2	23	25
Left Ventricular Failure	-	3	3
Congestive Heart Failure(mild)	1	2	3
Arrhythmia	1 ?	-	1 ?
Cerebral Thrombosis	-	1	1
Intermittent Claudication	-	1	1
Phlebitis	-	1	1
Major Operation	-	3	3
Shoulder pain	1	3	4

Eleven of the 15 cases experiencing effort pain after the myocardial infarct, had also experienced pain prior to the infarct (two of them have since died). Five who had suffered effort pain prior to the infarct, have experienced no pain since returning to activity. All are still alive. In 25 cases, the blood pressure has returned to, or has risen to, a hypertensive /

hypertensive level. Fifteen of the cases, were known to have been hypertensive prior to the myocardial infarct; in seven the previous blood pressure level was unknown; while in one case the blood pressure had been in the normal range. Four cases who had been definitely hypertensive prior to the infarct showed no return to this hypertensive level. The possible arrhythmia recorded may have been the cause of the sudden death in the male who died just prior to a routine examination. Shoulder pain was associated with limitation of movement of the shoulder particularly abduction and external rotation. It was little influenced by heat and massage, but in each case slowly became less marked and less disabling over a number of months. The three major operations performed were (1) for a stone in the common bile duct; (2) prostatectomy and (3) a mid thigh amputation of a leg. This last operation was carried out in the 7th week after myocardial infarction.

(Case No. 25 page 320).

Females too, have shown frequent complications.

TABLE LXV. /

TABLE LXV. Complications occurring in 15 females after myocardial infarction treated with anti-coagulants.

	Died Subsequently	Still Alive	Total
Angina Pectoris	1	7	8
Recurrence of) Myocardial Infarction)	1	1	2
Hypertension	2	12	14
Left Ventricular Failure	-	1	1
Congestive Heart Failure(Mild)	-	3	3
Peripheral Neuritis	-	1	1
Cardiac Neurosis	-	1	1
Cancer	-	1	1
Troublesome Extra-Systoles	1	-	1

The eight cases experiencing effort pain after the infarct had all previously experienced pain. Three other cases were free of the effort pain they had suffered prior to the infarct. Of the 14 cases showing hypertension after the infarct, the blood pressure had previously been high in 12; in one the previous level was unknown; and in one it had been within normal limits. The fifteenth case showed no return of a hypertension previously present.

(7) Electro-cardiographic changes: In 43 cases, electrocardiograms have been taken at intervals after the myocardial infarct. Nine records have returned to within normal limits (3 posterior, 5 anterior, and 1 /

1 atypical). One other record has been normal throughout. Return to normality of the record is not associated with freedom from symptoms however, or indeed with survival. One male showing such a return to normality has since died.

X-ray examination has not revealed a single case of cardiac aneurysm formation.

(8) After care: This has been exactly similar to the routine adopted in the management of the survivors of the conservatively treated series.

(page 149).

XII. COMPARISON of the CLINICAL COURSE of the SURVIVORS of MYOCARDIAL INFARCTION TREATED (a) CONSERVATIVELY and (b) WITH ANTI-COAGULANTS.

The number of cases in each series, which have been followed up, and reported in detail in sections VII. and XI., are similar, - 37 males and 13 females treated conservatively, and 39 males and 15 females treated with anti-coagulants. As in section X. the two series will be referred to as the control and treated series. The period of observation of the control cases has been much longer than that of the treated cases. For accurate comparison of the subsequent mortality rates in the two series, only those cases in the control series who died during the first $2\frac{1}{2}$ years among males and $1\frac{1}{2}$ years among females, will be considered. Eight of 37 males in the control series died in the first $2\frac{1}{2}$ years, but only 4 of the 39 males in the treated series died during the same period - mortality rate of 21% and 10% respectively. Four of 13 females in the control series, and 3 of 15 females in the treated series died in the first $1\frac{1}{2}$ years - mortality rates of 31% and 20% respectively. Survivorship tables for the two series have been constructed. (Table LXVI. page 204).

TABLE LXVI. Survival tables for 1000 cases of each sex in a theoretical control and treated series.

	Period of obser- vation after in- farct.	Number of in- patients ob- served.	Number alive at end of period.	Probability of surviv- ing period.	Probability of not sur- viving period.	Calculated num- ber alive at end of each period.	Number dyin- g in each per- iod.
Female							
A Control	1 yr.	13	13	1	0	1000	0
	1 1/2	13	10	0.77	0.23	770	230
	2	10	9	0.90	0.10	693	77
B Treated	1 yr.	15	13	0.87	0.13	870	130
	1 1/2	8	7	0.89	0.11	774	96
	2	5	5	1.0	0.	774	0
		-	-	-	-	-	-
Male							
A Control	1 yr.	37	32	0.86	0.14	860	140
	1 1/2	31	29	0.93	0.07	800	60
	2	27	26	0.96	0.04	780	20
	2 1/2	25	25	1.0	0	780	0
		24	24	1.0	0	780	0
B Treated	1 yr.	39	38	0.97	0.03	970	30
	1 1/2	24	23	0.96	0.04	931	39
	2	15	14	0.93	0.07	866	65
	2 1/2	11	11	1	0	866	0
		5	4	0.80	0.20	693	173

Fewer deaths have occurred during this limited follow up period among the cases receiving anti-coagulant therapy than among the control series, except during the 2-2 $\frac{1}{2}$ year period among the treated males, when too few cases were observed to allow accurate construction of a survivorship table. An equal proportion of the deaths in each series have resulted from a cardiac cause - 71%.

The grading of cases according to functional capacity after the infarct is similar among the males of the two series. Twenty-five males in the control series and 27 in the treated series were in cardiac grade IIA, but only one male in the treated series remained in grade I. as opposed to 4 in the control group. Seven females in each series were in grade IIA but in the treated series eight were in grade IIB as opposed to 2 in the control series. A similar number of cases in each series returned to work - 25 males in the control series and 24 in the treated series. Only 2 women in each series were fit for much housework.

With the exception of hypertension and arry-
the
thmias/incidence of complications in the two series has been similar. In the treated series 25 males and 14 females developed hypertension after the myocardial infarct, as opposed to the minimum figures of 13 males and 3 females in the control series. Only one doubtful /

doubtful arrhythmia occurred in the treated series in contrast with the 4 cases in the control series. A non-fatal recurrence of myocardial infarction has occurred thrice in each series. Shoulder pain was observed in the treated series, but attention was not paid to this complication in the control series. No case of cardiac aneurysm formation has been detected in the treated series.

A return to normality of the electro-cardiogram was noted in each series - 29% of the cases in the control series who had follow up records taken showed a return to within normal limits, while 21% of the records in the treated series have also returned to within normal limits.

There is little difference between the two series, in the course pursued during the months and years after the myocardial infarct apart from (1) the lower mortality rate in the treated series during the first $1\frac{1}{2}$ years (female) and $2\frac{1}{2}$ years (male) after the myocardial infarct and (2) the higher incidence of hypertension after myocardial infarction in the treated series. Whether these two points of difference are chance findings or whether they are due in some way to the administration of anti-coagulants during the acute phase of infarction, must await investigation of a larger series of cases, and a longer period of observation. It is possible, however, that they provide corroborative evidence of the suggested effect of anti-coagulants in limiting the extent of myocardial damage.

XIII. OBSERVATIONS on the CLOTTING CHANGES
FOLLOWING MYOCARDIAL INFARCTION.

(a) Investigation of the clotting changes :

The Waugh-Ruddick heparin retarded clotting test was briefly described in section IV page 98. Using this test, serial observations have been made every few days on 12 cases of acute myocardial infarction treated conservatively. In addition 22 cases treated with anti-coagulants were investigated before treatment was begun, and again after its completion, in the 17 surviving cases. It is convenient to use the clotting time of tube 9 (containing $\frac{7}{10}$ ths unit of heparin) when comparing serial observations on one patient or single observations on a group of patients. Waugh & Ruddick state that in a series of 50 healthy adults the clotting time of tube 9 ranged between 64 mins. and 88 mins. with the average time of 71 mins.. Personal observations would suggest that 64 mins. is not the lower limit of normality, times of 56 and 54 minutes having been observed in healthy individuals. The temperatures at which the test is carried out is of extreme importance. The practice of the originators of the test was adhered to and all investigations were made at a room temperature of 18-20°C.. Raising the temperature to 37°C. greatly shortens the duration of the test but, although narrowing the range of normality, also reduces the difference between the normal and the abnormal.

Of the 12 conservatively treated cases on whom serial observations were carried out, four died, after 9, 10, 12 and 16 days. All 12 cases showed a progressive shortening of the clotting time of tube 9 i.e. they developed an enhanced clotting tendency. This was then followed by a return to normality. (Figure 17). In 10 cases the change was detected in the first week after the infarct - 3rd day, 2 cases; 4th day, 3 cases; 5th day, 3 cases; 6th day, 1 case; 7th day, 1 case. As daily tests were not done, it is possible that the change may have been present for one or two days before being detected. In one case, there was little variation in the clotting time of tube 9 until the 14th day after the infarct. This patient died 2 days later. The 12th case was not investigated until the 9th day after his infarct, by which time tube 9 was clotting quickly. (34 mins.). Excluding the case which died on the 9th day and which was not investigated after the 7th day, and the case dying on the 16th day which showed no changes before the 14th day, the maximum shortening of the clotting time of tube 9 was observed on the following days after the myocardial infarct - 7th day, 1 case; 9th day 2 cases; 10th day 2 cases; 11th day 1 case; 12th day, 1 case; 14th day 1 case; 15th day, 1 case; and 17th day 1 case. The shortest clotting time observed for tube 9 in these cases was - 38 mins. 1 case; 34 mins. 2 cases;

32 mins. 2 cases; 30 mins. 2 cases; 28 mins. 2 cases; and 26 mins. 1 case. Finally in the 8 survivors a return to normality was observed on the following days after the infarct - 14th, 18th, 20th, 22nd, 25th, 25th, 28th, and 34th days. These are

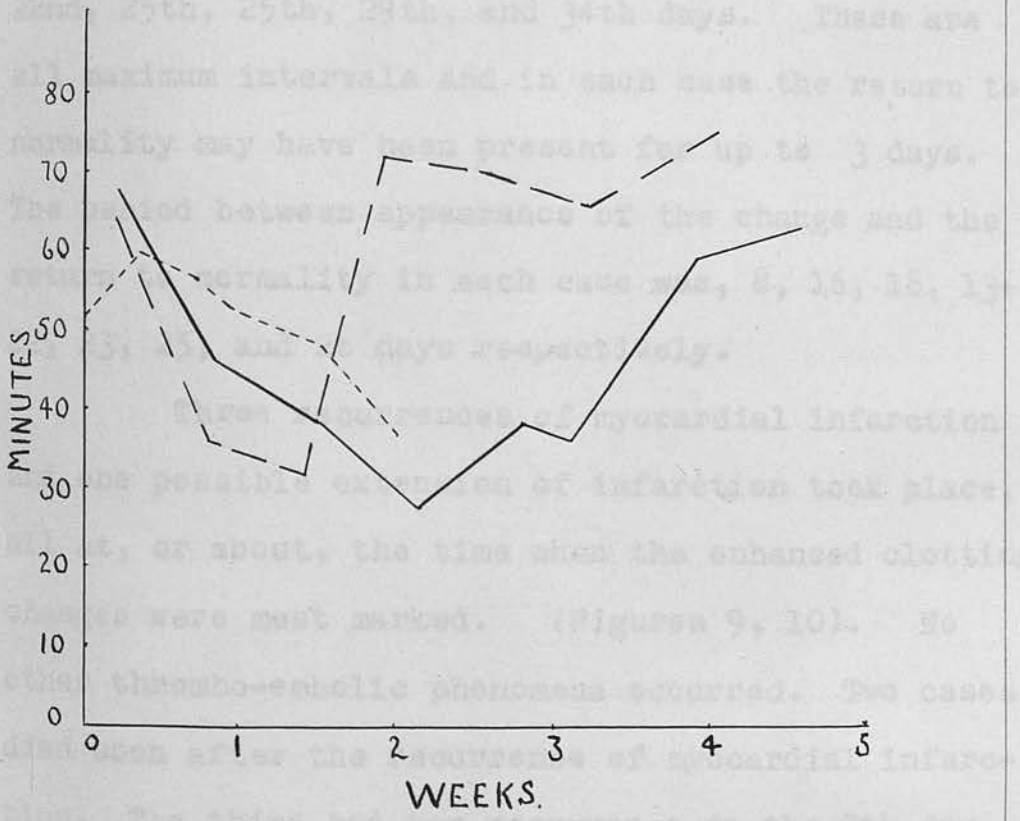


Figure XVII. The clotting time of tube 9 (Waugh-Ruddick heparin retarded clotting test) is recorded, and illustrates 3 varieties of changes after myocardial infarction. One case died on the 14th day.

Of the remaining 2 deaths, one occurred suddenly in a patient in heart failure who was receiving digitalis, while the other was due to left ventricular failure.

Two of the cases developing a recurrence of myocardial infarction while their blood showed a clotting tendency showed an unexpected change in the

32 mins. 2 cases; 30 mins. 2 cases; 28 mins. 2 cases; and 26 mins. 1 case. Finally in the 8 survivors a return to normality was observed on the following days after the infarct - 14th, 18th, 20th, 22nd, 25th, 25th, 29th, and 34th days. These are all maximum intervals and in each case the return to normality may have been present for up to 3 days. The period between appearance of the change and the return to normality in each case was, 8, 16, 18, 13+, 22, 23, 25, and 26 days respectively.

Three recurrences of myocardial infarction and one possible extension of infarction took place, all at, or about, the time when the enhanced clotting changes were most marked. (Figures 9, 10). No other thrombo-embolic phenomena occurred. Two cases died soon after the recurrence of myocardial infarction. The third had her recurrence on the 7th day and by the 18th day her clotting times were within the normal range. The fourth case had a possible small extension of her infarct on the 14th day and the clotting changes did not regress until the 25th day.

Of the remaining 2 deaths, one occurred suddenly in a patient in heart failure who was receiving digitalis, while the other was due to left ventricular failure.

Two of the cases developing a recurrence of myocardial infarction while their blood showed a clotting tendency showed an unexpected change in the days /

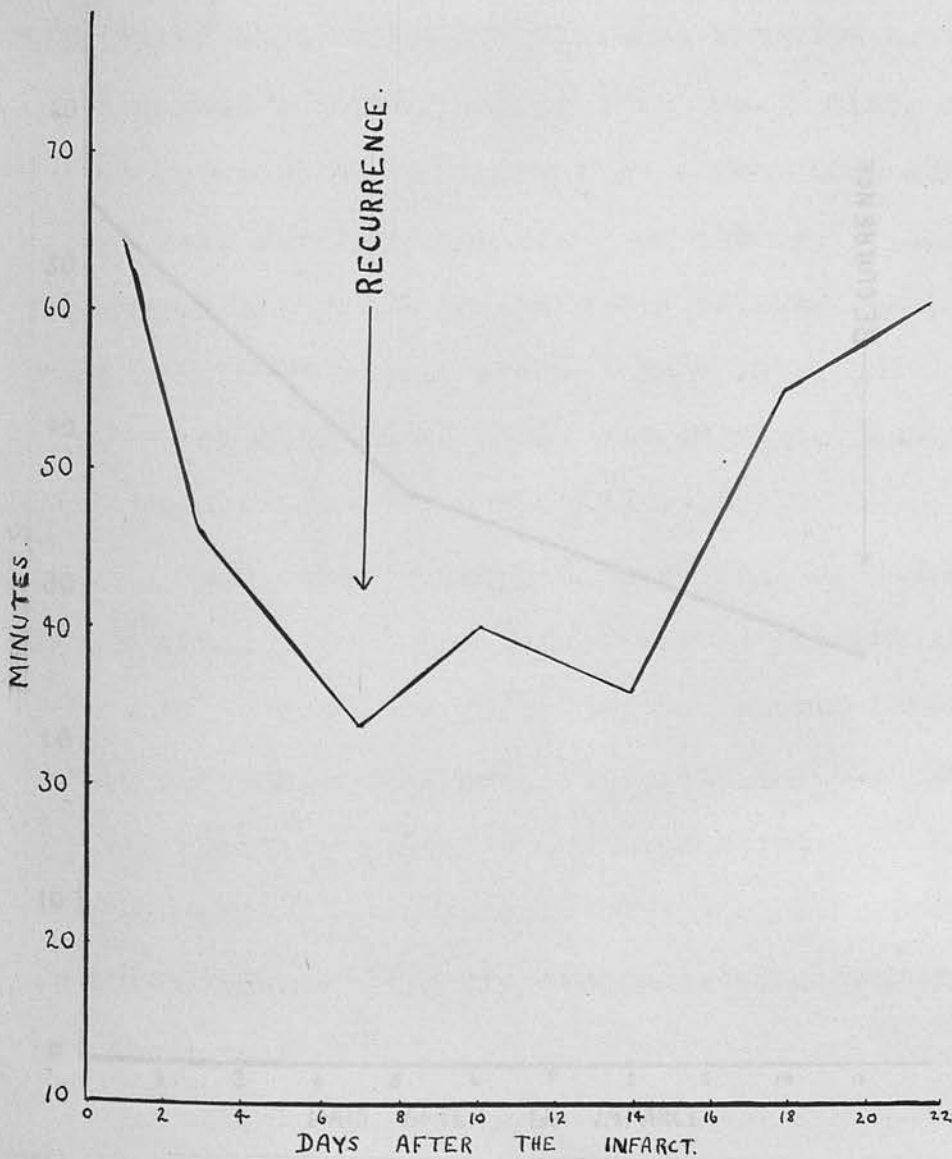


Figure IX. The graph records the clotting time of tube 9 (7/10ths unit of heparin / 2 c.c. saline) of the Waugh-Ruddick heparin retarded clotting test, at intervals of a few days, after myocardial infarction, and demonstrates the development of a clotting tendency. A recurrence of myocardial infarction occurred while the enhanced clotting was present.

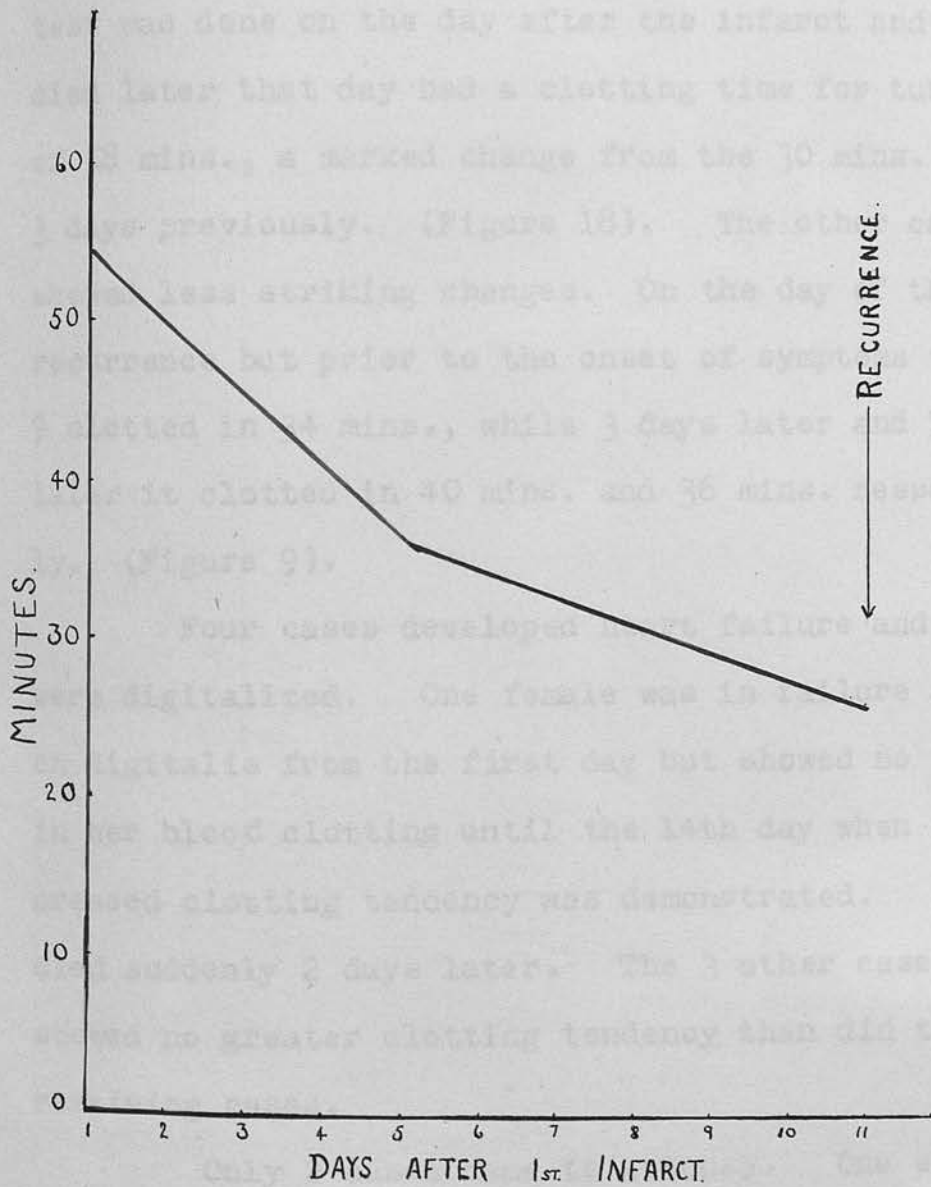


Figure X. As in figure IX, the clotting times of tube 9 are recorded, and the development of a clotting tendency is demonstrated. A recurrence of myocardial infarction with death occurred while enhanced clotting was present.

days succeeding the recurrence. One in whom the test was done on the day after the infarct and who died later that day had a clotting time for tube 9 of 58 mins., a marked change from the 30 mins. of 3 days previously. (Figure 18). The other case showed less striking changes. On the day of the recurrence but prior to the onset of symptoms tube 9 clotted in 34 mins., while 3 days later and 7 days later it clotted in 40 mins. and 36 mins. respectively. (Figure 9).

Four cases developed heart failure and 2 were digitalized. One female was in failure and on digitalis from the first day but showed no change in her blood clotting until the 14th day when an increased clotting tendency was demonstrated. She died suddenly 2 days later. The 3 other cases showed no greater clotting tendency than did the remaining cases.

Only 2 cases came to autopsy. One showed no evidence of mural thrombus formation - the female who had no change in her clotting time until the 14th day, while the other, whose clotting changes had begun on the 3rd day, and who died on the 12th day, after a recurrence of myocardial infarction had extensive mural thrombus.

Among the 22 cases investigated prior to anticoagulant treatment the clotting time of tube 9 varied depending on the time interval after the myocardial /

The results observed were as follows:

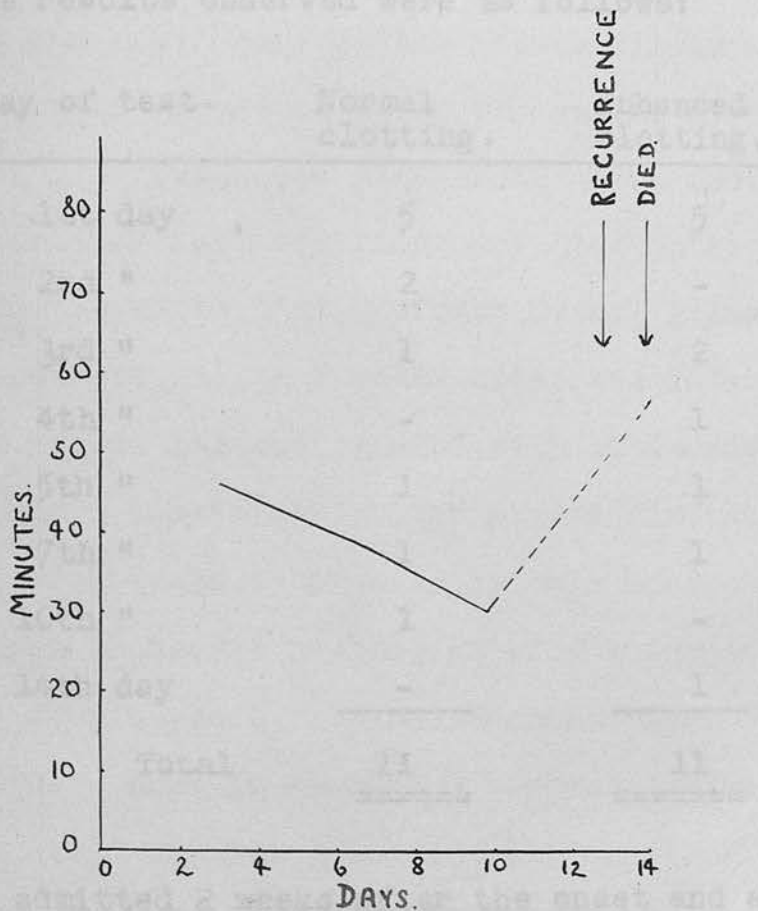


Figure XVIII. As in figure 17, the clotting time of tube 9 is recorded. The changes between the time of 30 mins. on the 10th day, the recurrence on the 13th day, and the 58 mins. recorded on the 14th day are unfortunately not known.

The five treated cases showing an advanced clotting tendency on the day of the myocardial infarct, and one other untreated case dying on the 14th day also showed this change (this case is not mentioned elsewhere in this section) were discussed in section IV.

Changes in Plasma Fibrinogen:

Plasma fibrinogen levels have been estimated

myocardial infarct.

The results observed were as follows:

Day of test.	Normal clotting.	Enhanced clotting.
1st day	5	5
2nd "	2	-
3rd "	1	2
4th "	-	1
5th "	1	1
7th "	1	1
10th "	1	-
14th day	-	1
Total	<u>11</u> =====	<u>11</u> =====

One case admitted 2 weeks after the onset and after 2 embolic episodes had a clotting time for tube 9 of 24 mins.. In the 17 cases surviving the infarct the test was repeated about 7-10 days after dicoumarol had been stopped. In each instance it was within normal limits.

The five treated cases showing an enhanced clotting tendency on the day of the myocardial infarct, and one other untreated case dying on the 1st day who also showed this change (this case is not mentioned elsewhere in this section) were discussed in section IV.

(b) Changes in Plasma fibrinogen :

Plasma fibrinogen levels have been estimated in /

in 8 cases after myocardial infarction, one treated with anti-coagulants and 7 treated conservatively. All showed a rapid rise in the plasma fibrinogen content, reaching almost to twice the normal level. (Figure 19). Two cases died on the 12th and 16th days. In 5 of the remaining cases the level fell to within the upper limits of the normal plasma fibrinogen content in 3 - 4 weeks after the infarct. The last case - the one treated with anti-coagulants - had a persistently high plasma fibrinogen level after 6 weeks. Presumably this increase must result from increased production of fibrinogen by the liver. Fibrinogen B has been demonstrated on only 3 occasions - once in each of 3 persons. The prothrombin time was not significantly shortened in any of the 70 cases of myocardial infarction treated with anti-coagulants.

(c) Discussion:

Why is it that after myocardial infarction thrombus should form on the endocardial surface of the infarcted area, either in the ventricle or auricle, and also, on occasions, in the pulmonary and peripheral arteries and veins? Also why should these changes be manifest mainly during the first 3 weeks after the infarct? What has upset the mechanism maintaining the normal fluid state of the blood? According to the Schmidt-Fuld Morawitz theory of blood coagulation, the change takes place in two stages -

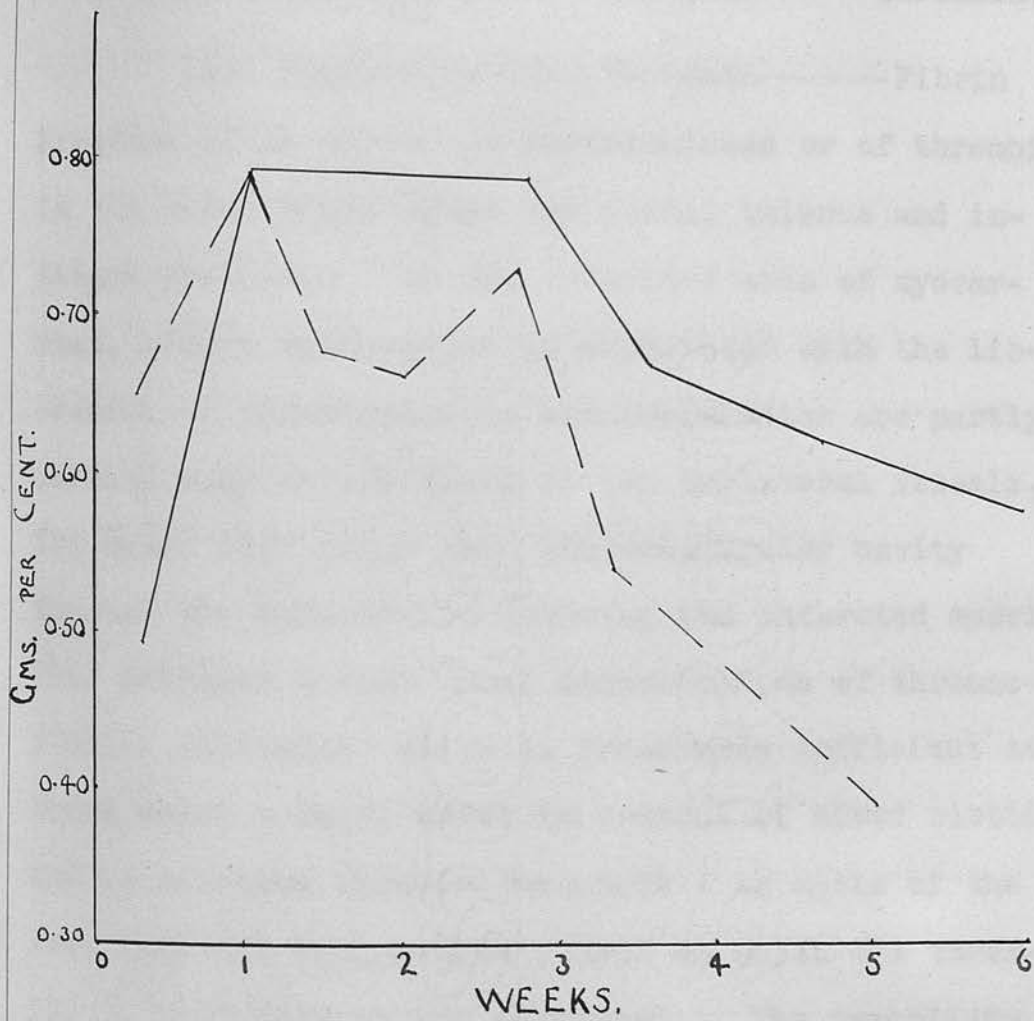


Figure XIX. Changes in the plasma fibrinogen content after myocardial infarction, as occurred in 2 cases.

stages -

Thrombokinase

(1) Prothrombin——Calcium.——Thrombin.

(2) Fibrinogen——Thrombin——Fibrin

Presence of an excess of thrombokinase or of thrombin in the blood might upset the normal balance and initiate clotting. In the infarcted area of myocardium, tissue destruction is associated with the liberation of thromboplastic substances which are partly carried away in the blood by the collateral vessels, but which also exude into the ventricular cavity through the endocardium covering the infarcted muscle. This produces a high local concentration of thromboplastic substance which is presumably sufficient to bring about a local upset in control of blood clotting and to initiate thrombus formation - in spite of the fact that the endocardium itself on which the thrombus is laid down is not infarcted. The immobility of the infarcted area relative to the remainder of the myocardium no doubt plays a part in not dislodging the thrombus once it has formed. The thrombus then acts as a foreign body in the blood stream on which further thrombosis occurs. The peripheral thrombotic episodes may be related to the excess of thromboplastic substances escaping into the blood stream and favouring initiation of blood clotting, but local vessel disease probably plays a part in determining the site of thrombosis. Peripheral infarcts /

Evidence

infarcts, resulting either from local arterial thromboses or from embolic arterial occlusion, would add their quota of thromboplastic substances to the blood stream.

What is the defence mechanism of the body against such excessive and continued production and liberation into the blood stream of thromboplastic substances? Much of the normal anti-clotting mechanism of the body is provided by heparin, or by a substance or substances derived from heparin. Heparin is the internal secretion of the mast cells of Ehrlich. It is believed to have five actions whereby it interferes with each stage of the clotting mechanism. (1) Along with a plasma co-factor it prevents the conversion of prothrombin to thrombin, (2) it is an anti-thrombokinase, (3) again in association with a plasma co-factor it is a strong anti-thrombin, (4) it prevents agglutination and disintegration of platelets, and (5) it causes fibrinolysis of a fresh clot. The mast cells of Ehrlich are distributed throughout the body around the capillaries and small vessels, with the maximum concentration in the liver and lungs. From that perivascular position they pass their secretion directly into the blood stream. How is the activity of these cells regulated? Under what stimulus is heparin formed and secreted? Is secretion continuous or intermittent? Are all the mast cells functioning at one time or is there /

there a large reserve? The physiology of heparin is not known.

Does any upset in the clotting mechanism favouring the occurrence of thrombosis, act as a stimulus to the mast cells and increase the secretion of heparin? If this enhanced clotting tendency is marked and long continued, will exhaustion of the mast cells result or will a stage be reached at which the cells are working to capacity but are not capable of maintaining the normal balance between the "clotting" and "anti-clotting" factors in the blood. A method of estimating the amount of heparin circulating in the blood is required, which does not involve the clotting time of blood in the technique.*

The changes in the heparin retarded clotting test following myocardial infarction could be explained by this lack of balance between thromboplastin production in the infarct and heparin secretion by the mast cells, but to what degree the mast cells respond by increasing heparin production, and whether the development of a marked clotting tendency indicates temporary exhaustion of these cells or not, must await further investigation. Are there any inferences which may be drawn from the clotting changes observed? Does absence of any change mean that no mural thrombus has formed or will form? On the other hand, does presence of a marked change imply

*

Since the section was written, the method described by Jaques and his associates (1949) has been noted in the literature. This involves precipitation of the heparin from citrated plasma by N - octylamine and reprecipitation with brucine.

that mural thrombus has formed? The two autopsy cases investigated and previously cited would lend some weight to both possibilities. The considerable variation from case to case in the duration of the clotting change, no doubt reflects the extent of myocardial damage and the activity of the system of mast cells in each case. With increasing age the efficiency of these cells may well diminish.

That anti-coagulant therapy does counteract this upset in the clotting mechanism, although apparently not completely in every instance, may be inferred from the relative absence of thrombo-embolic phenomena during anti-coagulant therapy and from the absence of mural thrombus at autopsy in adequately treated cases, even in those showing an enhanced clotting tendency prior to treatment.

XIV. SPECIFIC TREATMENT of the SHOCK ASSOCIATED
with ACUTE MYOCARDIAL INFARCTION.

In the two series of 170 cases reported in sections V. and IX., 4 deaths were due entirely to persistence of a severe degree of shock, and in one male who died in early congested heart failure, persistence of shock was doubtless a contributory factor. Until recent years, specific anti-shock treatment was discouraged, apart from warmth, the head low position, and the judicious use of stimulants such as adrenaline. The presence of shock was thought to be a protective mechanism, reducing to a minimum the strain on the damaged myocardium. The fact that this "protection" might sometimes be bought at the price of death from shock along was unfortunate but unavoidable. Shock i.e. peripheral circulatory failure, not only reduces the blood pressure and venous return to the heart, but also impairs the supply of blood to the myocardium. Wiggers (1947) demonstrated that in dogs persistence of a severe post-haemorrhagic hypotension for 135 minutes or more resulted in death from progressive myocardial insufficiency, even although the blood volume was restored by transfusion. Prinzmetal and his associates (1949) have shown that in dogs with myocardial infarction, if the degree of shock induced by bleeding is severe, not only is the amount of blood reaching /

reaching the infarcted area from the collateral vessels greatly reduced, but the remaining normal myocardium also becomes ischaemic and damaged. Ballooning of the infarcted area with each systole becomes marked. Restoration of the blood volume by transfusion results in a disappearance or lessening of this ballooning.

Human beings who develop myocardial infarction following coronary artery occlusion already have an impaired coronary blood flow due to the arteriosclerotic narrowing of the arteries. The risk of generalized myocardial ischaemia during a period of severe shock, is greater than in the experimental animal. Specific anti-shock treatment is therefore imperative in all cases showing a severe degree of shock at the time of their myocardial infarct.

Therapy should be instituted as soon as possible after the shock develops, as the longer the hypotension exists, the more coronary insufficiency and myocardial damage can be expected. If the patient has been shocked for a long period of time, the prognosis is poor and may be hopeless, because of irreversible changes in the myocardium. Even if the shock be relieved the patient will still die of heart failure. That is the risk in every case, either because of the myocardial changes while the shock persists or because of the size of the original infarct. Myocardial rupture is unlikely if treatment is begun early.

Prinzmetal (1949) recommends that treatment should /

should consist of (1) transfusion of whole blood or plasma, or glucose solution, and (2) administration of pressor agents - adrenaline 3-4 minims (1:1,000 solution) every 15 minutes, caffeine, or coramine. Plasma is the fluid of choice as there is often haemo-concentration due to vomiting and profuse sweating. If pulmonary oedema is present, plasma should be administered cautiously if at all, and chief reliance should be placed on the pressor drugs. Inevitably cases will be treated who would recover without any specific treatment, or who would die regardless of the treatment, but between these two extremes are the cases where treatment of shock is life-saving.

Our own experience of specific anti-shock treatment is limited to 3 cases, one in the treated series, and two in neither series. The methods adopted were (1) the head low position in bed, (2) warmth, (3) oxygen, (4) plasma infusion, (5) coramine hourly or 2 hourly. Only 2 cases received coramine.

The first case treated is reported in detail on page 293. Specific anti-shock measures were instituted 42 hours after the onset of symptoms, 1 pint of plasma and 11 oz. of 6% glucose being given over 28 hours. For about 24 hours there was considerable improvement but evidence of heart failure then developed and she died on the morning of the 5th day. Autopsy showed very extensive myocardial damage.

The second case (Case number 33 page 337) was treated within 6 hours of the onset of symptoms. One pint of plasma was given over 5 hours. The response was striking and within 18 hours of the onset she had improved greatly. Evidence of mild left ventricular failure developed on the third day, but cleared after 2 days. After 2 weeks, when an electro-cardiogram was obtained the record indicated that the degree of myocardial damage was slight.

The third case was first seen 12 hours after the onset of symptoms. She was severely shocked, but also showed evidence of left ventricular failure. In view of this plasma was not given. Twelve hours later, the degree of shock was greater but the chest was clear. Plasma infusion was begun forthwith but the patient died 2 hours later.

These 3 cases do little more than indicate (1) the importance of early treatment of the shock, and (2) the risk of heart failure following recovery from the shock. In the first case, the infusion was definitely given at too slow a rate.

XV. CORONARY ARTERY EMBOLISM.

Embolic occlusion of a coronary artery is a rare event. In 1941, Hamman reported a series of 40 cases, including 19 reported by Saphir 9 years earlier. Hamman cited 6 possible sources of the embolus but stated that bacterial vegetations on the mitral and aortic valves were the site of origin in about 50% of cases. He stressed the facts that death might occur suddenly, but that if the immediate effects of the embolic occlusion were withstood, the ultimate prognosis was good.

Of the 170 cases of myocardial infarction reported in sections V. and IX., one case had resulted from an embolic occlusion of a coronary artery. This was a female aged 63 years with mitral stenosis and auricular fibrillation, who was in congestive heart failure. The embolus lodging in the coronary artery was one of a series of small emboli thrown out from the left auricle during the course of one day. Although the myocardial infarct produced was small it probably contributed to an increase in the congestive heart failure and to death 5 days later. At autopsy, the coronary arteries were healthy. No embolus could be found in any of the major trunks.

During the years 1945 to 1949, forty-five cases of subacute bacterial endocarditis came under the care of Dr. A. Rae Gilchrist in the Royal Infirmary Edinburgh.

Three cases sustained one embolic occlusion of a coronary artery with myocardial infarction; one case suffered two such occlusions; while in a fifth the sudden onset of left ventricular failure with rapid death was thought to be due to a sudden myocardial infarct. All had rheumatic heart disease; four having both mitral stenosis and aortic incompetence, while the fifth had mitral stenosis alone. Two were females and three were males. Their ages were 20 years and 32 years; and 18 years, 31 years, and 57 years respectively.

Four of the six infarcts were associated with dramatic symptoms at the onset - sudden pain across the praecordium, radiating through to the back and up the right side of the neck and accompanied by breathlessness and restlessness; sudden severe substernal pain and collapse; pain in the praecordium spreading up to the left shoulder and worse on breathing or coughing; sudden extreme distress and breathlessness with continuous production of a little blood-stained sputum. One infarct was apparently symptomless being demonstrated electrocardiographically; while the sixth took place prior to the patient's admission to hospital and could not be co-related with any particular symptoms.

Two cases died as a direct result of the coronary embolism with myocardial infarction - the man aged 57 years who developed left ventricular failure and died in 40 minutes, and the female aged

20 years who was extremely shocked and died 18 hours after her second myocardial infarct. None of the four remaining infarcts materially altered the prognosis in any case, but were rather an incident, a temporary upset, in the course of the disease. The cause of death in these four cases was (1) cerebral embolus, (2) second coronary embolus, (3) mesenteric embolus, and (4) sudden cardiac tamponade for which no cause could be found. Each case survived the myocardial infarct by 15 days, 3 weeks, 6½ months, and 2 weeks respectively.

Autopsy was carried out on all five cases. Only one, the male aged 57 years, had arteriosclerotic changes in his coronary arteries, and this only in the anterior descending branch of the left coronary artery. No embolus was found in any artery, but the female who died 6½ months after her infarct had a firm ante-mortem clot completely obstructing the lumen of the second inch of the anterior descending branch. This was partially organized and recanalized. The vessel wall was not arteriosclerotic and presumably consecutive thrombosis had occurred behind the original embolus. No area of myocardial infarction was demonstrated in the case of the male dying in 40 minutes. The exact size of the original infarct 3 weeks previously was not determined in the female who died 18 hours after her second infarct. The anterior wall of the left ventricle was affected.

Two cases had an infarct of moderate size, while in one case it was small, being confined mainly to the posterior papillary muscle and the adjoining posterior wall of the left ventricle. The female dying after 6½ months showed an apical infarct with slight aneurysmal bulging of the scar.

These five cases bear out the views expressed by Hamman. They also draw attention to the incidence of coronary artery embolism in bacterial endocarditis - 5 cases in a series of 45, or 11%.

The standard leads were recorded in all cases, but a full set of precordial leads, i.e. V1 to V6, was recorded in only 36 cases during the acute phase. The remaining 27 cases had their initial record taken while in bed in the ward - in 10, leads V2, and V4 were recorded; in 17, leads V2, V4, and V6; and in one lead V1, V4, V5, V6. At a later date, a full set of precordial leads was obtained in all but 6 of these cases. Augmented unipolar limb leads were also obtained in all but these 6 cases.

The cases have been grouped according to the electrocardiographic pattern as -

anterior infarction	34 cases
XVI. / or infarction	15 "
antero-posterior infarction	2 "
high lateral infarction	1 "
bundle branch block	2 "
Right	4
Left	2
Apical record	
Dorsal record	

XVI.

ELECTROCARDIOGRAPHY.

Serial records obtained during the acute and healing stages in 65 cases of myocardial infarction have been analysed. Follow up records have also been taken in many of the survivors. The cases have been grouped according to the site of the lesion, and the diagnostic features for each group are discussed. The leads taken were (a) standard limb leads, (b) augmented unipolar limb leads, and (c) unipolar praecordial leads. The standard leads were recorded in all cases, but a full set of praecordial leads i.e. V₁ to V₆ was recorded in only 38 cases during the acute phase. The remaining 27 cases had their initial record taken while in bed in the ward - in 16, leads V₂, and V₄ were recorded; in 10, leads V₂, V₄, and V₅; and in one leads V₂, V₄, V₅, V₆. At a later date, a full set of praecordial leads was obtained in all but 8 of these cases. Augmented unipolar limb leads were also obtained in all but these 8 cases.

The cases have been grouped according to the electrocardiographic pattern as -

Anterior infarction	34	cases
Posterior infarction	15	"
Antero-posterior infarction	2	"
High lateral infarction	1	"
Bundle branch block	5	"
Right	4	
Left	1	
Atypical record	6	"
Normal record	2	"

The diagnostic features of each group will be discussed in detail.

(a) Anterior infarction - 34 cases.

In all cases, diagnostic changes were recorded in the praecordial leads, while in only 14 cases (41%) were the changes in the standard limb leads diagnostic of infarction. An even smaller number - 10 cases (29%) - showed diagnostic changes in the unipolar limb leads (lead aVL in anterior infarction). However 2 other cases showed suggestive changes in standard lead I, and five cases, including the two just mentioned, showed suggested changes in lead aVL.

Anterior infarction is associated with changes in the QRS complex, ST segment, and T wave in standard lead I, and less commonly in lead II. Reciprocal changes in the ST segment and T wave appear in lead III. (Figure 20). The following changes were observed in this series in the records obtained during the acute phase -

(1) Seven cases showed a Q wave in lead I with shift of the ST segment in lead I and/or lead III and T wave changes in lead I.

(a) Two showed ST elevation and T inversion in lead I with ST depression in lead III. (T in lead III was upright).

(b) Two showed ST elevation in lead I but no ST shift in lead III, and with a flat or inverted T wave in lead I.

(c) /

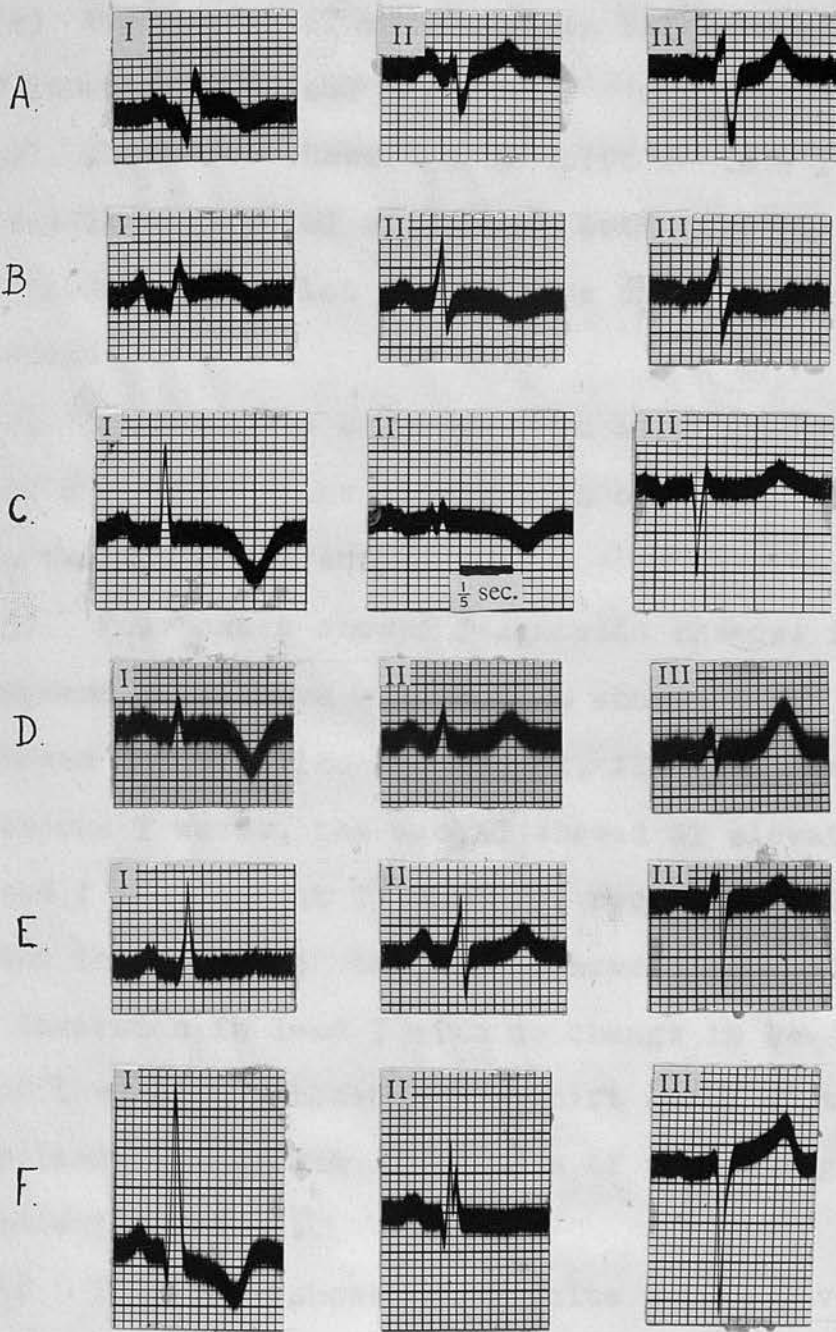


Figure 20: Changes in the standard limb leads associated with infarction of the anterior surface of the heart (A to E.). For comparison, the picture of "marked left axis deviation" is also shown (F.).

(c) One showed ST elevation in leads I and II with T inversion in lead I.

(d) Two cases showed no ST shift in lead I, but depression of the ST segment in both leads II and III; T (lead I) was flat in one case and inverted in the second.

(2) Three cases showed a Q in lead I, no ST shift and a change in the T wave. In one it was flat and in two it was inverted.

(3) Four cases showed diagnostic changes in the ST segment and T wave without QRS abnormality. One showed ST elevation in leads I, II and III with no obvious T waves, the second showed ST elevation in lead I with a flat T wave, and reciprocal ST depression in lead III; the third showed ST elevation and T inversion in lead I with no change in lead III; and the fourth showed no ST shift and a flat T wave in lead I, but with depression of the ST segment in leads II and III.

(4) Two cases showed a definite T wave inversion of coronary type in lead I (and lead II in one case) but no Q wave in lead I and no shift of the ST segment in any lead.

The remaining 18 cases who gave no evidence of anterior infarction in the standard limb leads showed (1) left axis deviation, 11 cases, (2) upright initial deflections in all three leads, 3 cases, (3) upright initial deflection in leads I and II and low /

low voltage initial deflection in lead III, 1 case.

(4) Upright initial deflection in lead I and low voltage initial deflections in lead II and III, 3 cases. Eight cases showing left axis deviation had an initial Q wave in lead I; two showed ST depression with T inversion in lead I and six had T inversion with no ST shift. The inverted T wave in lead I of left axis deviation differs in character from the T wave inversion of myocardial infarction. (Figure 20).

The depth of the Q wave in lead I in the 8 cases showing left axis deviation, and in the 10 cases showing diagnostic changes of myocardial infarction was as follows -

Depth of Q I.	Left Axis Deviation	Number of Cases.	Anterior Infarction
0.5 mm.	1		3
1.0 mm.	3		1
1.5 mm.	2		1
2.0 mm.	2		4
3.0 mm.	0		1

This would suggest that a Q in lead I of 2 mm. or more, is more likely to be associated with anterior infarction than not; while the reverse holds true if Q is 1.5 mm. or less - unless the initial deflections are of low voltage.

Five cases showed a Q in lead II as well as in lead I but only 2 of these cases showed other evidence of myocardial infarction.

Three cases had initial deflections of low voltage in all three leads (i.e. under 5 mm. in all leads). One showed a Q 0.5 mm. in depth and an inverted T wave in lead I; the second had a Q 1 mm. in depth, ST elevation and T inversion in lead I; while the third showed a small R wave as the sole initial deflection in lead I with a flat T wave, and the ST segment in lead III was depressed.

Changes in the ST segment have been mentioned with each type of diagnostic picture discussed. To briefly recapitulate, changes were observed in 11 cases. Eight showed ST elevation in lead I - twice with associated ST elevation - in lead II (1 case), and in leads II and III (1 case); three times with ST depression in lead III; and three times with no associated or reciprocal ST shift. Three other cases showed depression of the ST segment in lead III with no associated shift in lead I, but in one the ST segment was also depressed in lead II.

T wave inversion of coronary type occurred in lead I in 9 cases. Seven were associated with other diagnostic signs of infarction. Six other cases showed a flat T wave in lead I in all of whom diagnostic changes of infarction were present.

T wave inversion, not of coronary type occurred in lead I in 8 cases, in 2 cases the T wave was diphasic and in 2 the T wave was flat. In the remainder the

T wave in lead I was upright (7 cases) but in 3 of these cases T in lead I was lower than T in lead III.

The diagnostic changes observed in the first record of the standard leads were -

(1) (a) QI, ST shift (I and/or III) TI inversion	6	cases
(b) " " " TI flat	2	"
(2) (a) QI, TI inversion	1	"
(b) " " flat	1	"
(3) (a) ST shift (lead I) TI inversion	1	"
(b) ST shift (leads I and/or III) TI flat	3	"
(4) TI inversion	2	"

Six cases in whom the T wave in lead I was initially flat or upright, developed T wave inversion of coronary type in subsequent records.

The unipolar limb lead from the left arm commonly shows the changes diagnostic of anterior infarction, while the right arm and left leg leads may show reciprocal changes. As in the standard leads, changes in the QRS complex, ST segment, and T wave occur. (Figure 21). Records were obtained in 32 of the 34 cases showing anterior infarction in the precordial leads, and in only 10 cases could a definite diagnosis be made from lead aVL. Five other cases showed suggested changes. Of the 14 cases showing diagnostic changes in the standard limb leads only 9 showed diagnostic changes in aVL; two showed suggestive changes, one had a record of very low voltage, and one with a vertical heart showed no changes; the fourteenth case did not have unipolar limb leads recorded. /

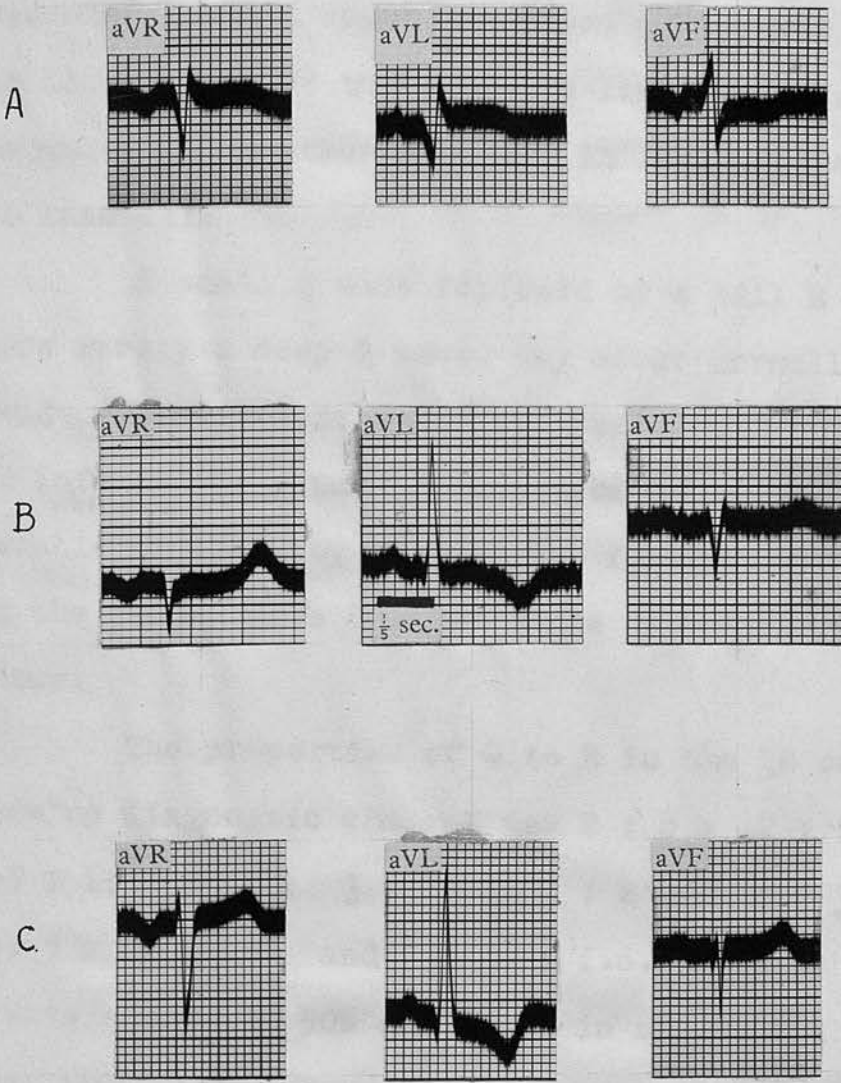


Figure 21: The changes associated with infarction of the anterior surface of the heart (A & B) and with hypertrophy of the left ventricle (c) are illustrated. (Unipolar limb leads.)

recorded. Only one case showed diagnostic changes in lead aVL where the standard limb leads had shown no abnormality other than a T in lead I lower than T in lead III.

A small q wave followed by a tall R wave or more rarely a deep Q wave, may occur normally in lead aVL. Before it can be taken as an indication of infarction, Q in aVL should be 0.04 second in duration and 50% or more of the following R wave. In the acute stage ST and T wave changes should also occur.

The proportion of Q to R in the 10 cases showing diagnostic changes was 2 : 8 ; 2 : 6 ; 3.5 : 1 ; 2 : 3 ; 3 : 7 ; 1.5 : 2.5 ; 1 : 3 ; 2 : 5 ; 5 : 4 ; and 2 : 7. i.e. only 4 showed a Q wave more than 50% of R, but in none was the Q wave less than 25% of R. In 8 cases the Q wave had a duration of 0.04 second, and in the remaining 2 cases, it was just a fraction under 0.04 second. Two of the 5 cases showing suggestive changes had a Q wave of 0.04 second duration, and the proportion of Q to R was, 3 : 9 ; and 2 : 10. T was shallow inverted in these two cases. Two other cases showed R as the initial deflection, but were followed by T inversion of the coronary type. The fifth case showed an R with ST elevation and a low upright T wave.

In /

In eleven other cases, lead aVL suggested the presence of left ventricular hypertrophy. (Figure 21). Seven showed a small q wave followed by a tall R and inverted T wave. Two had depression of the ST segment. In no case did the Q wave measure 0.04 second, and the proportion of Q : R was 1 : 18; 1 : 15; 1 : 15; 1 : 12; 1 : 15; 2 : 21; 0.5 : 11.

The praecordial leads provided evidence of myocardial infarction in all 34 cases. A diagnosis could be made in the presence of one of 4 combinations of changes. (Figure 22).

(1) Development of Q waves plus temporary ST elevation and T waves which are still upright, flat or inverted.

(2) Progressive diminution in the size of the initial r wave in leads passing from the right side of the praecordium towards the left side, plus changes in the ST segment and T wave. This diminution in r may stop abruptly at any lead, being replaced by a tall R.

(3) Combination of diminution in the r wave and the development of a Q wave in the leads from the right side to the left, plus changes in the ST segment and T wave.

(4) No abnormality of the initial deflections and changes in the ST segment and T wave alone.

The numbers presenting these features in this series were - /

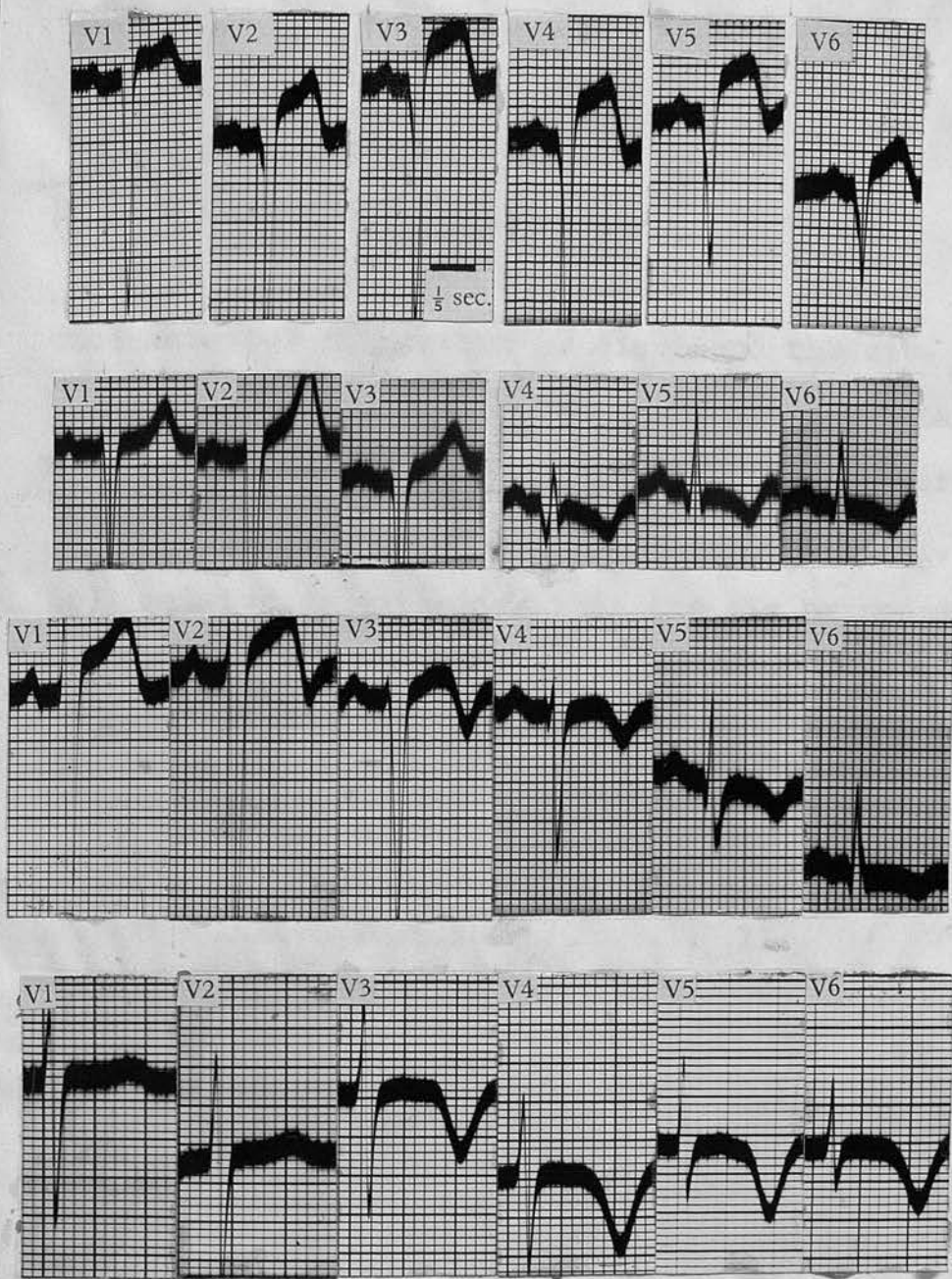


Figure 22: The four patterns occurring in the praecordial leads in infarction of the anterior surface of the heart are illustrated - (A) deep Q waves, (B) diminishing r waves + Q waves, (c) diminishing r waves; all plus ST & T wave changes, (D) T wave changes alone.

were -

Q waves 12 cases.

Diminishing r waves 6 cases.

Diminishing r waves + Q waves 6 cases.

ST & T wave changes alone 10 cases,

Once anterior infarction is diagnosed the site of infarction may be localized as (a) antero-septal, involving mainly leads V_2 V_3 and V_4 , (b) antero-lateral involving mainly leads V_3 V_4 V_5 and V_6 , (c) massive or extensive when the six praecordial leads are all involved and (d) central involving V_3 and V_4 or possibly one lead alone. In this series the infarcts were grouped as -

Extensive 8

Antero-septal 11

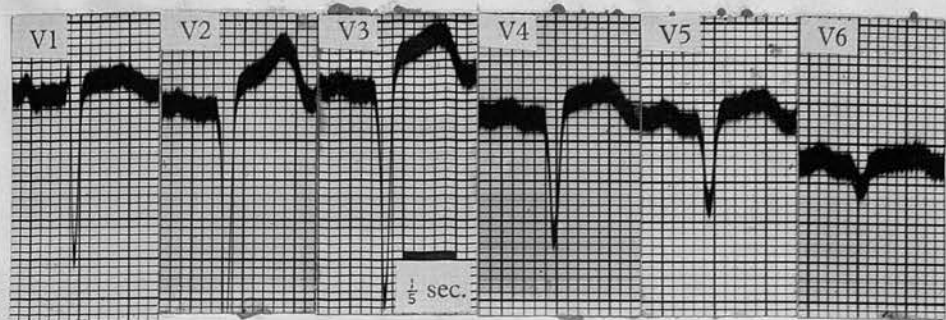
Antero-lateral. 14

Central 1.

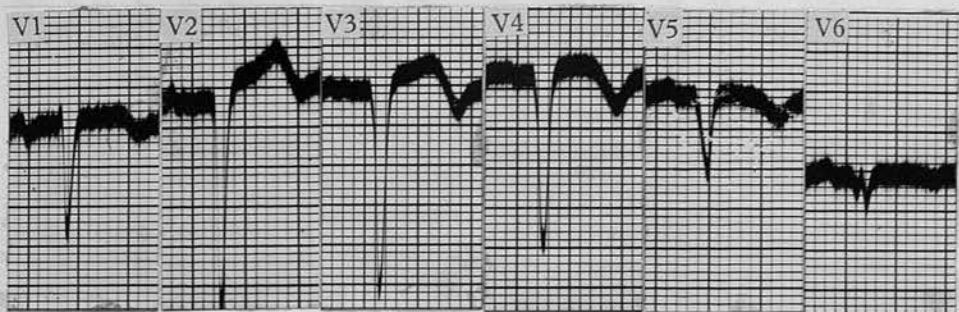
With 5 exceptions all cases showed elevation of the ST segment on admission. This was evident in 2 or more leads - V_1 & V_2 (1 case); V_1 - V_3 (4 cases); V_1 - V_4 (3 cases); V_1 - V_5 (5 cases); V_1 - V_6 (3 cases); V_2 - V_3 (1 case); V_2 - V_4 (1 case); V_2 - V_5 (8 cases); V_2 - V_6 (3 cases). Two cases showed the maximum ST shift in V_3 and V_4 - 6 mm. in each case, and five in V_4 and V_5 . e.g. 14 mm. and 12 mm., but in all remaining cases the maximum ST elevation was present in V_1 , V_2 or V_3 , commonly V_2 or V_3 . Persistence of ST elevation, particularly in leads /

leads towards the right of the praecordium, is common and is not abnormal, being recorded also in healthy subjects. Twenty-six cases showed persistent ST elevation during convalescence - V_1 (1 case); V_1-V_2 (1 case); V_2 (4 cases); V_1-V_3 (6 cases); V_1-V_4 (6 cases); V_1-V_5 (6 cases); V_2-V_5 (2 cases). In 18 cases the elevation was 3 mm. or less, and the maximum recorded was 7 mm. in V_3 . None of these cases had a cardiac aneurysm.

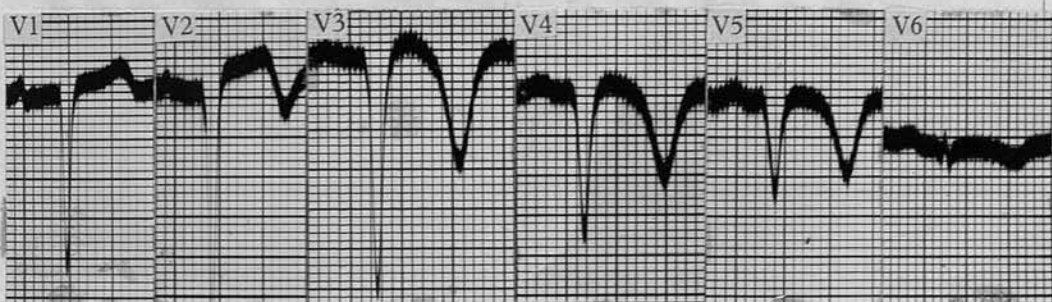
In the first record obtained, 22 cases had inverted T waves in one or more chest leads; 4 had diphasic T waves; in 3 the T waves were flat; while in 5 they were still upright. All developed T wave inversion and in 17 cases this was over 5 mm. in depth, being very deep - 15, 15 or 16 mm. in some cases (Figure 23). In the majority of cases the deep T waves were recorded in 3 praecordial leads - V_3-V_5 (5 cases) V_4-V_6 (5 cases), but four times it occurred in 4 leads - V_2-V_5 (1 case); V_3-V_6 (3 cases). One case showed this T wave change only in V_4 and V_5 , one in V_2 , and one in V_1 . This deep inversion of the T wave in the praecordial leads either appeared very soon after the infarct - 6 cases; or was delayed until during the 3rd week - 8 cases, 4th week - 2 cases, 6th week - 1 case. These changes regress gradually in most cases, the T inversion becomes less deep, and fewer leads show a T wave of over 5 mm. deep, until finally all leads show /



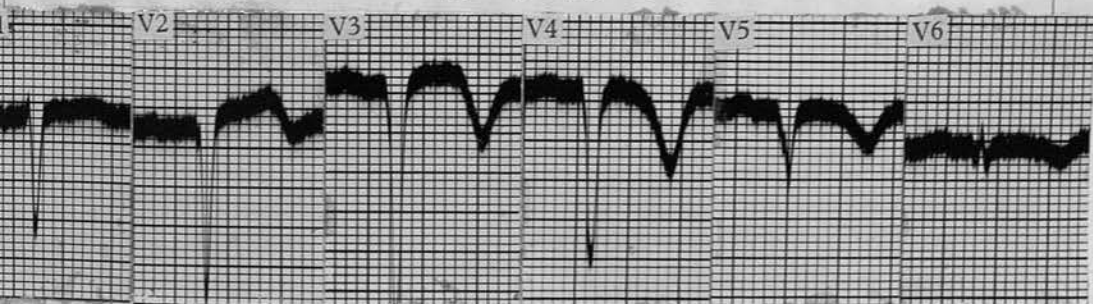
5 · 8 · 48



20 · 8 · 48.



14 · 9 · 48.



2 · 11 · 48

Figure 23: The successive changes in the T waves in praecordial leads, during the first 3 months after infarction of the anterior surface of the heart are illustrated.

show a T wave of less than 5 mm., or a flat or upright T wave. In 15 cases the time taken for this change to occur is known - 2 weeks, (3 cases); 3 weeks (1 case); 4 weeks (1 case); 5 weeks, (4 cases); 8 weeks (1 case); 10 weeks (3 cases); 12 weeks (2 cases).

Five cases have also shown a high upright T wave in chest leads to the right of the praecordium - V_1 (1 case); V_2 (3 cases); and V_1 and V_2 (1 case). The adjacent lead to the left showed a low upright T (3 cases); a diphasic T (1 case) or an inverted T wave (1 case). These high T waves appeared after 2 days, 6 days, 7 days, 12 days, and 21 days respectively.

Correlation of the changes in the standard limb leads with those in the praecordial leads shows that -

(1) Of two cases with T wave changes alone, in the standard leads, one had T wave changes alone in the praecordial leads, and one showed diminution in the height of r from V_1 to V_3 with associated ST and T wave changes.

(2) Of 4 cases with ST and T wave changes only, in the standard leads, 3 showed Q waves, and one the combination of diminishing "r" waves and Q waves in the praecordial leads.

(3) Of 6 cases with Q waves ST shift and T wave changes in the standard leads, 3 showed Q waves in the /

the praecordial leads, and 3 the combination of diminishing r waves and Q waves.

(4) Of 4 cases with Q and T wave changes in lead I, two showed Q waves in the praecordial leads, one the combination of diminishing r waves and Q waves, and one diminishing r waves alone.

(5) Of the 18 cases showing no diagnostic changes in the standard leads, (a) eleven with left axis deviation showed Q waves (3 cases); diminishing r waves and Q waves (2 cases); diminishing r waves (3 cases); ST and T wave changes alone (3 cases). (b) Seven remaining cases showed Q waves (1 case); diminishing r waves (1 case); and ST and T wave changes alone (5 cases).

Reversing the correlation, the following association is found -

Praecordial Lead Findings.

Limb Leads.	Q waves	r + Q	r	ST & T
Left Axis Deviation	3	2	3	3
Nil Abnormal	1	0	1	5
ST & T	3	1	+	-
Q, ST shift T.	3	3	-	-
Q. T.	2	1	1	-
T	-	-	1	1
	12	7	6	9

The only conclusion that may be reached is that the more changes there are in the limb leads, the more likely is the patient to have Q waves or a combination of /

of diminishing r waves & Q waves in the praecordial leads. If no changes are observed in the limb leads, or if they are confined to the T waves, the changes in the praecordial leads will probably also be confined to the T waves.

One case is worth commenting on further. (Figure 24). On admission one week after his infarct, he showed diminishing r waves in V_1 to V_3 , ST elevation in those leads, and ST depression in V_4 to V_6 . T was deeply inverted in $V_2 - V_4$, inverted in V_5 and diphasic in V_6 . Two days later, after an attack of pain in the chest, there was no change in the initial deflections, but the ST shift was less, and was confined to V_1 and V_2 . T was upright in all six praecordial leads. One week later the record had returned to the same pattern as shown on admission but the T waves were deeper. Why should this be? Clinically it was thought that he had not sustained a fresh myocardial infarct, and he was receiving anti-coagulants at the time of the upset. Was the pain that of prolonged coronary insufficiency, and was the change in the E.C.G. similar to that sometimes seen after exercise in a patient with angina pectoris? Viable muscle was still present in varying thickness over the anterior surface of the heart and prolonged ischaemia may have altered the repolarization of this layer of muscle, producing the changes observed in the chest leads.

Arrythmias /

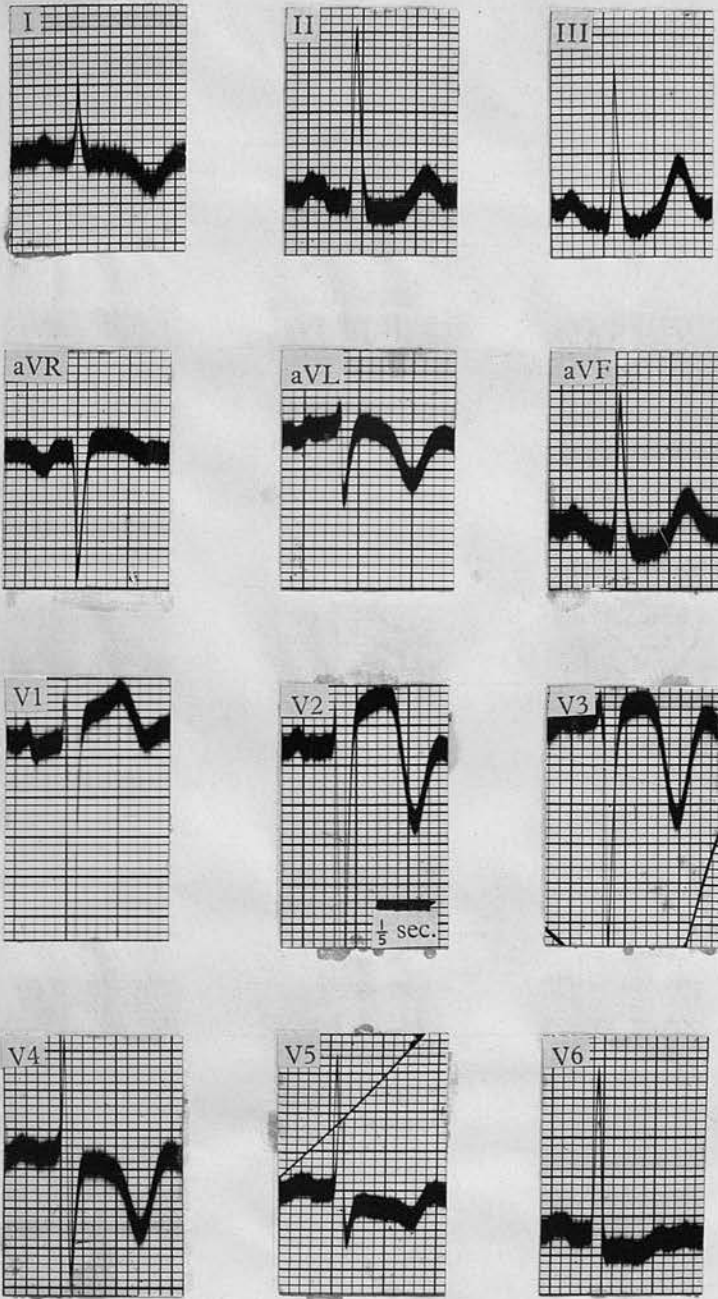


Figure 24 A 9.3.49. (Case 24):
 Record taken 7 days after the onset of symptoms,
 revealing infarction of the antero-septal segment
 of myocardium.

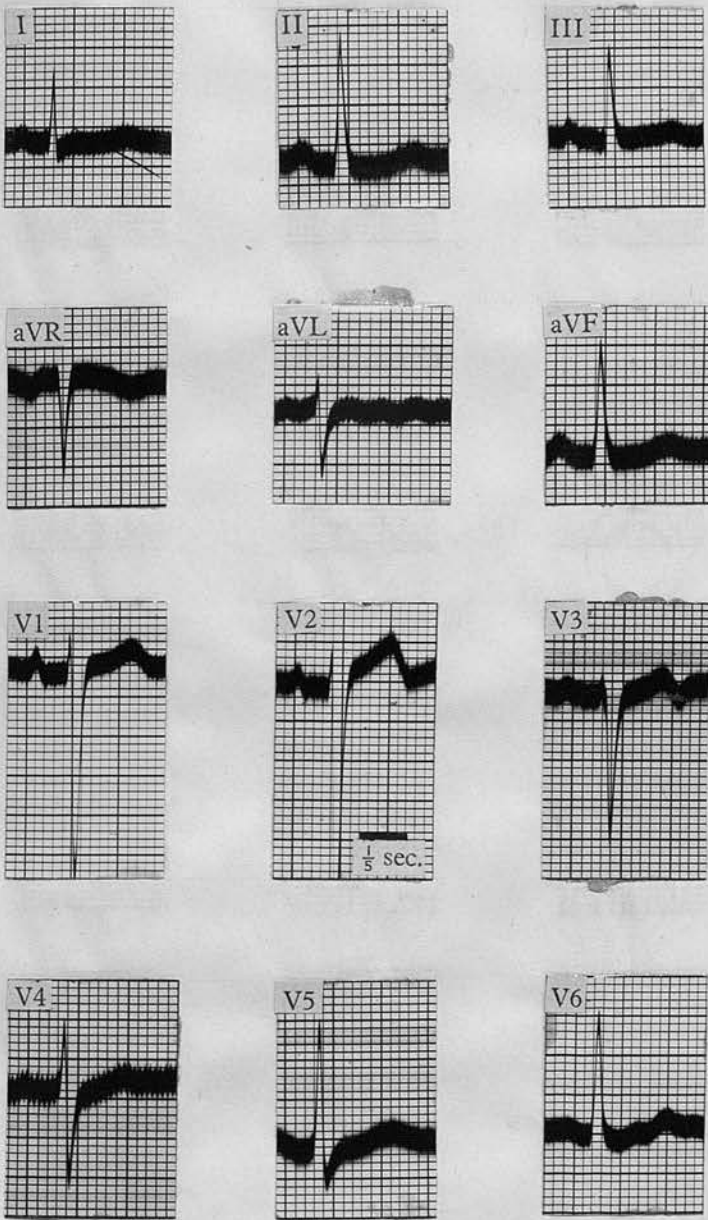


Figure 24 B. 11.3.49. (Case 24) :
 Record taken 3 days later after a prolonged attack
 of chest pain showing marked regression of the
 signs of myocardial infarction.

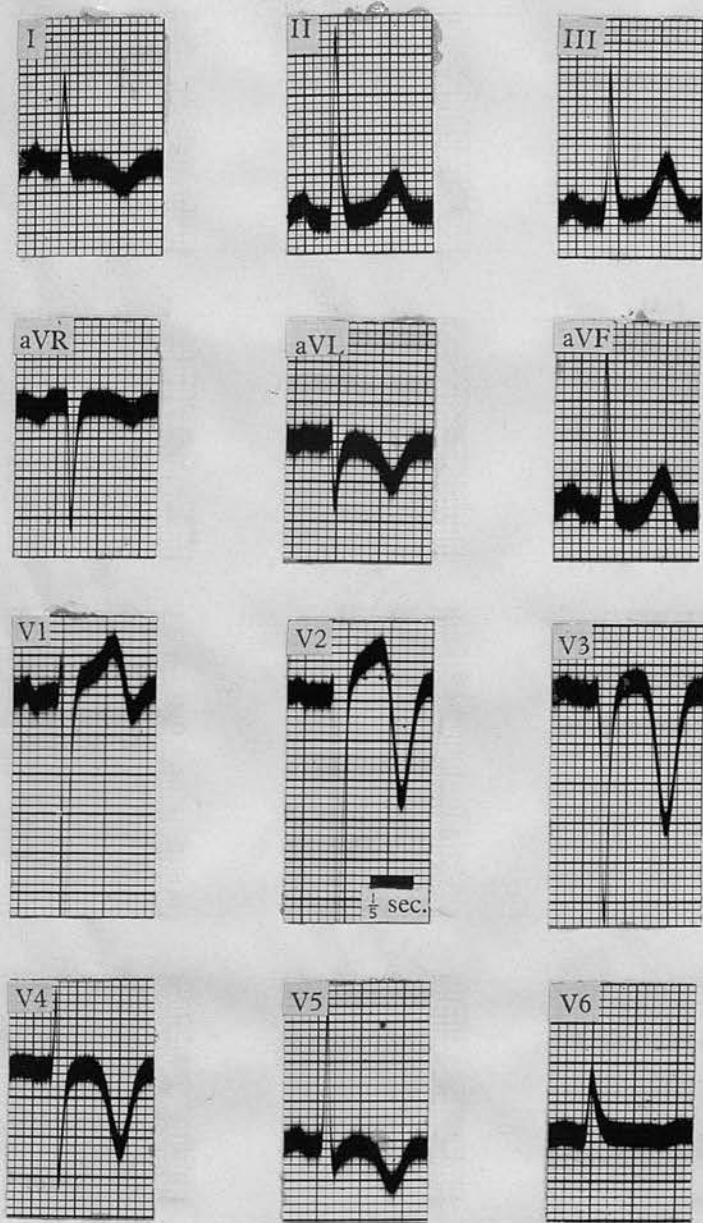


Figure 24 C.

18.3.49.

(Case 24):

The changes of myocardial infarction are again evident, the record being similar to that obtained on admission.

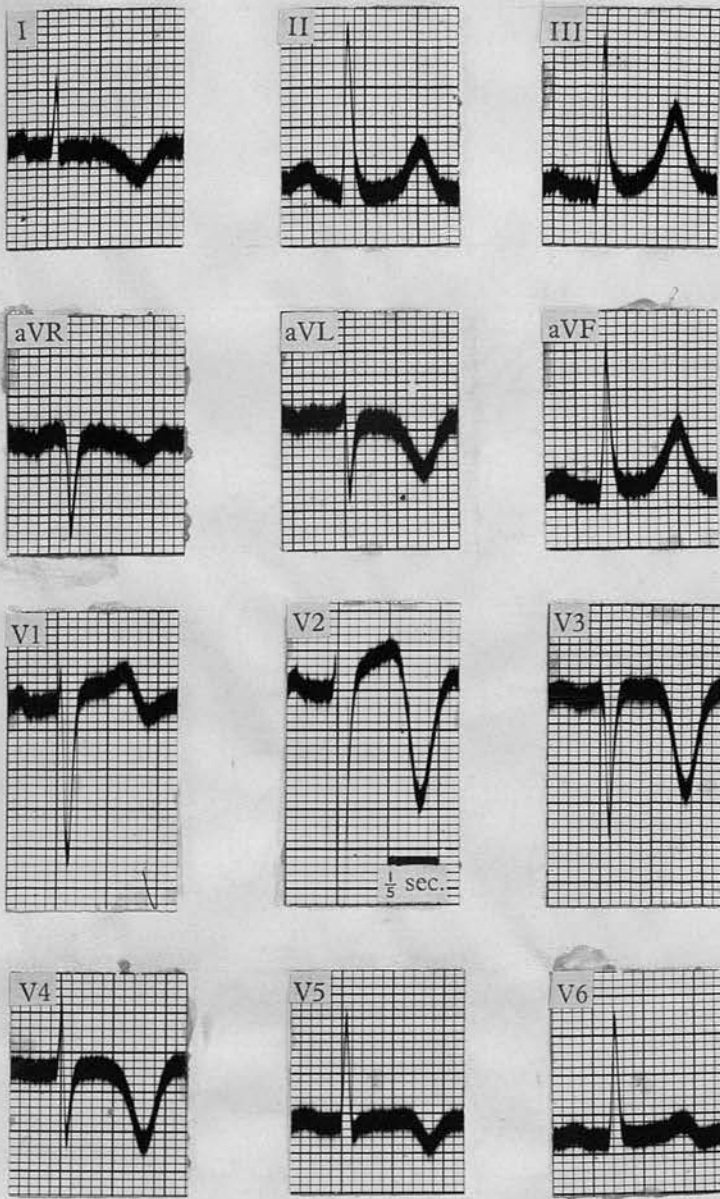


Figure 24 D. 29.3.49. (Case 24) :

The changes recorded are those associated with healing of the infarct.

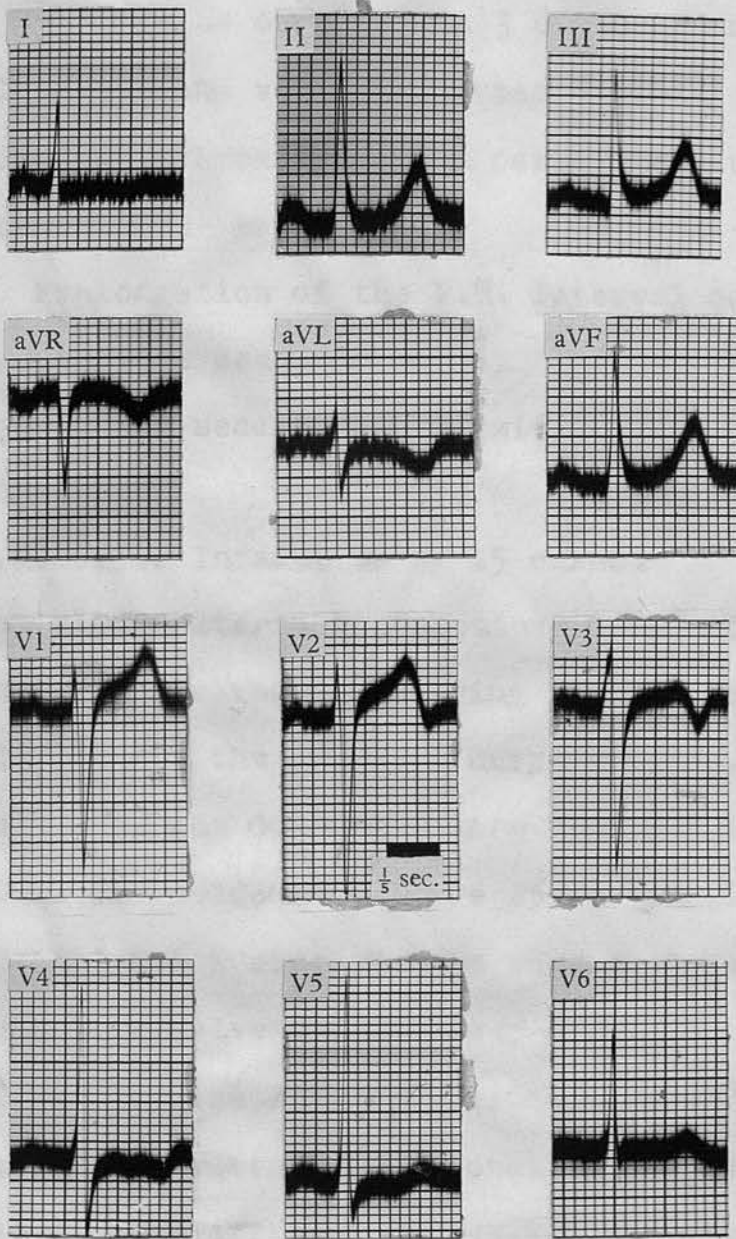


Figure 24 B.

17.1.50.

(Case 24) :

In the nine months from the onset, the changes of myocardial infarction have regressed markedly.

Arrythmias occurred in 3 cases - auricular fibrillation, and ventricular tachycardia; supra-ventricular tachycardia; and partial heart block with Wenchebach periods.

Prolongation of the P.R. interval occurred in 5 cases - 0.22 second 3 cases; 0.24 second 1 case; and up to 0.30 second 1 case (with the Wenchebach periods).

(b) Posterior Infarction - 15 cases.

Diagnosis of posterior infarction is made from the characteristic changes occurring in standard leads II & III and in the left leg unipolar lead. The praecordial leads do little more than provide corroborative evidence (Figure 25). In all cases, classical Q and T wave changes were observed in lead III but only twelve cases showed similar changes in lead II. In lead III Q was either the sole initial deflection, (7 cases) or it constituted 50% or more of the initial deflection (8 cases). In lead II Q was the sole initial deflection in only 2 cases. In all but one of the remaining 10 cases showing Q in lead II it was less than 33% of the succeeding R wave. Eight cases showed depression of the ST segment in lead I and eight cases showed elevation of the ST segment in lead III. In six cases the two features were associated so that ST shift occurred in a total of 10 cases. On admission the T wave in lead III was upright in 6 cases (3 of whom had ST shift) /

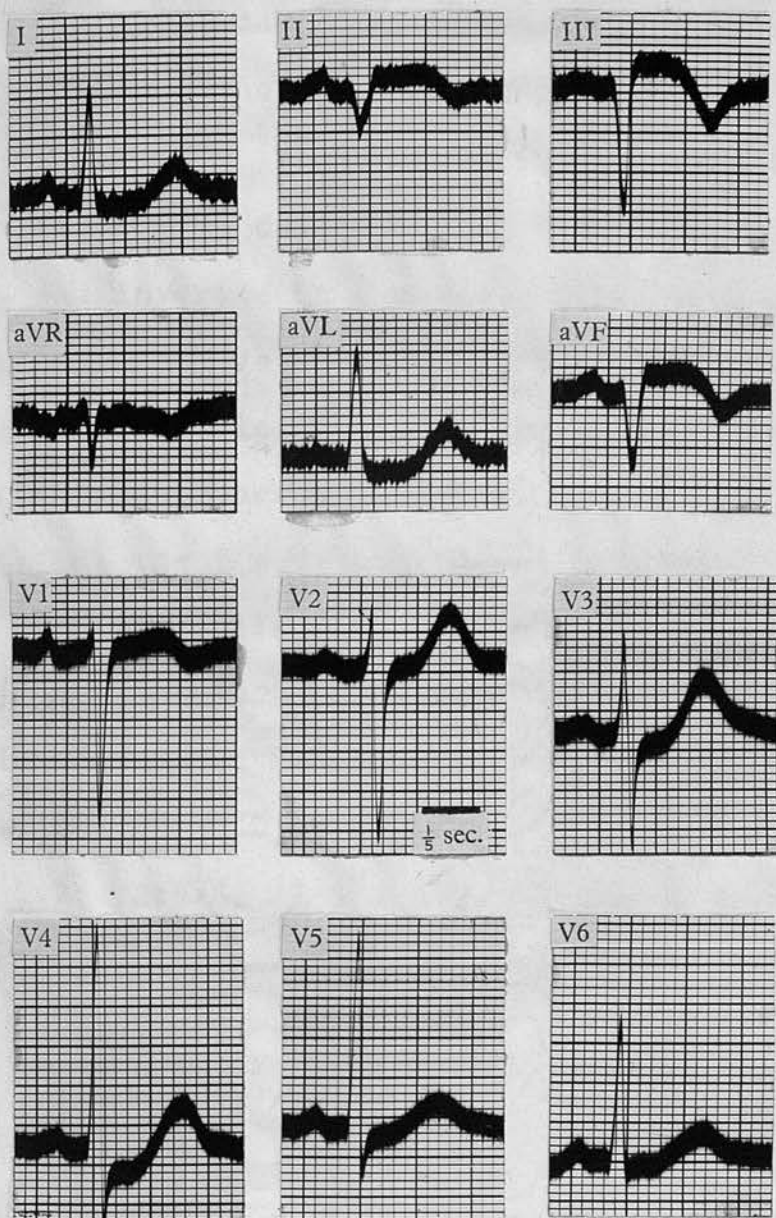


Figure 25. Infarction of the posterior surface of the heart.

shift) flat in 3 cases (2 of whom showed ST shift,) and inverted in the six remaining cases (5 of whom showed ST shift). In lead II the T wave was upright in 5 cases, diphasic in 3 cases, flat in 2 cases, and inverted in 5 cases. With the passage of time, the T wave became inverted in lead III in all cases and in lead II in 12 cases. One case showed a flat T wave in lead II. Two other cases died before the T wave had become inverted.

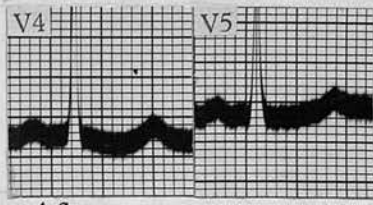
Unipolar limb leads were recorded in 11 of the 15 cases. Four showed Q as the sole initial deflection in lead aVF, and six showed a QR deflection. The ratio of Q to R in these cases was 2:4; 3:6; 5:4; 3:7; 2:5.5; 3.5 : 3.5. In two Q was less than 50% of R. One case showed a small q wave, small r wave, and deeper S wave with an upright T wave. Q was only 1 mm. in depth.

The duration of the Q wave is important. In 3 cases it was just under 0.04 second, in six it was definitely 0.04 second, while in 2 cases it lasted for 0.06 second.

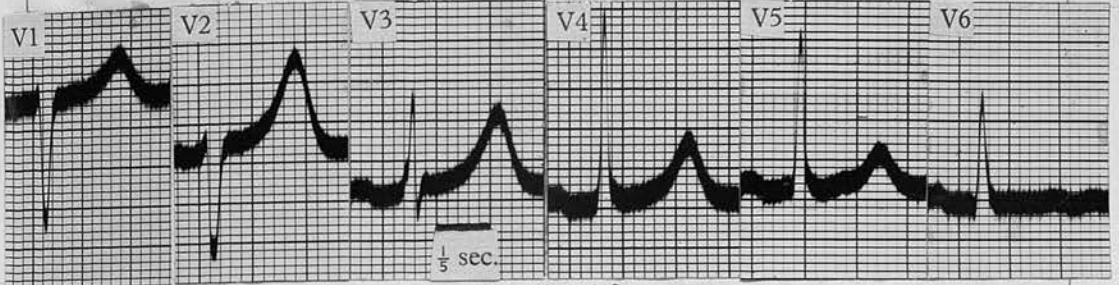
In 8 cases corroborative evidence of posterior infarction was found in the praecordial leads viz. depression of the ST segment. This was commonly most marked in V_3 , V_4 or V_5 , and never exceeded 5 mm., being 1, 2 or 3 mm. as a rule. This ST depression was temporary, disappearing within a few days. One case who did not show ST depression on admission developed /

developed it after 7 days, and the shift was maintained until his death 3 weeks after the infarct. Seven cases showed elevation of the ST segment in leads to the right of the praecordium when first examined - V_2 , 4 cases; $V_1 - V_2$, (1 case); $V_1 - V_3$, 1 case; $V_1 - V_4$, 1 case. Only two had concomitant depression of the ST segment in leads further to the left, and the remainder had an iso-electric ST segment (one later developed ST depression as mentioned above). Five other cases later developed elevation of the ST segment giving a total of 10 showing this change (2 of the 7 cases showing this change on admission had died). - V_1 & V_2 , 1 case; $V_1 - V_3$, 4 cases; V_1 to V_4 , 1 case; $V_1 - V_5$ 1 case, $V_2 - V_3$, 1 case, $V_2 - V_4$, 2 cases.

As the ST depression in the chest leads disappears the T waves become high upright, but the two changes may be present together. Leads V_2 , V_3 & V_4 show the high T waves most frequently. Nine cases developed high upright T waves, in two cases before the ST depression had subsided. (Figure 26). Of the six who did not show this change, 2 died early, 1 died after 3 weeks, 2 had earlier suffered an anterior infarct, and only one had an uneventful course. Very high T waves may be recorded, reaching as high as 19 mm. in one case. The interval within which the T waves became high varied considerably - 1st day, 2 cases; 2nd day, 2 cases; 4th day, 1 case; 7th /



1. 4. 49.

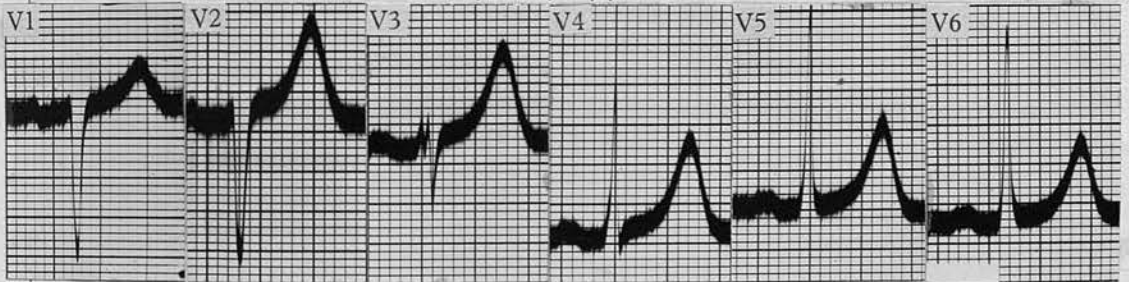


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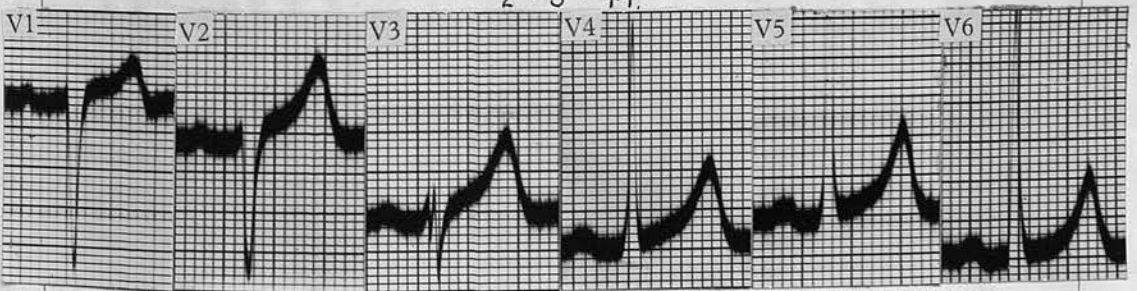
9. 4. 49.



15. 4. 49.



2. 5. 49.



12. 1. 50.

Figure 26. The successive changes over 9 months of the T waves in praecordial leads, in a case of infarction of the posterior surface of the heart.

7th day, 1 case; 11th day, 1 case; 14th day, 1 case; 21st day 1 case. Initially these high T waves appeared in V_2 alone, 3 cases; V_1-V_3 , 1 case; V_1-V_4 , 1 case; V_2-V_3 , 1 case; V_2 & V_4 , 2 cases; V_3-V_4 , 1 case. In all but three cases, the number of leads showing such a change increased and the maximum number involved were, V_1-V_3 , 1 case; V_1-V_4 , 2 cases; V_1-V_6 , 2 cases; V_2-V_6 , 1 case. With the passage of time these high T waves tended to become lower and to be present in fewer leads. After 7 months, two cases still show high T waves in V_2-V_5 and V_2-V_6 ; after 10 months only V_2 was involved in one case; 2 other cases showed the characteristic T wave in V_3 , and V_1 to V_4 ; while after 1 1/2 years another has still high T waves in V_2 & V_3 .

Two cases showed arrhythmias - both had auricular fibrillation and one had also complete heart block. Three cases showed prolongation of the PR interval - 0.22 second, 2 cases; and 0.40 second 1 case. One died, but in the other two it returned to within normal limits.

(c) Antero-Posterior Infarction - 2 cases:

Two cases gave evidence of infarction of both the anterior and posterior surfaces of the heart. In each, the standard limb leads and the left leg unipolar lead showed changes characteristic of infarction of the posterior surface of the heart, and the precordial /

praecordial leads demonstrated involvement of the anterior surface.

The first case showed a large Q wave in leads II & III with elevation of the ST segment and upright (II) and flat (III) T waves respectively. Lead aVF showed a deep Q 4.5 mm. deep, a tall R, 10 mm. high, ST elevation and a flat T wave. The ST segment in leads aVR + aVL was depressed, and the T waves were low upright. The praecordial leads showed extensive anterior infarction with the most marked changes in the antero-septal region - Q in V₁ - V₄; and QR in V₅ and V₆. The ST segment was elevated in all leads. T was upright in V₁ + V₂, flat in V₃ and V₄, inverted in V₅ & V₆. (Figure 27). At autopsy, infarction of the anterior and posterior surfaces of the heart and of the inter-ventricular septum was demonstrated.

The second case showed the classical limb lead changes of posterior infarction and the corroborative ST depression in V₃ to V₆. Initially leads V₄ & V₅ showed a small Q wave. This increased in size, the ST depression disappeared and the T waves became diphasic in V₁ & V₂ and inverted in V₃ to V₆.

Neither case showed the T wave changes in the praecordial leads which are common in posterior infarction.

(d) /

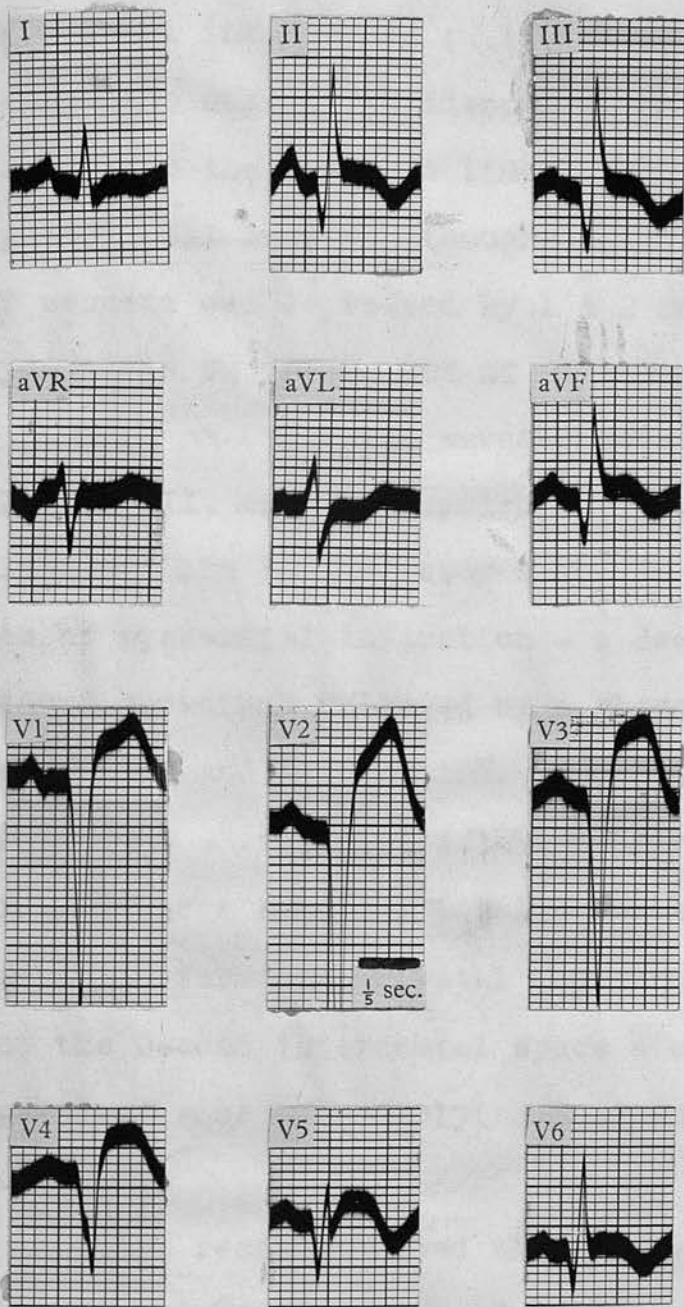


Figure 27. (Case 12): Antero-posterior infarction.-
 Leads II, III, and aVF indicate infarction of the
 posterior surface of the heart, while the praecordial
 leads reveal anterior infarction.

(d) High lateral infarction ; 1 case.

One case showed no definite evidence of myocardial infarction in either the standard limb leads or the unipolar praecordial leads, although in leads II and III the ST segment was depressed by 1 & 2 mm. respectively, and in V_4 and V_5 the ST segment was also depressed 3 and 2 mm.. The T waves were upright in leads I, II and III, and high upright in V_2 , V_3 & V_4 . The unipolar left arm lead however showed the classical changes of myocardial infarction - a deep Q wave of 0.04 second duration, followed by a shorter R wave, ST elevation and T inversion. The right arm and left leg leads showed ST shifts. (Figure 28). Additional leads were taken vertically above V_4 , V_5 and V_6 , up to the first intercostal space above V_4 and V_5 , and the second intercostal space above V_6 , but none gave evidence of underlying dead muscle. (Figure 28C).

Subsequent records showed the following changes.

- (1) Subsidence and disappearance of the ST shift in standard leads II and III.
- (2) Decrease in height of the T wave in lead I, for it to become first flat, and then shallow inverted.
- (3) Disappearance of the ST depression in leads V_4 and V_5 .
- (4) Development of ST elevation in leads V_1 to V_3 and later V_4 .
- (5) Increase in the height of the T waves in V_2
 V_3 /

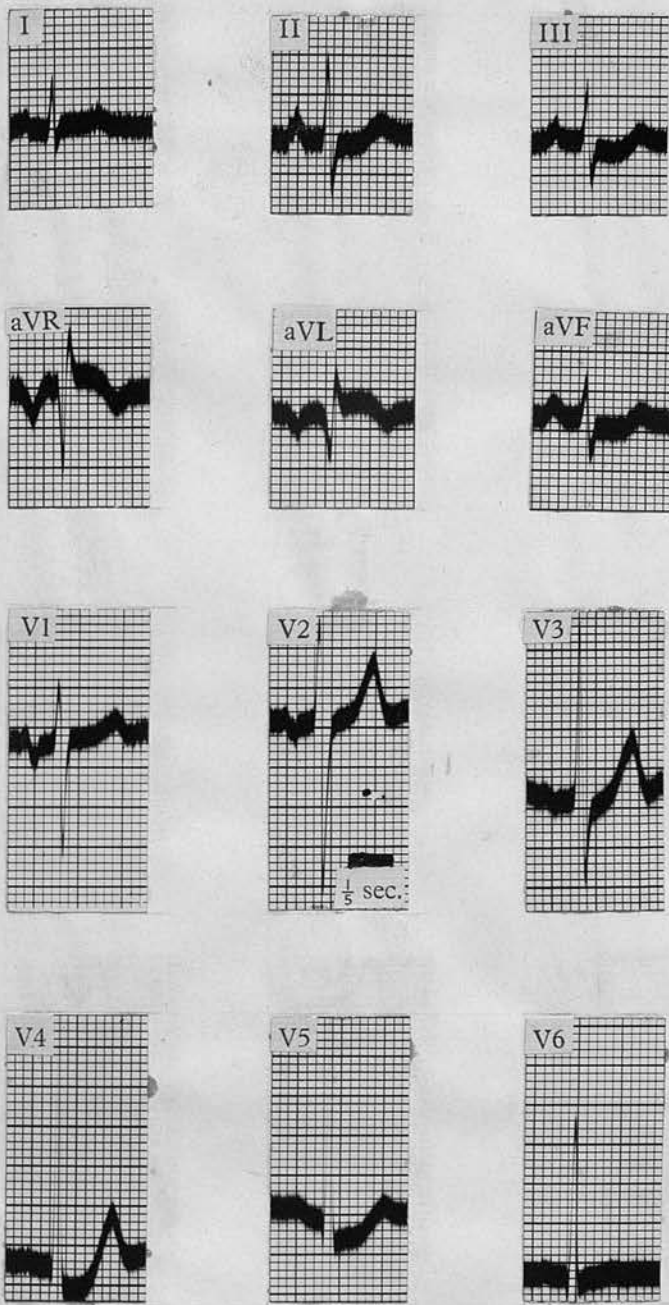


Figure 28A

(11.6.49).

(Case 17):

The changes in lead aVL, with the absence of diagnostic changes in the standard limb leads, or praecordial leads, indicate infarction of the high lateral aspect of the heart.

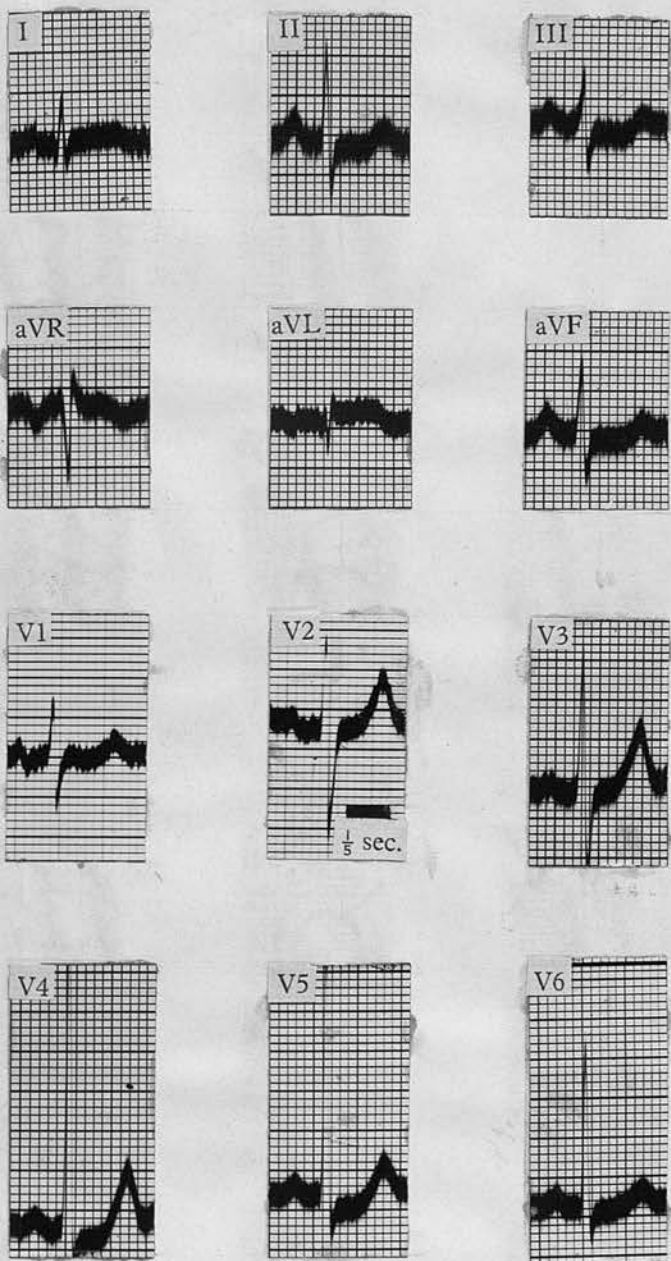


Figure 28 B.

14.6.49.

(Case 17):

Three days later, little change in the form of the record.

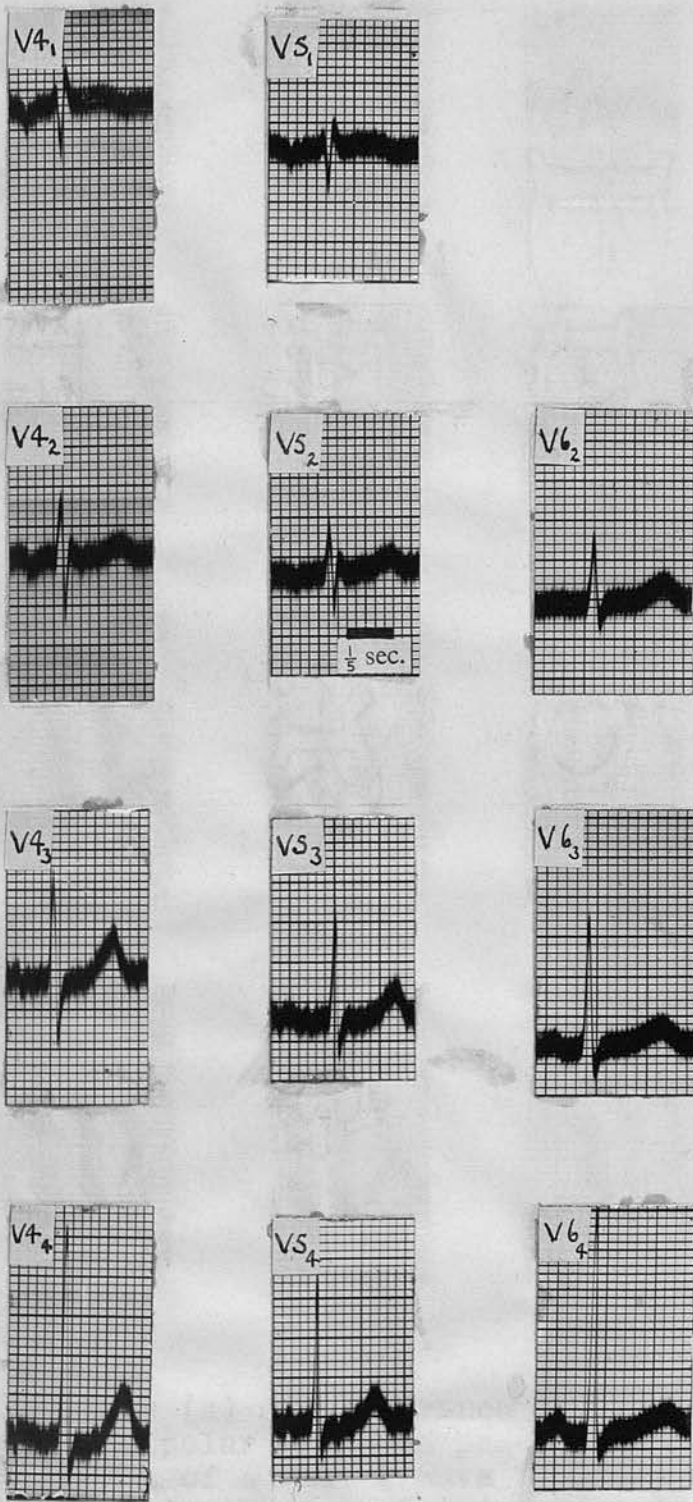


Figure 28C. 14.6.49. (Case 17) :

Leads taken from the interspaces above V₄, V₅, & V₆ -
 (a) 1st, (b) 2nd, (c) 3rd and (d) 4th interspaces -
 do not indicate infarction of the underlying muscle.

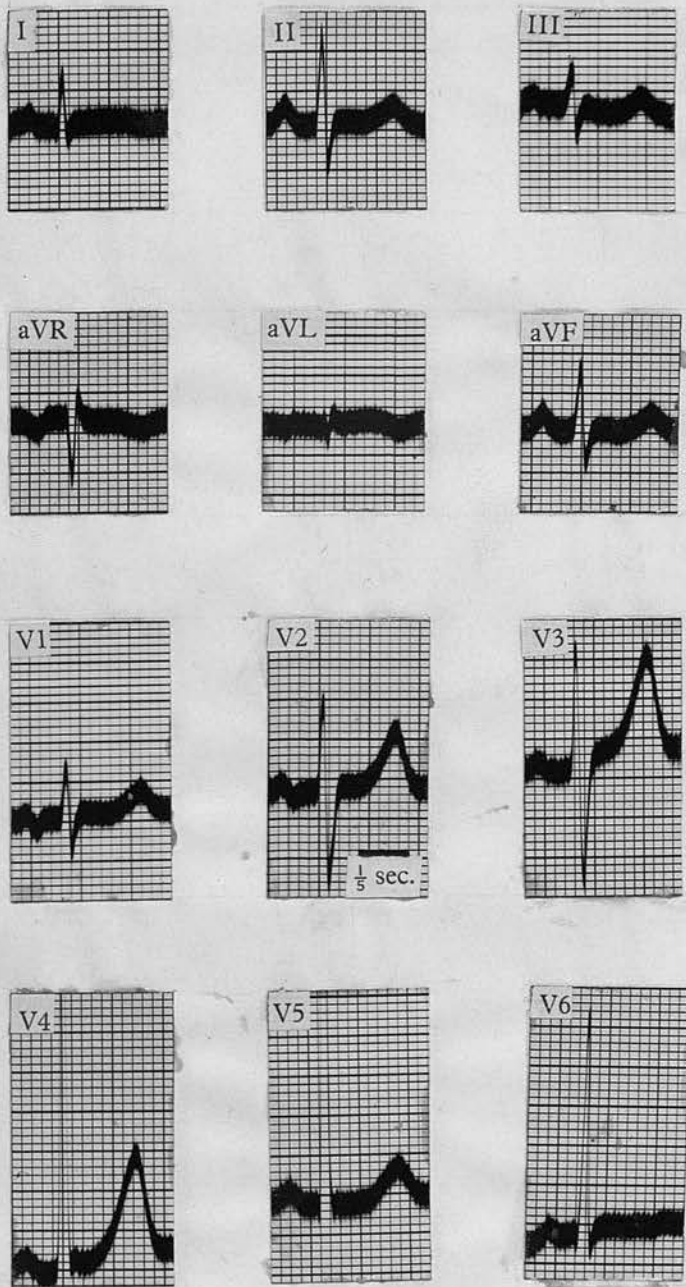


Figure 28 D.

22.6.49.

(Case 17).

The record shows (a) disappearance of the ST shift in standard, unipolar limb and praecordial leads, (b) development of a flat T wave in lead I and an inverted T wave in aVL, and (c) increase in the height of T in the praecordial leads.

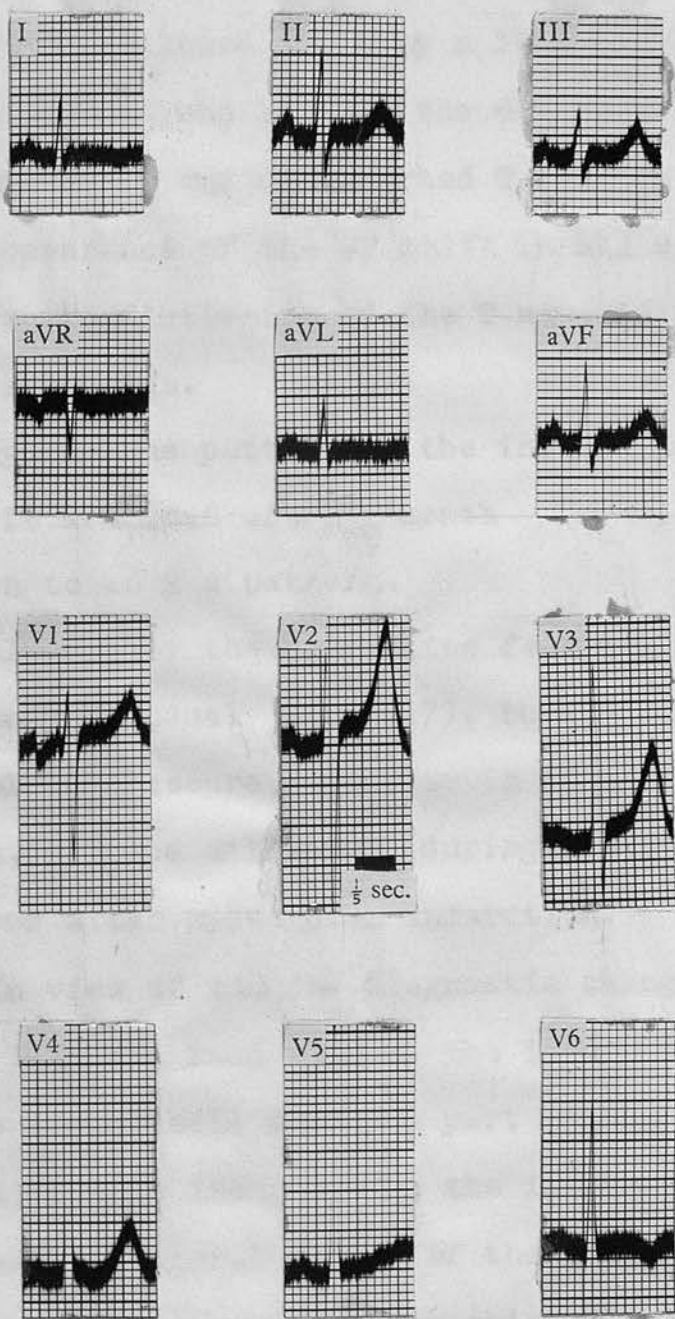


Figure 28 E. (5.7.49). (Case 17):

The record though abnormal is no longer diagnostic of myocardial infarction.

V₃ V₄ and V₅, followed later by a lessening of the height of T in V₃ and V₄, and the development of a flat T wave in V₅ and an inverted T wave in V₆.

(6) Disappearance of the ST shift in all unipolar limb leads and flattening of the T wave in the right and left arm leads.

(7) Change in the pattern of the initial deflection in the left arm lead after 1 month - from the initial QR pattern to an R s pattern.

Clinically the presenting features of the case were somewhat unusual (Case 17), but he showed the fall in blood pressure, the rise in blood sedimentation rate, and the mild fever during the first 3 days, which occur after myocardial infarction.

In view of (1) the diagnostic changes in the unipolar left arm lead and (2) the inability to demonstrate dead muscle over any part of the front of the heart, it was thought that the infarcted area was on the postero-lateral aspect of the heart towards the base. Support was lent to this by (1) the initial ST depression in leads V₄ and V₅, (2) the presence of high upright T waves in leads V₂, V₃ and V₄, and (3) the progressive increase in the height of the T waves in the praecordial leads, followed later by a decrease in these T waves.

The patient died suddenly and unexpectedly when reporting as an outpatient 6 weeks after his discharge. At autopsy a myocardial infarct was demonstrated /

demonstrated affecting the postero-lateral wall of the left ventricle and extending up to the base of the heart. The infarct involved the full thickness of the muscle wall. It was oval in shape and measured 7 cms. by 5 cms..

(e) Bundle Branch Block - 5 cases.

Four cases showed evidence of right bundle branch block, and one of left bundle branch block. All four with right bundle branch block died in heart failure, whereas the one patient showing left bundle branch block still survives.

(1) Right Bundle Branch Block :

Three cases showed the rare type of right bundle branch block, and one the Wilson type. In all four cases the praecordial leads gave evidence of recent infarction of the anterior surface of the heart, but in no case did the standard limb leads suggest myocardial infarction. Three showed a QR pattern of initial deflection in the praecordial leads, but in the fourth, the initial deflection was positive. All showed elevation of the ST segment - $V_1 - V_5$, 2 cases; V_2 & V_4 , 2 cases. The T waves were flat, diphasic or inverted in all cases. In two the lesion was mainly antero-septal in position, and in one it was mainly antero-lateral. The fourth case showed deep Q waves in the only two chest leads recorded - V_2 & V_4 and its exact extent was not determined.

All /

All four cases died - 3 in congested heart failure and one in left ventricle failure - but in one the occurrence of a variety of arrhythmias precipitated death (Case number 11). Two cases came to autopsy. The male who showed the rare type of bundle branch block, with r s R deflections in V_1 to V_3 , and ST elevation with flat T waves in V_1 to V_5 (Case number 10. Figures 29 and 30), had an infarct involving the greater part of the interventricular septum up almost to the auriculo-ventricular ring, and extending to involve the adjacent anterior and posterior walls of the heart. The infarcted section of the anterior wall was intra-mural in position, hence the absence of Q waves in the overlying praecordial leads.

The second autopsy case also showed rare type bundle branch block, but had well marked QR waves in the praecordial leads. (Figure 31). The patient had been admitted with her third myocardial infarct within 1 month (case number 9). At autopsy, the greater part of the anterior and posterior walls of the left ventricle, and of the interventricular septum were infarcted, with the most recent infarct situated in the upper part of the septum.

These cases demonstrate that (1) in the presence of right bundle branch block, the praecordial leads show up an associated myocardial infarct, and that (2) infarction of the upper part of the interventricular septum may be associated with a lesion of the /

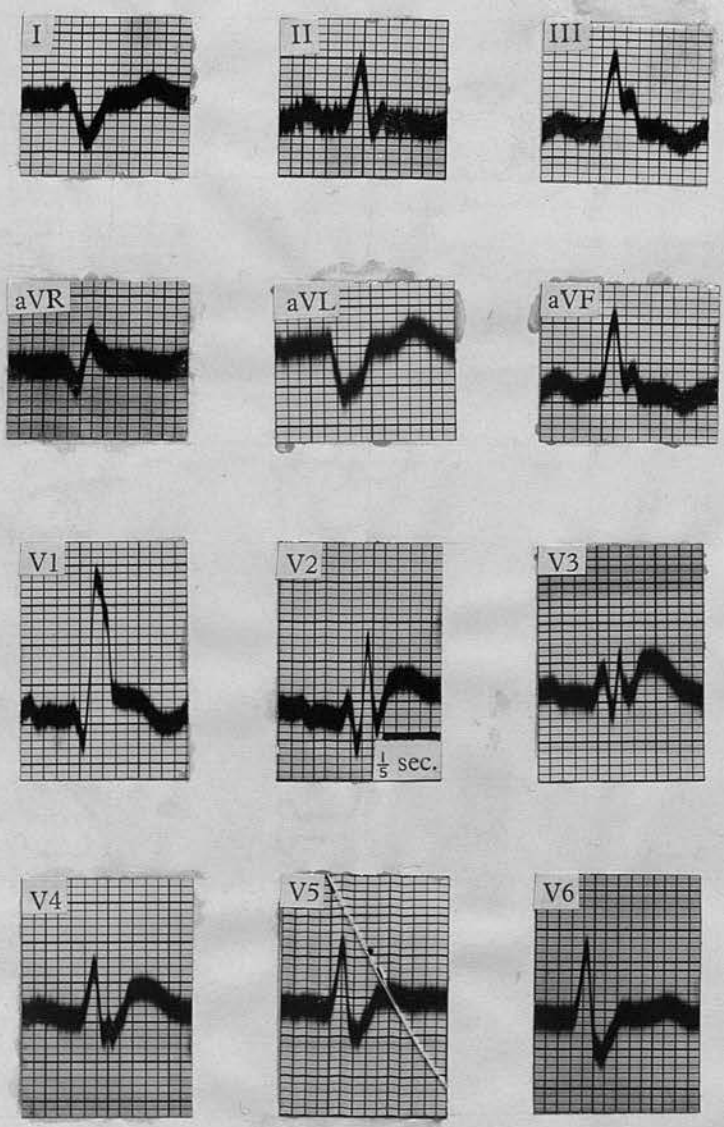


Figure 29. (Case 10): Rare type right bundle branch block, with evidence of anterior myocardial infarction in the praecordial leads.

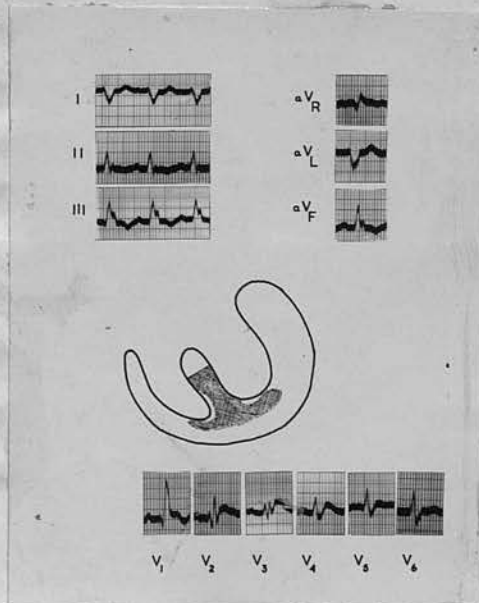
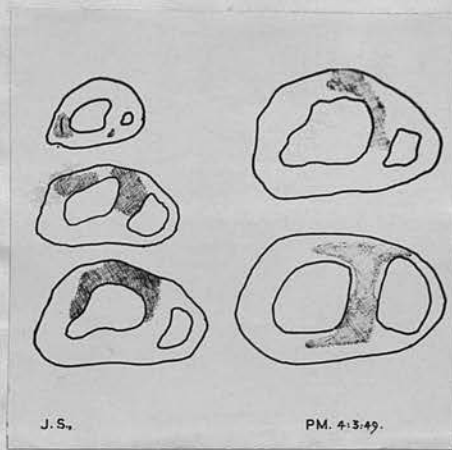


Figure 30. A diagrammatic representation of the site of myocardial infarction - mainly of the inter-ventricular septum, but with intra-mural extension anteriorly and posteriorly - in the case whose E.C.G. is shown in figure 29 (Case 10). The upper limit of infarction in the septum has not been defined.

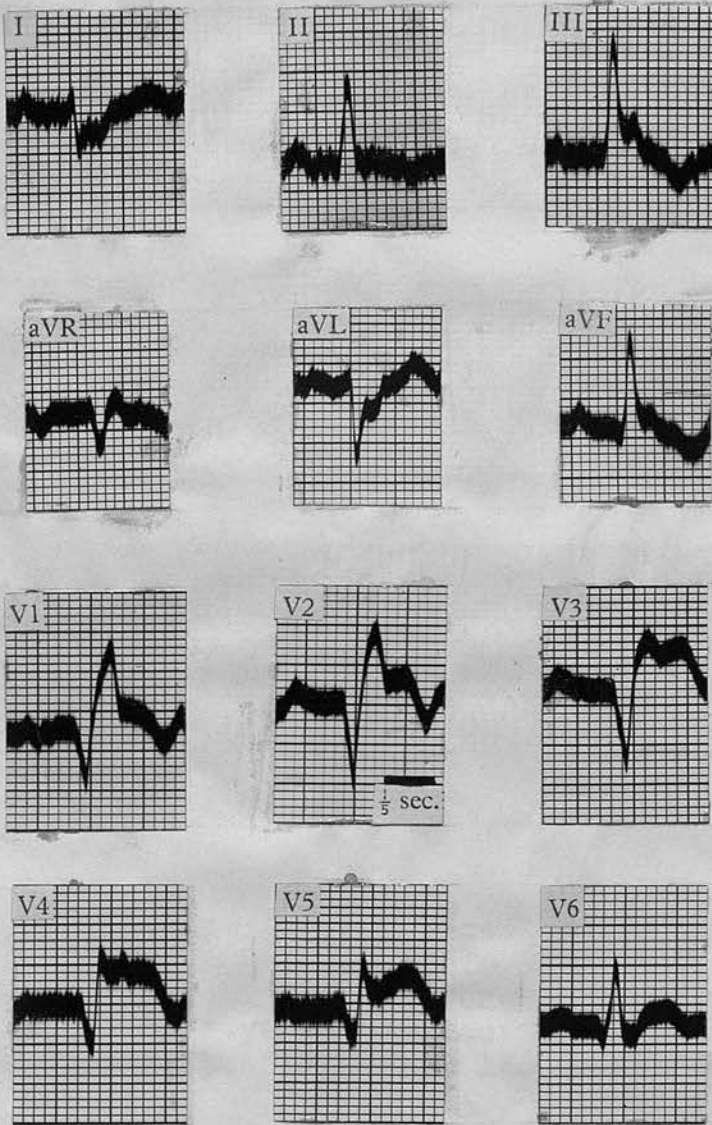


Figure 31 A (Case 9). Rare type right bundle branch block, with infarction of the anterior surface of the heart.



Figure 31 B. (Case 9). Successive changes in rhythm recorded in the days before death. (A) partial heart block with Wenckebach periods, (B) normal sinus rhythm, (C) Auricular fibrillation. All records have been taken by lead II.

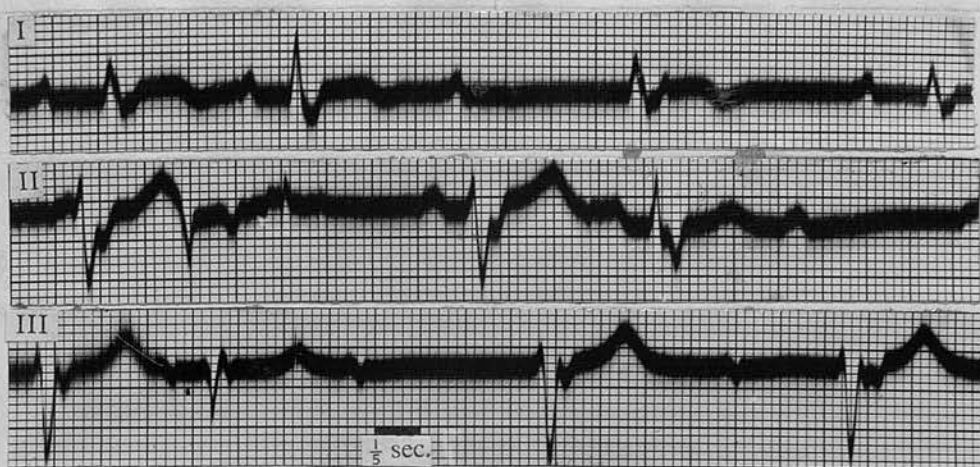


Figure 32 A. (Case 11): The record shows A./V. dissociation with ventricular extra-systoles; the auricular rate being 65/min., and the basic ventricular rate 44/min.. Wilson type bundle branch block is present.

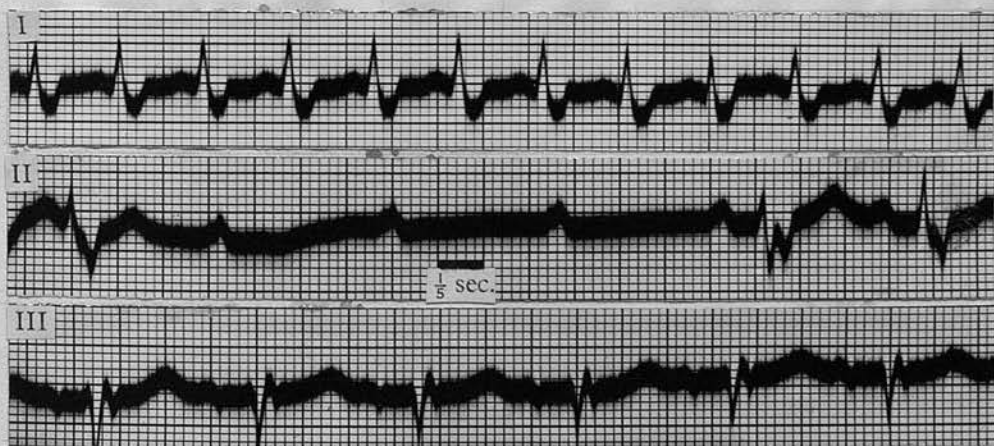


Figure 32 B. (Case 11): The record shows (1) Auricular paroxysmal tachycardia, (2) short Stokes-Adams attack with ventricular arrest for 3 seconds, and (3) 1 : 1 A.V. conduction. Wilson type bundle branch block is present.

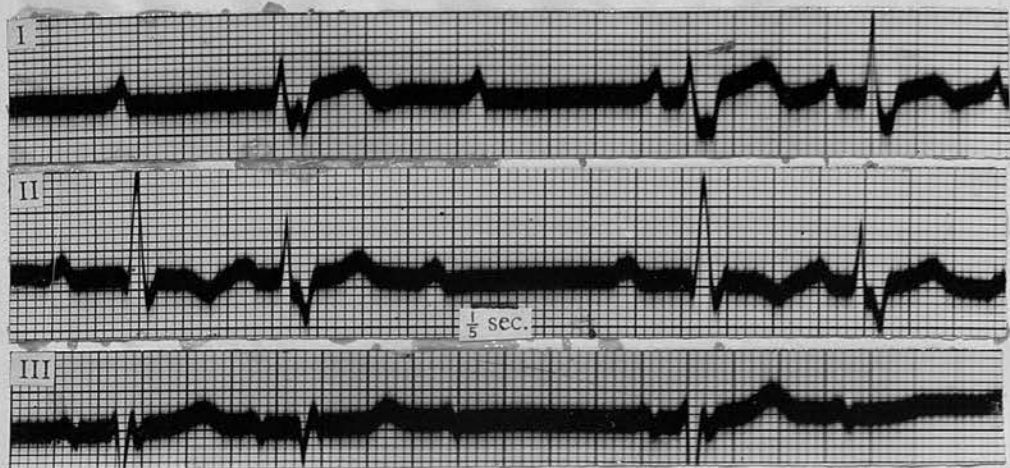


Figure 32 C. (Case 11): Alternating complete heart block and 1 : 1 A.V. conduction. Wilson type bundle branch block persists.

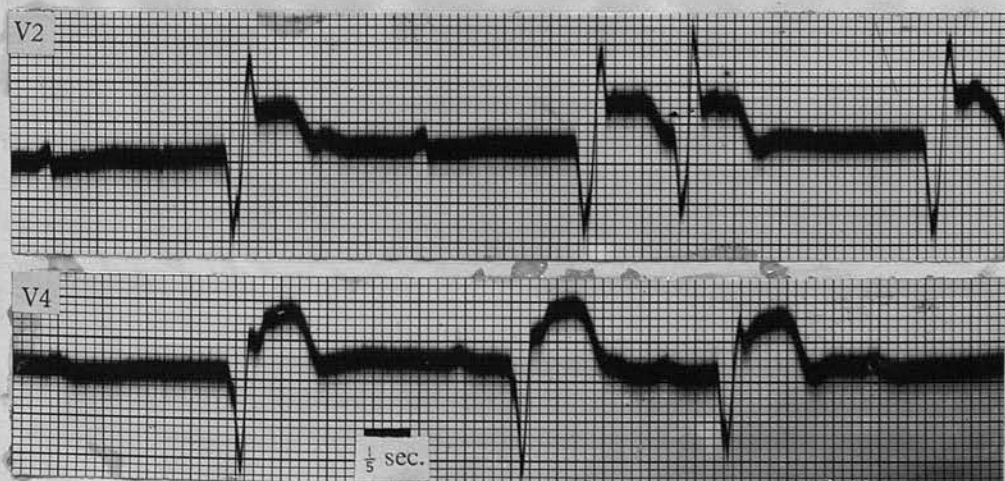


Figure 32 D. (Case 11): Praecordial leads V2 & V4 indicate recent anterior myocardial infarction.

the right conducting bundle.

Arrhythmias occurred in two of the four cases - partial heart block with Wenchebach periods, and auricular fibrillation in one, and partial heart block, complete heart block, paroxysmal auricular tachycardia, and Stokes-Adams attacks in the other. (Figure 32).

(2) Left Bundle Branch Block :

A diagnosis of myocardial infarction could not be made from the records obtained on admission or during the first 3 weeks. Thereafter, defective conduction in the left bundle alternated with normal intraventricular conduction. This variation in conduction was entirely dependent on heart rate. At a slow rate - under 60/min. - normal intraventricular conduction prevailed, but an increase in heart rate resulted in defective conduction through the left bundle. With normal intraventricular conduction, the standard limb leads showed marked left axis deviation and no evidence of myocardial infarction; the unipolar left arm lead showed R as the sole initial deflection with an inverted T wave; while praecordial leads V_5 & V_6 showed an R_s deflection with ST depression and T inversion. The remaining praecordial leads showed certain abnormal features however - the initial r wave remained of the same height in V_1 to V_3 - 2 mm., and in V_3 the initial deflection was polyphasic r s R' s' r'' s''. The ST segment was elevated in V_1 /

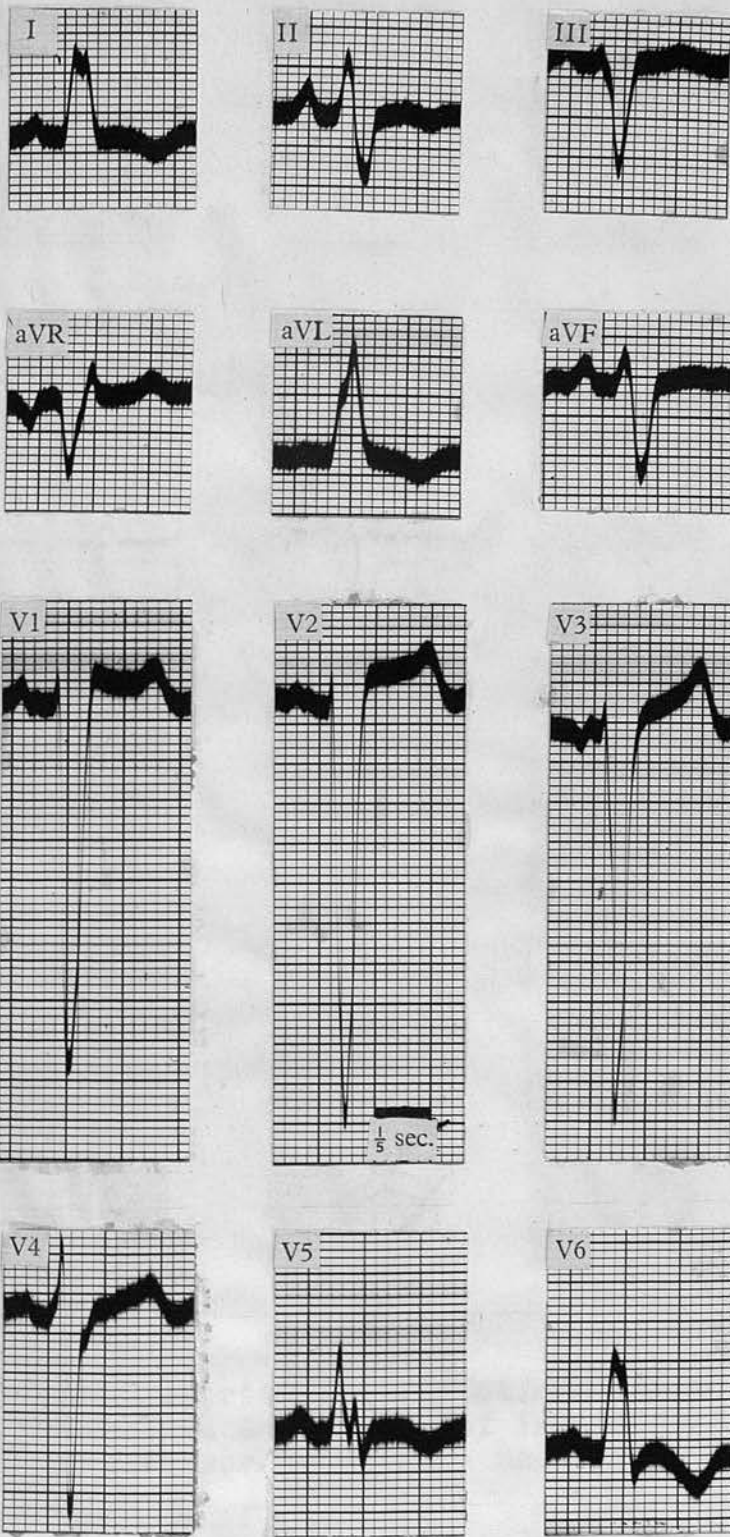


Figure 33 A. 28.4.49. (Case 29):
Left bundle branch block.

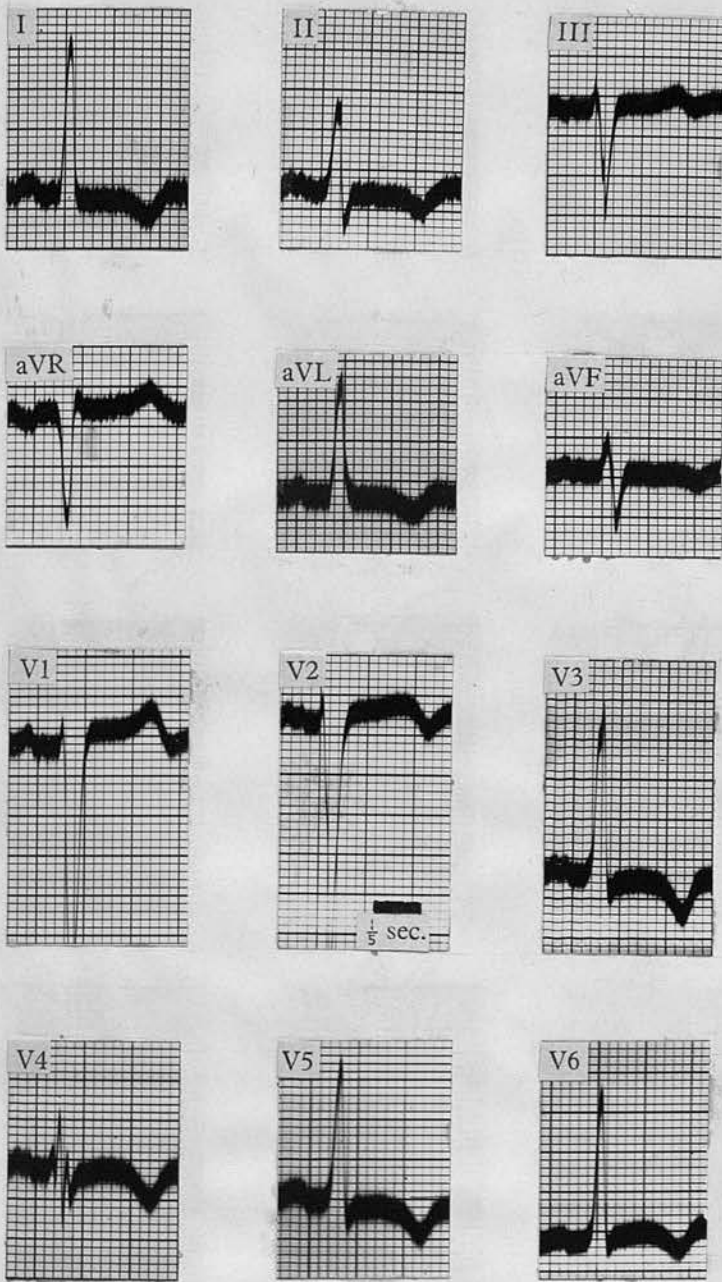


Figure 33 B. 18.5.49. (Case 29):
 Normal intra-ventricular conduction at a slow heart rate with changes suggestive of intra-mural damage of the anterior surface of the heart.

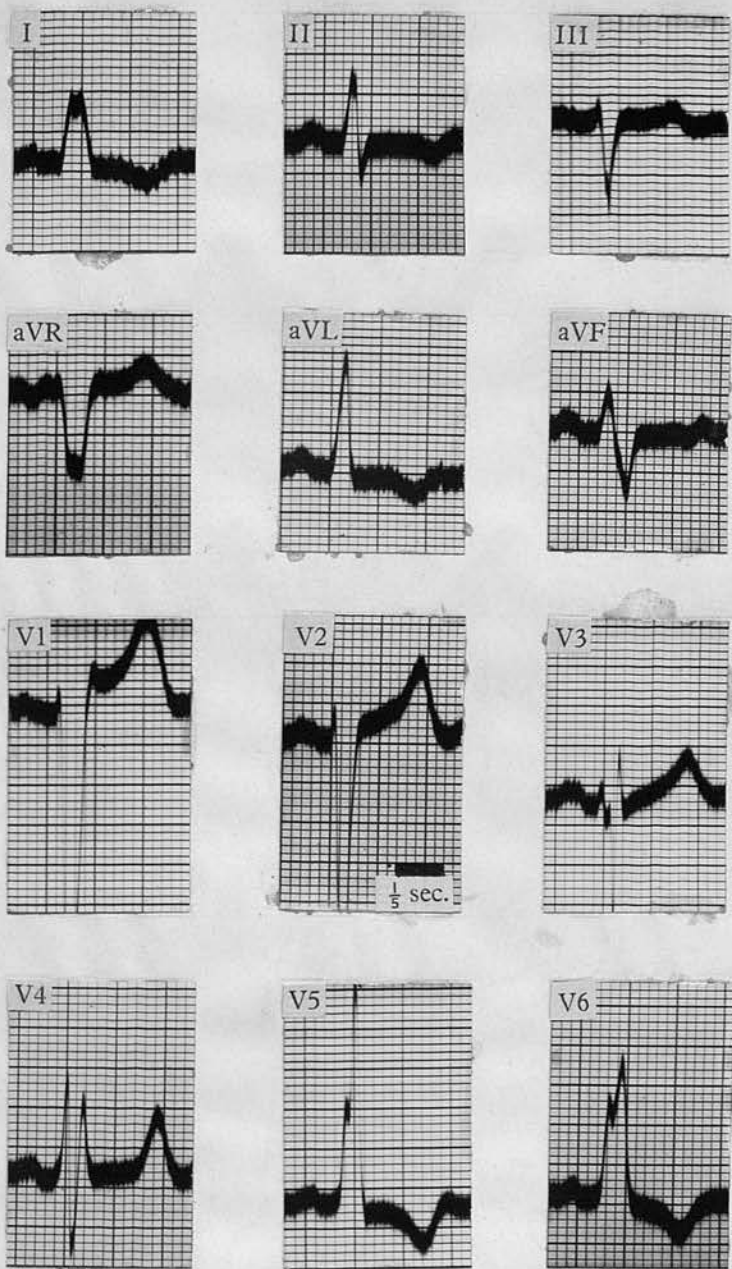


Figure 33 C 28.5.49. (Case 29):
 Varying bundle branch block and normal intra-
 ventricular conduction.

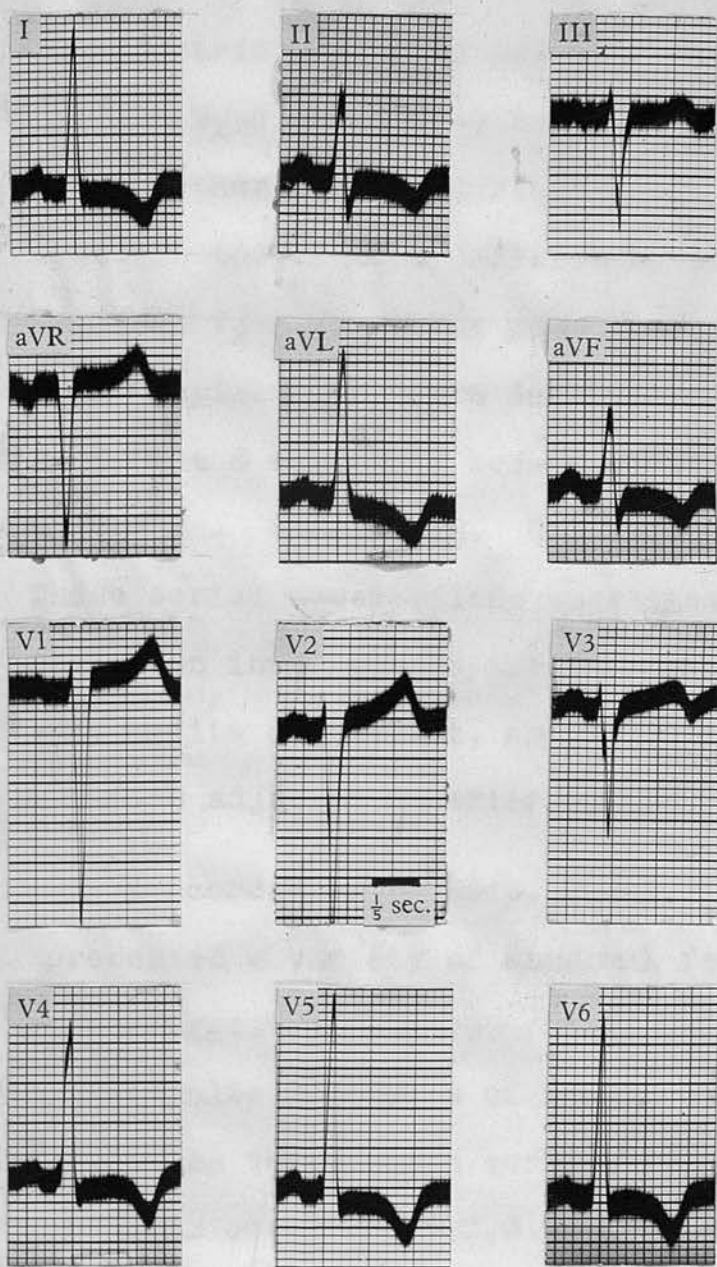


Figure 33 D 31.5.49. (Case 29):
 Normal intra-ventricular conduction.
 Regression of the evidence of intra-mural
 infarction in the praecordial leads.

V_1 & V_2 , iso-electric in V_3 and depressed in V_4 . T was upright in V_1 , diphasic (+) in V_2 and inverted in V_3 & V_4 . Further records during normal conduction, showed changes in the initial deflections in V_3 and in the T waves in V_2 & V_3 . The polyphasic initial deflection was replaced by an rS deflection with splintering of the S wave. T became upright in V_2 and diphasic in V_3 . (Figure 33, Case Number 29).

These serial observations suggested that the area of infarction involved the interventricular septum including its upper part, and extended very slightly into the adjacent anterior wall of the heart.

(f) Atypical Records - 6 cases.

Six cases presented a variety of abnormal features, which although suggestive of myocardial damage, did not permit a definite diagnosis of infarction to be made. The changes recorded in each case will be discussed and in 2 cases the E.C.G. and autopsy findings will be correlated.

(1) Mrs O.B. (Figure 34). Three records were obtained, one the day after the onset, and two during the succeeding month. In none did the initial deflections in the standard limb leads suggest infarction, but in the first record, the ST segment in lead I was depressed by 1 mm., while in lead III it was elevated by 1 mm. The T waves were flat, but later became inverted in lead I and upright in leads II & III. The unipolar limb leads indicated that the /

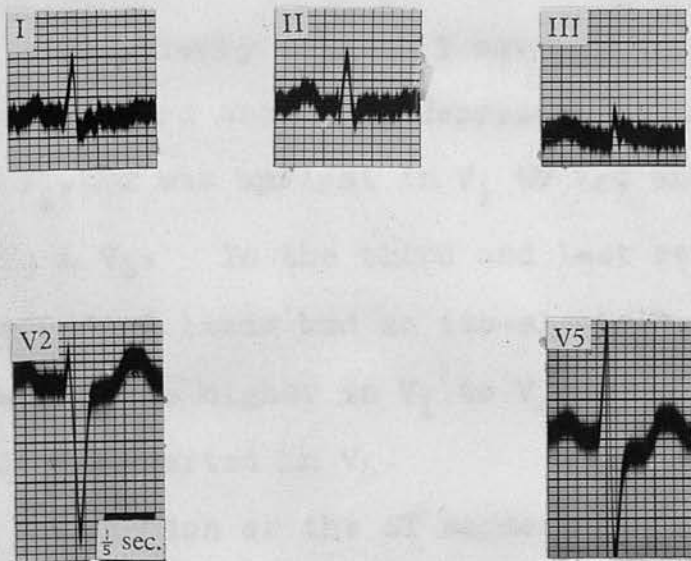


Figure 34 A 1.6.49. Initial record showing ST shift in leads I & III and V2 & V5, with flat T waves in leads I, II & III.

the heart was vertical in position. The praecordial leads showed no abnormality of the initial deflection but in V_2 & V_5 (the only chest leads recorded on the first occasion) the ST segment was depressed, 1 mm. & 2 mm. respectively and the T waves were upright. The second record showed ST depression confined to V_4 V_5 & V_6 , T was upright in V_1 to V_4 , and diphasic (\mp) in V_5 & V_6 . In the third and last record all six praecordial leads had an iso-electric ST segment, the T waves were higher in V_1 to V_4 , upright in V_5 , and shallow inverted in V_6 .

Depression of the ST segment in the praecordial leads is seen in posterior infarction and in severe myocardial ischaemia. The ST shift observed in the standard leads - depression in lead I and elevation in lead III - is of the type observed in posterior infarction and not in generalized myocardial ischaemia. In the absence of QRS changes indicative of infarction, these temporary ST changes may have resulted from a small intra-mural infarct in the posterior wall of the left ventricle.

(2) Mrs S. (Figure 35). Two records were obtained, the first on the day of the onset of symptoms, and the second 2 days later. Lead III showed a small Q wave 3 mm. deep, and a tall R wave 15 mm. high. The ST segment was iso-electric and T was diphasic (\mp). Lead II showed no Q wave, but both leads /

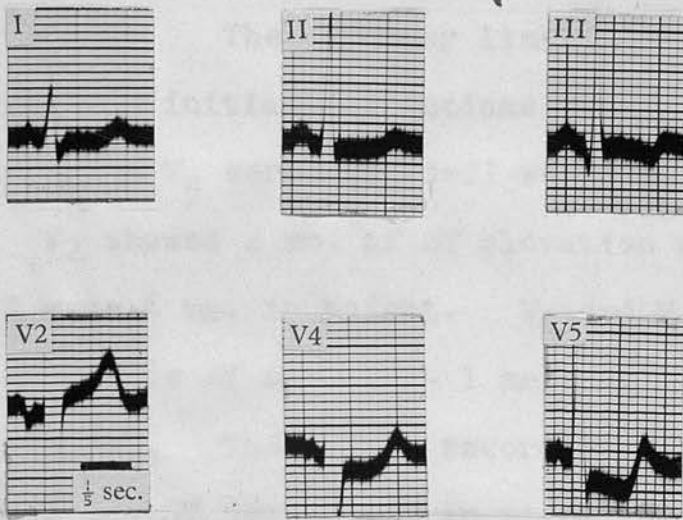


Figure 35A: 17.7.48.

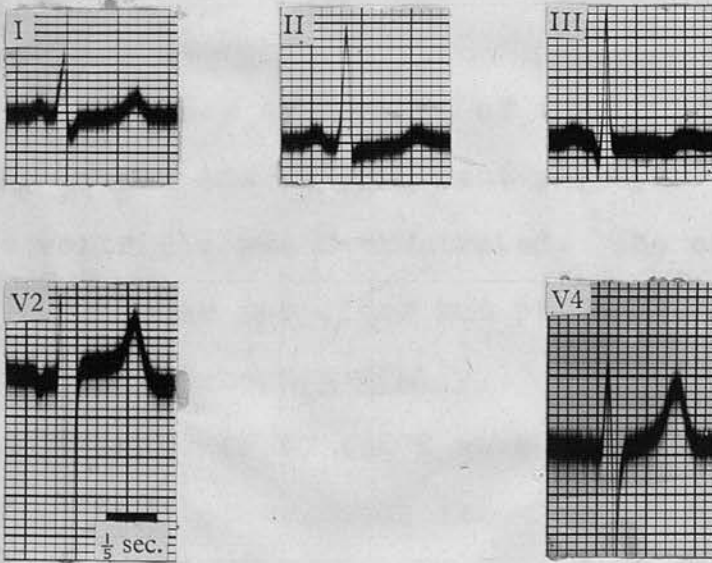


Figure 35 B. The ST depression in leads I & II, and in V4 & V5 (35A), together with the development of high upright T waves in V2 & V4 (35 B), are changes associated with posterior myocardial infarction but the QRS changes of a trans-mural lesion are absent.

leads I & II showed 1 mm. of ST depression with upright T waves. The unipolar limb leads were not recorded. The initial deflections in the praecordial leads (V_2 , V_4 & V_5 were recorded) were within normal limits. V_2 showed 2 mm. of ST elevation with an upright T wave 6 mm. in height. V_4 and V_5 showed depression of the ST segment - 1 mm. & 3 mm., and upright T waves. The second record showed (1) persistence of the ST depression in standard leads I & II, (2) inversion of T in lead III, (3) disappearance of the ST depression in lead V_4 (V_5 was not recorded), (4) slight increase in the height of the T wave in V_2 (now 7 mm.) and development of a high upright T wave in V_4 (8 mm.).

At autopsy infarction of the posterior papillary muscle and the adjacent posterior wall of the left ventricle was demonstrated. The exact depth of the infarct was not clear but probably some viable muscle remained subepicardially.

The type of ST and T wave changes observed in the standard and praecordial leads are known to occur in infarction of the posterior wall of the heart, the absence of Q waves of significant depth in leads II & III would indicate that the infarct is intra-mural in position.

(3) /

(3) T.A. (Figure 36). Only 3 records were obtained, the first 2 days after the onset of symptoms, the second 10 days later, and the third 3 months later. The standard limb leads showed no significant abnormality of the initial deflections; the ST segments were iso-electric; but the T waves were upright in lead I and shallow inverted in leads II & III. Praecordial leads V_2 & V_4 were recorded. The initial deflections were of normal pattern, the ST segments were flat and the T waves were both high upright (8 mm. and 6 mm. respectively). The second record showed (1) no change in the standard limb leads except that T in lead I had become diphasic (\pm) and T in leads II & III was more steeply inverted. (2) ST elevation of 1 mm. had developed in V_1 & V_2 , and (3) the T waves in V_1 , V_2 and V_3 were high upright (6 mm., 12 mm. and 8 mm. respectively). The unipolar limb leads were recorded, the left leg lead being of low voltage and W shaped with an initial q of 1 mm.; T was inverted. The Q wave was less than 0.04 second in duration. The third and last record showed (1) A diphasic T wave in lead I. (2) ST elevation of 2 mm. in leads V_1 , V_2 , and V_3 . (3) Increase in the height of the T waves in V_1 , V_2 , V_3 and V_4 (6 mm., 15 mm., 15 mm., & 5 mm. respectively.)

The QRS changes of myocardial infarction were absent but (1) the T waves were inverted in leads II /

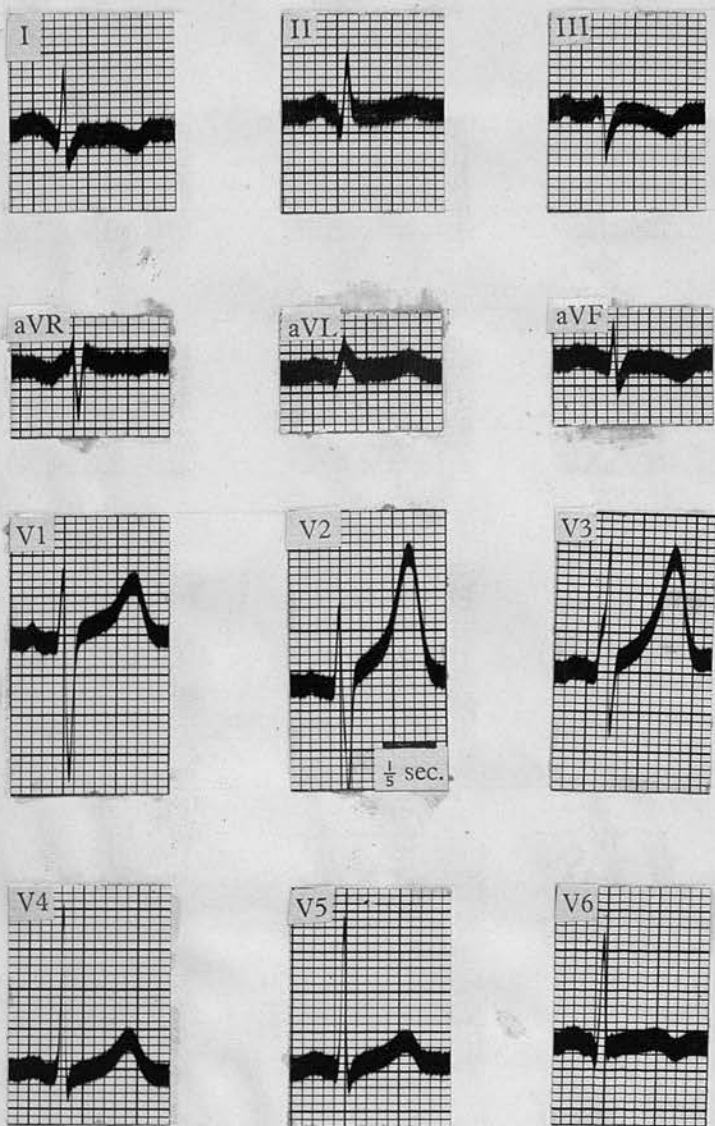


Figure 36. 21.12.48. The record is abnormal in respect of (1) the T wave changes in lead I & III and aVF, and (2) the very high T waves in V₁ to V₃. The change may indicate intra-mural damage³ of the posterior aspect of the heart, possibly towards the base.

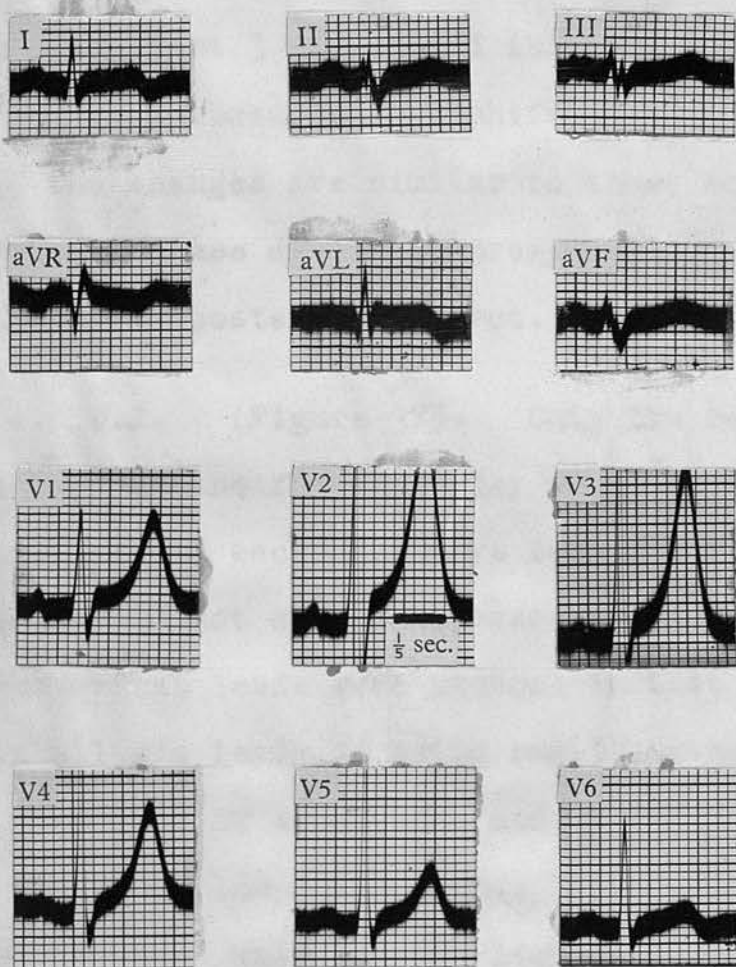


Figure 37 A. 6.2.48. The limb leads are not indicative of myocardial infarction but the praecordial leads show (1) R greater than S in all six leads, and (2) high upright T waves in V1 to V5.

II & III and had increased in depth in the first 10 days, (2) the T waves in the praecordial leads were high and over the 3 months had increased in height. Apart from the absence of ST shifts in the initial record, the changes are similar to those observed in the preceding case and would prompt the diagnosis of an intra-mural posterior infarct.

4. W.J. (Figure 37). Only two records were obtained, the first one day after the onset of symptoms and the second 10 days later. The standard limb leads did not suggest myocardial infarction. The praecordial leads were unusual in that R exceeded S in all six leads, S being small throughout. V_1 to V_5 showed ST elevation and high upright T waves (10 mm., 18+ mm., 19 mm., 11mm., and 6 mm. respectively). The unipolar limb leads indicated that the heart was horizontal. The second record showed an increase in the height of T in V_5 .

Is it that the high T waves in the praecordial leads permit the diagnosis of a posterior intra-mural infarct in the absence of other changes ?

5. Miss M.F. (Figure 38). Three records were obtained in the space of 1 week, the first being about 7-10 days after the onset (which was very indefinite). Leads I & II showed a tall R wave with iso-electric ST segments and T waves. Lead III showed a deep Q, short r, ST elevation (1 mm.) and T /

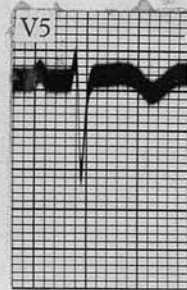
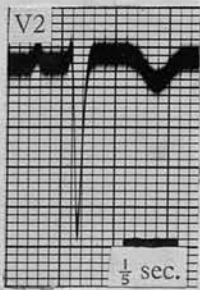
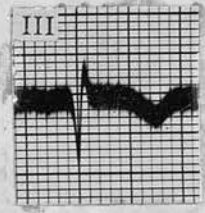
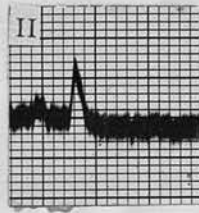
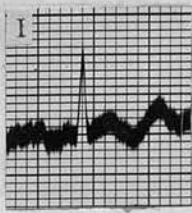


Figure 38A. 9.12.48. Lead III is of the form seen in posterior infarction, but lead II does not support the diagnosis. Lead V2 & V5 show T inversion of coronary type.

... in lead III
 ... by the depth of T inversion in
 ... development of very shallow
 T inversion in lead II, (3) increase in the
 depth of T inversion in leads V2 & V5.

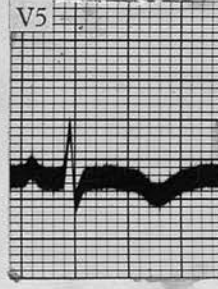
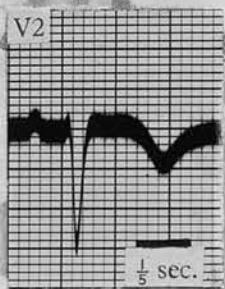
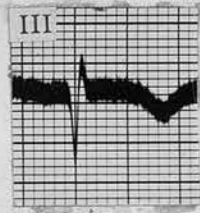
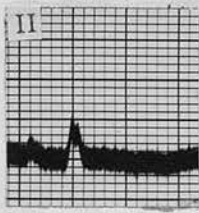
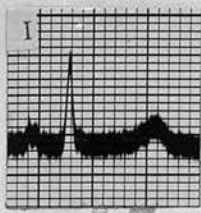


Figure 38 B. 11.12.48. There is little change in the form of the record apart from (1) subsidence of the ST elevation in lead III with increase in the depth of T inversion in that lead, (2) development of very shallow T inversion in lead II, (3) increase in the depth of T inversion in leads V2 & V5,

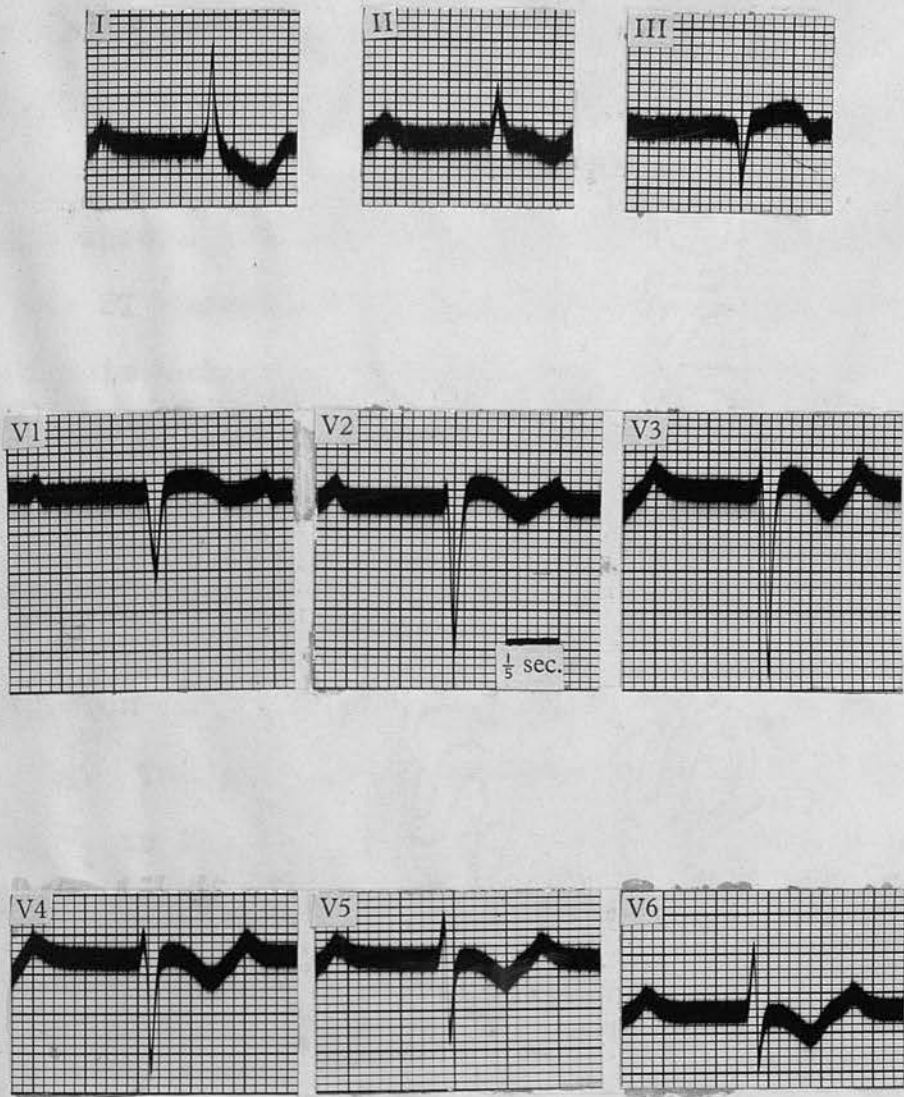


Figure 38 C. 16.12.48. The ST segment & T waves in the limb leads are distorted, due to digitalis. The prolongation of the PR interval to 0.44 second may also be a digitalis effect. In the praecordial leads T is inverted in V1 to V6, and is closely followed by the succeeding P wave giving a false diphasic appearance.

T inversion. Praecordial leads V_2 & V_5 were recorded. Both showed an r S pattern with very little increase in the height of r from V_2 to V_5 - 1.5 to 3 mm.. The ST segment was elevated in V_2 (1 mm.) and flat in V_5 . T was inverted in both leads. Subsequent records showed the following changes (1) disappearance of the ST elevation in lead III, but in the third record this had reappeared and was associated with ST depression in lead I. (2) From being flat, T in lead I became first upright and then inverted; T in lead II also became inverted. (3) The praecordial leads showed ST elevation in V_1 , V_2 , & V_3 , with shallow T inversion in V_1 to V_4 and diphasic (\mp) T waves in V_5 and V_6 . The initial deflections were of r S type from V_1 to V_5 , but in V_6 R exceeded S. The unipolar limb leads were recorded. The left leg lead was of low voltage and r s in form with an upright T wave, while the left arm showed R as the sole initial deflection ST elevation and an inverted T wave. Partial heart block was present in the last record. This defect and the T wave changes in standard and praecordial leads were probably related to digitalis administration.

From a serial study of the records two suggestions might be advanced -

(1) The T wave changes in V_1 to V_5 might be due to intra-mural infarction of the anterior surface of the heart, mainly artero-septal in position. The small r waves in V_1 to V_5 might be associated with such a happening /

happening and not with rotation of the heart - although the r waves do increase in height progressively from right to left. The development of an inverted T in lead I and the changes in the left arm lead would fit in with the diagnosis of intra-mural infarction.

(2) The ST elevation and T inversion in lead III, followed 2 days later by subsidence of the ST shift and deepening of the T inversion are changes which occur in posterior infarction. In lead II of the corresponding records T was flat and shallow inverted. In the absence of diagnostic QRS changes, could these findings indicate intra-mural posterior infarction. Lead aVF was not recorded before digitalis was given.

Clinical details may help correlate these two possibilities. The patient was in left ventricular failure which was progressing to congestive heart failure. She had suffered two pulmonary infarcts and had also had an embolus in her right popliteal artery, i.e. she was having thrombo-embolic episodes in both the pulmonary and peripheral circulations. There was no evidence of peripheral phlebothrombosis. Was there mural thrombus in both sides of her heart? Had this possibly formed on each side of an infarcted interventricular septum? Was the myocardial infarct primarily of the interventricular septum with slight intra-mural extension to the anterior and posterior surfaces of the heart giving the electro-cardiographic picture already detailed? Presumably the infarct did /

did not extend to the upper part of the septum as intraventricular conduction was normal. It is possible, however, that the pulmonary emboli may have arisen from mural thrombus in an infarcted right auricle, but the disturbance noted in auriculo-ventricular conduction did not occur until digitalis was administered.

Autopsy correlation of the site of infarction with the electrocardiographic changes and the clinical picture would have been most instructive, but permission to examine the body was refused.

6. A.H. (Figure 39). A tentative diagnosis of infarction of the interventricular septum was also made in this case from the records obtained. The initial deflections in the standard leads were not abnormal, but the ST segment was depressed in leads I & II and the T waves were shallow biphasic ($\bar{+}$). T in lead III was low upright. Praecordial leads V_2 , V_4 , & V_5 were recorded. The initial deflections in V_4 & V_5 were much smaller than in V_2 , and r in V_4 was less than in V_2 . The ST segment was elevated in V_2 (1 mm.), flat in V_4 , and depressed in V_5 (2 mm.). The T waves were upright. Unipolar limb leads were not recorded. Seven days later two changes were observed - (1) a short splintered r was the sole initial deflection in V_5 and was smaller than the r wave in V_2 , (2) the T wave in V_5 was diphasic /

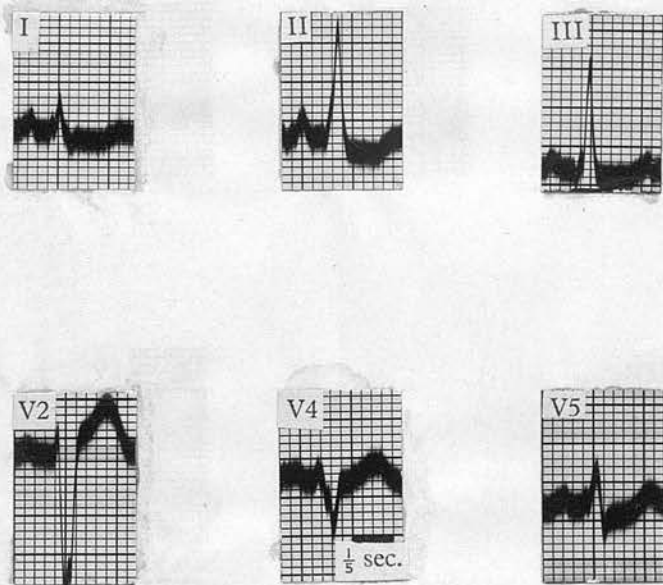


Figure 39 A. 7.3.49. The record is not diagnostic of myocardial infarction, but (1) the ST depression with low diphasic T waves in leads I & II, (2) the form of the initial deflection in V4, and (3) the ST depression in V5 are abnormal.

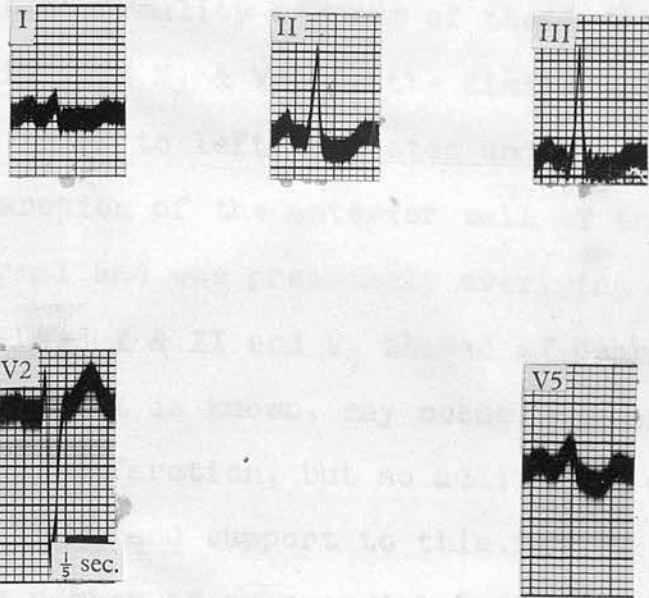


Figure 39B. 14.3.49. There is little change apart from the form of the initial deflection in V5. The persistence of ST depression may be a digitalis effect. In both records myocardial damage in the region of leads V4 & V5 might be suspected.

...anterior wall of the left ventricle was demonstrated. There was no extension posteriorly. At the apex there was an old small infarct.

Discussion:

From these 6 cases it may be suggested that certain electro-cardiographic features indicate (1) anterior infarction of the posterior wall of the heart, and (2) infarction of the lower part of the interventricular /

diphasic (\pm). The ST depression persisted in standard leads I & II and in V_5 but this may have been associated with digitalis administration.

The abnormality in form of the initial deflection in lead V_4 & V_5 and the diminution in height of r from right to left suggested underlying intramural infarction of the anterior wall of the heart. V_2 was normal and was presumably overlying undamaged muscle. Lead I & II and V_5 showed ST depression, a change which, it is known, may occur in these leads in posterior infarction, but no additional changes observed would lend support to this finding. Although the number of praecordial leads available for analysis was few, a tentative diagnosis was made of infarction of the interventricular septum in its lower part, with extension to involve the anterior wall of the heart, and just possibly extension to the posterior wall. At autopsy infarction of the anterior one third of the interventricular septum and of the adjoining anterior wall of the left ventricle was demonstrated. There was no extension posteriorly. At the apex there was an old small infarct.

Discussion:

From these 6 cases it may be suggested that certain electro-cardiographic features indicate (1) intra-mural infarction of the posterior wall of the heart, and (2) infarction of the lower part of the interventricular /

interventricular septum with slight extension anteriorly and/or posteriorly. Only by a correlation of the clinical, electrocardiographic, and autopsy findings in all atypical cases, will the following criteria be proved correct or refuted.

(1) Intra-mural infarction of the posterior surface of the heart.

(a) No QRS changes in leads II, III or aVF.

(b) ST shift in the standard leads, ST depression in lead I and possibly lead II, associated with ST elevation in lead III; ST depression in the praecordial leads to the left of the sternum (mainly V_4 to V_6). These shifts are of short duration and may be missed if an early record is not obtained.

(c) Development of T inversion in lead III and possibly also in lead II.

(d) ST shift in the unipolar limb leads, particularly depression in lead aVL and elevation in lead aVF, and development of an inverted T wave in aVF.

(e) Development of high upright T waves in the praecordial leads particularly V_2 to V_4 , with a progressive increase, during the first few weeks or months, in the height of the T waves, and possibly in the number of leads involved. The more leads showing this change, the more definite the diagnosis. The leads to the right of the praecordium may also show ST elevation, but this is not part of the diagnostic /

diagnostic picture. The incidence of high T waves in the praecordial leads of healthy individuals must be assessed before too much emphasis is placed on this feature as an isolated finding. High T waves in the praecordial leads are known to occur at the edge of an infarct. Of the 34 cases showing anterior infarction in this series five developed high upright T waves in V_1 and/or V_2 . In posterior infarction high T waves are common in the praecordial leads. This may be because the infarct is located on the diaphragmatic surface of the heart and the praecordial leads pick up the potential variations at its edge. But the one case of high posterolateral infarction also developed high T waves in the praecordial leads and there was no question of the leads being near the edge of the infarcted area. In this case also the infarct involved the full thickness of the muscle wall. The second atypical case described had the same high T waves and autopsy showed an intra-mural infarct involving the posterior papillary muscle and the adjoining posterior wall of the left ventricle. These two autopsy cases would suggest that the high T waves in the praecordial leads are not due to the electrodes being near the edge of the infarct, but rather to the infarct being opposite the electrodes and with the healthy anterior muscle wall intervening. That this last factor is essential /

essential is suggested by the fact that neither case who sustained a posterior infarct after a previous anterior infarct developed high T waves in the praecordial leads.

The findings in the high-postero - lateral infarct would also suggest that the criteria listed for an intra-mural posterior infarct, may at times be associated with a through and through lesion towards the base of the heart.

(2) Infarction of the lower part of the inter-ventricular septum :

(a) Evidence of intra-mural damage over the front of the heart, either mainly antero-septal or antero-lateral.

(b) Changes in the ST segment in standard leads and possibly also in the praecordial leads associated with posterior infarction.

(c) Duration of the QRS complex within normal limits.

(g) Normal records - 2 cases :

Two cases diagnosed clinically as having sustained a myocardial infarct and whose course in hospital was compatible with this diagnosis had E.C.G. records apparently within normal limits. However the experience gained by a study of the atypical cases and the one case showing a high postero-lateral infarct would stimulate the suggestion that one case was /

was not within normal limits, and that in fact infarction of the postero-lateral aspect of the left ventricle had taken place. (Figure 40).

Standard lead I showed a q 1 mm. in depth followed by a tall R and a low upright T wave. The unipolar left arm lead showed a low voltage initial deflection with Q 1.5 mm. and R 3 mm. T was flat. The Q wave measured 0.04 second and was 50% of the height of R. The praecordial leads showed no abnormality of the initial deflections, but ST elevation was present in V₁ to V₄ (maximum of 4 mm. in V₁ & V₂) and the T waves were upright in all 6 leads. In V₂, V₃ and V₄, the T waves measured 6 mm. 5 mm. and 5 mm. respectively. Additional leads taken vertically above V₂ V₃ V₄ V₅ & V₆ showed no evidence of underlying dead muscle.

Subsequent records showed (1) slight reduction in the size of the Q wave relative to R in the left arm lead - 2: 5 ; (2) slight variation in the T wave in that lead - from flat to low upright and back to flat; (3) increase in the height of the T waves in the praecordial leads V₂, V₃, & V₄, 9 mm., 10 mm., and 6 mm. respectively, and development of high T waves in leads V₁ & V₅ (5 mm. each).

A diagnosis of high postero-lateral infarction is hazarded on the basis of (1) the findings in the unipolar left arm lead, and (2) the successive changes in the T waves in the praecordial leads.

In /

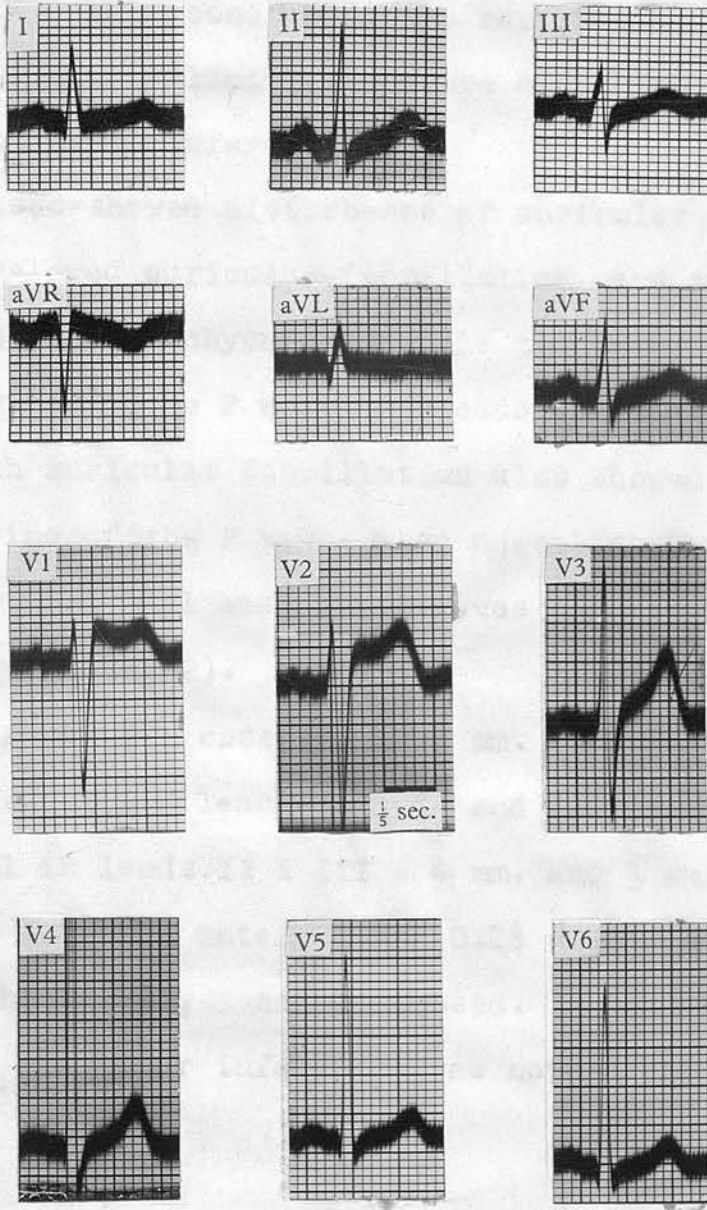


Figure 40. An apparently normal record obtained after a clinical myocardial infarct.

In the second case, the record was consistently within normal limits. (Figure 41).

(b) Auricular Infarction :

Seven cases showed disturbance of auricular activity. Four developed auricular fibrillation, and two auricular paroxysmal tachycardia, while the seventh showed splintering of the P waves in leads II & III. One case with auricular fibrillation also showed marked splintering of the P waves when normal rhythm was restored. Within 1 week the P waves were normal in form. (Figure 42).

An eighth case showed 1 mm. of depression of the PQ segment in leads II, III and aVF. The P waves were tall in leads II & III - 4 mm. and 3 mm. respectively. The PR interval was 0.18 second. Within a week these changes had regressed.

Auricular infarction was not examined for at autopsy.

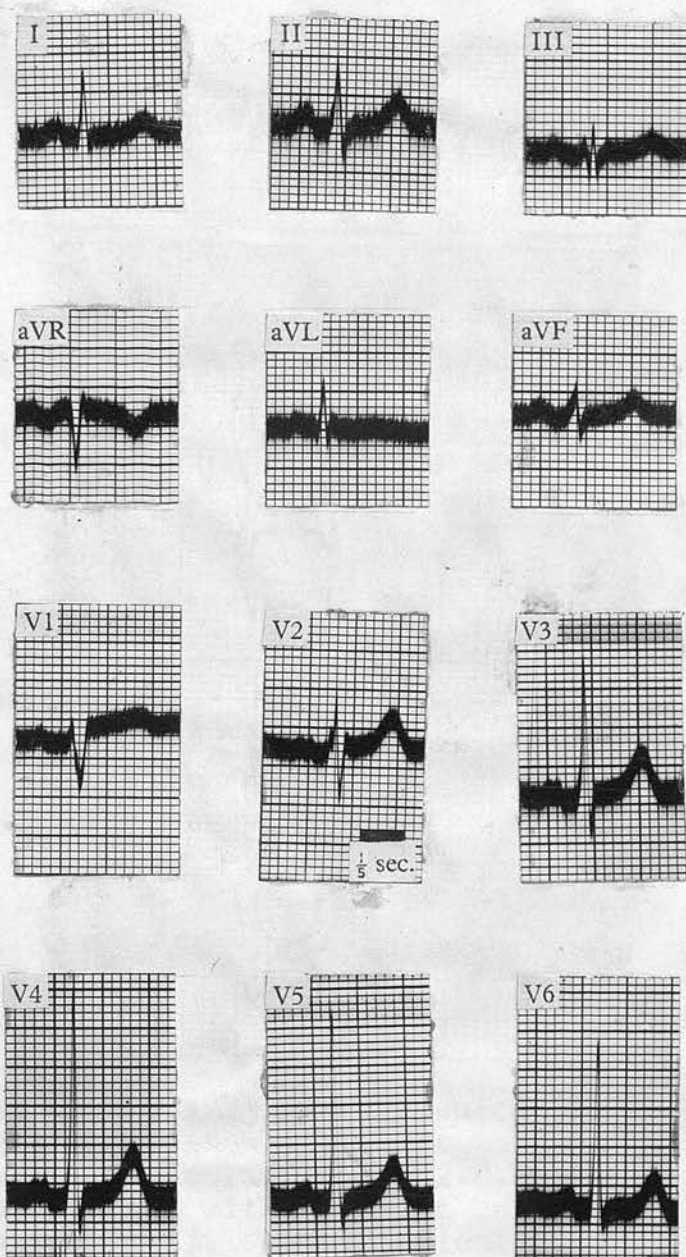


Figure 41. (Case 31): A normal electrocardiogram in a case of recent myocardial infarction.



Figure 42. (Case 23). The successive records taken by lead II show (a) auricular fibrillation with rapid ventricular rate (12.8.48), (b) auricular fibrillation with frequent ventricular extrasystoles (14.8.48), (c) ventricular tachycardia (14.8.48), (d) normal rhythm with splintered P waves (17.8.48), and (e) normal rhythm with normal P waves (24.8.48).

XVII. CONCLUSIONS.

1. (a) The number of deaths certified as due to coronary thrombosis has increased yearly between 1937 and 1947. The increase has been more striking among females than males.

(b) Ageing of the population does not account for the increase.

(c) The incidence of deaths due to coronary thrombosis is highest in the 6th and 7th decades among males, and in the 7th decade among females.

2. (a) The rate of development of the arterio-sclerotic process in the coronary arteries is the fundamental factor determining when capillary rupture will occur in a plaque and arterial occlusion result from the superimposed thrombosis.

(b) Fragility of the capillaries throughout the body may play a minor role in facilitating this capillary rupture and haemorrhage in the arterio-sclerotic plaque.

(c) An upset in the control of intravascular blood clotting resulting in an enhanced clotting tendency may favour the occurrence of thrombosis in a diseased coronary artery. As with other endocrine glands, the mast cells of Ehrlich may become less efficient in later life than in youth, and in the elderly this change may be associated with an enhanced clotting tendency.

3. /

3. (a) In a series of 100 cases of myocardial infarction (70 males and 30 females) treated conservatively, 30 males and 16 females died during the first 6 weeks, the mortality rate being 43% and 53% respectively.

(b) Heart failure developed after the infarct in 31 cases, and of these 27 (87%) died.

(c) Twenty-four cases suffered one or more thrombo-embolic complications, a recurrence of myocardial infarction being the most common event. Twelve cases (50%) died, but in only 4 cases was the episode directly responsible for death.

(d) Fourteen cases showed one or more arrhythmias and of these ten died.

(e) Heart failure was primarily responsible for 50% of all deaths.

(f) Digitalis therapy of heart failure was associated with sudden death in 6 cases, but was not associated with the occurrence of embolic complications.

(g) Excluding cases dying during the first week, endocardial mural thrombus was found in 13 out of 15 cases coming to autopsy, and of these, 10 showed peripheral or pulmonary infarcts.

(h) Massive infarction of the heart was not associated with any constant clinical picture.

3. (a) The immediate prognosis in myocardial infarction is dependent on (1) age, (2) heart size, (3) /

(3) cardiac grade prior to the infarct, (4) severity of shock at the onset, (5) level to which the systolic blood pressure drops, (6) pulse pressure, (7) pulse rate, (8) character of the heart sounds, (9) occurrence of complications, particularly, heart failure, thrombo-embolic episodes and arrhythmias, (10) sex - the elderly female does^{/not} fare so well as the elderly male.

(b) The prognosis is poor if several or all of the following features are present in any one case - (1) elderly patient, (2) enlarged heart, (3) cardiac grade II B or III, (4) severe degree of shock at the onset, (5) systolic blood pressure of under 100 mm.Hg., (6) pulse pressure of under 30 mm. Hg., (7) pulse rate of over 100/min., (8) poor quality heart sounds, tic-tac or gallop rhythm, or inaudible heart sounds, (9) occurrence of any or all of the complications mentioned.

(c) On the other hand, the prognosis is good if not one of these features is present.

(d) The presence of one or two "bad" prognostic features is compatible with recovery, but in such a case, any complication is of grave significance.

(e) The presence of angina pectoris prior to the infarct favoured recovery rather than death.

(f) Thrombo-embolic complications, particularly a recurrence of myocardial infarction, were important in determining prognosis among males in cardiac grade

IIA who had also cardiac enlargement. Of the six cases suffering such an upset, five died.

5. (a) Complications occurring during the months and years after myocardial infarction are frequent. The most common are a recurrence of myocardial infarction, angina pectoris, return of, or development of, hypertension, and the occurrence of heart failure.

(b) Fifty per cent. of the recurrences of myocardial infarction take place within 1 year of the observed infarct, but there is no time limit after which myocardial infarction will not recur.

(c) A reduction in functional capacity is commonly observed after myocardial infarction, but in cases previously in cardiac grade I, and to a less extent IIA, it may be slight.

(d) About 60% of the males who survive the infarct will return to some form of work. A few will be fit for strenuous work. Less than 50% of the female survivors will be fit for ordinary household duties.

(e) In about 25% of cases the electrocardiogram will return to within normal limits, after myocardial infarction, and in a further 10-15% it will remain abnormal, but be no longer diagnostic of infarction. The time within which this regression of signs will occur has not been determined from this investigation.

(f) Proper management determines to a large extent the degree of well being of the patient in the months /

months and years after myocardial infarction.

6. (a) The ultimate prognosis in myocardial infarction centres on the possibility of a recurrence of infarction. Seventeen of 24 deaths occurring during the follow-up period in this conservatively series were probably due to such an event. No case still surviving has had a recurrence.

(b) Leaving aside the unpredictable, the course after myocardial infarction is determined by the efficiency of the remaining heart muscles.

(c) The young tend to survive and the elderly to die, but a higher proportion of elderly males survive, than do elderly females.

(d) Among males the following features are associated with survival rather than death -

1. Factors present prior to the infarct:
 - (i) No effort pain.
 - (ii) No previous infarct.
 - (iii) Body weight within normal limits.
 - (iv) Cardiac grade I.
 - (v) Presence of hypertension.
2. Factors arising immediately after the infarct.
 - (i) No shock at the onset.
 - (ii) Good quality heart sounds.
 - (iii) Systolic blood pressure above 100 mm. Hg.
 - (iv) Pulse rate under 100/min.

3. Factors developing after the infarct.

- (i) Cardiac grade I or IIA.
- (ii) Freedom from recurrence of myocardial infarction.
- (iii) Freedom from effort pain.
- (iv) Development of hypertension.
- (v) Regression of the electrocardiographic signs of myocardial infarction.

(e) The group of females surviving the infarct is too small for similar analysis.

7. (a) In a series of 70 cases of myocardial infarction (46 males and 24 females) treated with anti-coagulants during the first 3 weeks after the infarct, 7 males and 9 females died during the first 6 weeks - sex mortality rates of 15% and 37.5% respectively.

(b) Heart failure developed in 23 cases (33%) with a 57% mortality.

(c) Eight patients experienced 9 thrombo-embolic episodes while anti-coagulant therapy was theoretically adequate. Recurrence of myocardial infarction occurred once. Three cases died, but in only one case was the episode directly responsible for death.

(d) Seven cases showed one or more arrhythmias and of these five died.

(e) Heart failure was primarily responsible for 50% of all deaths.

(f) Digitalis therapy of heart failure was associated with sudden death in 3 cases.

(g) /

(g) One adequately treated case showed a minimal degree of mural thrombus formation at autopsy, and one other case dying in congestive heart failure showed terminal thrombosis in a small pulmonary artery. No mural thrombus was found in the other cases, nor were peripheral or pulmonary infarcts demonstrated.

(h) All cases dying and coming to autopsy had large or massive myocardial infarcts.

8. Anti-coagulant therapy has undoubtedly brought about an improvement in the immediate prognosis after myocardial infarction.

(a) Male mortality has been reduced from 43% to 15% and female mortality from 53% to 37.5%.

(b) While adequate anti-coagulant therapy was maintained, thrombo-embolic complications were reduced from 24% to 11%. Only one death was directly due to a thrombo-embolic episode, as compared with 4 in the control series.

(c) Mortality rate among cases developing heart failure was reduced from 87% to 57%.

(d) Males in cardiac grade IIA showed greatest improvement - the mortality rate being reduced from 42% to 4%; while females showed improvement only among those in cardiac grade IIB, the mortality dropping from 83% to nil.

(e) The males in cardiac grade IIA who had also cardiac enlargement suffered no thrombo-embolic complication and only one died.

9. The evidence adduced indicates that the improvement in prognosis in the treated series is due, not only to a reduction in thrombo-embolic complications, but to limitation of the extent of myocardial damage. Anti-coagulant therapy maintains the patency of the collateral vessels, so preventing or minimising concentric enlargement of the infarcted area.

10. Absence of the layer of endocardial mural thrombus has not resulted in any increase in deaths due to rupture of the infarct.

11. Anti-coagulant therapy for a period of 3 weeks after the infarct is adequate in the great majority of cases. Only one case in the treated series had a thrombo-embolic episode after treatment was completed.

12. Treatment with dicoumarol must never be lightly undertaken. Strict control of treatment is necessary to avoid greater danger to the patient than he runs from his myocardial infarct.

13. (a) The complications occurring during the months and years after the myocardial infarct in the treated series, have been similar to those in the control series.

(b) Seven deaths have occurred during the follow up period of which 4 were probably due to a recurrence of myocardial infarction.

(c) /

(c) In all, six recurrences have taken place, three within one year of the "treated" attack.

(d) 60% of the males have returned to some form of work, but only 14% of the surviving females are fit for their normal housework.

(e) Hypertension returned or developed in 25 of 39 males and 14 of 15 females.

(f) Troublesome shoulder pain has developed in 4 cases.

(g) In 21% the electrocardiogram has returned to within normal limits.

(h) No case has developed a cardiac aneurysm.

14. To what extent, if any, anti-coagulant therapy during the first 3 weeks of the acute phase, influences the ultimate prognosis, requires further study over a prolonged period, and with a larger series of cases. To date fewer deaths have occurred in the treated series than in the control series, over the same follow up period. A greater number in the treated series have become hypertensive after the infarct, possibly as a result of limitation of the size of the infarct and thereby maintenance of the myocardial efficiency.

15. (a) The blood develops an enhanced tendency to clot after myocardial infarction. There is considerable individual variation in the rapidity of onset of this change, in the degree of change, and in the duration.

(b) /

(b) Commonly this clotting tendency develops during the first week, reaches its maximum about the end of the second week and disappears during the fourth week.

(c) Recurrence of myocardial infarction has occurred while a marked clotting tendency was observed in 3 cases, but other thrombo-embolic phenomena have not taken place.

(d) It is suggested that (1) development and maintenance of a marked clotting tendency indicates the presence of endocardial mural thrombus, while (2) absence of any change would mean that mural thrombus had not formed.

(e) The theory is advanced that heparin, the secretion of the mast cells of Ehrlich plays a dominant role in maintenance of the fluid state of the blood. Any change observed in the blood coagulation is the result of the interplay of two opposing forces - heparin secretion on the one hand, and on the other hand, substances promoting blood clotting such as arise in damaged or infarcted tissues.

(f) The plasma fibrinogen level rises after myocardial infarction, and commonly returns towards normal in the 3rd or 4th week.

(g) No change was observed in the prothrombin times at the onset of myocardial infarction.

16. Specific anti-shock therapy with plasma infusion, oxygen, warmth, and coramine, may relieve a severe degree of shock at the onset, and prove a life-saving measure.

17. Embolic occlusion of a coronary artery is a rare event except in subacute bacterial endocarditis. In the series reported, it occurred in 11% of cases, and was either associated with rapid death or did little beyond causing a temporary set back to the patient.

18. (a) Analysis of serial records in 34 cases of anterior infarction has shown that electrocardiographic evidence of myocardial infarction occurs in the standard limb leads in 41% of cases, in the unipolar limb leads in 29%; and in the praecordial leads in 100%.

(b) The diagnostic changes in the standard limb leads are well known. In the unipolar left arm lead a Q wave must be (i) 0.04 second in duration and (ii) at least 25% of the succeeding R wave, before it can be considered diagnostic of myocardial infarction. Associated ST and T wave changes occur as in standard lead I.

(c) Four diagnostic patterns indicate anterior infarction in the praecordial leads.

(i) Q waves plus ST & T wave changes.

(ii) Diminution in size of the initial r wave from right to left, plus ST & T wave changes.

(iii) /

(iii) Combination of diminution in size of the r wave, and Q waves, plus ST & T wave changes.

(iv) No abnormality of the initial deflection and ST & T wave changes alone.

(d) The more diagnostic features there are present in the standard leads, the more likely are Q waves or a combination of diminishing r waves and Q waves to be present in the praecordial leads.

(e) If no diagnostic changes are present in the limb leads, the changes in the praecordial leads will probably be confined to ST & T wave changes.

19. (a) Posterior myocardial infarction occurred in 15 of 65 cases analysed. Diagnosis was made from changes in the standard limb leads and from the left leg unipolar lead. In 8 cases the praecordial leads provided corroborative evidence.

(b) High upright T waves occur in the praecordial leads, particularly V_1 to V_4 during the healing stage of posterior infarction, but may also occur during the acute phase. Such changes persist for months or years.

20. Antero-posterior myocardial infarction, shows the changes of anterior infarction in the praecordial leads, and the changes of posterior infarction in the left leg lead, and standard leads II and III.

21. The unipolar left arm lead shows the changes of infarction when the high antero-lateral or postero /

postero-lateral aspects of the heart are involved. The praecordial leads do not suggest infarction, and exploration of the chest vertically above these leads reveals a high antero-lateral infarct, but not a high postero-lateral infarct.

22. (a) In cases of right bundle branch block complicating myocardial infarction, the praecordial leads reveal evidence of anterior infarction, but the standard limb leads do not. The unipolar limb leads may do so.

(b) Neither the limb leads nor the praecordial leads may show evidence of myocardial infarction in the presence of left bundle branch block. Only if the block is unstable, and normal intraventricular conduction supervene, may classical or atypical evidence of infarction be apparent.

23. (a) An apparently atypical electro-cardiogram showing (i) no QRS changes in the standard leads, (ii) T inversion in lead III and lead aVF, and possibly in lead II, (iii) the ST shifts of posterior infarction in the standard, unipolar limb and praecordial leads, and (iv) development of high upright T waves in the praecordial leads, is considered to be diagnostic of an intra-mural posterior infarct or occasionally a trans-mural posterior infarct at the base of the heart.

(b) /

(b) An investigation of the incidence of high T waves in the praecordial leads of healthy individuals is important in assessing the importance of the criteria listed above.

(c) Infarction of the lower part of the interventricular septum may give the following features, (i) evidence of intra-mural damage over the front of the heart, either mainly antero-septal or antero-lateral, (ii) shift of the ST segment in the standard leads and possibly also in the praecordial leads associated with posterior infarction. (iii) QRS complex of normal duration.

24. Auricular infarction is evidenced by a disturbance of auricular rhythm or by splintering or notching of the P waves.

25. Occasionally the electrocardiogram may remain within normal limits in cases of undoubted myocardial infarction.

XVIII.

SUMMARY.

1. A historical review of myocardial infarction in all its clinical aspects is presented.
2. The increasing importance of myocardial infarction as a cause of death has been investigated by a study of the annual reports of the Registrar-General for Scotland between 1937 and 1947.
3. The aetiology of coronary thrombosis with myocardial infarction is briefly reviewed and two clinical factors of possible importance are reported.
4. The clinical details of a series of 100 cases of myocardial infarction treated conservatively are detailed, and the features of importance in estimation of immediate prognosis discussed. The survivors have been followed up and the clinical course pursued has been analysed to determine the factors governing ultimate prognosis.
5. A series of 70 cases treated with anti-coagulants has been similarly analysed and compared with the conservatively treated series, to determine the value of this measure in (a) immediate prognosis, and (b) ultimate prognosis.
6. Clotting changes which occur after myocardial infarction are presented and tentative suggestions made as to the response of the body to the presence of a mass of infarcted tissue.
7. Specific anti-shock therapy is summarised and experience with 3 cases cited.

8. /

8. Embolic coronary artery occlusion is briefly mentioned and six cases are listed. The incidence of coronary artery embolism in subacute bacterial endocarditis is presented.
9. Serial electro-cardiograms obtained in 65 cases using standard limb leads, augmented unipolar limb leads, and unipolar praecordial leads, have been analysed, and the features of diagnostic importance stressed.
10. The conclusions are presented.
11. Finally clinical details of 35 cases are reported.

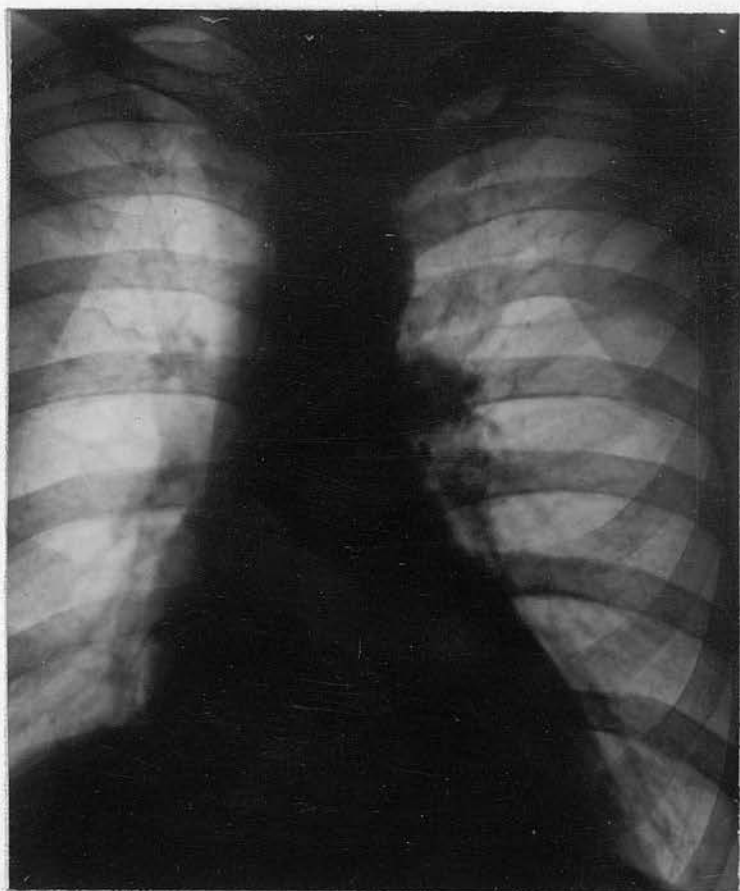
Thirty-five cases are reported in detail.

Thirty-one are included in the two series reported in sections V. and IX.; one had subacute bacterial endocarditis; one was treated plasma; and two were investigated to demonstrate the clotting changes after myocardial infarction. All were selected as showing some feature of interest either in onset, clinical course after the infarct, or follow up period. Cases 1 to 8 were treated conservatively. Seven survived the infarct although 3 had a stormy course. Two have developed a cardiac aneurysm. Cases 9 to 31 were treated with anti-coagulants. Eight (cases 9 to 16) died in the ward from a variety of causes. Five (cases 17 to 21) died after their discharge; while ten (cases 22 to 31) are still alive. Case 32 developed a myocardial infarct during the course of subacute bacterial endocarditis and later died following a cerebral embolus. Case 33 received anti-shock treatment and made a good recovery; while cases 34 and 35 were treated conservatively and the serial change in blood clotting, demonstrated by means of the Waugh Ruddick heparin retarded clotting test, were studied. Both died and came to autopsy.

Case Number 1: D.E. 43 years: Admitted on 17.4.39 having had a myocardial infarct that morning. Premonitory pains had been experienced during the preceding /

preceding 5 days. E.C.G. examination showed an anterior myocardial infarct. Convalescence was uneventful. He was allowed up on 22.5.39 and was discharged home on 3.6.39. X-Ray examination on 18.4.39 showed the heart to be of normal size and shape. (Figure 43).

On 1.8.39 he was seen again when it was recorded that his cardiac apex was thrusting in character. X-Ray examination suggested the development of a cardiac aneurysm. (Figure 44). In October '39 he returned to work as a clerk. He was slightly short of breath on exertion but was otherwise well. Early in November '39 he suddenly felt a fluttering in the region of his heart and at the same time had a feeling of tightness beneath the upper sternum. He had no pain and was not short of breath. After 33 hours the palpitation suddenly stopped, and after 3 days he returned to work feeling perfectly fit. Thereafter he was well, until June '40, when he had an exactly similar attack of palpitation lasting 24 hours. On 22.7.40 while in bed he developed a sensation of hard thumping in his chest and his pulse was not so fast as in the other attacks (his own observation). At times he felt very short of breath. The thumping sensation came and went at intervals for 2 days, during which he continued at work. Intermittently he felt a stinging pain behind his sternum which was quite unrelated to exercise. He reported on 29.7.40 when /

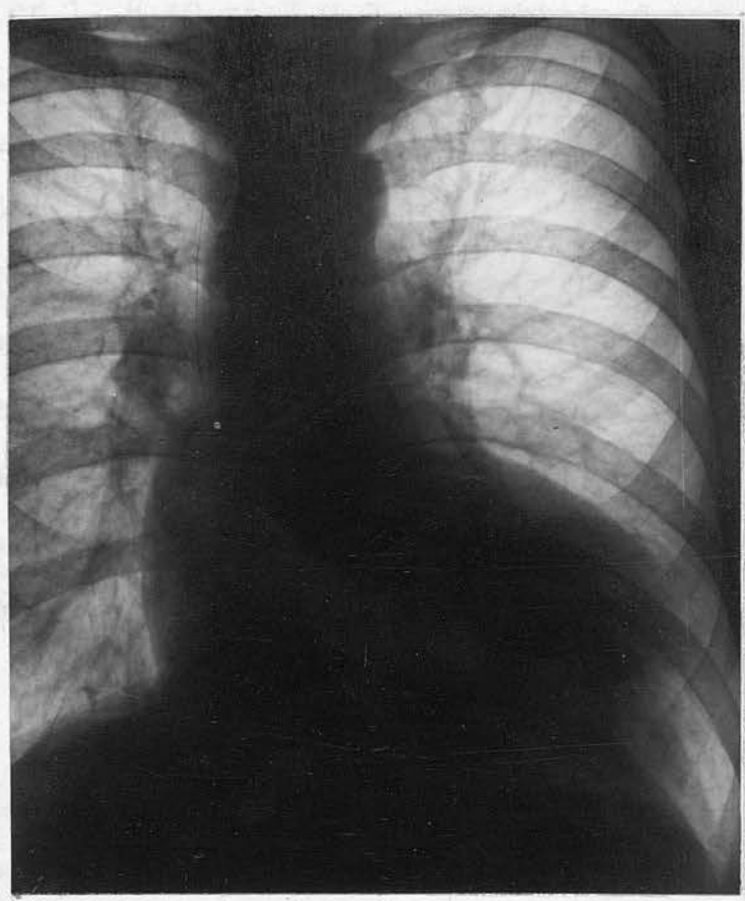


18.4.39.

Figure 43. Case I. One day after
the myocardial infarct. Heart size
within normal limits.

When I-ray examination showed a definite cardiac aneurysm. (Figure 43).

During a similar attack of angina in the



1.8.39.

Figure 44. Case I. Three and a half months after the myocardial infarct. Development of cardiac enlargement with bulging of the left ventricle.

the other heart was in the left lateral position almost in the anterior axillary line. The cardiac impulse was for the most part in the left lateral position. The chest leads gave evidence of an old anterior infarct, but did not substantiate the diagnosis of left bundle branch block suggested by the limb leads. (Figure 47)

when X-Ray examination showed a definite cardiac aneurysm. (Figure 45).

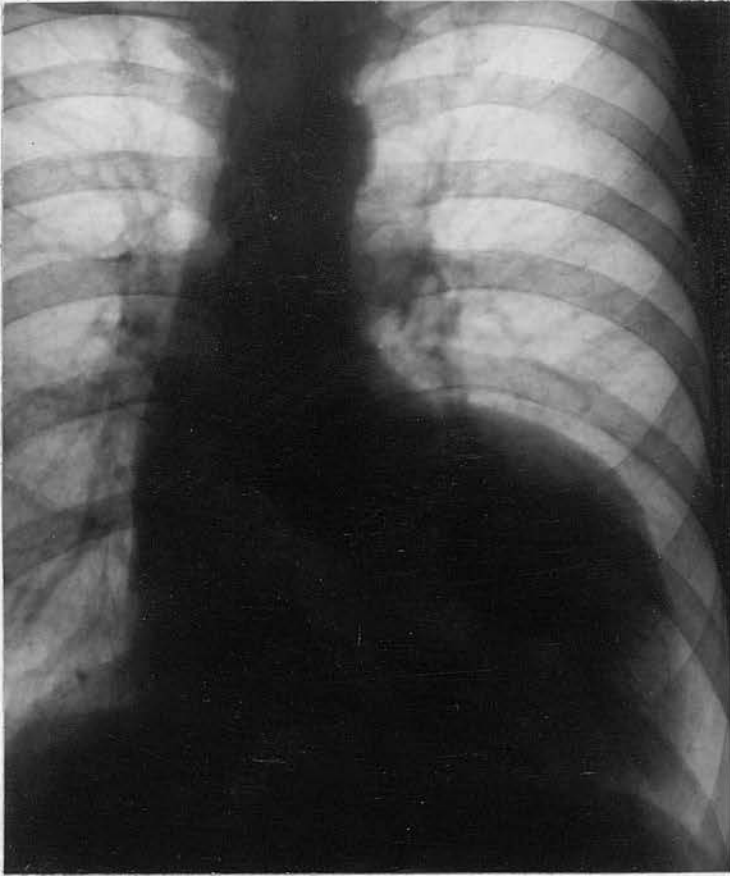
During a similar attack of thumping in the chest on 13.8.40 an E.G.C. was obtained, and showed a ventricular tachycardia at a rate of 150/min.. After $3\frac{1}{2}$ hours the attack ceased spontaneously, but he was admitted for observation, and was given quinidine 0.2 Gm. t.i.d. He continued to take this after his discharge. Thereafter he remained well, and continued at work. He was not short of breath unless he hurried and had no pain in the chest on exertion. He did not feel tired. During the war he acquired an allotment and dug it himself, only giving it up in 1947.

When he next reported in June '48 his main trouble was that of dyspepsia. Later it was found that he had a large duodenal ulcer. On examination the apex beat was in the 6th left interspace almost in the anterior axillary line. The cardiac impulse was forcible. The pulse rate was 86/min. with frequent extra-systoles, and the blood pressure was $\frac{136}{86}$. X-Ray examination showed little change in heart size or in size of the aneurysm over the 8 years since 1940 (Figure 46). E.C.G. examination however showed a prolongation of the initial deflections in all standard leads to 0.12 second. The chest leads gave evidence of an old anterior infarct, but did not substantiate the diagnosis of left bundle branch block suggested by the limb leads. (Figure 47).



29.7.40.

Figure 45. Case I. Fifteen and a half months after the myocardial infarct. Cardiac enlargement with more definite cardiac aneurysm formation.



24.6.48.

Figure 46. Case I. Nine years after the myocardial infarct. Relatively little change from 29.7.40, in the size and shape of the heart.

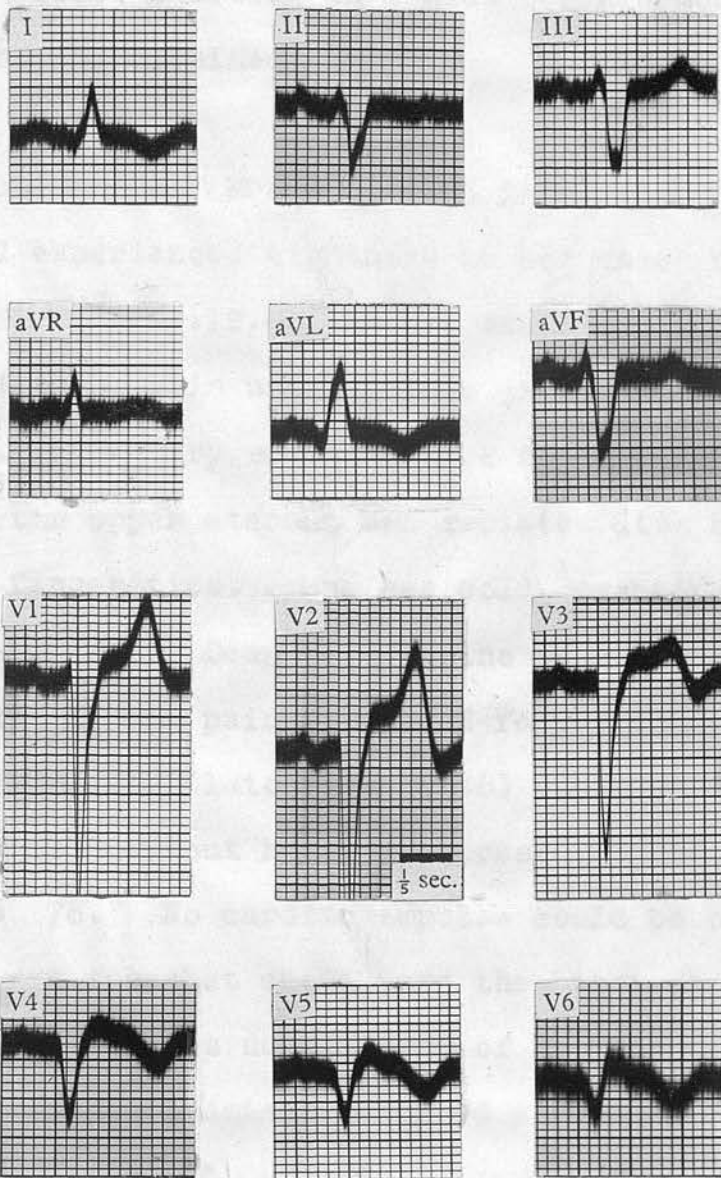


Figure 47. 24.6.48. (Case 1):
 Nine years after the myocardial infarct. The limb leads show widening of the QRS complex suggestive of a bundle branch conduction defect, but the six praecordial leads recorded fail to substantiate this.

Since starting on a diet for his duodenal ulcer he has remained well.

Case Number 2: Mrs J.R. 55 years. For 9 months she had experienced tightness in her chest on exertion. During 9.12.46 she had several short attacks of substernal pain unrelated to exertion and at 10 p.m. had a very severe attack of pain which began behind the upper sternum and radiated down both arms to the finger tips. She was cold, sweating, and felt nauseated. Despite morphine and inhalation of amyl nitrite the pain persisted for $3\frac{1}{2}$ hours. On admission 7 days later (16.12.46) she was still hypertensive - $\frac{140}{104}$, but her blood pressure subsequently fell to $\frac{116}{76}$. No cardiac impulse could be palpated as she was somewhat obese, and the heart sounds were faint. There was no evidence of heart failure. An E.C.G. taken on admission showed a recent posterior myocardial infarct.

Convalescence was uneventful and on 28.1.47 she was discharged home. Hypertension had returned, the B.P. being $\frac{154}{94}$ on 27.1.47. E.C.Gs had shown evidence of healing but X-Ray examination suggested the possible development of a cardiac aneurysm. (Figure 48A and B).

After 3 months at home she felt fit for light housework, but would rest every second afternoon. She had no tightness in the chest or shortness of breath on exertion, but did get a numb feeling in both /

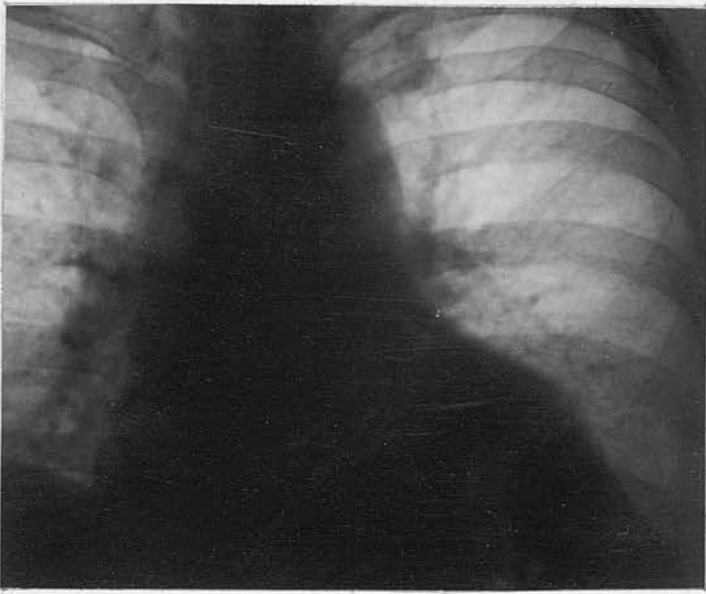


Figure 48 A. Case II. 21.1.47.

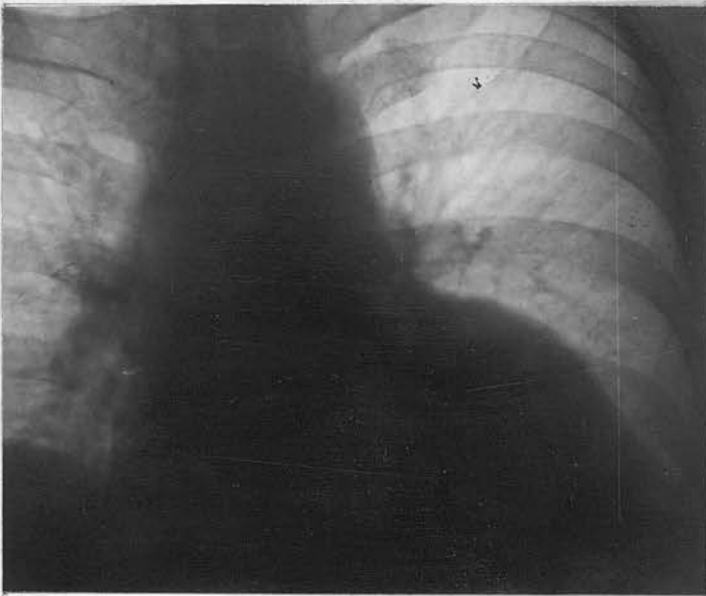


Figure 50 A. Case II. 1.6.49.

Antero-posterior view of heart showing initial slight bulging in the middle of the border of the left ventricle (figure 48 A) and subsequent development of marked bulging of the outline of the left ventricle (Figure 50A).

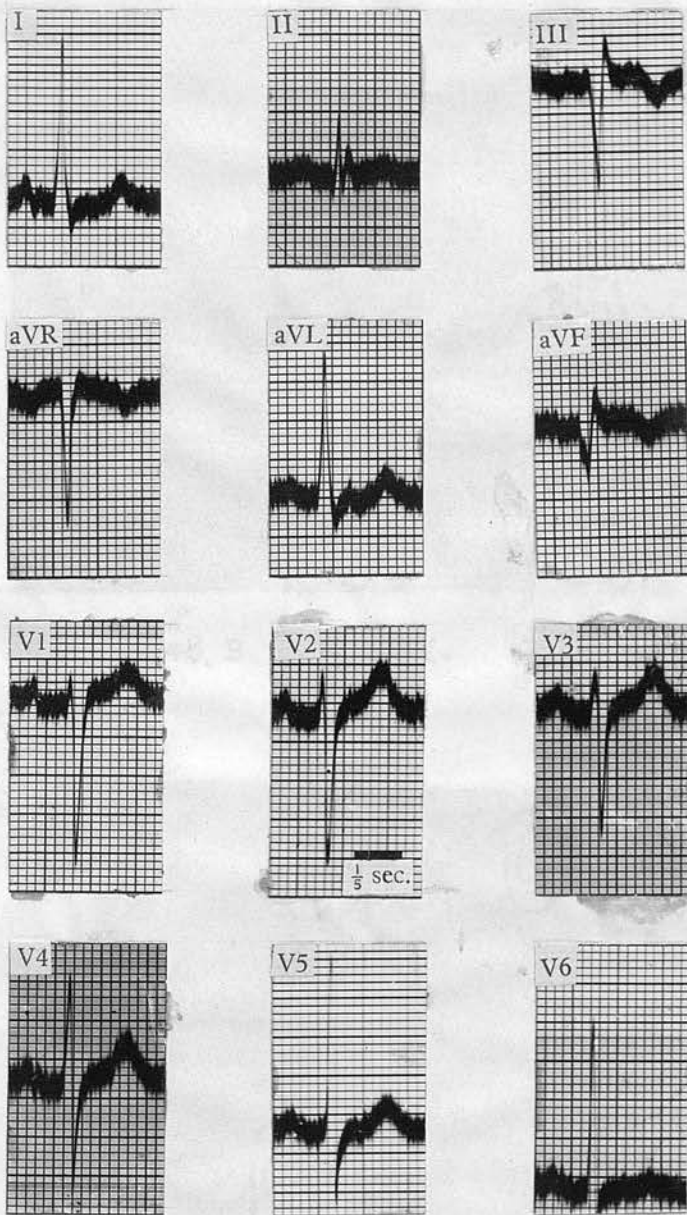


Figure 49. 1.6.49. (Case II) :
 The record is that of an old healed posterior infarct.

Left anterior wall
 heart showing
 aneurysm formation



Figure 48 B Case II. 21.1.47.

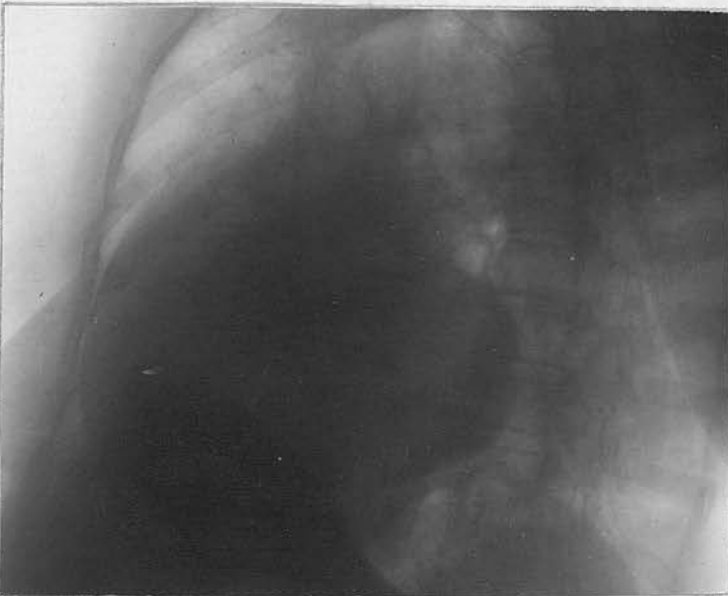


Figure 50 B Case II. 1.6.49.

The heart sounds were faint. The chest was clear.
Left anterior oblique view of the heart showing definite cardiac aneurysm formation (Figure 50 B).

both arms. When seen again on 14.6.49 she was feeling well. Her blood pressure had risen being $\frac{210}{124}$. Again no cardiac impulse could be felt. Her weight had increased and she was very obese, being 3 stones over her standard weight. The E.C.G. showed evidence of an old posterior infarct (Figure 49). X-Ray examination in the left anterior oblique position however showed a definite cardiac aneurysm. (Figure 50A and B).

She has continued to lead a quiet life and has remained well.

Case Number 3. J.M. 41 years. Admitted on 21.11.39. Thirteen days previously while at work, he had experienced very severe substernal pain which did not radiate. It was burning and crushing in character, and his chest felt as if it were being "drawn from the sides towards the middle". Even when he arrived home and got to bed, the pain persisted. He had never experienced such pain before. On admission the pulse was regular $\frac{65}{\text{min.}}$, and of good volume. The blood pressure was $\frac{115}{80}$. The radial arteries were palpable but not tortuous. The apex beat was in the 5th left interspace 4" from the midline. The heart sounds were faint. The chest was clear. E.C.G. examination suggested a posterior myocardial infarct. He was kept at rest in bed and discharged home on 4.12.49.

After $5\frac{1}{2}$ months he returned to work, having a light /

light job for $1\frac{1}{2}$ years. Later he returned to his usual work/as a commercial traveller, and took up golf again. Thereafter he played golf frequently, and entered for some of the major amateur tournaments. During 1942 and 43 he was in the Home Guard. Walking uphill against a wind, or hurrying after a meal would cause slight anginal pain, and very occasionally he would have to stop. He never had a return of severe persistent chest pain. When seen in June '48 the blood pressure was $\frac{126}{88}$, and the E.C.G. no longer indicated old myocardial infarction. He was fit for most things. Fluoroscopy was carried out in June '49 and an inactive segment was detected on the lateral border of the left ventricle.

Case number 4: J.M. 60 years. On 5.4.43 while at his work as a porter-signalman he suddenly felt weak, had a tight feeling in his chest, and became very breathless. He broke out in a sweat and felt very cold. In about 20 minutes this passed off and he carried on with his work, which included climbing a 40 ft. lamp standard. At the end of the day he felt weak and unsteady on his feet and was taken home by car. Prior to this he had been very fit and during the preceding 2 months had been doing very heavy work.

When admitted on 12.4.43 E.C.G. examination showed a posterior myocardial infarct. He was kept in /

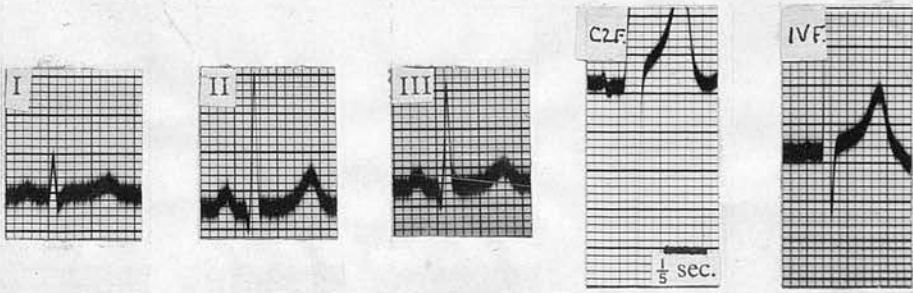
in bed until 11.5.43 and was discharged home 4 days later. Within 2 weeks he was doing many small jobs about the house but did not begin work again for 8 months. Since then he has been employed as a dispatcher of diving suits. He finds this more strenuous than his previous work as a porter but is not short of breath, and can hurry up a stair of 67 steps without distress. Not only is he working 9 hours each day, $5\frac{1}{2}$ days in the week, but he travels 15 miles to and from work each day, walking the first 3 miles in the morning. His day starts at 4.15 a.m.. He is not hypertensive - $\frac{152}{86}$, but has arterio-sclerotic peripheral vessels. It would be hazardous to diagnose myocardial infarction from his E.C.G. on 11.2.49.

Case Number 5: G.J. 49 years. Admitted on 27.5.43 complaining of severe pain across the front of the chest and down the inside of both arms to the fingertips. His chest felt tight and he was short of breath, restless, and sweating. Morphine $\frac{1}{4}$ gr. s.c.i. relieved the pain after 2 hours. During the 10 days prior to admission he had experienced substernal pain on exertion. This had rapidly increased in severity. On admission the heart sounds were faint; the blood pressure was $\frac{116}{78}$; the peripheral arteries were thickened and tortuous. E.C.G. examination showed no abnormality, but the T wave in lead I was slightly lower than T in lead III. He remained well /

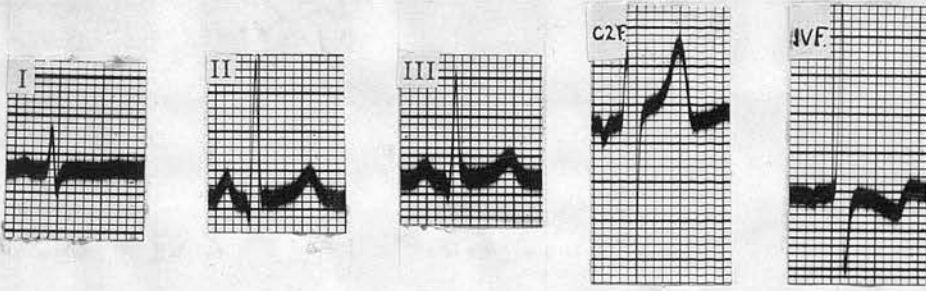
well for 4 days, but thereafter had frequent attacks of anginal pain while in bed. These varied in severity, some being relieved by inhalation of amyl nitrite or by sucking nitroglycerine $\frac{1}{100}$ gr., but others required morphine for their relief. During each attack of pain the blood pressure rose e.g. to $\frac{182}{110}$. From 6.6.43, $\frac{1}{100}$ gr. nitroglycerine was given 2 hourly but with only slight lessening of the pain. Daily E.C.Gs. showed variations in the T waves in lead I and CIVF. (Figure 51). On 9.6.43 he had a particularly severe attack of substernal pain, which required morphine for its relief. An E.C.G. on that day showed evidence of myocardial infarction. (Figure 52). Again on 11.6.43, after a very severe attack of pain, the E.C.G. indicated fresh myocardial damage. Thereafter he remained free of pain. He was kept at rest in bed and was well sedated with phenobarbitone. Five weeks after his second infarct he was allowed up and 8 days later was discharged home. E.C.Gs. taken at intervals showed evidence of healing (Figure 53).

After his discharge his activities were considerably restricted by effort pain. He could avoid this only by walking slowly or by going for less than $\frac{3}{4}$ mile. In cold weather the pain would come on very easily. On 27.12.43, while in bed he developed a very severe substernal pain which gripped him like a vice, and passed down to the fingers of both hands.

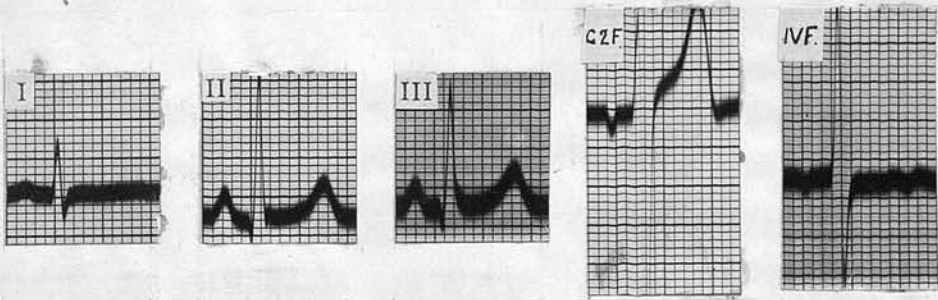
He /



27. 5. 43.



31. 5. 43.



7. 6. 43.

Figure 51. Successive T wave changes in lead I and lead CIVF during period while anginal pain was easily induced.

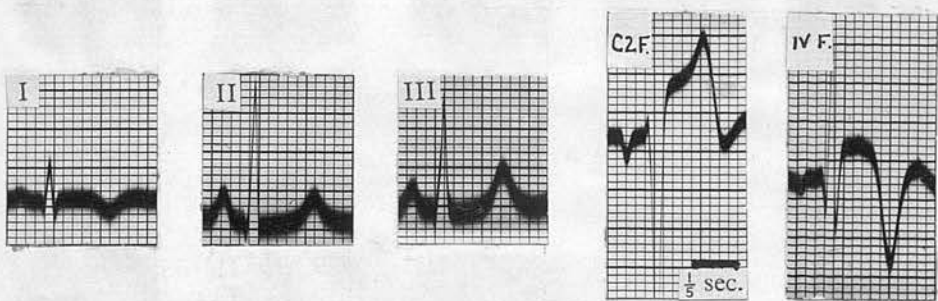


Figure 52 A

9.6.43.

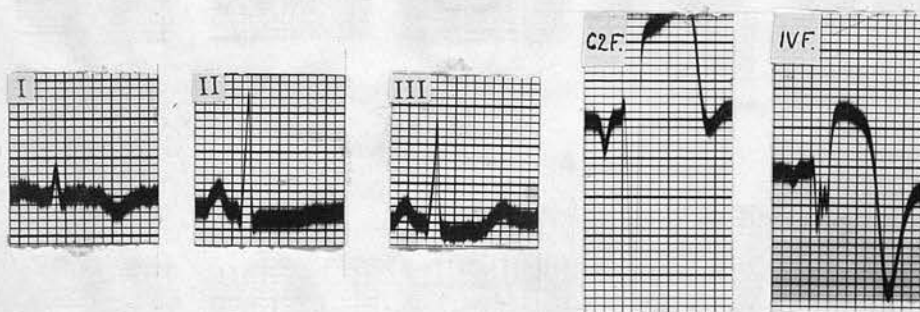
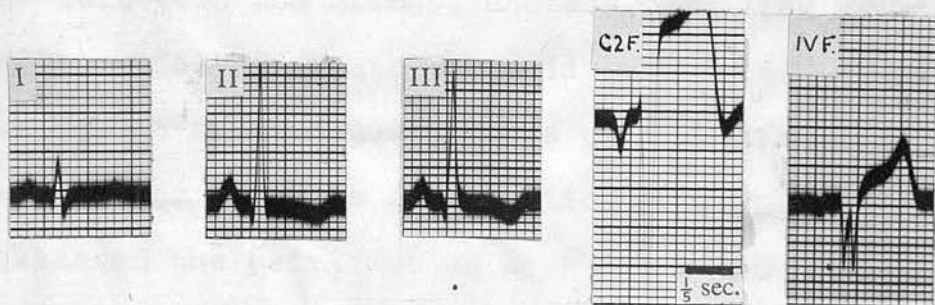


Figure 52 B.

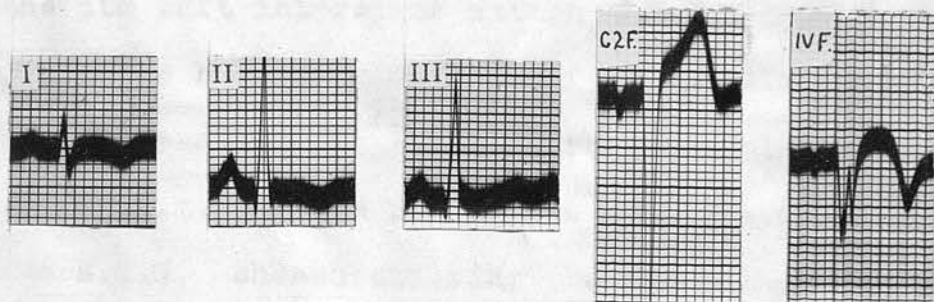
11.6.43.

(Case 5):

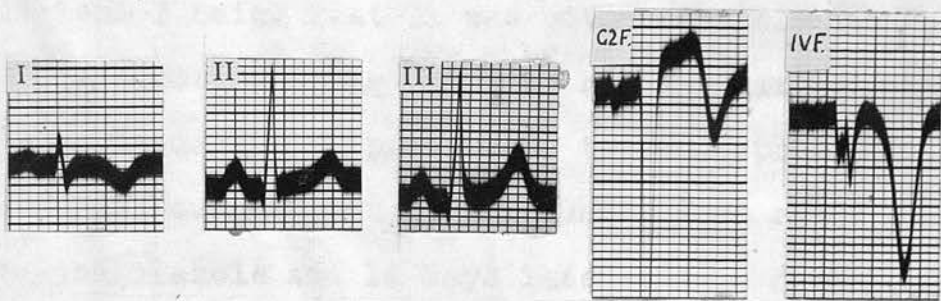
The records, taken at an interval of 2 days, both show evidence of fresh anterior myocardial infarction.



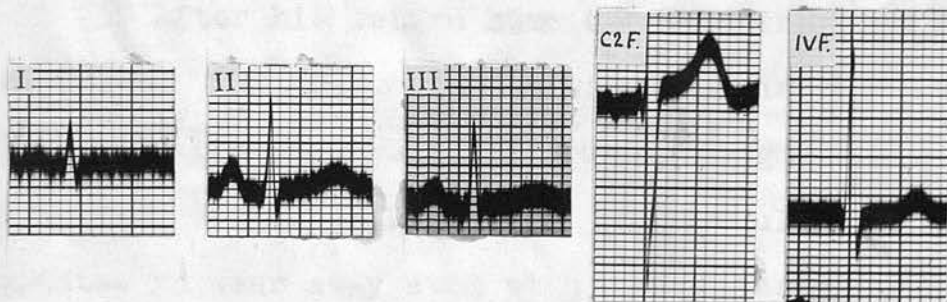
15. 6. 43.



19. 6. 43.



28. 6. 43.



6. 1. 44.

Figure 53. Healing changes after the infarct with eventual return to normality.

He felt cold and clammy, and was trembling all over. He also felt nauseated but did not vomit. He was afraid to move because of the pain. After 3 hours his doctor gave him an injection of morphine. This relieved the pain, but an ache persisted for 5 nights. On 6.1.44 he was re-admitted. The apex beat was in the 5th left interspace within the mid-clavicular line, the heart sounds were of good quality, and the blood pressure was $\frac{106}{70}$. There was no leucocytosis - 7,200/c.m. and the B.S.R. was normal - 4 mm./hr.. The E.C.G. showed striking changes being no longer diagnostic of myocardial infarction. Apart from T in lead I being flat it was not definitely abnormal. After 2 weeks during which he had no pain and felt well he developed pneumonia, type II. pneumococci being recovered from his sputum. This responded to sulphathiazole and 16 days later he was discharged to a convalescent home.

After his return home the pain in the chest returned. He was greatly disabled, being unable to walk more than 100 yards without feeling pain in the chest and inside both elbows. This would take 10-15 minutes to wear away even with the aid of nitro-glycerine. While the pain was present he would be short of breath. Frequently he had attacks of pain while in bed at night. Because of the severity of the pain and the ease with which it was induced, he spent many months in bed, and between 1944 and 1947 was /

was up for only about 3 months each year. In 1947 however he felt better and was able to work in a bookshop for a year. The pain was still frequent but not so severe. His hours of work were from 8 a.m. to 7 p.m. and by the end of a day he was very tired. He began to notice that he was having pain in the calves on exertion, but commonly pain in the chest would come on first and stop him before he felt pain in the legs. In January '48, he retired to bed, because of the severity of the chest pains and also because of the development of spontaneous short attacks of irregular palpitation and breathlessness.

When seen on 23.9.48 he was far from well.

The apex beat was in the 5th left intercostal space just outside the mid-clavicular line. The heart sounds were normal but were accompanied by a systolic murmur of moderate intensity in the mitral area. The blood pressure was $\frac{146}{86}$. There were frequent extra-systoles. An E.C.G. was within normal limits, but showed ventricular extra-systoles. (Figure 54). His exercise tolerance was extremely limited, and in spite of sucking nitroglycerine he had to stop 3 times when asked to walk 30 yards on the level. While resting after this exertion, one short attack of palpitation occurred during which he temporarily lost consciousness & only occasional weak pulse beats reached the wrist. Unfortunately an E.C.G. was not being taken at the time, nor was his heart auscultated.

Ten days later he died, death being certified as due to Angina Pectoris.

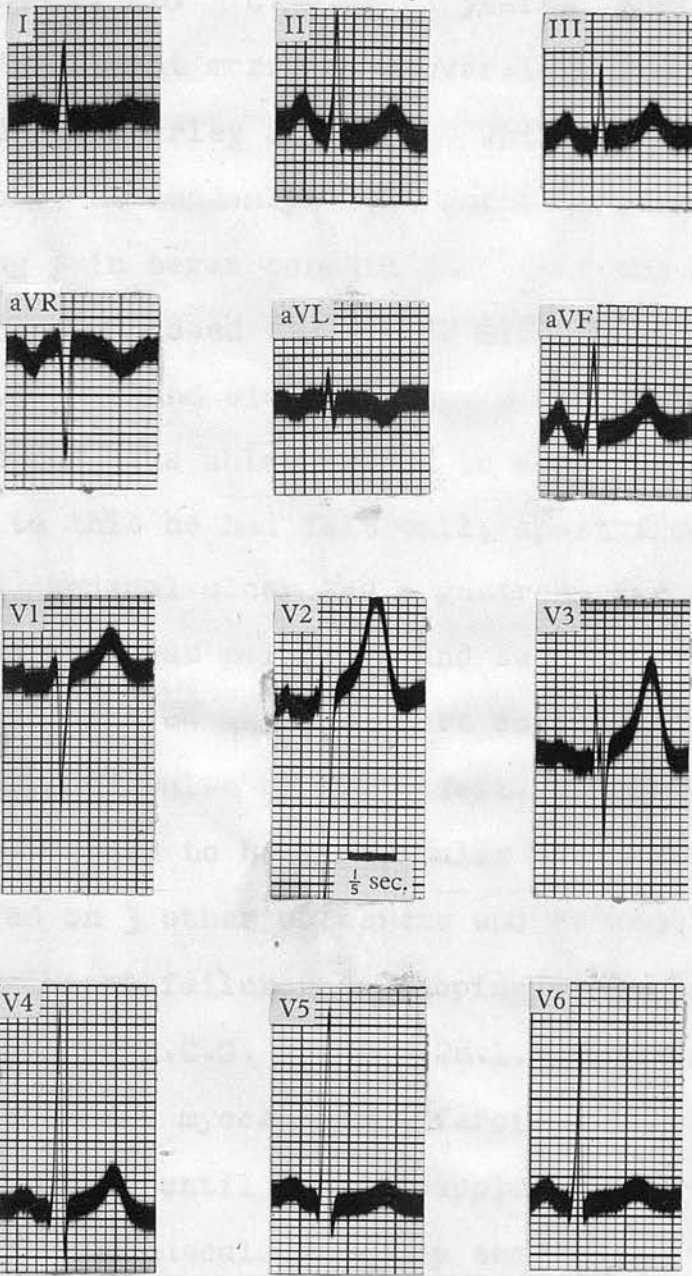


Figure 54. 23.9.48. (Case 5) :

The record is no longer diagnostic of anterior infarction but leads I and aVL are abnormal and suggestive of old infarction.

Case Number 6. C. H. 61 years. Admitted on 18.1.47. That morning he overslept and had then rushed to Waverley Station. While standing on a platform, he suddenly broke out in a cold sweat. A gnawing pain began beneath the lower end of his sternum and passed through to his back. He felt faint, dizzy and sick, and was a little short of breath, but was able to walk to a first aid post. Prior to this he had felt well, apart from trouble with a duodenal ulcer and a gastro-enterostomy. On admission he was pale cold and sweating. The blood pressure was $\frac{104}{64}$ and the heart sounds were faint. No cardiac impulse could be felt. On the 5th day he was noticed to have auricular fibrillation. This recurred on 3 other occasions and he went into congestive heart failure, developing ankle and sacral oedema. An E.C.G. done on 28.1.47 showed evidence of an anterior myocardial infarct. Digitalis was given but not until it was supplemented by neptal 2 c.c. intra-muscularly every second day, did the oedema clear. After the second day of digitalis therapy the auricular fibrillation ceased. Subsequent E.C.G.s. showed a marked disturbance of auricular activity - periods of auricular arrest and ventricular escape, interrupted by occasional, conducted sinus beats; varying form of the P wave indicating a changing site of stimulus production; spells showing prolongation of the P-R interval. (Figure 55).

After /

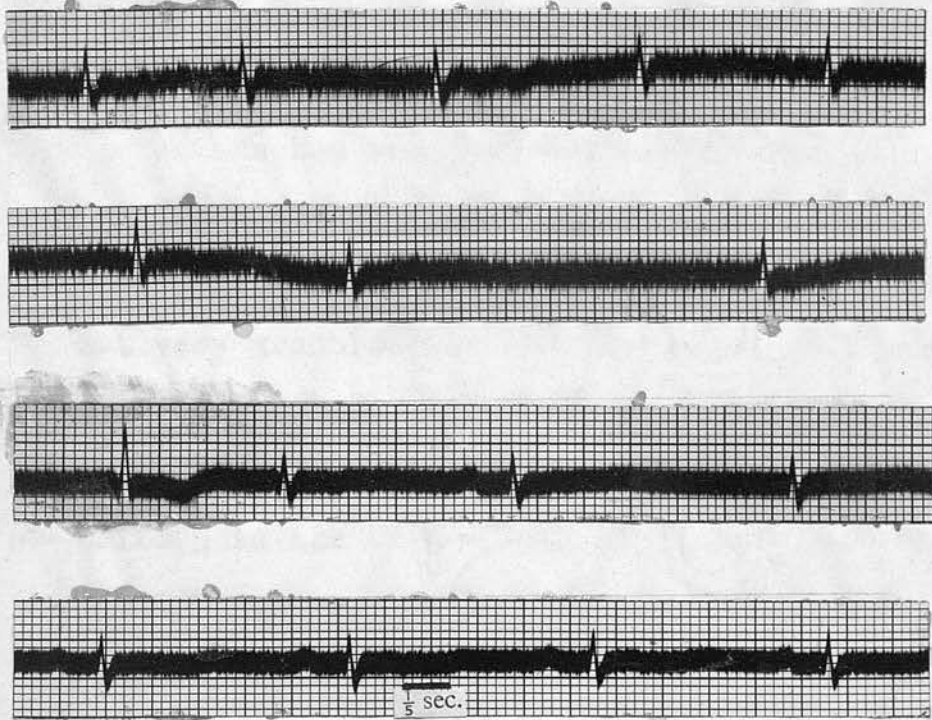


Figure 55. (Case 6): Varying auricular rhythm in the days following myocardial infarction. All records illustrated are of lead II. (A) Auricular fibrillation, (B) no evidence of auricular activity and a slow ventricular rate, (C) one normal conducted beat during a period of apparent auricular standstill. (D) normal sinus rhythm.

After 4 weeks, normal sinus rhythm prevailed. He was discharged home on 22.2.47.

He has remained well apart from occasional trouble with his stomach, and is working as a foreman-chauffeur. He is breathless on exertion but this is not very troublesome, and may partly be due to anaemia. His E.C.G. done on 16.9.48 was within normal limits.

In his youth this man represented Great Britain in the Olympic Games, taking part in the cycling events.

Case Number 7: S.R. 63 years. For 2-3 months he had been short of breath on exertion and for 1 month had experienced effort pain. While reporting as an outpatient on 5.12.45, he suddenly collapsed, becoming ashen-grey in colour, cold, clammy, and practically unconscious. No pulse could be felt and the heart sounds could only just be heard. He was admitted, kept as warm as possible and given coramine 1 c.c. 2 hourly. The blood pressure was recorded as $\frac{62}{50}$. An E.C.G. taken that day showed a recent posterior infarct with defective A.V. conduction, and sinus bradycardia.

He rallied amazingly however and with relief of the shock, remained seriously ill but not in immediate danger of death. The blood pressure varied around $\frac{92}{72}$, and did not rise above 100 mm. Hg. for 2 weeks. The pulse rate varied between 80-90/min., except /

except on 8.12.45 when E.C.G examination showed complete heart block with a ventricular rate of 50/min. Probably this arrhythmia did not last for more than one day.

His first setback was a urinary infection which did not respond to 0.5 gm.Q.I.D. of sulphanilamide, given for 11 days, or later to 0.5 Gm sulphadiazine Q.I.D. for 15 days, but which cleared quickly on penicillin 25,000 units 3 hourly for 9 days. While the infection was persisting he went into congestive heart failure, for which he was given first digoxin 0.25 mgm t.i.d. and later digitalis $1\frac{1}{2}$ gr t.i.d.. While receiving digitalis he developed a phlebothrombosis in the right calf. Only when mercurial diuretics were given in addition to the digitalis from the 7th week onwards was a diuresis produced and the oedema relieved. When he was discharged 13 weeks after the infarct, it was arranged that he carry on with digitalis and that injections of mersalyl be given twice weekly.

In July '46 - 7 months after his infarct - he felt sufficiently well to begin work as a watchman of coal waggons. It was light work but his hours were long - 2 p.m. to 11 p.m., 5 days a week. He was short of breath on exertion, but this did not induce pain in the chest until early in 1949. When seen in September '48, he had not taken any digitalis for a long time, and had only been having 1 injection of mersalyl every second week. His heart was enlarged - the /

- the apex being in the 6th left interspace, just outside the mid-clavicular line. He had become hypertensive - the blood pressure being $\frac{180}{120}$. X-Ray examination showed some left ventricular enlargement, and the aortic arch was on the right side. E.C.G. examination still indicated posterior myocardial infarction.

Case Number 8: Mrs H.M. 65 years. While walking upstairs on 5.11.47, she suddenly became acutely short of breath, and had to stop and rest. It was so troublesome, and she felt so weak, that she had to go to bed. She was unable to lie flat and had to be propped well up. Each night thereafter she woke up short of breath and had to sit upright to get relief. For about 6 months previously, she had been short of breath on exertion and had had a troublesome cough. When admitted on 26.11.47, she was in mild congestive heart failure. E.C.G. examination suggested anterior myocardial infarction. Death occurred suddenly 5 days later. At autopsy a very extensive myocardial infarct was found, extending from the apex on to both anterior and posterior walls for a distance of about 8 cms. and also into the inter-ventricular septum. The coronary arteries were markedly atheromatous, but no thrombus was found.

Case Number 9: Mrs M.G. 61 years. She was well until 1 month prior to her admission on 9.12.48.

During that month she had 3 attacks of myocardial infarction, being admitted after the third. Although confined to bed from the onset she had experienced repeated short attacks of pain in the chest which were relieved by nitroglycerine.

On admission she was in considerable distress, being sick frequently. Chest pain was still severe. Her skin was grey, cold, and clammy, and she was very thirsty. The pulse was rapid irregular and of poor volume - 100/min., many beats being dropped at the wrist. The blood pressure was $\frac{112}{80}$. The heart sounds were faint and of poor quality. E.C.G. examination showed an extensive anterior infarct, partial heart block with Wenchebach periods, and right bundle branch block. (Figure 31). Anti-coagulant therapy was begun. The shock persisted in severe degree and on 10.12.48 she was dying solely from peripheral circulatory failure. The skin was cold and clammy. No pulse could be felt at the wrist and the blood pressure was $\frac{90}{70}$. Treatment to counteract the shock was instituted. She was kept as warm as possible, given oxygen, and one pint of plasma was given over 16 hours and followed by 11 oz. of 6% glucose over 12 hours. There followed a marked improvement in her general condition. On 11.12.48, the pulse became of quite good volume, and the blood pressure rose to about $\frac{118}{80}$.

E.C.G. /

E.C.G. examination showed auricular fibrillation with a high ventricular rate (Figure 31). There was no evidence of heart failure. This developed one day later however and she died early on 13.12.48.

Autopsy examination revealed a recent myocardial infarct in the upper part of the inter-ventricular septum, with a very thin covering layer of mural thrombus. The remainder of the septum and the greater part of the anterior and lateral wall of the left ventricle, was also infarcted, the lesion being at least 2 weeks old. The coronary arteries were atheromatous and the left main artery was blocked just distal to its origin.

Case Number 10: J.S. 61 years. For 1 year he had felt easily tired and had experienced pain across the chest and down both arms on exertion. This was relieved by resting for 5 minutes. One month prior to admission the chest pain became severe and was very easily induced. It did not pass off so quickly as usual when he rested. Since that change he felt more tired and also became short of breath while in bed. In the evenings his ankles were swollen. Although feeling far from well, he carried on with his work as branch manager of a Co-operative store. On 26.2.49 while in bed - about 10.30 p.m. - he felt severe pain across the chest and down both arms. He became short of breath and began sweating. The pain and /

and breathlessness persisted until the 28th. when he got up and went to see the doctor. He felt very weak and tired.

When admitted on 2.3.49 he looked exhausted. His skin was grey and cold and he was sweating profusely. His lips were cyanosed. The pulse was rapid and of poor volume - 118/min., and the blood pressure was $\frac{110}{90}$. No heart sounds could be detected. The neck veins were distended, the liver was distended to 2 fingers beneath the costal margin and there was oedema of both ankles. In the left lung there were many fine crepitations but the right lung was dry. In spite of being propped well up and given oxygen his respirations remained persistently rapid - 38/min. but were not periodic. E.C.G. examination showed rare type bundle branch block and also evidence of anterior infarction in the chest leads.

(Figure 29). He died 24 hours after admission, the blood pressure having fallen to $\frac{74}{64}$.

Autopsy examination showed a large myocardial infarct involving mainly the septum but extending on to the anterior wall of the left ventricle, and partly on to the posterior wall. (Figure 30).

Case Number 11 : E.O. 65 years. Admitted on 9.5.48, having sustained a myocardial infarct during the preceding night. He was pale and cold and was sweating /

sweating slightly. His lips were cyanosed. The cardiac impulse could just be felt, the apex being in the fifth left interspace just outside the mid-clavicular line. The heart sounds were very faint and pericardial friction was audible over and to the left of the sternum. The pulse was regular 80/min., but was poor in volume. The radial artery was thickened. The blood pressure was $\frac{140}{90}$.

Praecordial pain persisted during 9.5.48, and morphine $\frac{1}{4}$ gr. s.c.i. was given at 11.30 a.m., 5.30 p.m., and 11 p.m.. Anti-coagulant therapy was begun, forthwith. An E.C.G. taken on 11.5.48 showed an anterior infarct with Wilson type right bundle branch block. Cough was very troublesome - he had been a miner all his life - and he had difficulty in bringing up the thick muco-purulent sputum. On examination of the chest there were numerous coarse crepitations in all areas but mainly at the lung bases. Penicillin 200,000 units b.i.d. was begun on 12.5.48. His general condition deteriorated and on 13.5.48, the neck veins were distended, the liver was palpable, and there was sacral oedema. The blood pressure was falling daily, being $\frac{90}{64}$ on 15.5.48. The cough was more troublesome. On 18.5.48 he complained of sudden sensations of faintness and on auscultation of the heart a variety of arrhythmias was detected over the space of about 5 minutes. An E.C.G. was obtained and the arrhythmias are illustrated, leads /

leads I II and III (Figure 32A) show complete A/V. dissociation with ventricular extra-systoles. From lead I the auricular rate is 65/min. and the basic ventricular rate 44/min. (Figure 32B) was taken immediately after the preceding record. It shows auricular paroxysmal tachycardia in lead I and in the first two complexes of lead II. Thereafter there is ventricular standstill for 3 seconds while the auricles continue beating at 83/min.. After this Adam-Stokes attack, 1 : 1 A/V conduction occurs with a P-R interval of 0.20 second. This normal rhythm is at a rate of 83/min.. The next record (Figure 32C) shows alternating complete heart block and 1 : 1 A/V conduction. Chest leads V2 and V4 show a deep Q, tall R wave, and marked ST elevation with a Pardee type of T wave, indicating anterior infarction. Throughout all the records there is right bundle branch block of Wilson type.

The arrhythmias persisted and in the early hours of 19.5.48 he died. Autopsy was refused.

On 22.4.49 . . . complained . . .

Case Number 12 : Mrs G.P. 53 years. For one year she had experienced pain in the left arm and chest on exertion. At 9 p.m. on 14.4.49, she suddenly felt severe jabbing pain in both elbows, particularly the left. It rapidly spread up both arms and across the chest, and also down both arms to the fingertips. It was very severe and she had a slight gripping feeling /

feeling in her chest. She was not short of breath, did not sweat and did not feel sick. When admitted on 15.4.49 she was not shocked, but was slightly cyanosed. Her pulse was rapid, 124/min., regular in time and in force, and of quite good volume. The radial artery was thickened and slightly tortuous. The blood pressure was $\frac{196}{132}$. The apex beat was in the 5th left interspace just outside the mid-clavicular line, and the heart sounds were tic-tac in character. There was no evidence of heart failure. An E.C.G showed extensive myocardial damage involving both the front and back of the heart. (Figure 27).

Anti-coagulant therapy was begun on 15.8.49. Pericardial friction developed on 16.8.49 and persisted for 3 days. It was associated with pain at the left shoulder. During the succeeding days her general condition remained fairly satisfactory, her pulse rate slowly fell, and the blood pressure fell slightly - 104/min. and $\frac{148}{110}$ respectively on 20.4.49. During the nights of 19.4.49 and 22.4.49 she got out of bed. On 22.4.49 she complained of slight discomfort on palpation in the right hypochondrium, and within 24 hours the neck veins were distended and the liver had enlarged to 1 finger's breadth beneath the costal margin. Her heart rate had increased slightly - 120/min. but the blood pressure was well maintained - $\frac{150}{110}$. On 25.4.49 she was in gross congestive heart failure. The liver edge was 4 fingers /

fingers beneath the costal margin, there was a trace of ankle oedema, the pulse was almost impalpable, and the blood pressure could just be recorded - $\frac{86}{70}$. The heart sounds were faint and tic-tac in character. The lung fields were clear. During the morning she died.

At autopsy there was a very extensive myocardial infarct involving the anterior wall of the left ventricle, the apex, part of the posterior wall of the left ventricle and also the inter-ventricular septum. There was also an old posterior infarct about the size of a florin.

There was a diffuse haemorrhagic pericarditis, but no mural thrombus in the left ventricle. No infarcts in the lungs or in the systemic circulation were found.

The coronary arteries were very arteriosclerotic, and the first $1\frac{1}{2}$ inches of the anterior descending branch of the left coronary artery was blocked by a thrombus.

Case Number 13 : Mrs M.W. 54 years. She was admitted on 10.7.47 having had a myocardial infarct that morning. She was severely shocked and was in considerable pain. The pulse was regular, 96/min., except for occasional extra-systoles, and was of poor volume. The blood pressure was $\frac{130}{108}$. No cardiac impulse could be felt and heart sounds could just be heard. /

heard. They were tic-tac in character. During 11.7.47 chest pain persisted, being only slightly relieved by morphine. Shock was still severe, the blood pressure being $\frac{126}{100}$. Anti-coagulants were begun. Pain and shock were still present on 12.7.47. Extra-systoles were frequent, and the blood pressure had fallen to $\frac{62}{50}$. The tic-tac rhythm had given place to a gallop rhythm. Two "fits" each lasting a few minutes occurred. In these she suddenly lost consciousness, and became rigid but did not twitch. It was thought clinically that they were due to ventricular paroxysmal tachycardia, but no E.C.G. record of a paroxysm was obtained. There were frequent ventricular extra-systoles, sometimes in pairs. Quinidine 0.2 Gm. t.i.d. was begun but she died shortly after the first dose.

At autopsy the infarct was found to involve the apex and the inter-ventricular septum. There was no mural thrombus. The anterior descending branch of the left coronary artery was blocked.

Case Number 14: Mrs H.L. 62 years. On 4.12.47 she developed a myocardial infarct and five days later had a recurrence, which was symptomatically more severe. She was admitted on 11.12.47. She was restless and cold, but her general condition was quite good. The pulse was rapid and regular 104/min. and the vessel wall was palpable. The blood /

blood pressure was $\frac{118}{82}$. No cardiac impulse could be felt and the heart sounds were faint. There was no evidence of heart failure. E.C.G. examination showed an anterior myocardial infarct. Anti-coagulants were begun, but during the evening of 12.12.47 she died suddenly.

At autopsy there were about 100 c.c. of clotted blood in the pericardial sac, which had escaped from 2 sites of myocardial rupture on the anterior wall of the left ventricle. The infarct involved the apex, interventricular septum and the anterior wall of the left ventricle.

Case Number 15 : Miss J.L. 67 years. She was admitted on 3.12.47 having had a myocardial infarct 5 days previously. During the night she had risen to go to the bathroom and on the way there she suddenly felt as if she were going to be sick. She felt very weak and went straight back to bed where she was violently sick. There was a slight feeling of tightness in her chest, at times she felt as if she was about to choke. She thought she was going to die. Two days previously she had experienced severe tightness across the chest while walking, and had had to stop several times. After a long rest in a chair, the tightness had not recurred.

On admission she was in no distress. The pulse was slightly irregular due to frequent extrasystoles - rate 62/min. The blood pressure was

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76. The peripheral arteries were not thickened. No cardiac impulse could be felt, and the heart sounds were faint. There was no evidence of heart failure. E.C.G. examination showed a recent posterior infarct.

Anti-coagulant therapy was begun, but in spite of this she had an embolus in her left leg on 5.12.47 and a cerebral embolus on 7.12.47. This caused an extensive lesion - a complete left-sided hemiplegia, hemianaesthesia, and hemianopia. Her general condition deteriorated. She developed a hypostatic pneumonia and died on 21.12.47. Autopsy was not carried out. Throughout her stay in hospital the B.S.R. was high, being 105 mm./hr. on admission, and there was a leucocytosis, - 15,000/cm. on admission.

Case Number 16 : W.S. 61 years. For 7 years he had experienced pain across the front of the chest on exertion, and with it a feeling of tightness in the chest and mild breathlessness. In the past few months the pain had spread to the left arm. On 8.11.48 while going down the steps into the Brasserie in Piccadilly, London, he suddenly felt nauseated, broke out in a sweat and staggered against the wall. He collapsed on the floor and was unconscious for a few minutes. After resting for half an hour he went to the Saville theatre, and after the performance took /

took a taxi to his hotel. He went to bed, and slept only to awaken 1 hour later - about 11 p.m. with severe substernal pain. He felt short of breath and a little sick, but did not sweat. The pain eased a little but he did not sleep again. Next day 9.11.48 he caught the 10 a.m. train back to Edinburgh. The pain was still present and he felt exhausted. Twice he tried to be sick. At Edinburgh he was met and taken home by taxi, and was put straight to bed. On 10.11.49 he was admitted to the ward. His skin was greyish cold and clammy and his lips were cyanosed. He was not in pain but was very restless. The pulse was rapid - 96/min. and of poor volume, with frequent extra-systoles. The radial arteries were thickened and tortuous and the blood pressure was $\frac{96}{64}$. No apex beat could be felt. The heart sounds were faint. In the right axilla there were a few fine crepitations. The E.C.G. showed depression of the ST segment with diphasic T waves in leads I and II and in V5 and V6, Anti-coagulant therapy was begun. His general condition deteriorated, congestive heart failure developing. On 12.11.48 he was exhausted restless and very ill. Digoxin was given intravenously - 1 mgm. at mid-day and 0.5 mgm. at 8 p.m. and continued by mouth on the following day (13th) - 0.25 mgm. t.i.d.. After slight temporary improvement the congestive heart failure increased. Neptal 2 c.c. i.m.i. was begun on 16.11.48 and given every second day. There was little response and he died on 20.11.48.

At autopsy both right and left coronary arteries were very arteriosclerotic, but no thrombosed segment was found. There was diffuse infarction of the whole of the left ventricle, mainly subendocardial in position and not involving the full thickness of the muscle. In one small pulmonary artery thrombosis had taken place.

Case Number 17: D.B. 48 years. He was admitted on 8.6.49, having collapsed about $\frac{3}{4}$ hour previously. He had been out delivering coal and was found lying unconscious beside his lorry. On admission he was semi-conscious, groaning, and resentful of interference. No evidence of an intra-cranial lesion could be detected. The only positive finding was that of tenderness in the epigastrium and as he gave a history of vague dyspepsia for 1 month - when he recovered consciousness - he was observed as a possible case of perforation of a peptic ulcer. He was hypertensive - $\frac{176}{104}$, but his heart was not enlarged, and his heart sounds were of a quite good quality. A routine E.C.G. done 4 days after admission revealed definite evidence of myocardial damage, in lead aVL in particular, but with corroborative changes in leads II & III and V4 and V5. (Figure 28 A & B). Anti-coagulant therapy was begun and he was kept at rest in bed. E.C.Gs. taken from interspaces above the normal chest leads failed to show evidence of a high /

high lateral infarct - as suggested by lead aVL. However the blood pressure fell progressively, reaching $\frac{104}{74}$ on the 12th day and the B.S.R. rose to 90 mm./hr. on the 8th day. No leucocytosis was detected. Convalescence was uneventful. Serial E.C.Gs. showed subsidence of the evidence of myocardial infarction. On 12.7.49 he was discharged to Convalescent House.

On 30.8.49 he reported. Apart from mild dyspeptic symptoms he was feeling well. While stripping to have his chest examined, he suddenly said that he felt queer, collapsed, and died. His wife later reported that 2 weeks previously he had very temporarily lost consciousness while sitting in a barber's chair.

At autopsy there was a large oval healed myocardial infarct, about 5 cms. by 7 cms. in size, at the base of the left ventricle on its posterolateral aspect.

Case Number 18 : Mrs M.P. 56 years. For one year she had been short of breath and had a feeling of tightness in her chest on exertion. She also had occasional attacks of nocturnal dyspnoea, and frequently had epistaxis. At 4 a.m. on 3.4.49 she woke with a tight feeling in her chest. This gradually became worse and pain supervened. She had to gasp for breath. At 5 a.m. she was given morphine $\frac{1}{4}$ gr. /

$\frac{1}{2}$ gr. and this relieved the pain. On admission she was extremely cyanosed. The pulse was rapid, 100/min. but of quite good volume. The blood pressure was $\frac{140}{100}$. No cardiac impulse could be felt; the heart sounds were faint and tic-tac rhythm was present. Many fine crepitations were heard in both lung fields. Oxygen was given and anti-coagulants were started. Within 24 hours she was much improved, and thereafter made an uneventful recovery. E.C.G. examination on 8.4.49 did not reveal evidence of myocardial infarction but a later record on 29.4.49 showed that she had sustained a posterior infarct. On 27.5.49 she was discharged home.

Three weeks later (18.6.49) she was re-admitted with a recurrence of myocardial infarction - an anterior infarct not involving the full thickness of the muscle. She was not acutely ill but the blood pressure fell from $\frac{180}{110}$ recorded by her own doctor to $\frac{124}{86}$ within 48 hours. Pericardial friction developed and persisted for several days. The heart sounds were faint. Her general condition remained good and after $3\frac{1}{2}$ weeks she was discharged to rest at home (12.7.49).

She remained well, but on 14.8.49 she had a second recurrence and died soon after the onset.

Case Number 19 : Mrs A.P. 62 years. At 11 a.m. on 24.4.47 she felt sudden severe pain in the epigastrium. /

epigastrium. It was burning in character and moved up behind the sternum. She went to bed immediately but could not lie still. She was sick twice. She was not short of breath, but had a choking feeling. Two days previously she had experienced a few similar attacks of pain while going about the house. They had passed off in 1-2 minutes.

On admission she was pale. but her lips and nails were cyanosed. She was complaining of severe substernal pain. The pulse was regular, 90/min., and of quite good volume. The blood pressure was $\frac{150}{90}$. The peripheral arteries were thickened and tortuous. No cardiac impulse could be felt, but the heart sounds were of good quality. There was no evidence of heart failure. E.C.G. examination showed a recent anterior myocardial infarct. Anti-coagulant therapy was begun. Convalescence was uneventful apart from the development of haematuria due to the dicoumarol. The blood pressure fell to $\frac{96}{66}$ on the fifth day.

On 13.6.47 she was discharged home. Six months later she reported complaining of buzzing in the right ear and palpitations. She was fit for light housework and was not short of breath unless she hurried. She was hypertensive - $\frac{160}{100}$ and a gallop rhythm was present. The palpitation was due to frequent extra-systoles, for which quinidine was prescribed.

On 11.1.48 however she had a second myocardial infarct and died within an hour of the onset.

Case Number 20: R.A. 56 years. For six years he had experienced pain in the left side of the chest on exertion. It passed through to the back and down the left arm to the fingers. During the first 3 years it was not too troublesome and he was able to carry on with his work as a cattleman. Thereafter it became more severe and more easily induced until walking 10 yards would bring it on. Excitement also brought it on, and each time he had to rest for 10-15 minutes before it passed away. In 1946 he began using nitroglycerine and by June '48 was using 120 tablets in a week. During that month he had an attack of pain which lasted 30 minutes and was not relieved by nitroglycerine. During the following nights he tended to waken up short of breath and was therefore kept in bed for 2 weeks. On rising the effort pain was more severe and more easily induced, and he was soon using 240 tablets of nitroglycerine in the week. He was not fit for even the lightest of work. On 19.9.48 he developed a severe pain in the chest about 10 a.m. which was not relieved by nitroglycerine. It persisted until late on the evening of the 20th.. He was a little short of breath, but did not sweat or feel sick.

On 27.9.48 he was admitted. He was of medium height, thick set, and of a florid complexion. The apex beat was in the 5th left interspace outside the mid clavicular line. The heart sounds were of good /

good quality. The peripheral arteries were thick and tortuous and the blood pressure was $\frac{174}{110}$. E.C.G. examination showed a small anterior myocardial infarct, not of recent origin. He was kept at rest in bed, given phenobarbitone 1 gr t.i.d., and was begun on dicoumarol therapy. Any exertion in bed, particularly after eating precipitated chest pain.

In spite of adequate dicoumarol dosage he had a fresh myocardial infarct on 7.10.48, the chest pain beginning at 8 p.m. It was relieved at 11.30 p.m., by an intravenous injection of morphine 1/6th gr., and papaverine 1 gr.. During the pain, a well marked gallop rhythm was present and his blood pressure was raised - $\frac{240}{150}$. E.C.G. examination next day suggested that a posterior infarct had developed. The next 3 weeks were uneventful, but he frequently had coupled rhythm due to regularly recurring ventricular extra-systoles. On 30.10.48 he had a second episode of severe chest pain, associated with the presence of a gallop rhythm and a raised blood pressure $\frac{240}{150}$. Papaverine $1\frac{1}{2}$ gr. intravenously relieved the pain and the blood pressure fell to $\frac{204}{124}$. Prior to the pain he had coupled rhythm, but during the pain, the heart rate was regular at 86/min.; after the pain had been relieved, the extra-systoles returned. After this episode there was a mild leucocytosis - 11,400/c.m. on 31.10.48, but no rise in the B.S.R. or fall in the blood pressure. Pain was easily induced thereafter, and /

and on 12.11.48 he was begun on a compound tablet containing papaverine 2 grs., erythrol tetranitrate $\frac{1}{2}$ gr., phenobarbitone $\frac{1}{2}$ gr., and atropine sulphate $\frac{1}{100}$ gr. four times daily. Nitroglycerine was also given if required, but gradually the frequency of pain was reduced. A gradual increase in his activities was allowed, but on 26th November he woke at midnight with severe chest pain which was not relieved by nitroglycerine. The pain persisted for 4 hours and he became short of breath and sweated profusely. E.C.G. examination showed no change, and over the succeeding days there was no leucocytosis or rise in the B.S.R.. The blood pressure fell very temporarily to $\frac{146}{100}$. Thereafter he felt well and had only one further slight attack of pain in the chest. This was associated with a rise in blood pressure to $\frac{234}{144}$ but no gallop rhythm was detected.

He was allowed up on 11.12.48 and very gradually increased his activities. Before walking he sucked a tablet of nitroglycerine. Soon his confidence increased, and with it his exercise tolerance. Dicoumarol, which had been given from the day of admission, was stopped on 13.12.48 - a total of 11 weeks treatment. He was also put on a 1200 calorie diet to reduce his weight. On 12.1.49 he was discharged home, with instructions to continue the diet and the tablets of papaverine etc., and to use nitroglycerine as required.

Thereafter /

Thereafter he reported once every 3 months.

March '49 - three weeks after his discharge from the ward he developed pain at the left shoulder and down the left arm to the fingers. Movement of the shoulder, particularly abduction increased the pain and the fingers felt stiff. He was doing very little, and was not having too much chest pain. The blood pressure was ²³⁰140. His weight had increased slightly rather than fallen.

June '49 : Cough was his main complaint, particularly on lying down in bed. He had to use 4 pillows at night, otherwise he became short of breath.

While up and about he had his good days when he could walk half a mile on the level without trouble, and his bad days when he could hardly move without the pain coming on. For 2 months his ankles had been swelling slightly in the evenings. The pulse was rapid - 100/min. and the blood pressure was high - ¹⁹⁰136. There were many fine crepitations in both lungs. Digitalis and mersalyl were recommended but only digitalis was given.

August '49 : He was feeling better. At night the cough was much less troublesome and he only needed 1 pillow. His feet still became swollen occasionally. He had stopped the papaverine tablets, and the effort pain was more easily induced. He was using 120 tablets of nitroglycerine per week, twice the number that he used while also taking the papaverine.

November /

November '49 : For one month he had taken no digitalis and was short of breath, requiring 4 pillows in bed once more. His feet were also swollen and his abdomen was tending to swell. He was not taking the papaverine and was still requiring 120 tablets of nitroglycerine per week. His exercise tolerance was very poor. The heart sounds were of quite good quality, and the blood pressure was high - $\frac{196}{134}$.

Shortly after midnight on the night of 12th January 1950, he died at home during an attack of chest pain.

Case Number 21 : P.C. 44 years. He was formerly a miner and had developed pneumoconiosis. For 14 months he had not been fit for work. During these months he had noticed substernal pain coming on with exertion and making him stop. It gradually came on more easily until he could only walk about 10 yards in comfort. At 6 p.m. on 7.6.47 he suddenly felt severe pain beneath the sternum, and passing through to the back. He was restless and broke out in a cold sweat. After 3 hours he was sick.

When admitted early on 11.12.47 he was mildly shocked. The pulse was rapid - 114/min and of poor volume. The blood pressure was $\frac{114}{96}$. No cardiac impulse could be felt but the heart sounds were of good quality. E.C.G. examination showed an anterior myocardial infarct. He was in left ventricular failure /

failure and within 24 hours developed an infarct in the left lung. He was propped up in bed, and treated with sedatives, oxygen and aminophylline. The chest was strapped to relieve the pain. Anti-coagulants were also given. Within 4 days his lungs had cleared and he felt well, as long as he remained propped up. The blood pressure fell progressively reaching $\frac{74}{58}$ on the 8th day. Thereafter it remained consistently low with a small pulse pressure. Progress was satisfactory until 20/6/47 when he began having attacks of cardiac asthma. Digitalis was given, 3 grs. t.i.d. and was taken for 8 days. It produced marked improvement and was therefore continued in courses. On 16.7.47 he was discharged home.

August '47: Feeling better than he has done for years. Cough troublesome in the evenings. Pain in the chest and breathlessness on exertion.

November '47: The slight improvement has been maintained. He can walk uphill to the town without pain, but still requires 3 pillows in bed at night. Taking digitalis - 1 week on and 1 week off. The blood pressure was higher - $\frac{118}{88}$.

May '48: Little change in his general condition, except that his peptic ulcer is now causing trouble. He is using about 8 half tablets of nitroglycerine each day.

June '49: He reported by letter. Again the stomach is causing most trouble.

November /

November '49: On 16.11.49 he was admitted with a pontine haemorrhage and died on the next day.

Autopsy examination showed an old fibrous infarct about 3.5 mm. in thickness. The apex, anterior wall of the left ventricle and the lower half of the inter-ventricular septum were all involved. A recent adherent antemortem thrombus was found over the endocardial surface of the apex, but there was no evidence of fresh infarction,

Case Number 22: Mrs M.H. 60 years. She was well until January '48, when she began to experience substernal pain on exertion. It was associated with breathlessness and both would pass off as soon as she rested. On 5.4.48 the pain came on more severely and was not relieved by resting. It persisted until just after she was admitted to the ward on 7.4.48. During these 2 days she was very troubled with flatulence and bringing up wind relieved the pain slightly. On admission, her pulse was rapid - 136/min., the blood pressure was raised - $\frac{240}{140}$, the heart sounds were very loud and at the apex a pre-systolic gallop could be clearly heard. The apex beat was in the 5th left interspace in the mid-clavicular line. She was not shocked, and there was no evidence of heart failure.

Substernal pain returned while an E.C.G. was being /

being taken on 8.4.48. This record (Figure 58) showed the well marked S T and T wave changes of coronary insufficiency. On the evening of the following day she again had substernal pain, but on this occasion it was more severe than ever before. She became pale, cold, and slightly cyanosed, and broke out in a sweat. The blood pressure fell to $\frac{148}{102}$ and the gallop rhythm was marked. E.C.G. examination on 10.4.48 showed evidence of anterior myocardial infarction. (Figure 59). Treatment with anti-coagulants was begun and continued for 3 weeks. For 7 days she was seriously ill. The blood pressure fell to $\frac{116}{80}$ and the pulse rose to 124/min.. The heart sounds were of poor quality. Frequently tic-tac rhythm or gallop rhythm was detected. Pulmonary congestion developed and on the 7th day pericardial friction was detected. The myocardial infarct was very extensive, involving the greater part of the front of the heart, as shown by leads taken from the 1st, 2nd, 3rd and 4th interspaces above the normal chest leads. (Figure 60). Nevertheless, convalescence thereafter was uneventful. After $5\frac{1}{2}$ weeks she was allowed up and one week later (25.5.48) was discharged home.

Four months later (September '48) she was well, but was not doing much. Her hypertension had returned, the blood pressure being $\frac{204}{120}$. Her weight had increased so she was put on to an obesity diet. By November '48 she was doing all her housework and was /

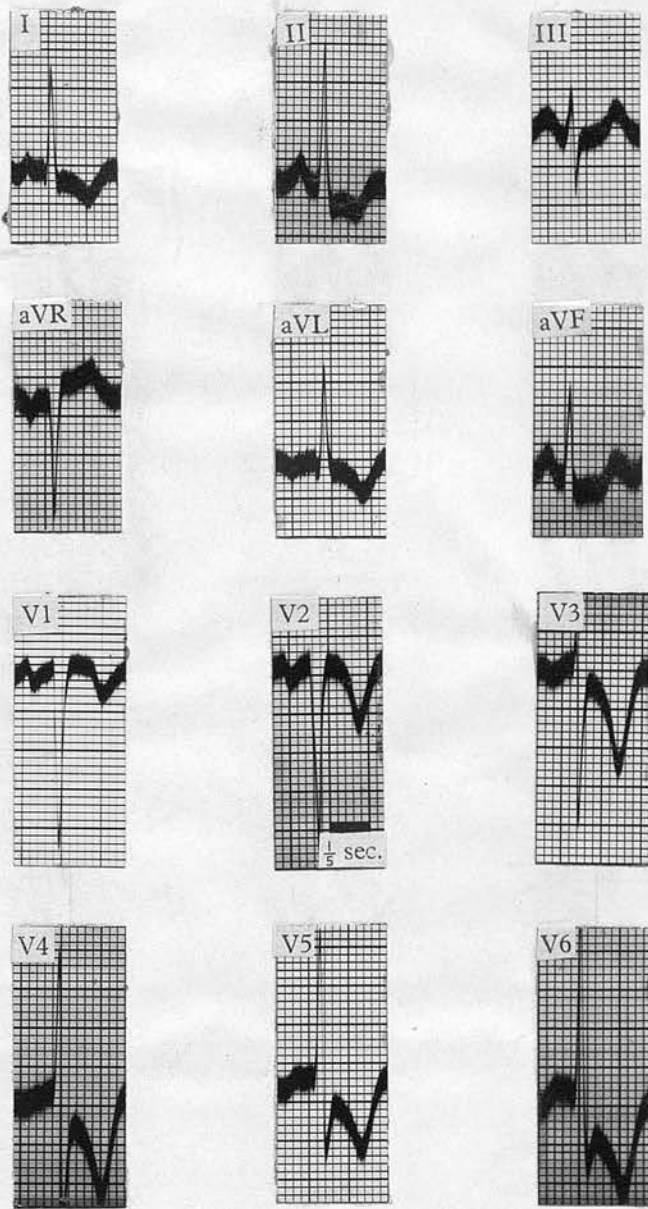


Figure 58. 8.4.48. (Case 22):
 Record taken during an attack of coronary ischaemic
 pain, in a hypertensive person, shows changes
 associated with myocardial insufficiency.

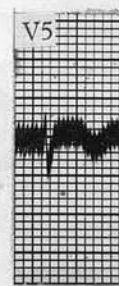
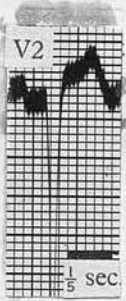
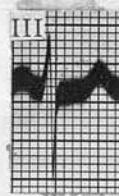
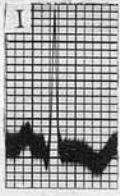


Figure 59.

10.4.48.

(Case 22):

Anterior myocardial infarction.

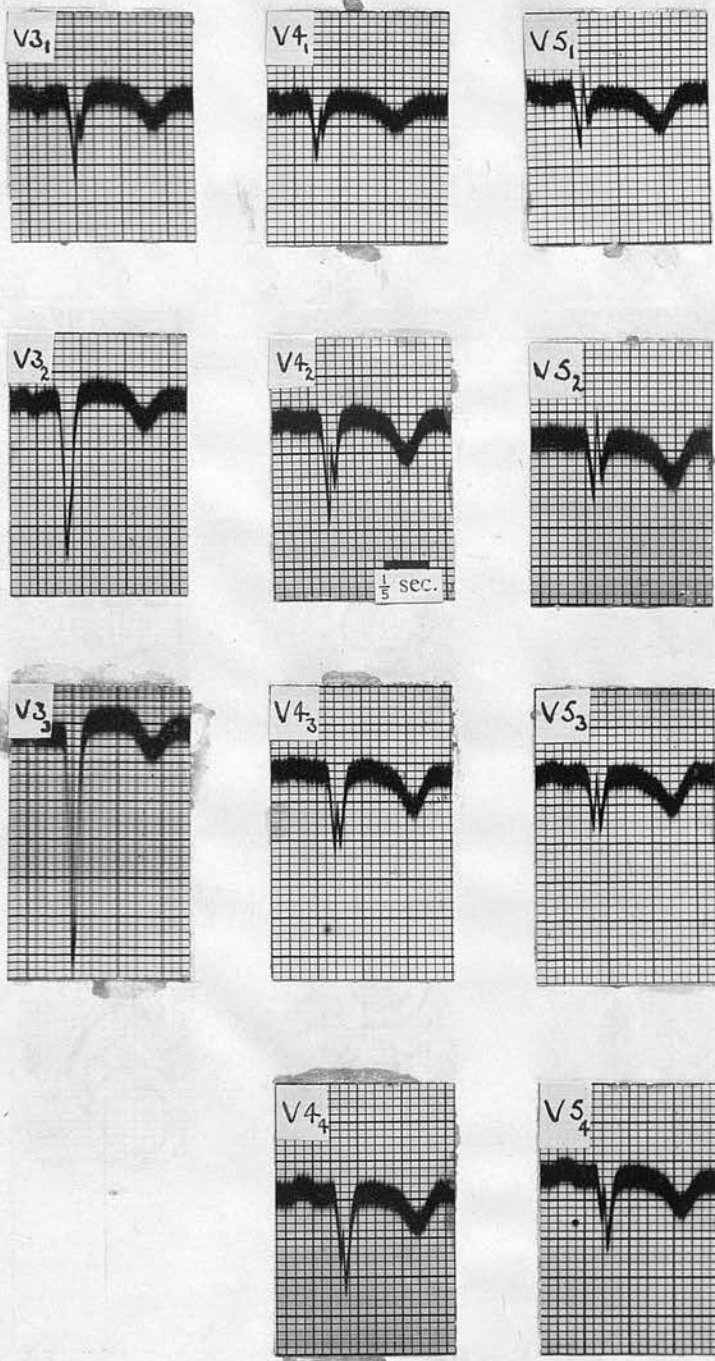


Figure 60B. 30.4.48. (Case 22):
 Leads taken vertically above V₃, V₄ & V₅ reveal
 extensive myocardial damage.

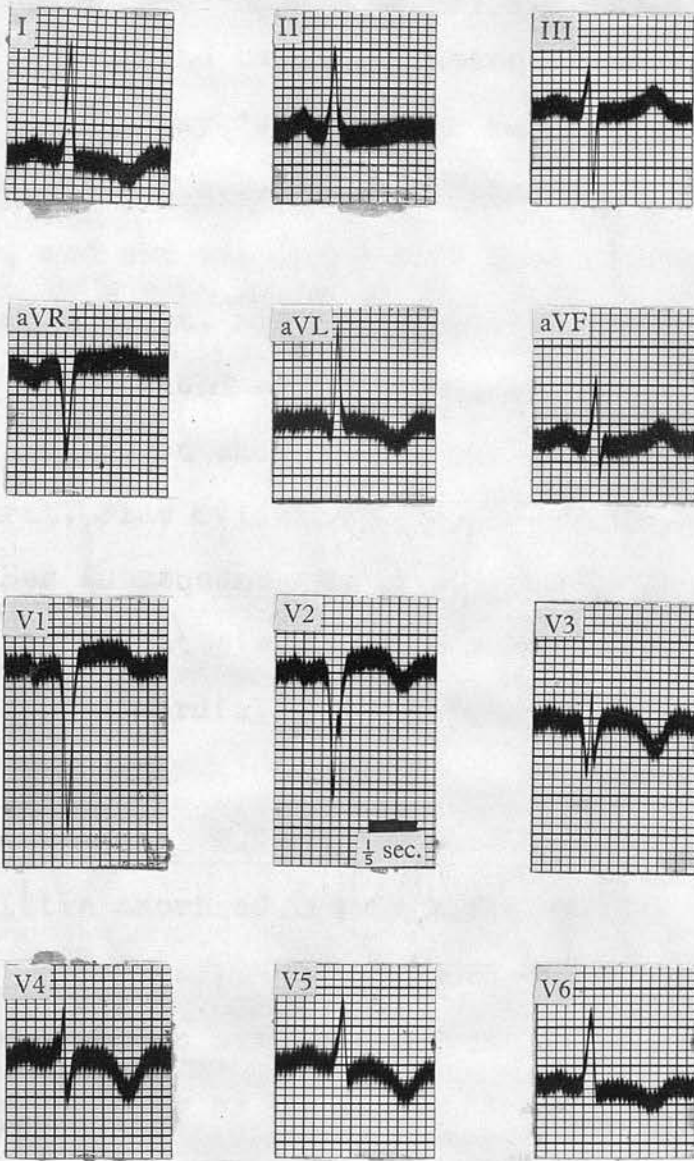


Figure 61. 1.12.49. (Case 22):
 The record is that of an old healed anterior infarct,
 but also suggests left ventricular hypertrophy.

was feeling stronger. On hills, she was a little short of breath and had a sensation of tightness in the chest. In May '49 when she was next seen, even this shortness of breath and tightness in the chest had gone, and she was doing more than before her myocardial infarct, now being quite fit for all her washing. The blood pressure was still high - $\frac{224}{118}$. E.C.G. examination showed evidence of the old myocardial infarct, plus evidence of hypertension.(Figure 61).

Her subsequent course was marred by an attack of infective hepatitis, but she showed no evidence of coronary or myocardial insufficiency.

Case Number 23: T.R. 63 years. On 9.8.48 he felt a little short of breath while walking to work in the morning, and after going about 100 yards he felt a sudden severe pain across the front of his chest. Almost immediately he began sweating profusely. In spite of feeling very weak, he walked another 100 yards before catching a tram into town. There he put an order into a shop and then took another tram up the Bridges to his place of business. After climbing 2 flights of stairs he collapsed into a chair. All this time the pain in the chest was very severe and was also felt in the throat. He was short of breath and his chest felt tight. He was still sweating profusely. After a rest he took a taxi home and went to bed. The pain persisted until the night of the 10th /

10th - about 36 hours in all - but returned prior to his admission on 11.8.48. When first seen he was very shocked. His skin was grey and cold, and he was sweating profusely. His pulse was 64/min., and was irregular both in time and in force. The blood pressure was $\frac{90}{64}$. The apex beat was in the 5th left interspace in the mid-clavicular line. It was forcible, rapid and irregular, the heart rate being about 180/min.. The heart sounds were of quite good quality. The lung fields were quite clear; the respirations were Cheyne-Stokes in character. E.C.G. examination showed auricular fibrillation at about 180/min.. (Figure 42) and the chest leads showed evidence of anterior myocardial infarction.

He was put at rest in bed, given phenobarbitone 1 gr. t.i.d. and was begun on anti-coagulants. On 13.8.48 the neck veins were distended. As the arrhythmia with rapid ventricular rate and marked pulse deficit persisted, it was thought advisable to give digitalis in an attempt to slow the ventricular rate. Digoxin 0.5 mgm. t.i.d. was given on the 12th and thereafter reduced to 0.25 mgm. t.i.d. Oxygen was also begun. The heart rate slowed and the pulse rate rose with some slight improvement in his condition, but on 13.8.48 there were frequent extra-systoles and on 14.8.48 he had runs of paroxysmal ventricular tachycardia (Figure 42). Quinidine 0.2 Gm. five times in the day was begun and given along with the digoxin. /

digoxin. Late on 15.8.48 he reverted to normal rhythm. The digoxin was stopped but the quinidine was continued for 3 days. Thereafter convalescence was uneventful. E.C.Gs. showed splintered P waves (17.8.48 Figure 42) which soon reverted to normal form (24.8.48). Records taken from the interspaces above V2 V3, V4 and V5 showed widespread infarction of the lateral surface of the heart.

After 7 weeks in hospital he was discharged home. Four months later he felt sufficiently fit to return to work and since then has worked 4½ hours each day 5 days a week. He is a watchmaker and has his own business, so that he can regulate his work as desired. Apart from being short of breath on hills and stairs and when walking against a wind he feels well. He is somewhat tired in the evenings, but his feet are never swollen. His blood pressure is maintained at about $\frac{144}{74}$.

Case Number 24: E.W. 63 years. He was admitted on 9.3.49, having had a myocardial infarct 7 days previously. Prior to this he had been fit. He looked exhausted but was not shocked. The pulse was regular and of quite good volume. The blood pressure was $\frac{170}{122}$. The radial artery was slightly thickened and tortuous. A cardiac impulse was felt but the apex beat could not be located. The heart sounds were of good /

good quality. There was no evidence of heart failure. E.C.G. examination showed an antero-septal infarct not involving the full thickness of the muscle wall (Figure 24 A). Anti-coagulant therapy was begun.

Early on 11.3.49 he felt quite severe pain at the lower end of the sternum, and with it tightness in the chest. Nitroglycerine gave very temporary relief and it was not until 10 mgms. of physeptone were given that the pain was eased. The tightness in the chest persisted all day. An E.C.G. showed a remarkable reversion towards normal (Figure 24B) but when this was repeated on 18.3.49 it again showed an antero-septal infarct. The blood pressure fell to $\frac{118}{78}$ on 16.3.49 - 2 weeks after the onset. On 23.3.49 and 27.3.49 he was troubled by short attacks of nocturnal dyspnoea but this did not recur until 15.4.49 when there was also a definite pad of sacral oedema. Aminophylline 0.24 Gm. intravenously relieved the dyspnoea. Digitalis was begun and produced a quick response. He was discharged home to bed on 19.4.49 with instructions to continue the digitalis.

July '49 : Feeling fairly well, but short of breath on the hills. No swelling of the feet. Stopped digitalis 1 month ago. Return of hypertension $\frac{168}{96}$.

October '49 : Back at light work 1 month. Feeling fit, but has difficulty in walking up the hill out of the dockyard where he works. He has to stop three times for 1-1 $\frac{1}{2}$ minutes because of shortness of breath.

Pain /

Pain and stiffening of the right shoulder developed 3 weeks before he reported and he cannot lift his arm properly.

January '50: Has had pain in the chest on walking uphill or against a wind for about 2 months. At the same time he is short of breath. He stopped work in November '49., on account of the pain and has felt better since then. The pain in the right shoulder is still present, and has not been appreciably relieved by heat and massage. The blood pressure is higher ¹⁷⁴100. Weight steady. E.C.G. examination showed regression of the evidence of myocardial infarction.

Case Number 25: J.D. 67 years. He was recommended for admission on account of (1) pain, stiffness, and coldness of the left leg from the knee downwards of 10 days duration, and (2) difficulty in speaking of 2 days duration. Both had been of sudden onset. Fourteen days previously he had suddenly felt pain across his shoulders and in the mid-line posteriorly. It was very severe and within 5 minutes he was sick. The pain persisted for 3 $\frac{1}{2}$ days, but was not so severe as to keep him awake, and apart from it he felt fairly well. It was suspected that he had sustained a myocardial infarct and that the presenting complaints were embolic manifestations. E.C.G. examination showed an extensive anterior infarct. He was admitted on 17.11.48 and anti-coagulant therapy was begun /

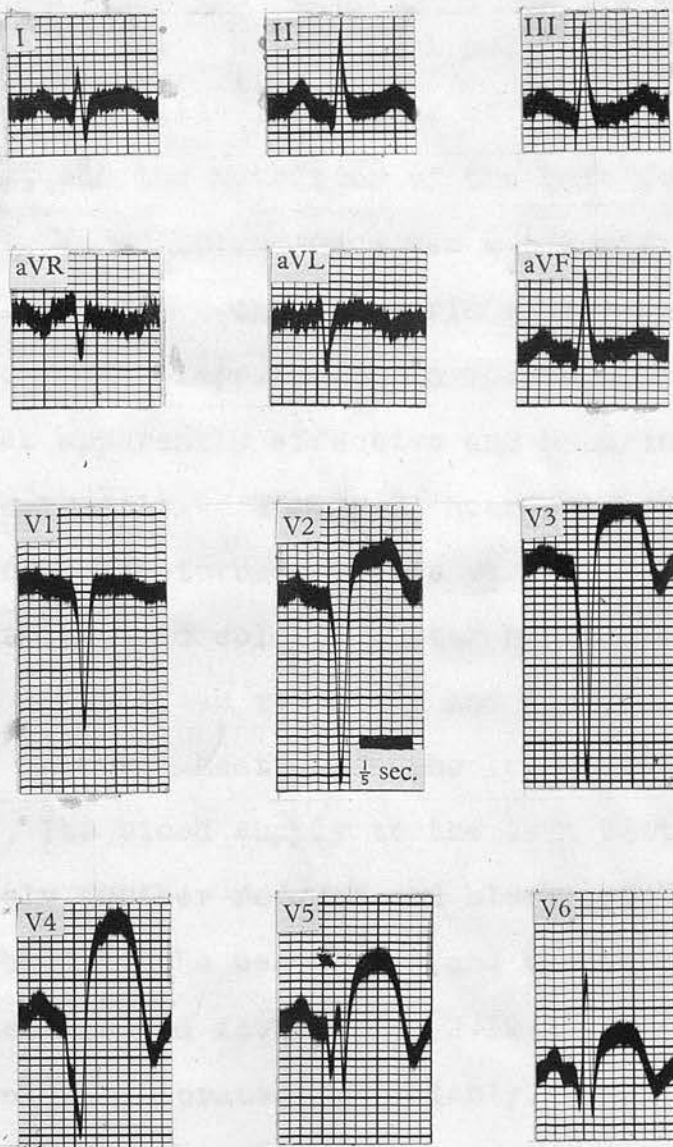


Figure 62. 17.11.48. (Case 25) :
 The record reveals extensive anterior myocardial damage. The marked ST elevation in the praecordial leads would suggest recent infarction, but in fact 14 days had elapsed between the onset of symptoms and his admission to hospital.

begun forthwith. No arterial pulsation could be felt in the popliteal fossa or at the ankle in the left leg, and the nutrition of the left foot was impaired. In addition there was a phlebitis of the left calf veins. While heparin was being given the local condition improved. On the 5th day the dicoumarol was apparently effective and heparin was stopped abruptly. Within 24 hours the pain in the left foot had returned and was very severe. The foot was pale and cold and later became a mottled blue. Heparin was restarted and given for a further 3 days. Reflex heating of the left arm was also begun. The blood supply to the left foot had been definitely further reduced and black patches appeared on the big toe, the second toe, and the heel. He had a persistent mild fever. On 2.12.48, his general condition deteriorated appreciably. He became more febrile and confused, and left ventricular failure developed. Penicillin 100,000 units 4 hourly and digoxin 0.25 mgm. t.i.d. were begun on 3.12.48. He improved slowly. The heart failure cleared, and he became less toxic and confused. Dicoumarol was stopped on 7.12.48 and on 13.12.49 he was transferred to a surgical ward for a mid-thigh amputation on the following day. Recovery was uneventful and on 5.1.49 he was discharged to Convalescent House.

On 31.1.49 he was feeling well and was able to be about with the aid of crutches. An artificial limb was later fitted, but his activities are restricted.

Case Number 26 : Mrs J.S. 68 years. This lady first came under our care in May '48. During the night of 11-12 May, she was twice wakened by severe pain across the front of her chest which passed through to the back, and down the left arm to the fingertips. She was short of breath and felt her chest tight as if she could not expand it. She began sweating and felt sickly. On each occasion the pain lasted about 15 minutes and she was able to sleep thereafter. For 1 month she had experienced similar pain on exertion. It had gradually come on more and more easily until walking across the room would bring it on. Resting for 2-3 minutes always relieved it. During the early hours of 5th May '48 she had had one very short attack of pain while in bed. Seven years previously and 2 years previously she had experienced similar severe attacks of pain while in bed and each time had been kept in bed for some weeks.

On admission, she was very nervous and overwrought. Her blood pressure was $\frac{252}{110}$ with pulsus alternans down to 230 mm. Hg.. The pulse was slow - 68/min. and the radial arteries were thickened and tortuous. The apex beat was in the 5th left interspace within the mid clavicular line and was very forcible. The heart sounds were very loud and clear cut. There were a few fine crepitations in each axilla, but no other evidence of heart failure.

E.C.G. /

E.C.G. examination showed marked T wave changes in leads I and II and in the chest leads. (Figure 63A).

Anti-coagulant therapy was begun and continued for 3 weeks. Convalescence was uneventful. The blood pressure fell to $\frac{148}{70}$ on the 9th day, but before her discharge home on 22.6.48 had risen to $\frac{220}{102}$.

On 3.8.48 she reported. She was doing very little and was feeling easily tired. She was short of breath on exertion but had no pain in her chest or arm. In the evening her feet were a little swollen. Hypertension was marked $\frac{250}{120}$. The E.C.G. showed a marked regression towards normal. (Figure 63B). Two months later she was feeling better. She was resting each afternoon, and in the evening had no ankle swelling.

On 28.11.48 she was re-admitted with her fourth myocardial infarct. She had wakened about 3 p.m. from her sleep after lunch with very severe praecordial pain radiating to the back and down the left arm. As before she was mildly shocked. The pain eased somewhat after half an hour but persisted until relieved by morphine. On this occasion the heart sounds were not of good quality and the mitral 1st sound was split. The pulse was 78/min. and the blood pressure $\frac{180}{110}$. E.C.G. examination again showed striking T wave changes. (Figure 63C).

Anti-coagulant therapy was begun and convalescence was uneventful until severe bleeding occurred from an /

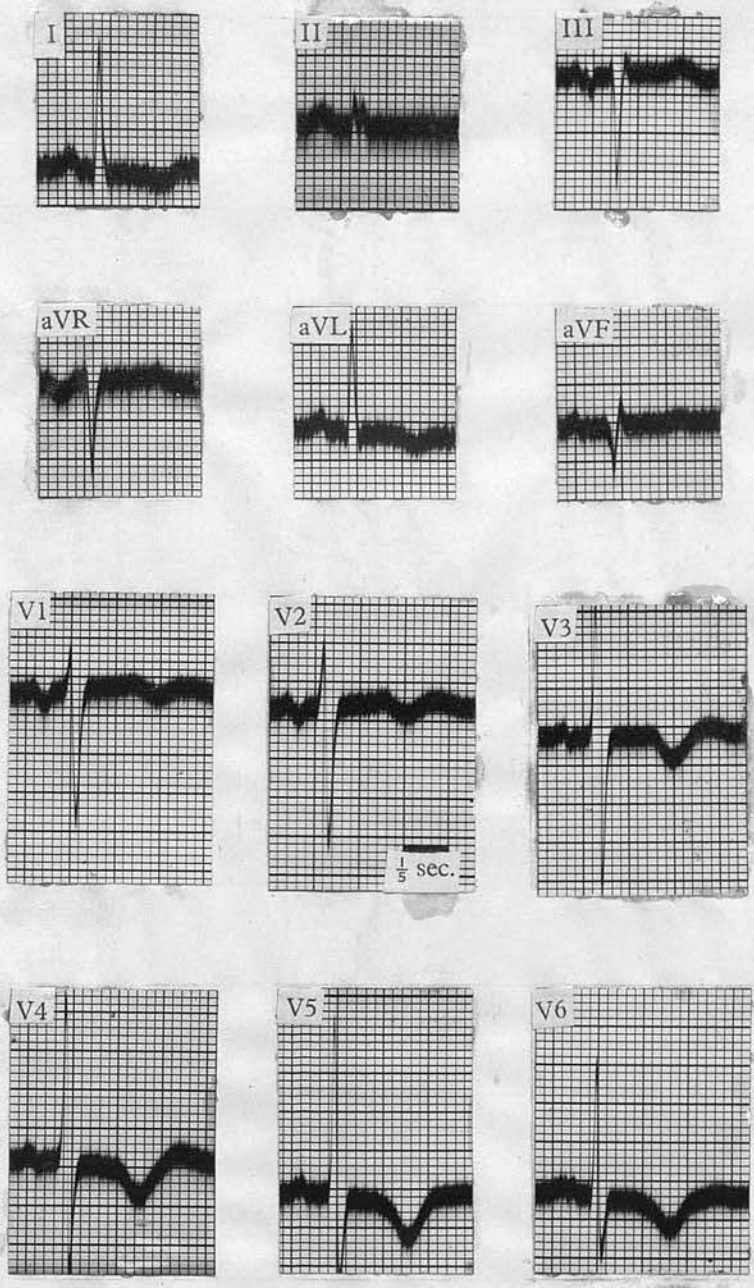


Figure 63 A. 12.5.48. (Case 26):
 The T wave changes in the praecordial leads indicate intra-mural damage over the front of the heart.

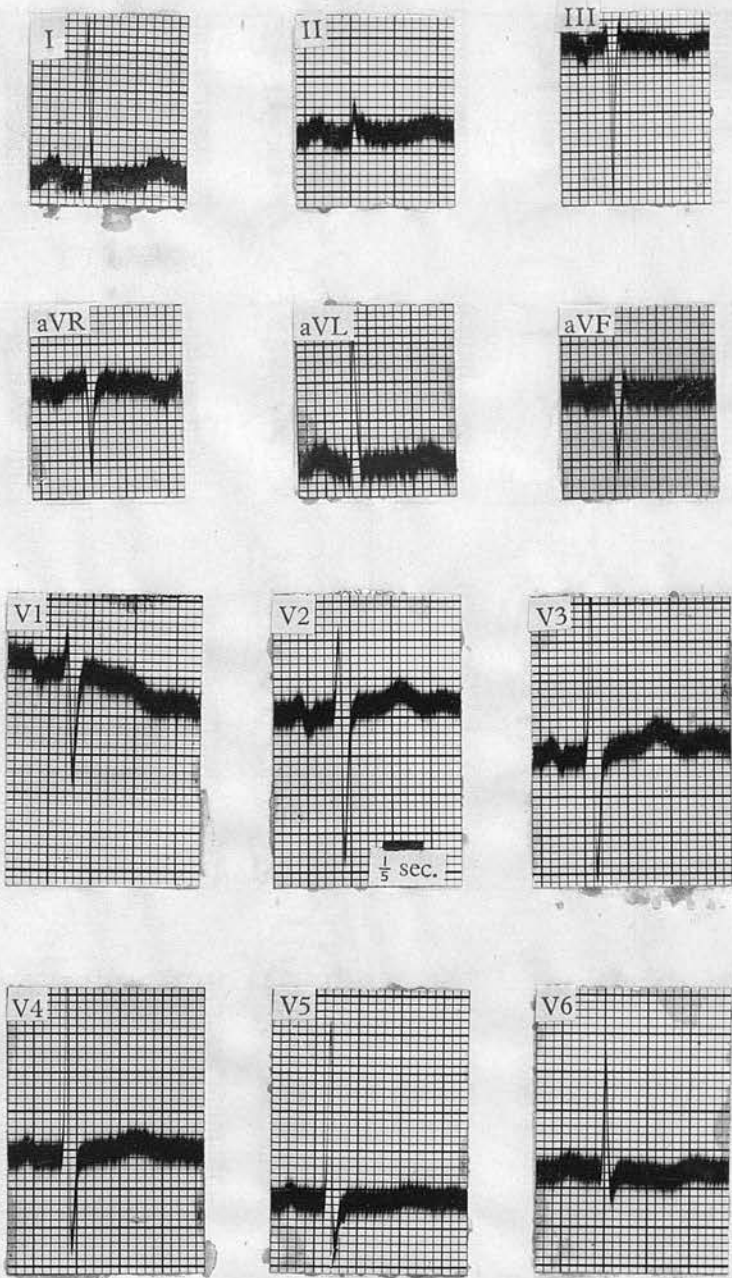


Figure 63 B. 3.8.48. (Case 26):
 All evidence of myocardial infarction has disappeared, the record now suggesting left ventricular hypertrophy.

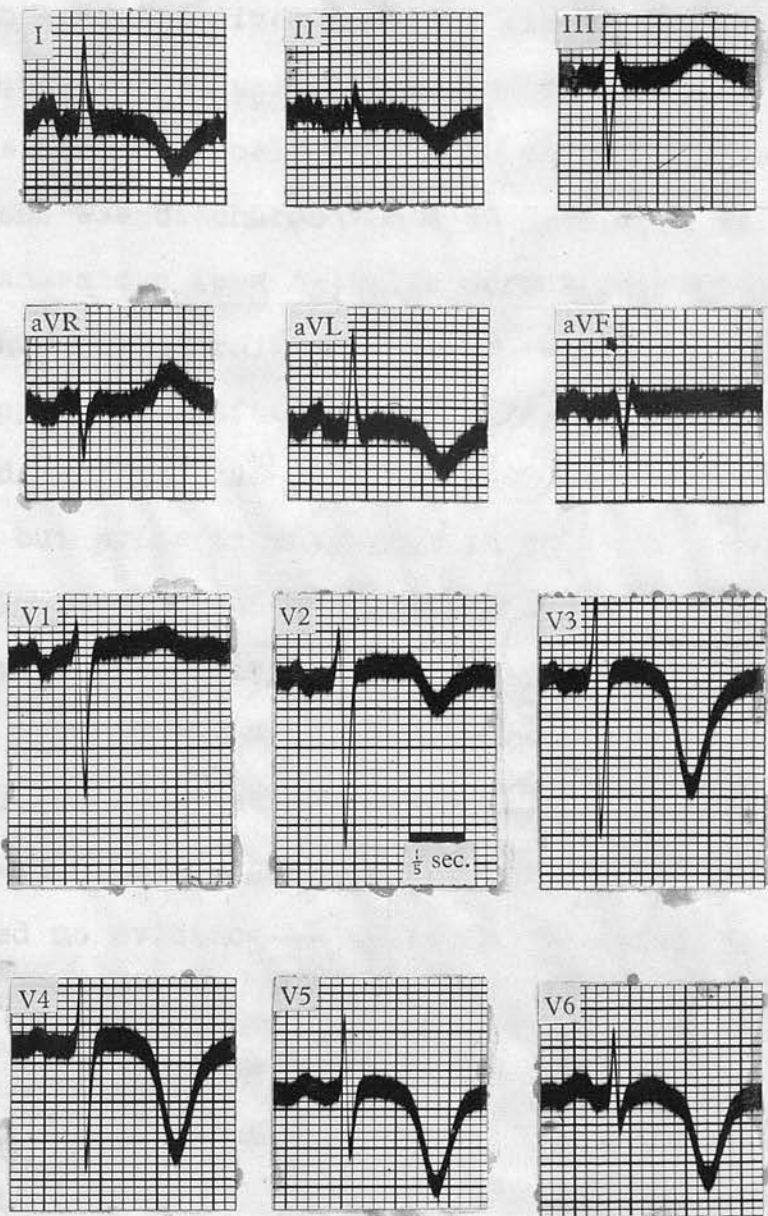


Figure 63 C. 30.11.48. (Case 26):
 The T wave changes in leads I and II, aVL, and
 the praecordial leads, indicate intra-mural damage
 over the front of the heart.

an unsuspected diverticulitis (later demonstrated by barium enema examination). Transfusion with 3 pints of packed cells restored the situation however and she was discharged home on 25.1.49. While she was anaemic a loud systolic murmur developed over the whole praecordium, and after the transfusion it disappeared. After the myocardial infarct the blood pressure had slowly fallen to $\frac{140}{70}$ on the 10th day, but prior to discharge it rose to $\frac{168}{90}$. E.C.G. examination showed some regression of the marked T wave changes.

In March '49 she reported. She was feeling tired, and was not fit for much, but was otherwise well. Her blood pressure was $\frac{260}{120}$, and her E.C.G. showed no evidence of myocardial infarction. (Figure 63D).

On 8th May '49, she had her fifth myocardial infarct, being wakened by pain at 1 a.m.. This persisted in spite of morphine, until shortly after her admission. She was slightly shocked. The heart sounds were of poor quality and the first mitral sound was split. The second pulmonary sound was louder than the second aortic sound. The blood pressure was $\frac{212}{86}$, and the pulse rate 66/min.. E.C.G. examination showed T wave changes but these were less striking than on previous occasions. (Figure 63E). Anti-coagulants were begun and continued for 3 weeks. The blood pressure fell to $\frac{150}{66}$ /

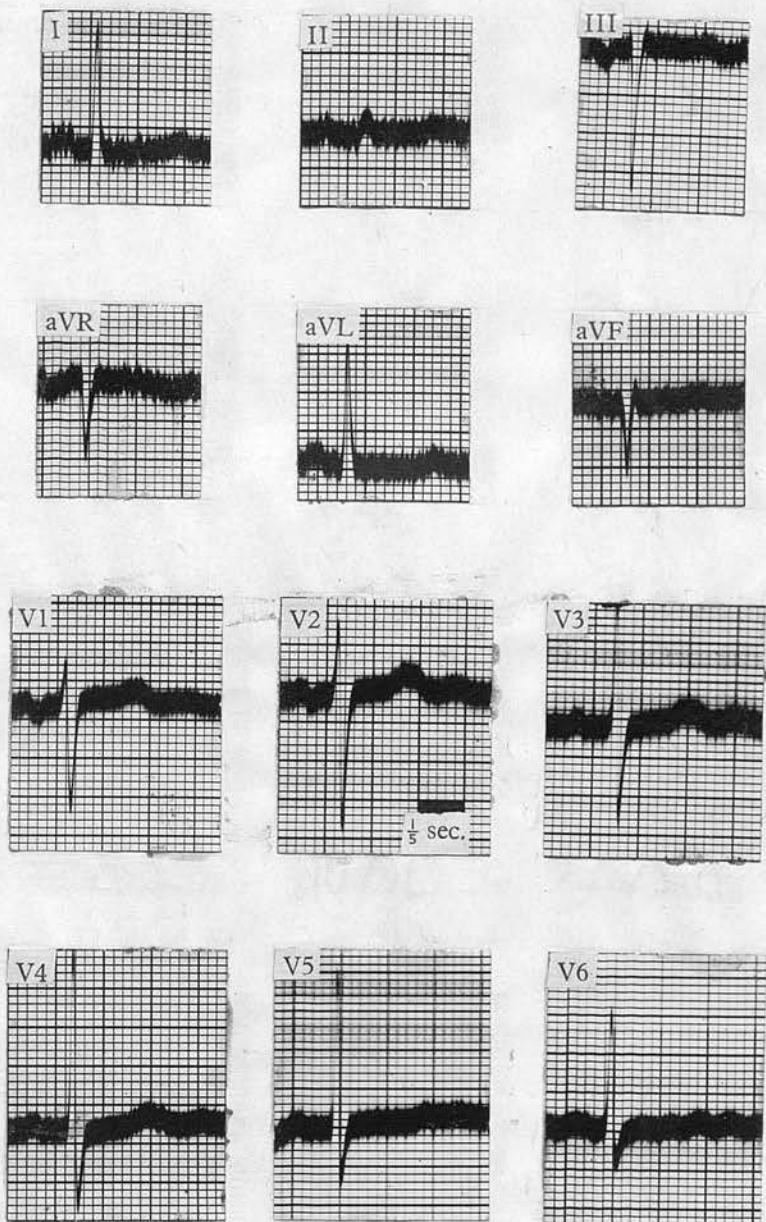


Figure 63 D. 22.3.49. (Case 26):
 Although not within normal limits the record is
 no longer diagnostic of myocardial infarction.

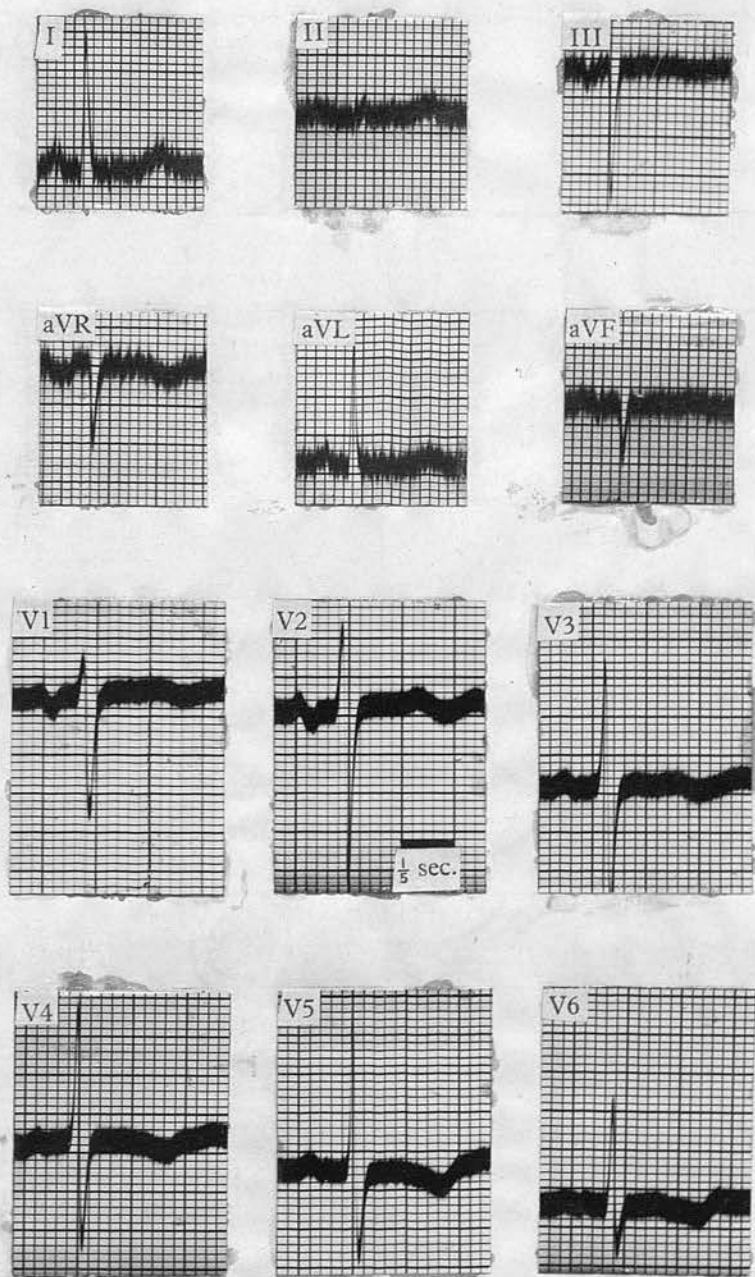


Figure 63 E.

11.5.49.

(Case 26).

The T wave changes in the limb and praecordial leads suggest fresh intra-mural damage over the front of the heart.

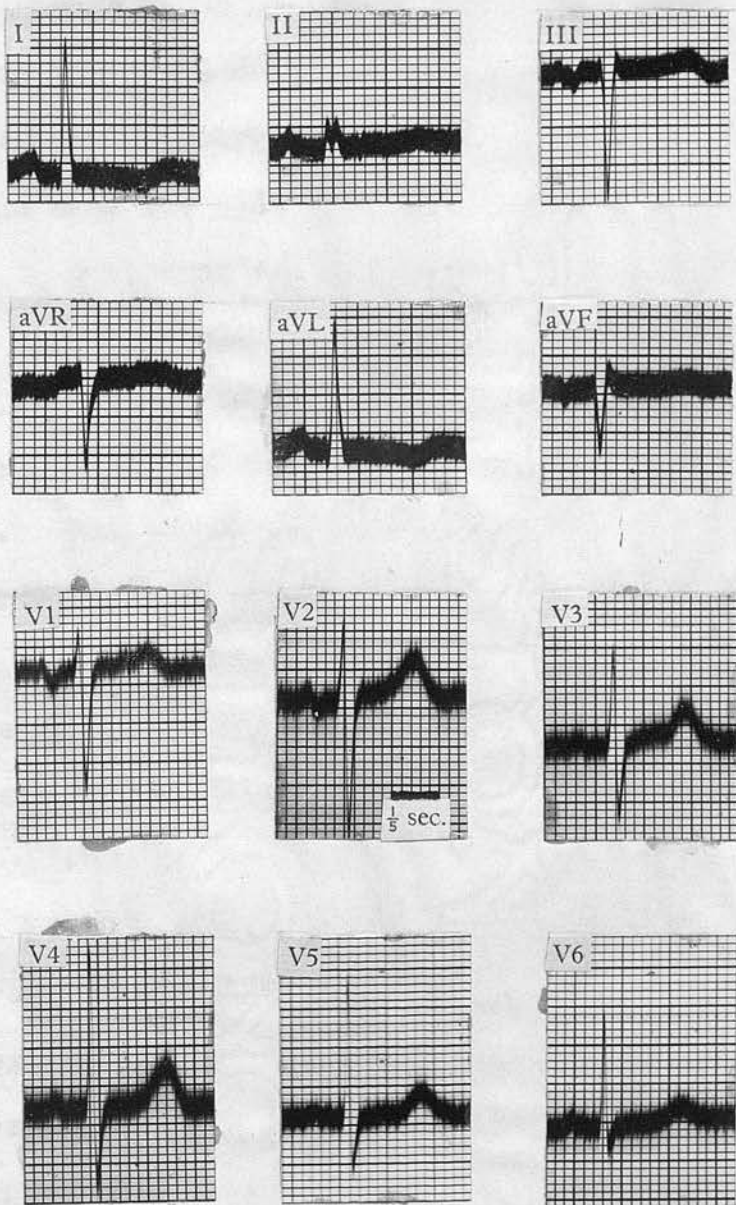


Figure 63 F. 20.12.49. (Case 26):
 Apart from the presence of marked left axis deviation in the standard leads, the record is not abnormal.

150

66 on the third day and rose thereafter, being 210
 100 before her discharge. Convalescence was uneventful and she was allowed home on 21.6.49.

She reported in August '49. She was feeling well. While walking she was a little short of breath, but had no pain in the chest. If she were up for too long, her feet would swell in the evenings. Her blood pressure was 230
 110. Four months later there was little change except that her ankles were no longer swelling and her blood pressure was higher - 280
 134. E.C.G. examination showed no evidence of myocardial infarction. (Figure 63F).

Case Number 27: Miss A.D. 69 years. For 10 years she had experienced crushing praecordial pain on exertion. The pain radiated up the left side of her neck but not to either arm. It was associated with breathlessness. Gradually the pain came on more easily and was more severe, and latterly walking 30 yards would bring it on. She had to stop and in about a minute the pain passed away. Nitroglycerine might prevent the pain coming on.

On 25.5.48, just after rising, she felt very severe praecordial pain. She became cold, broke out in a sweat and felt dizzy. Nitroglycerine had no effect on the pain, which persisted all day and night but eased off somewhat on 26.5.48. She was sick /

sick several times that day. About mid-day on 27.5.48 the pain returned and remained present until after she was admitted on 28.5.48. She looked exhausted. The pulse was slow, 62/min., and of quite good volume. The blood pressure was $\frac{132}{68}$. The radial artery was thickened but not tortuous. The apex was in the 5th left interspace inside the mid-clavicular line. The heart sounds were faint and in the mitral area there was a soft systolic murmur. In each lung field there were many loud fine crepitations. E.C.G. examination showed a posterior infarct, with first degree heart block, the P.R. interval being 0.44 second. Anti-coagulant therapy was begun. Pericardial friction was audible on 30.5.48 and persisted for 48 hours. After 4 days the evidence of left ventricular failure lessened, and thereafter, only a few crepitations were heard in each lung field. Convalescence was uneventful, and she was allowed home on 19.7.49. Her activities were somewhat restricted by troublesome arthritis of both knees. The excessive prolongation of the P.R. interval shown electro-cardiographically did not persist. On 3.6.48 it was 0.24 second, on 12.6.48, 0.22 second, and on 18.6.48 0.20 second.

September '48 : She was not feeling well and was spending most of the day in bed. Her ankles were oedematous, the liver was not enlarged but was tender on palpation, and fine crepitations were to be heard at /

at both lung bases. The blood pressure was $\frac{220}{110}$.

She was begun on phenobarbitone and digitalis.

December '48: Feeling better; fit for more. No swelling of the ankles. Still pain in the chest on exertion. Sleeping well. Has taken no digitalis for 3 weeks. Still hypertensive $\frac{220}{110}$.

June '49: Feeling much better and stronger. Gets pain in the chest occasionally while walking - taking about 3 nitroglycerine tablets per day. No swelling of ankles. Blood pressure now $\frac{180}{96}$. E.C.G. examination showed no evidence of posterior myocardial infarction, but rather indicated left ventricular hypertrophy.

Case Number 28: J.J. 59 years. About 8.30 p.m. on 14.10.47 he was walking up the High Street towards the Tron Church when he suddenly felt severe pain across the front of the chest and down the inside of both arms to the wrist. He stopped at once and sat down. He felt weak and queer. After 10 minutes he walked home - 150 yards downhill - and climbed to his house on the second floor of a tenement. He was sick and then went to bed, but did not sleep much. He was very restless all night. The pain persisted. In January '47, he had had a similar attack of pain in the chest and arms which began at 8 p.m. and lasted most of the night. He was then off work for 2 weeks, but thereafter felt fit. On severe /

severe exertion he felt a tightness in his chest.

He was a big thick set man. His pulse was regular in time and in force, 80/min., the vessel wall was not thickened and the blood pressure was

130
92. No cardiac impulse could be felt. The heart sounds were faint. There was no evidence of heart failure. E.C.G. examination showed a recent posterior myocardial infarct. Anti-coagulant therapy was begun.

Auricular fibrillation supervened on the third day and within a few hours of the onset of the arrhythmia left ventricular failure developed. Pericardial friction appeared on the same day. Digoxin 0.25 mgm. q.i.d. was begun. The neck veins were distended on 19.4.47 and the breathing was periodic in character. This was causing considerable distress. The digoxin was therefore increased to five times in the day and aminophylline 0.2. Gm. was given by mouth with each dose. This gave some symptomatic relief, but was stopped after 4 days. The rhythm of his heart varied daily between auricular fibrillation and normal rhythm, but repeated variation on any one day was never detected. Between 17.10.47 and 2.11.47 auricular fibrillation was detected on 6 occasions. After 2.11.47 normal rhythm persisted. The pericardial friction also persisted for many days, being heard for the last time on 8.11.47.

While /

While the rhythm was unstable, left ventricular failure and mild congestive heart failure supervened. Two courses of digoxin by mouth were given - one has already been referred to. After 2.11.47 however recovery was uneventful. He was discharged home on 2.12.47.

January '48 : Feeling well, but has pain and tightness in the chest on exertion.

February '48 : Returned to his old work - railway carter - 10 days ago, although it had been arranged that he get a light job. He was feeling tired and was having pain in the chest on exertion and also sometimes during the night. For 3 nights he had been a little short of breath on first lying down and during the night before he reported, he had been wakened by a severe attack of nocturnal dyspnoea. His heart sounds were almost tic-tac in character and his blood pressure was $\frac{130}{90}$. He was stopped from working and sent home to rest for a month.

Digitalis was begun. This resulted in considerable improvement and 4 weeks later he was feeling much better. His blood pressure was $\frac{160}{100}$.

May '48 : Has been at work for 3 weeks - as a telephone attendant. Feels well as long as he does not hurry or do too much. Still on digitalis.

May '49 : He had to give up his light job 4 weeks previously. Generally he was not feeling well. The tightness in the chest and breathlessness, were fairly /

fairly easily induced and he was tired by the end of the day. In addition he had vague dyspeptic symptoms and was losing weight. No cause for this was found apart from very bad teeth. His blood pressure had fallen again to $\frac{120}{80}$. E.C.G. examination was not diagnostic of myocardial infarction.

Case Number 29 : R.L. 53 years. He was well until 7.4.49. About 8.30 a.m. he had a burning pain across his chest and with it was a little short of breath and sweated slightly. This persisted until 10 a.m.. Thereafter he felt well, but on exertion, he experienced a tightness across his chest. On 23.4.49 he woke about 4 a.m. with the same burning pain across his chest. It lasted $\frac{3}{4}$ hour, and he felt quite well on rising next morning. On 26.4.49 it returned while he was walking round to the Local in the evening. It was very severe and he had to go home to bed. His chest felt tight, but he did not sweat or feel short of breath. The pain persisted until shortly before he was admitted on 27.4.49. His pulse was rapid - 104/min. and was of poor volume. The blood pressure was $\frac{150}{120}$, and the radial arteries were thickened and tortuous. No cardiac impulse could be felt. The heart sounds were faint and gallop rhythm or tic-tac rhythm was frequently detected. E.C.G. examination showed left bundle branch block (Figure 33A). He was kept

at rest in bed and anti-coagulant therapy was begun. The blood pressure fell to $\frac{106}{80}$ on the third day, and the B.S.R. rose to 40 mm./hr. on the 5th day. Convalescence was uneventful.

E.C.G. examination showed a persistence of the left bundle branch block until 13.5.49 when at a heart rate of 56/min, normal intra-ventricular conduction was present. The record then showed evidence of slight anterior infarction. (Figure 33B). Further records revealed that the bundle branch block was unstable, varying with the heart rate. At a rate of under 60/min., conduction was normal, but over 70/min, bundle branch block was present.

On 7.6.49 he was discharged home. Six weeks later he was feeling well and had been doing quite a bit of gardening. His blood pressure was raised - $\frac{160}{108}$. and E.C.G. examination revealed left bundle branch block; the heart rate being 68/min.. He has since remained well and has returned to his work as a warehouseman.

Case Number 30: W.W. 58 years. He was well until 7 days before his admission. During that week he had three attacks of severe crushing sub-sternal pain with accompanying breathlessness, coming on once while he was working and twice while he was walking uphill. On each occasion he had to sit down and rest for 10-15 minutes before feeling all /

all right again. On the morning of 13.10.47 he woke early in the morning with severe pain in the chest. It persisted for 2 hours and he then fell asleep again. During the day he felt quite well. An E.C.G. done on that day showed shallow sharp inversion of the T wave in leads C2F and IVF. An exercise test - 9,396 foot pounds in 2 mins. - caused no pain and produced only transient changes in the record.

On 14.10.47 he woke at 2 a.m. with the same severe crushing substernal pain. It continued without remission for 19½ hours - until 9.30 p.m. He was restless and could not find a comfortable position. About mid-day he got up and had a walk for 5 minutes to see if that would help. All the time he felt hot and sweated profusely. During the afternoon he was sick. Nitroglycerine had no effect in relieving the pain and morphine was required.

On admission he was shocked. The pulse was of poor volume, - 72/min. and the blood pressure was $\frac{148}{82}$. The heart sounds were faint and the first sound in the mitral area was split. There was no evidence of heart failure. E.C.G. examination showed a very extensive anterior infarct, involving the whole of the front of the heart.

Anti-coagulant therapy was begun at once. Convalescence was uneventful. The blood pressure fell to $\frac{104}{70}$ on the 11th day. There was no leucocytosis but the B.S.R. rose to 68/mm./hr. on the 5th day. /

day. On 25.11.47 he was discharged to the Astley Ainslie Hospital.

Prior to his admission to hospital he had been employed as a gardner. It was thought that he would not be fit for this work and when he reported in February 1948, he was advised to seek lighter employment. He was feeling well but was short of breath on the hills unless he walked slowly. His blood pressure was becoming higher - $\frac{120}{90}$. An E.C.G. showed an extensive healed anterior infarct, and an exercise test produced definite changes in the T wave of the chest leads.

When next seen in July '48, he was working as a caretaker, with his wife to help him. He was feeling well. Six months later - January '49, there was little change but his blood pressure was higher - $\frac{166}{106}$ and his weight had increased. He was begun on an obesity diet.

In September '49 he was feeling well, and was working 7 days a week. His duties as caretaker included tending several furnaces and although he was tired at the end of the day he was otherwise well. He was short of breath only on the first exercise of the day. His weight had come down by 10 lbs. and his blood pressure had fallen to $\frac{114}{74}$.

Case Number 31 : J.D. 52 years. For two years he had complained of pain, tightness in the chest, and /

and breathlessness on exertion. The pain was situated over the left side of the chest and did not radiate. He worked as a coalman and first experienced the pain after climbing 4 flights of stairs carrying a 112 lb sack of coal. Gradually it came on more easily and he would feel it after climbing one flight of stairs. Each time it would pass away in 2-3 minutes if he rested. Nitroglycerine would relieve it more quickly. For 6 months, he had felt easily tired and he frequently wakened about 6 a.m. with shortness of breath. Sitting upright relieved this in 10 minutes.

On 1.10.48 he woke at 4 a.m. with severe pain in the left side of his chest. His chest felt tight and he became very short of breath. Soon he began sweating and felt sickly. At 6 a.m. he fell asleep. When he woke at 10 a.m. the pain was still present, but he got up and walked round with his lorry all day. He felt weak and giddy and could not lift a bag of coal. About 10 p.m. the pain passed away and he slept quite well. From that day until he was admitted on 6.10.49 he got up and moved about but felt very easily tired and the left-sided chest pain came on very easily.

On admission the pulse was 84/min. and the blood /

heart sounds were of poor quality. Digitalis was

still being taken and veronal tablets were

given in addition.

November /

blood pressure $\frac{160}{114}$, the radial arteries were palpable and slightly tortuous. No cardiac impulse could be felt but the heart sounds were of good quality. There was no evidence of heart failure. E.C.G. examination showed a normal record. Nevertheless he was treated as a case of myocardial infarction and given anti-coagulants for 3 weeks. The blood pressure fell gradually to $\frac{126}{94}$ after 14 days, and the B.S.R. rose to 16 mm./hr. on the second day in hospital. Convalescence was uneventful and on 9.11.48 he was discharged to the Astley Ainslie Hospital.

Since then he has reported at intervals of 1 - 3 months. Although he has tightness in the chest and is short of breath on exertion, there has been no return of pain.

March '49 : Reported that he was easily tired, and breathless if he hurried. For 2 weeks his feet had felt a little swollen in the evenings. His weight was increasing. The blood pressure was raised - $\frac{184}{118}$. He was given an obesity diet, and was begun on digitalis.

July '49: His general condition had deteriorated. For 3 weeks, he had been waking almost nightly at 3 a.m. because of breathlessness and had to sit up for $\frac{1}{2}$ - $\frac{3}{4}$ hr.. The blood pressure was $\frac{164}{110}$. The heart sounds were of poor quality. Digitalis was still being taken and mersalyl twice weekly was given in addition.

November /

November '49 : He was feeling better and only occasionally had nocturnal dyspnoea. The blood pressure was still raised - ¹⁵⁸110. The E.C.G. was still within normal limits. (Figure 41).

Case Number 32 : C.B. 31 yrs. He was being treated with penicillin for subacute bacterial endocarditis, superimposed on rheumatic heart disease, 2,000,000 units being given daily. At 9 p.m. on 7.5.48 - the 37th day of treatment - he suddenly felt pain like a weight across the praecordium, which radiated through to his back and up the right side of his neck. He felt short of breath and wanted to move about in bed. Coughing and deep breathing had no effect on the pain. It persisted for 4½ hours until relieved by morphine. A few crepitations developed at each lung base but cleared in 3 days. E.C.G. examination on 8.5.48 showed no evidence of myocardial damage, but 2 days later there was S T depression in V4 and T in V5 had become inverted. On 14.5.48 V5 also showed conspicuous S T depression with sharp T inversion in V5 and V6, and 4 days later the S T shift had practically disappeared. The block pressure showed little variation but there was a slight increase in pulse rate - 100/min. to 120/min., and a moderate leucocytosis occurred - 16,000/cm on 8.5.48. On 18.5.48 he suddenly became unconscious, having had a cerebral embolus. He never /

never completely regained consciousness and died 5 days later.

At autopsy a small infarct of the posterior wall of the left ventricle was demonstrated.

Case Number 33: Miss C.S. 56 yrs. On the morning of 10.8.49 she underwent an operation for removal of a cataract from her left eye. During the afternoon she suddenly felt faint and had a fluttering sensation in her chest for a few seconds. Thereafter she felt exhausted, but was not short of breath and did not feel sick. When seen 4 hours later she was very shocked - the skin was pale cold and moist, the lips were cyanosed, the heart sounds were faint and of poor quality, the pulse was slow 56/min. but was of poor volume, and a blood pressure of $\frac{78}{56}$ could just be detected. The peripheral arteries were thickened and tortuous. In the aortic area faint systolic and diastolic murmurs were heard.

At one stage while she was being questioned it was thought that she had died - her voice died away, her jaw fell forward, and her breathing which had been irregular stopped for a short time. However she revived. The most likely diagnosis was considered to be that of a painless myocardial infarct and it was decided to institute specific anti-shock treatment. She was kept warm, oxygen was given, and coramine /

Coramine, 2 c.c., was given 2 hourly. Plasma was begun 6 hours after the onset and 1 pint was given in 5 hours. Her position in bed was not altered lest the pressure inside her eye be increased. Morphine 1/6th gr. s.c.i. was given after the plasma had been run in.

Within 18 hours there was a striking improvement. She was still feeling weak but otherwise well. The heart sounds were louder and of better quality; the pulse was of good volume, and the blood pressure was $\frac{130}{78}$. On the third day she was slightly short of breath and fine crepitations were detected in each axilla. The neck veins were not distended. After two days her breathing ceased to trouble her and the lung fields became clear. The blood pressure rose to about $\frac{130}{90}$. On the 15th day an electrocardiogram was obtained. It showed no definite evidence of myocardial infarction, but T was sharply inverted in V1., diphasic in V2, very low upright in V3, and low upright in V4 to V6. On the same day the B.S.R. was 35 mm./hr.. Follow up electrocardiograms showed minor T wave changes in the chest leads. By the end of the 5th week, the B.S.R. had fallen 10 mm./hr.. She was allowed up in the middle of the 5th week and was discharged home 2 weeks later.

When seen 2 months later she was feeling fairly well, but was only fit for light housework and was resting each afternoon. Her E.C.G. showed

T wave inversion in V1 to V4. T was flat in V5 and low upright in V6.

Her aortic incompetence was considered to be associated with marked arterio-sclerotic changes in her aorta and aortic valve cusps. The W.R. was negative and she gave no history of rheumatic fever.

Case Number 34 : Mrs M. McL. 59 years. For 6 years she had experienced pain in the chest and neck on exertion. It was very disabling and in April '49 she had the upper thoracic ganglia on the left side injected with alcohol. This did not relieve the pain on exertion to any great extent, but produced a troublesome neuritis in the left arm. She was admitted on 14.10.49, and after being at rest in bed for 16 days, developed a myocardial infarct. She was severely shocked, and within 2 hours of the onset had gone into left ventricular failure. Morphine $\frac{1}{4}$ gr. was given. She was propped up in bed and kept warm. Oxygen was started. Six hours later she was cold, cyanosed and had marked Cheyne-Stokes respirations. The blood pressure had fallen to $\frac{84}{74}$. Digoxin 1 mgm was given intravenously, and digoxin 0.25 mgm t.i.d. by mouth was continued for 5 days thereafter. Neptal 1 c.c. intravenously was given every second day. After 1 week the pulmonary congestion cleared and she began to feel stronger. The blood pressure was still low - $\frac{100}{80}$ and /

and the heart sounds were still faint. Attacks of breathlessness developed on the 10th day and recurred. Neptal was continued and oxygen was given, but digoxin was not restarted until the 14th day. She died quite suddenly on the 16th day. E.C.G. examination after the infarct showed the development of a left bundle branch block.

Investigation of the clotting changes in the blood, by means of the Waugh-Ruddick heparin retarded clotting test, showed no departure from normal until the 14th day after the onset, when tube 9 clotted in 34 minutes.

At autopsy, the entire anterior wall of the left ventricle and the inter-ventricular septum were involved in a large infarct. There was no endocardial mural thrombus. The coronary arteries were arteriosclerotic. A thrombus of recent origin occluded the upper part of the anterior descending branch of the left artery. Beyond this thrombus, the artery became extremely narrow and thin walled. This was thought to be a congenital defect of the artery.

Case Number 35: W.B. He was admitted on 13.1.50 having sustained a myocardial infarct 2 days previously. E.C.G. examination showed an extensive anterior infarct. Blood examination on 14.1.50 - by means of the Waugh Ruddick test - gave /

gave the clotting time of tube 9 as 46 minutes. Four days later (18.1.50) tube 9 clotted in 38 minutes and on 21.1.50 it clotted in 30 minutes. Convalescence was uneventful until 23.1.50 when he complained of pain across the chest and up to the left shoulder. It was not too severe but he was slightly short of breath. On auscultation, marked pericardial friction was audible. This persisted until 24.1.50 when he died quite suddenly. The clotting test had been repeated on 24.1.50 when tube 9 clotted in 58 minutes.

At autopsy a large infarct, involving the apex and anterior wall of the left ventricle and the adjoining inter-ventricular septum was demonstrated. The infarcted wall had ruptured just above the apex, and the pericardial sac was filled with blood. On the endocardial surface of the inter-ventricular septum there was a massive mural thrombus. The coronary arteries were arteriosclerotic, but no thrombosed segment was demonstrated.

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