SERUM GLUTAMIC OXALACETIC TRANSAMINASE ASSAY

IN THE DIAGNOSIS OF

ACUTE MYOCARDIAL INFARCTION.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

C O N T E N T S.

VOLUME I.

Introduction. ... ... P.1.

Methods and Materials.. ... 3.

Estimation of Serum Transaminase Activity .. 3.

Conditions in which Serum Transaminase Assay was Performed. 4.

a) Normal Controls. 4.

b) Acute Myocardial Infarction. 4.

c) Angina Pectoris at rest. 4.

d) Cardiovascular diseases other than Acute Myocardial Infarction and Angina Pectoris at rest. 4.

e) Diseases outwith Cardiovascular system. 4.

The History and Findings on Clinical Examination. ... ... 5.

Electrocardiographic Studies. ... 5.

a) Electrocardiographic Technique .. 5.

b) Criteria used in electrocardiographic interpretation. ... .. 5.

Post mortem and Histological Studies .. 6.

Ancillary Methods employed in the diagnosis of Acute Myocardial Infarction. ... .. 7.

a) Body Temperature. ... .. 7.

b) Erythrocyte Sedimentation Rate .. 7.

Page

Tests of Liver Function. ... ... 7.

Criteria employed in assessing the degree of peripheral vascular failure in Acute Myocardial Infarction. ... . 8.

Criteria considered indicative of a guarded prognosis in Acute Myocardial Infarction. .. 8.

The Definition of the Normal Range of Serum Transaminase Activity. ... .. 8.

a) The effect of digestion and exertion on serum transaminase activity in normal subjects. .. .. 9.

b) Day to day variations in serum transaminase activity in normal subjects. 9.

c) The effect of sex and age on serum transaminase activity in normal controls. 10.

d) The effect of haemolysis of the red blood cells on serum transaminase activity. 10.

e) The effect of anticoagulant substances (in vitro) on transaminase activity .. 10.

f) Stability of the Enzyme. ... . 10.

The Sources of Serum Transaminase Activity in Normal Human Subjects and in Experimental Disease States. ... .. 11.

1) In normal human subjects. .. 11.
2) In experimental cardiac disease states. ... ... 11.

a) Acute myocardial infarction. 11.
b) Myocardial ischaemia. .. 12.
c) Pericarditis .. .. 13.

3) In experimental hepatic disease states. .. .. 13.

4) In experimental skeletal muscle injury. .. .. 14.

Page.

5) In experimental pulmonary infarction. .. 14.

6) In experimental cerebral infarction. ... 15.

7) In experimental infarctions of other organs. 15.

The Excretion of Serum Transaminase in Experimental Animals and in Normal and Diseased Human Subjects. ... .. 16.

a) Excretion of transaminase in urine .. 16.

b) Excretion of transaminase in the bile. 17.

Clinical Aspects of the cases of Acute Myocardial Infarction and Angina Pectoris at rest under consideration. ... . 19.

a) Angina pectoris on effort and at rest preceding acute myocardial infarction .. 19.

b) Angina pectoris at rest without electrocardiographic evidence of acute myocardial infarction. .. .. .. 20.

c) The determination of time of onset of acute myocardial infarction. .. .. 20.

d) Cases of acute myocardial infarction presenting with breathlessness or other signs but without pain. .. .. 21.

i) Left ventricular failure. .. 21.
ii) Cerebral thrombosis. .. 21.
iii) Marked peripheral vascular failure. 22.

e) Cases in which acute myocardial infarction was diagnosed on clinical grounds only.. 23.

The Classification of the Cases of Acute Myocardial Infarction under consideration, according to the Electrocardiographic Findings and a comment on the Accuracy of Electrocardiographic Diagnosis.. . 24.

Page.

The Results of Serum Transaminase Assay in Acute Myocardial Infarction. ... . 26.

1) The period of delay before serum transaminase activity rises following acute myocardial infarction. .. .. 26.

2) High levels of serum transaminase activity following acute myocardial infarction. .. 26.

a) In acute transmural myocardial infarction. .. .. 26.

b) In acute intramural myocardial infarction. .. .. 30.

c) In acute myocardial infarction, in which the diagnosis was based on the history, clinical findings and electrocardiographic patterns which, although grossly abnormal, were at no time diagnostic of acute myocardial infarction. .. .. .. 32.

d) In acute myocardial infarction in which the diagnosis was based on the history and clinical findings only. .. .. 32.

3) Normal or borderline serum transaminase activity following acute myocardial infarction. .. .. 32.

The Results of Post Mortem and Histological Examination in Cases of Acute Myocardial Infarction and Angina Pectoris at rest. ... ... 35.

Evidence of Hepatic Dysfunction following Acute Myocardial Infarction & an Investigation into the Relationship between Hepatic Dysfunction and increased Serum Transaminase Activity. ... .. 38.

The Correlation between the degree of Peripheral Vascular Failure and the level of Serum Transaminase Activity found following Acute Myocardial Infarction. ... . 40.

Page.

The Results of Serum Transaminase Assay and Electrocardiographic Examinations incases of Angina Pectoris at rest. ... . 42.

The Results of Serum Transaminase Assay, Electrocardiographic Examination, Post mortem Examination and Liver Function Tests in Cardiovascular conditions other than Acute Myocardial Infarction or Angina Pectoris at rest. .. .. 44.

1) Acute left ventricular failure and congestive cardiac failure due to ischaemic heart disease. .. .. .. 44.

2) Ischaemic Heart disease. .. .. .. 45.

3) Essential Hypertension .. .. .. 45.

4) Chronic cor pulmonale. .. .. .. 45.

5) Acute rheumatic fever. .. .. .. 46.

6) Chronic rheumatic valvular disease of the heart. .. .. 46.

7) Uraemic Pericarditis. .. .. .. 47.

8) Cerebral infarction. .. .. .. 47.

9) Acute pulmonary infarction. .. .. 47.

10) Thrombo-embolic conditions other than Acute pulmonary infarction. .. .. .. 51.

11) Dissecting Aneurysm of the Aorta. .. . 53.

12) Supraventricular Tachycardia and auricular fibrillation. .. .. 54.

The Results of Serum Transaminase Assay, Electrocardiographic Examination, Post Mortem Examination and Liver Function Tests in Diseases outwith the Cardiovascular System. .. .. 59.

1) Diseases of the Alimentary Tract. .. .. .. 59.

Page.

1. Diseases of the Alimentary Tract (ctd.) .. 59.

a) Peptic Ulcer .. .. .. 59.

b) Hiatus Hernia .. .. .. 60.

c) Steatorrhoea. .. .. .. 60.

2. Diseases of the Respiratory System. .. .. 61.

a) Pulmonary Tuberculosis. .. .. 61.

b) Bronchopneumonia and Pleurisy. .. 61.

c) Neoplasm of Lung. .. .. .. 61.

3. Diseases of the Endocrine Glands. .. .. 61.

a) Diabetes Mellitus .. .. .. 61.

b) Thyrotoxicosis. .. .. .. 62.

4. Cholelithiasis. .. .. 62.

5. Acute Pancreatitis. .. .. 62.

6. Jaundice. .. .. 64.

a(Obstructive jaundice due to neoplastic conditions. .. .. 64.

b) Jaundice due to hepatic cirrhosis. .. 65.

c) Jaundice due to haemolytic anaemia.... 65.

7. Lymphadenoma with hepatic involvement. .... 65.

8. Metabolic Disease of Bone. .. ... 65.

9. Uraemia and Oliguria. .. ... 66.

Serum Transaminase Activity compared with Pyrexia as an Index of Acute Myocardial Infarction. .. .. .. 66.

Serum Transaminase Activity compared with Erythrocyte Sedimentation Rate etc. /ctd over.....

(ctd)

	Page.
Serum Transaminase Activity compared with Erythrocyte Sedimentation Rate as a Diagnostic Aid in Acute Myocardial Infarction and Angina Pectoris at rest.	67.
Discussion of Results.	69.
Figures. (I:- P.27)	
(II:- P.29)	
(III:- P.31)	
(IV:- P.49)	
(V:- P.52)	
(VI:- P.55)	
(VII:- P.63)	
(VIII:- P.103)	
(IX:- P.105)	
(X:- P.109).	
Summary.	113.
Acknowledgments.	115.
References.	116.-121.

VOLUME II (over).....

C O N T E N T S.

VOLUME II.....

Appendix I. Page.

The Spectrophotometric Method of Glutamic Oxalacetic Transaminase Assay in Serum, Bile and Urine. . ... 1.

1) Historical Introduction. ... . 1.

2) Materials used and their preparation. .. . .. 2.

3) Description of procedure followed. .. . . 3.

4) Comments on the procedure. .. . . 3.

a) Practical considerations. . .. . . 3.

b) The accuracy, reproducibility and simplicity of the method. . .. . . 4.

Appendix II.

In this appendix are included the case histories, the electrocardiograms and the results of serum transaminase assay. .. .. 6.

(Please see index to case histories overleaf)

Appendix III. Tables: Nos. 1 - 19. .... 423.

No. 1: P. 424.
No. 2: P.425.
No.3: P. 427
No. 4: P. 428.
No. 5: P. 429.
No. 6: P. 430.
No. 7: P. 431.
No. 8: P. 432.
No. 9: P. 433.
No. 10 : P. 434.
No. 11 : P. 435.
No. 12 : P. 436.
No. 13 : P. 437.
No. 14 : P. 438.
No. 15 : P. 439.
No. 16 : P. 442.
No. 17 : P. 443.
No. 18 : P. 444.
No. 19 : P. 445.

Appendix IV. PLATES. NOS. 1 - 5. .... 446.

No.1: P. 447.
No. 2:P. 448.
No.3 : P. 449.
No.4 : P. 450.
No. 5 : P. 451.

/- over.

VOLUME II. (Appendix II).... CASE HISTORIES, 1 - 135.

History No.	Page.	History No.	Page.	History No.	Page.
1.	7.	46	193.	91	345.
2.	11.	47	196.	92	346.
3.	16.	48.	202.	93	347.
4.	19.	49	206.	94	348.
5.	21.	50	210.	95	351.
6.	25.	51	214.	96	354.
7.	29.	52	218.	97	355.
8.	32.	53.	221.	98	358.
9.	38.	54	224.	99	360.
10.	41.	55	228.	100	362.
11 .	45.	56	231.	101	365.
12.	52.	57	235.	102	369.
13.	56.	58	239.	103	372.
14.	59.	59	243.	104	373.
15.	62.	60	245.	105	374.
16.	65.	61	248.	106	379.
17.	70.	62	251.	107	381.
18.	75.	63	254.	108	385.
19.	79.	64	256.	109	388.
20.	84.	65	260.	110	391.
21.	90.	66	264.	111	392.
22.	94.	67	267.	112	393.
23.	97.	68	270.	113	394.
24.	101.	69	273.	114	395.
25.	103.	70	275.	115	395.
26.	116.	71	278.	116	398.
27.	122.	72	281.	117	400.
28.	125.	73	284.	118	401.
29.	128.	74	287.	119	403.
30.	131.	75	290.	120	405.
31.	138.	76	291.	121	406.
32.	142.	77	296.	122	407.
33.	146.	78	301.	123	409.
34.	150.	79	306.	124	410.
35.	154.	80	311.	125	411.
36.	157.	81	315.	126	412.
37.	162.	82	318.	127	413.
38.	166.	83	322.	128	414.
39.	168.	84	325.	129	415.
40.	171.	85	329.	130	417.
41.	174.	86	331.	131	418.
42.	179.	87	332.	132	419.
43.	183.	88	333.	133	420.
44.	187.	89	339.	134	421.
45.	190.	90	341.	135	422.

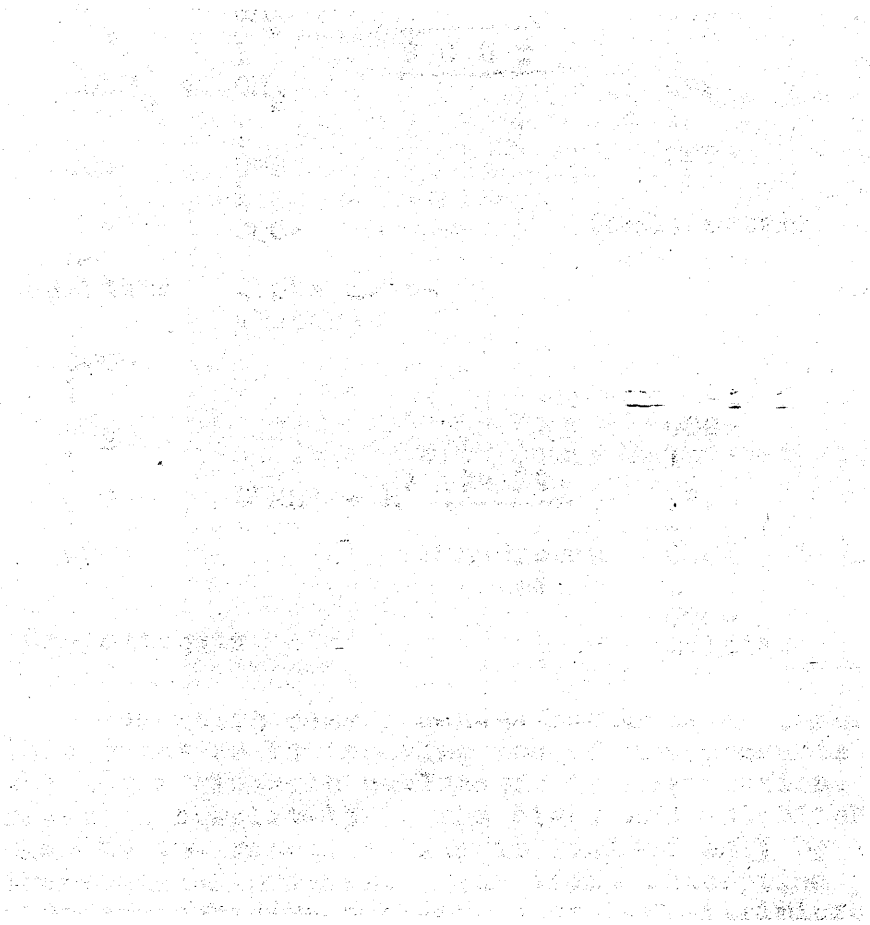
VOLUME I.

INTRODUCTION.

Transamination was defined by La Due and his associates (1954) as the enzymatic catalysed reversible transfer of the alpha amino nitrogen of an amino acid to the alpha-keto-acid with the synthesis of a second amino acid and a second alpha-keto-acid. Glutamic oxalacetic transaminase is an enzyme which catalyses the reversible transfer of an amino group from aspartic acid to alpha-ketoglutaric acid, yielding glutamic acid and oxalacetic acid. This enzyme, hereafter referred to as transaminase, is found widely distributed in animal tissues but is most concentrated in heart muscle. (Cohen 1940), (Awapara and Seale, 1952). The latter discovery led La Due and his co-workers to study its concentration in human serum in cases of myocardial infarction, after they had established the range of serum transaminase activity in normal adults. (La Due et al, 1954), (La Due and Wroblewski, 1955). In these studies, it was found that the transaminase activity of the serum was strikingly elevated during the first few days after acute myocardial infarction. These results have been confirmed by many workers e.g., Steinberg and Ostrow (1955); Kattus et al, 1956. The potential value of such a biochemical test as an aid in the detection of myocardial infarction is very great but it is not yet clear how much the test offers as a supplement to the clinical, electrocardiographic and other ancillary findings in the diagnosis of acute myocardial infarction.

The present study was undertaken with the object of assessing the value of the test, as a routine procedure, in the diagnosis of acute myocardial infarction by comparing it with other diagnostic techniques presently available in general hospital practice. Serum transaminase activity was also studied in angina pectoris at rest to determine the value of assay in differentiating between acute myocardial infarction and myocardial ischaemia. When the present investigation was begun it was known that the test was not specific for acute myocardial infarction since increased serum transaminase activity had been demonstrated in the presence of liver and other diseases. (La Due and Wroblewski, 1955). Therefore, it was decided to investigate liver function following acute myocardial infarction to discover if there was any relationship between impairment of liver function and increased serum transaminase activity. Serum transaminase activity was also investigated in diseases other than acute myocardial infarction to determine whether the lack of specificity of the test might lead to diagnostic error in those conditions which may closely resemble acute

/acute myocardial infarction e.g., dissecting aneurysm of the aorta, acute pulmonary infarction, acute pancreatitis etc., or which may accompany it e.g., cardiac arrhythmias.

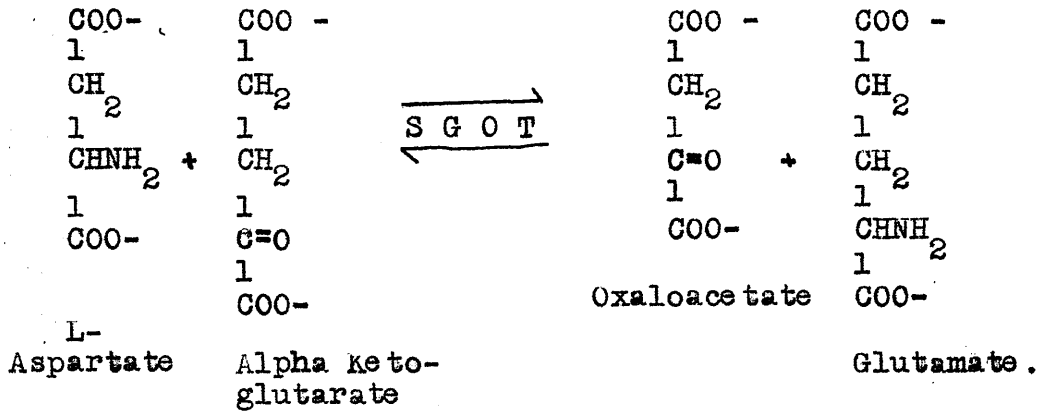


METHODS AND MATERIALS.

Estimation of Serum Transaminase Activity.

The transaminase activity of serum was estimated by the technique of Karmen (1955). Full details of this method are given in Appendix 1.

In this method, the transamination reaction is coupled with the reduction of oxalacetic to malate by reduced diphosphopyridine nucleotide in the presence of an excess of purified malic dehydrogenase; the reactions may be written thus :-



The malic dehydrogenase performs an important function in this reaction by removing one of the products in equilibrium in the serum glutamic oxalacetic transamination. This forces the reaction completely to the right and establishes a condition whereby the reaction rate is limited only by the amount of transaminase present. The light absorption peak of reduced diphosphopyridine nucleotide at 340 millimicrons is used to measure the transaminase reaction, spectrophotometrically, by observing the decrease in optical density at that wave-length as the reduced diphosphopyridine nucleotide is oxidised. Transaminase activity is expressed as units per ml. of serum per minute, one unit being defined as that amount of enzyme which will cause a decrease in optical density of 0.001/ml/min. under the standard conditions of the test.

Conditions in which Serum Transaminase Assay was performed.

a) Normal controls.

Serum transaminase activity was measured in 9 healthy people and in 16 patients attending surgical and orthopaedic out-patient departments suffering from conditions unrelated to cardiac or liver disease and in whom the history and clinical examination raised no suspicion of such disease. The results of these assays are presented in Table I (Appendix III).

Disease States.

Serum transaminase assays were performed in 135 patients suffering from a variety of diseases.

b) Acute myocardial infarction.

Serum transaaminase activity was measured following 67 attacks of acute myocardial infarction occurring in 57 patients. The majority of these patients received anticoagulant therapy and required daily venepuncture for estimation of prothrombin times. Blood obtained for this purpose was also used for serum transaminase assay and tests of liver function so that these seriously ill patients were not unnecessarily disturbed by the investigation. The results of these assays are included in the individual case histories in Appendix II and are presented in tabular form in Tables II, III, IV, V.and VI., (Appendix III).

c) Angina pectoris at rest.

Serum transaminase assays were performed following 25 attacks of angina pectoris occurring in 20 patients. These attacks of pain came on at rest and there was no electrocardiographic evidence of acute myocardial infarction following them. The results of assay in these cases are included in the individual case histories in Appendix II and are also presented in tabular form in Table VII, (Appendix III).

d) Cardiovascular diseases other than acute myocardial infarction and angina pectoris at rest.

Serum transaminase activity was measured in a variety of cardiovascular diseases in which there was no evidence of acute myocardial infarction or angina pectoris. Several of these patients suffered from more than one cardiovascular lesion. The results of serum transaminase assay in these conditions are included in the individual case histories in Appendix II. The conditions investigated are set out in tabular form in Table VIII, (Appendix III).

e) Diseases outwith cardiovascular system.

Serum transaminase activity was determined in a variety of diseases affecting systems other than the cardio-

/cardiovascular system. In these cases, there was no clinical and/or electrocardiographic evidence of acute myocardial infarction or angina pectoris. The results of serum transaminase assay in these conditions are included in the individual case histories (Appendix II). The conditions investigated are presented in Table IX, (Appendix III).

All serum transaminase assays were personally performed by the author. The number of assays totalled 533.

The History and Findings on Clinical Examination.

The history and clinical findings in each of the 135 patients studied are presented in Appendix II. Except for a few patients who died within a few hours of their admission to hospital, the author personally questioned and examined all patients suffering from cardiovascular diseases. The history and results of clinical examination are of the greatest value in determining whether or not acute myocardial infarction has occurred. Because of their relevance to the use of serum transaminase assay in the diagnosis of acute myocardial infarction, a special interest was taken in symptoms, prodromal to acute myocardial infarction, in atypical modes of presentation and in the determination of the exact time of onset of acute myocardial infarction.

Electrocardiographic Studies.

Electrocardiograms were examined in 100 out of the 135 patients included in this study. In certain cases duplicate electrocardiograms were not available for inclusion in this thesis. However, 179 electrocardiograms are available for inspection and they are included in the individual case histories in Appendix II.

a) Electrocardiographic Technique.

Electrocardiograms, serial where indicated, were recorded by a portable direct writing Cambridge electrocardiograph. The following leads were recorded: Leads I, II, III, aV.R., a.V.L., a.V.F., V2, V4, V6. These are the leads routinely recorded in the hospital in which this investigation was carried out. Since a limited number of chest leads were being used, great care was taken to place the praecordial electrodes accurately according to the recommendations of the Cardiac Society of Great Britain, 1949.

b) Criteria used in Electrocardiographic Interpretation.

In cases of suspected myocardial infarction, the electrocardiogram is usually considered to be the final criterion in determining whether acute myocardial infarction has occurred. In an investigation such as this, which seeks to compare one diagnostic technique with another, it is obviously desirable to avoid bias towards either and, consequently, the electrocardio-

/electrocardiograms were interpreted by an independent observer, Dr. A. J. V, Cameron, who was given a short note of the history of each case. He had no knowledge of the results of serum transaminase assay or other ancillary tests and the history and electrocardiograms in each case were known to him by a reference number only. Dr. Cameron employed diagnostic criteria which were essentially those of Goldberger (1953), although a different terminology from his was used in the description of the types of myocardial infarction. The term, transmural, was used to describe myocardial infarctions in which the electrocardiogram showed abnormal Q waves and abnormally shaped RS-T elevations. The diagnosis of infarction was not made from T wave changes alone unless abnormal Q waves were present and progressive T wave changes occurred in serial tracings. The term, intramural, was employed in preference to the term, superficial, used by Goldberger (1953), to describe myocardial infarctions in which the electrocardiogram did not show abnormal Q waves but revealed abnormally shaped RS-T elevations in one or more leads that faced a localised, epicardial surface of the heart. In this group, great importance was attached to observing sequential changes in the electrocardiogram. The term, subendocardial, (Goldberger,1953) was reserved for those myocardial infarctions in which the electrocardiographic patterns of acute coronary insufficiency persisted for more than 24 hours. No clear cut examples of this latter type of myocardial infarction were encountered in this study.

All electrocardiographic interpretations included in this study were those of Dr. A. J. V. Cameron.

Post Mortem and Histological Studies.

Post mortem examination was performed in 8 fatal cases of acute myocardial infarction and 3 of these fatal attacks had been preceded by attacks of severe angina pectoris. The liver and heart were examined histologically in 7 out of the 8 fatal cases of acute myocardial infarction. The degree of venous congestion of the liver was described as moderate when congestion was limited to the centre of the hepatic lobule and as severe when the whole lobule was involved in the congestion. The term, centrilobular necrosis of liver, was reserved for those cases in which necrosis was present in the centre of the lobule. Post mortem examinations were also carried out in 2 cases of dissecting aneurysm of aorta, 2 cases of mitral stenosis, 1 case of ischaemic heart disease, 1 case of alveolar carcinoma of lung, 1 case of malignant hypertension, 1 case of cerebral embolism with infarction, 1 case of hepatic cirrhosis, 1 case of perforated stomal ulcer and 1 case of adenocarcinoma of the pelvic colon.

ANCILLARY METHODS EMPLOYED IN THE DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION.

/ ctd over.

ANCILLARY METHODS EMPLOYED IN THE DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION.

It is well recognised that pyrexia and elevation of the erythrocyte sedimentation rate (E.S.R.) often occur following acute myocardial infarction and their presence in suspected myocardial infarction is usually regarded as providing evidence suggestive of the occurrence of acute myocardial infarction although neither test is specific for myocardial infarction. Such observations were made in this study in acute myocardial infarction, angina pectoris at rest and in a variety of other diseases.

a) Body Temperature.

Axillary temperatures were recorded. Temperatures of 99°F or above were considered abnormally high.

b) Erythrocyte Sedimentation Rate.

This was determined in the hospital wards by the method of Westergren (1926). Serial estimations of E.S.R. were made in most cases. Only the reading at the end of the first hour was recorded. The E.S.R. was considered to be abnormally accelerated if it was above 10 mm. in the first hour.

TESTS OF LIVER FUNCTION.

The following tests of liver function were performed in cases of acute myocardial infarction, of liver or biliary disease and of cardiac arrhythmia. The results of these tests in acute myocardial infarction are presented in Tables X,XI,XII, in Appendix III. The results in the other types of illness are included in the case histories in Appendix II.

1. Van den Bergh Reaction:- a) Direct. b) Indirect - quantitative bilirubin estimation. The method employed was that of King (1946) but a bilirubin instead of an artificial methyl red standard was employed. The normal range, by this method, was 0.5 - 1 mgm.per 100 ml.

2. Thymol Turbidity Test. The method employed was that of Maclagan (1944). The normal range of thymol turbidity is 0 - 4 units.

3. Zinc Turbidity Test. The method employed was that described by Kunkel (1947). The normal range is 2 - 8 units.

4. Alkaline Phosphatase. The plasma alkaline phosphatase was measured by the method of King and Armstrong (1934). The normal range is 3 - 13 units.

5. Total Plasma Proteins. These were measured by the usual procedure of micro-Kjeldahl digestion followed by Nesslerisation. The normal range was 6 - 8 g.per 100 ml.

6. Cephalin Flocculation Test. This flocculation technique (Hanger and Patek, 1941) was employed in a few cases, instead of the thymol turbidity test.

7. Bromsulphalein Test. The bromsulphalein test, using 5 mgm/kg. body weight, was employed (Helm and Machella,1942). Serial tests were performed in one patient in whom the first measurement had been made before the onset of acute myocardial infarction. The risk of a toxic allergic reaction to the dye, however rare, was considered too great for routine use of the test in acutely ill patients suffering from myocardial infarction.

Normal Range. When the sample of serum is taken 45 minutes after injection of the dye, there should be no retention of the dye in the blood.

8. Urine Tests. Bilirubin, urobilin and urobilinogen were determined qualitatively by the methods of Fouchet, Schlessinger and Erhlich,respectively,in several cases.

CRITERIA EMPLOYED IN ASSESSING THE DEGREE OF PERIPHERAL VASCULAR FAILURE IN ACUTE MYOCARDIAL INFARCTION.

The criteria used for assessing the degree of peripheral vascular failure present in cases of acute myocardial infarction were those of Davidson et al (1946). They are set out in Table XIII, (Appendix III).

CRITERIA CONSIDERED INDICATIVE OF A GUARDED PROGNOSIS IN ACUTE MYOCARDIAL INFARCTION.

The prognostic criteria employed were those of Russek and his associates (1951). The following criteria were considered indicative of a guarded prognosis:- Previous myocardial infarction, intractable pain, extreme degree of persistence of shock, significant enlargement of the heart, gallop rhythm, congestive cardiac failure, auricular fibrillation or flutter, ventricular tachycardia or intra-ventricular block, diabetic acidosis or other complicating serious disease states. Anticoagulant therapy was given in all cases of acute myocardial infarction whether or not signs of poor prognostic significance were present provided there was no contra-indication to the use of the drug.

THE DEFINITION OF THE NORMAL RANGE OF SERUM TRANSAMINASE ACTIVITY.

19 assays of serum transaminase activity were performed, under varying physiological conditions, in 9 healthy people who were either nurses or medical students and single determinations of serum activity were made in 16 patients who were attending surgical or orthopaedic clinics with disabilities unrelated to cardiac or liver disease and in whom

/whom the results of history-taking and clinical examination raised no suspicion of such disease. The results of these assays are presented in Table I.

The range of serum transaminase activity in control subjects in this series was 5 - 35 units/ml. with a mean serum transaminase activity of 17 ± 8 units. It will be noted in Table XIV that the range of serum transaminase activity found closely agreed with that found by other workers. Mean serum transaminase activity in this study is somewhat lower than that reported by other investigators. It should be noted that Baron et al (1956) applied a correction factor for variation in room temperature.

Since all recorded studies have shown that in normal subjects levels of serum transaminase activity above 40 units/ml. are not found and since duplicate analyses of the serum by the spectrophotometric method do not vary by more than 10 units (see Appendix I), the following ranges of serum transaminase activity have been arbitrarily defined:-

Normal.
Serum transaminase activity is considered to be normal to levels of 40 units.

Borderline.
Serum transaminase activity is considered to be borderline when it is in the range of 41 - 50 units.

High.
Serum transaminase activity is considered to be abnormally high when above 50 units.

a) The Effect of Digestion and Exertion on Serum Transaminase Activity in Normal Subjects.

In control cases 1 and 2., serum transaminase activity was estimated before, and five hours after, a strenuous game of rugby while, in control case 3., it was measured in the fasting state and three hours after a hearty meal. No significant alteration in serum transaminase activity was found following exercise or eating. It is generally agreed that exertion and the state of digestion have no effect on the levels of serum transaminase activity e.g., Steinberg and Ostrow (1955); Chinsky et al (1956).

b) Day to Day Variations in Serum Transaminase Activity in Normal Subjects.

In control cases 4, 5 and 8., serum transaminase activity was examined on three successive days (Table I). The variations found were insignificant, which is in agreement with the

/the experience of other workers e.g., Baron et al (1956).

c(The Effect of Sex and Age on Serum Transaminase Activity in Normal Controls.

No relationship between transaminase levels and sex or age of the control subjects was noted.

d) The Effect of Haemolysis of the Red Blood Cells on Serum Transaminase Activity.

In control case 6., the transaminase activity of clear serum was 15 units. The transaminase activity of an aliquot of the same specimen of blood in which haemolysis had been induced by contact with distilled water, was 126 units, transaminase being released from the red blood cells. This effect of haemolysis was recorded by La Due et al (1955) in their original papers and has since been confirmed by others e.g., Steinberg and Ostrow (1955). The importance of using non-haemolysed samples of serum and plasma in serum transaminase determinations is obvious. Although platelets also contain transaminase it remains to be determined whether variations in platelet numbers will significantly alter the assay. (Magalini and Stefanini 1956).

e) The Effect of Anticoagulant Substances (in vitro) on Serum Transaminase Activity.

It is generally agreed that transaminase assays on plasma specimens obtained with oxalate, citrate or heparin as anticoagulants are similar to those performed on serum derived from the same blood e.g., Kattus et al (1956). In control case 9., the serum and plasma transaminase activity of the same specimen of blood was 14 and 10 units respectively. Heparin was the anticoagulant used in obtaining the specimen of plasma.

f) Stability of the Enzyme.

The stability of serum transaminase is such as to facilitate its clinical usefulness. Freezing of the serum does not influence serum transaminase activity. For example, in control case 5., storage of the sera for 7 days at 4°C. did not significantly alter serum transaminase activity. Many workers have reported similar findings e.g., Chinsky and Sherry (1957).

THE SOURCES OF SERUM TRANSAMINASE ACTIVITY IN NORMAL HUMAN SUBJECTS AND IN EXPERIMENTAL DISEASE STATES.

1. In Normal Human Subjects.

Transaminase activity has been demonstrated in the serum and tissues of all animals studied e.g., Ames and Elvehjem, (1946); Goldstein et al (1956) and, so far, all tests of human serum have shown the presence of transaminase. The impressive amounts of the enzyme in tissues like the heart and liver are in marked contrast to the small amount of enzyme activity present in an equivalent amount of serum. (see below).

Glutamic Oxalacetic Transaminase Activity of Normal Human Tissues and Serum. (Wroblewski, 1957).

Normal Human Tissue.	Transaminase (Units/Gram of Wet Tissue).
Heart.	155,500.
Liver.	142,400.
Skeletal Muscle.	99,300.
Kidney.	90,900.
Pancreas.	28,300.
Spleen.	13,600.
Lung.	10,000.
Serum.	20.

The source of transaminase in normal human serum has not been determined nor has serum transaminase been isolated for comparison of its physical or immunological characteristics with purified tissue transaminase.

2. In Experimental Cardiac Disease States.

a) Acute Myocardial Infarction.

The alterations in transaminase activity associated with acute myocardial infarctions have been studied experimentally by techniques which do not simultaneously produce liver or skeletal muscle damage. Coronary occlusion by coronary artery ligation in the closed chest dog has been produced and the changes in serum transaminase activity correlated

/correlated with electrocardiographic and other observations, (Nydick et al, 1955; Rudolph et al, 1955). In all but one of these experiments involving production of acute myocardial infarction there was a concomitant rise of serum transaminase activity. When the dogs died from experimentally produced infarction or were killed at varying intervals following ligation of the coronary artery, Nydick et al (1955) determined transaminase activity in normal and infarcted heart muscle and showed that there was a rough correlation between the peak serum transaminase activity, the duration of the rise in serum transaminase activity and the size of the myocardial infarction produced. A myocardial infarction of less than 1 gm. of muscle mass in the dog was observed to produce elevations of serum transaminase activity above the normal range of activity. They postulated that the mechanism for the increase in serum transaminase activity following myocardial infarction was the leakage of the enzyme from the infarcted heart muscle into the serum, since they showed that infarcted muscle contained less transaminase than adjacent normal cardiac muscle of the same animal and that the older the myocardial infarction, the less transaminase activity demonstrable in the necrotic muscle. Merrill et al (1955) reported similar findings in their study of the infarcted myocardial tissues of the dog. Using an experimental technique (Agress et al, 1952), by which plastic microspheres were embolised into the coronary arteries of the closed chest dog, acute myocardial infarction of pre-determined extent was produced. (Agress et al, (1955). They demonstrated a rise in serum transaminase activity following each acute myocardial infarction and observed a relatively linear relationship between the peak rise in serum transaminase activity and the size of the myocardial infarction, estimated at autopsy examination. They found that infarction of as little as 10% of the cardiac muscle mass produced significant increases in serum transaminase activity. Thus, there is sound experimental evidence that serum transaminase activity results from leakage of the enzyme from infarcted cardiac muscle and that the rise in serum activity is roughly proportional to the size of the infarcted area of cardiac muscle.

b) Myocardial Ischaemia.

A study of myocardial ischaemia in dogs, produced by temporarily occluding the coronary arteries, produced further convincing evidence that the infarcted area was the source of increased serum transaminase activity in acute myocardial infarction. (Rudolph et al, 1957; Nydick et al, 1957). Nydick and his associates correlated the degree of myocardial ischaemia with changes in serum transaminase activity, in the electrocardiographic patterns and in heart tissue transaminase activity. They found that myocardial ischaemia of a degree sufficient to produce reversible changes typical of ischaemia

/ischaemia in the electrocardiogram did not cause significant increase in serum transaminase activity. They showed also that the transaminase content of heart tissue which had been rendered ischaemic was the same as that of non-ischaemic tissue. Significant increases in serum transaminase activity occurred only in those cases in which myocardial ischaemia had been prolonged enough to result in heart cell necrosis which was demonstrated at autopsy.

c) Pericarditis.

Agress et al (1956) produced pericarditis in dogs by placing sand, talc or alpha streptococci in the pericardial sac. They found significant elevation in serum transaminase activity only in those animals in which damage to the sub-epicardial cardiac muscle was demonstrated at autopsy and, further, that the peak levels of serum transaminase activity observed were proportional to the severity of the cardiac muscle damage. Normal serum transaminase activity was present in those animals in which pericarditis without underlying cardiac muscle damage was found. Nydick and his colleagues (1957) reported, that in experimental percarditis in dogs, serum transaminase activity increased only when histological evidence of subepicardial damage was present.

3. In Experimental Hepatic Disease States.

Increased serum transaminase activity has been demonstrated following the experimental production of virus hepatitis in mice with a transplantable mouse leukaemia, (Friend et al, 1955), and there seemed to be a relationship between this increase in serum activity and the size of the virus inoculum, the titre of the virus in the blood and the degree of liver necrosis demonstrated at autopsy.

Molander and his associates (1955) produced hepatocellular damage in rats by the gastric intubation of carbon tetrachloride and found high levels of serum transaminase activity. The height and duration of increased serum transaminase activity were proportional to the amount of carbon tetrachloride administered and to the extent of liver necrosis found at autopsy. They considered that serum transaminase activity was a highly specific index of hepatocellular injury. Molander and Friedman (1956) failed to demonstrate a decrease in rat hepatic tissues transaminase in carbon tetrachloride hepatitis even when serum transaminase activity was greatly increased. Ligation of the common bile duct of rats was rapidly followed by a rise in serum transaminase activity, (Chinsky and Sherry, 1957). Relief of the biliary obstruction was followed by a rapid return of the serum transaminase level to normal. Increased serum transaminase

/transaminase in this experimental situation was not associated with histological evidence of hepatic or cardiac necrosis.

The evidence, though incomplete, suggests that the source of serum transaminase activity is release of the enzyme from damaged parenchymal cells of the liver, in experimental conditions associated with hepatic cell necrosis. The findings in experimental biliary obstruction, unaccompanied by hepatic cell necrosis, suggest that the source of increased serum transaminase activity in this experimental situation may be interference with the excretion of the enzyme by the biliary route.

4. In Experimental Skeletal Muscle Injury.

Surgery in dogs resulting in injury to skeletal muscle is associated with a rise in serum transaminase activity and has been ascribed to release of the enzyme from skeletal muscle, which is a rich source. (Nydick et al, 1955).

5. In Experimental Pulmonary Infarction.

Rudolph and his associates (1957) ligated the right pulmonary artery or its lobar branches in dogs and observed increased serum transaminase activity proportional to the amount of lung tissue involved in each case. It should be noted, however, that although every effort was made to minimise the trauma of surgery, the controls used in this experiment were animals which had been subjected to thoracotomy. Agress et al (1956) produced acute pulmonary infarctions in dogs by injecting the dogs' own blood clot into the jugular vein after inducing increased vascularity of the lung by the preliminary injection of alpha naphthyl thiourea, a general tissue poison. The nine experimental animals sustained pulmonary infarctions of 0 - 50% of their lung tissue. Several of the experimental and control animals had increased serum transaminase activity although none had levels of activity above 50 units. There was no statistical difference between the groups and for this reason the increased serum transaminase activity was thought to be due to the use of alpha naphthyl thiourea. It should be noted also that the animals were sacrificed 40 hours after the experiment.

There is, therefore, no agreement as to whether or not acute pulmonary infarction results in increased serum transaminase activity. In those experimental animals in which

/which increased serum transaminase activity was found, the source of the enzyme is uncertain since,in one group of experiments, the increase in serum activity may have been due in part to release of the enzyme from skeletal muscle injury following surgery and, in the other group, to the use of a general tissue poison which may produce death of cells in many tissues.

6. In Experimental Cerebral Infarction.

Wakim and Fleiser (1956) produced acute cerebral infarction in dogs by the injection of red vinyl acetate into the carotid artery. They found that in normal dogs serum transaminase activity was consistently higher than the transaminase activity of cerebro-spinal fluid. Following the onset of acute cerebral infarction, there was a marked rise of transaminase activity in the cerebro-spinal fluid. In certain cases, this rise was followed by a slower and less well marked rise in serum transaminase activity while, in others, serum transaminase activity remained normal. The source of increased transaminase activity in the cerebro-spinal fluid was thought to be release of the enzyme from the damaged brain tissue, the brain having a high transaminase concentration. The rise in serum transaminase activity observed in some cases was considered to have resulted from a breach of the normal blood brain barrier by the brain lesion.

7. In Experimental Infarctions of other Organs.

Rudolph and his associates (1957) ligated renal, splenic and mesenteric arteries in dogs and produced infarctions in the organs supplied by these vessels. Increased serum transaminase activity was demonstrated following all these procedures. It was noted that, as the amount of tissue rendered necrotic was reduced, the amount of enzyme which appeared in the serum was commensurately less. Ischaemia of these organs of short duration was associated with normal serum transaminase activity.

Therefore, while the source of normal human serum transaminase activity is unknown, there is good experimental evidence that the necrosis of any enzyme-rich tissue may result in a significant increase of serum activity of the enzyme.

THE EXCRETION OF SERUM TRANSAMINASE IN EXPERIMENTAL ANIMALS AND IN NORMAL AND DISEASED HUMAN SUBJECTS.

Following experimental myocardial infarction, the observed increase in serum transaminase activity was much smaller than anticipated from the measured loss of transaminase activity from the infarcted myocardium and the dilution of this amount of transaminase in the plasma volume. (Agress et al, (1956) ; Nydick et al, 1955). This suggested either rapid removal of the enzyme or a diluting volume considerably greater than the plasma volume.

Dunn and his associates (1958) found that, following the intravenous injection of transaminase into dogs, three-quarters of the injected enzyme had disappeared from the blood stream within 20 - 72 hours, depending upon the amount injected. Equilibrium was reached between serum and lymph transaminase activity in 6 - 8 hours and marked the end of the rapid disappearance phase. It was deduced from this that the rapid disappearance of the enzyme was due to its diffusion into the interstitial fluid and that this accounted for the discrepancy between serum and tissue transaminase activity noted by previous workers. The exact mechanism of excretion of the enzyme is uncertain. The excretion of the enzyme in the urine and bile is discussed below.

a) Excretion of Transaminase in the Urine.

Dunn et al (1958) found no measurable amount of transaminase activity in the urine of dogs and no enzyme appeared in the urine following the intravenous injection of autogenous or homologous transaminase. They demonstrated that transaminase disappeared from the blood stream at the same rate in both nephrectomised animals and in sham-operated control animals indicating that no inactivation of the enzyme occurred in the kidney. They considered that the large molecular size of transaminase prevented its passage through the glomerular membrane and thus accounted for the absence of transaminase in the urine.

In the present study, a small number of observations was made which suggest that the excretion of transaminase in the urine in human beings is insignificant. In control cases 6 and 7., the transaminase activity of the urine was small and this is in agreement with the observations of Chinsky et al, 1956. (Table I). In cases 41 and 42., the serum transaminase activity was elevated following acute transmural myocardial infarctions and the transaminase activity in the urine was repeatedly examined in the days immediately following the onset of infarction when the serum transaminase activity was raised.

/raised. In neither case was significant elevation of the transaminase activity of urine found. Chinsky et al, (1956) also obtained evidence that significant amounts of transaminase are not excreted even when the serum levels are abnormally high. These findings show that transaminase is excreted by human kidneys in small amounts but the presence of normal serum transaminase levels when oliguria and/or azotaemia is present suggests that other routes of excretion may be of greater significance.(Chinsky and Sherry, 1957). For example, in Case 123., normal serum transaminase activity was found despite coincident uraemia secondary to prostatic retention of urine. In Case 96., serum transaminase levels were normal, despite the presence of severe oliguria. In Case 94., the serum transaminase activity was normal when anuria, uraemia and gross hyperkalaemia were present.

b) Excretion of Transaminase in the Bile.

In 1956, Chinsky and his associates suggested that biliary excretion may be a normal route of transaminase excretion. They had found that specimens of normal human bile obtained at laparotomy had transaminase activities in the range of 2,000 units i.e., 100 times the serum level, and that serum transaminase activity was significantly elevated in patients with obstructive jaundice in the absence of laboratory evidence of the presence of hepatic necrosis. They derived further evidence supporting this concept of the biliary excretion of transaminase from experiments in animals. In 1957., they found that ligation of the common bile duct of rats is rapidly followed by a rise in the level of serum transaminase activity, whereas sham-operated controls did not show significant changes in serum transaminase. The changes in serum transaminase activity following common duct ligation were not associated with histological evidence of hepatic or cardiac necrosis. Release of the experimentally induced common duct obstruction in the rat was followed by a rapid return of serum transaminase activity to normal. Dunn and his colleagues (1958) found the daily biliary excretion in 5 dogs with external biliary fistulae to be very high, (1,000 - 2,000 units/24 hours.) Following the elevation of serum transaminase levels by the intravenous injection of autogenous or homologous transaminase, they found no correlation between the serum transaminase level and the concentration and total excretion of the enzyme in the bile and, therefore, were uncertain whether the transaminase found in bile actually represents transaminase removed from the blood stream by the liver or whether biliary transaminase is formed in, and secreted by, the parenchymal cells of the liver.

In the present investigation, normal bile was not studied

/studied but serial estimations of transaminase activity in serum, bile and urine were made in three cases viz., cases 106, 100 and 99. In case 106., acute pancreatitis was found at operation and gallstones were present in the gall-bladder but not in the common bile duct. The naked-eye appearance of the bile was normal and liver function tests revealed no abnormality. The serum transaminase levels were consistently normal and the transaminase activity of urine low. The transaminase activity of bile obtained by drainage of the gallbladder was repeatedly found to be twice that of the serum. In case 100., the diagnosis of cholelithiasis was confirmed at operation. Gallstones were present in the gallbladder and there was a stone in the common bile duct. The results of liver function tests indicated biliary obstruction. Despite this, only borderline values of serum transaminase activity were found before operation and, following operation, serum transaminase activity was normal. Once again, the transaminase activity of urine was insignificant. The transaminase activity of bile obtained by drainage of the common bile duct by tube was $1\frac{1}{2}$ - 2 times the activity found in serum. In case 99., the diagnosis of cholelithiasis was confirmed at operation, many gallstones being found in the gallbladder but none in the common bile duct. Serum transaminase activity was normal both before and after operation and transaminase activity following operation was low on repeated examination. Transaminase activity of bile obtained by drainage of the gallbladder was 2 - 3 times that of the serum after operation.

In these three cases, very high levels of transaminase activity of the bile were not found but the levels of transaminase activity in the bile were consistently higher than those in the sera. Transaminase activity of the urine was consistently low.

These findings are regarded as possibly indicating biliary excretion of the enzyme. The discrepancy between the results of serum and bile transaminase assay in this study and those of Chinsky and his associates (1956, 1957) cannot be easily explained. It has been shown that common bile duct obstruction in the human subject may be associated with borderline levels of serum transaminase activity (Case 100). The low levels of transaminase activity found in the bile in this study may have been due to impairment of excretion of the enzyme by the liver, a consequence of disease in the biliary tract, although there was nothing to suggest significant liver damage in the tests of liver function performed, or due to contamination of the bile by other secretions during drainage.

CLINICAL ASPECTS OF THE CASES OF ACUTE MYOCARDIAL INFARCTION AND ANGINA PECTORIS AT REST UNDER CONSIDERATION.

Acute myocardial infarction may cause sudden death or may present with severe and characteristic chest pain or with breathlessness or other signs without pain. (Parkinson and Bedford, 1928).

Acute Myocardial Infarction presenting with chest pain.

Sudden prolonged chest pain was the presenting symptom of acute myocardial infarction in 57 out of the 67 attacks of acute myocardial infarction observed in this study. In one case (47b) the praecordial pain of myocardial infarction was overshadowed by pain due to renal infarction. Pain in the chest which occurs at rest is more difficult to assess than pain related to effort and a history of typical angina on effort is very helpful in the diagnosis of myocardial infarction since, if angina on effort is followed by pain at rest of similar character and radiation, then it is likely that the pain occurring at rest is also cardiac in origin. Therefore, the symptoms prodromal to acute myocardial infarction were studied.

a) Angina Pectoris on Effort and at rest preceding Acute Myocardial Infarction.

Angina pectoris on effort preceded the onset of acute myocardial infarction in 31 out of 67 attacks. In 16 of these 31 attacks, angina pectoris on effort had been present for over 3 months before the onset of the acute infarction. (Cases, 3, 7, 9, 11a., 12, 18, 20, 23, 25a, 27, 35, 36, 39, 45, 48, 51). In 5 of these attacks, angina on effort had become more easily induced in the last 3 months before the acute myocardial infarction. (Cases 9, 11a., 23, 25a, 48). In 5 attacks, angina pectoris on effort was succeeded by angina pectoris at rest. (Cases 11a, 18, 25a, 39, 48).

In 15 out of 31 attacks, angina pectoris on effort had made its first appearance during the last three months before the onset of acute myocardial infarction. (Cases, 2, 5, 6, 14, 15, 16, 26, 39,40, 46, 54, 59, 71, 77, 122). In 2 instances, angina pectoris on effort had occurred in isolated attacks 5 weeks and 3 weeks respectively before the onset of acute myocardial infarction. (Cases 5, 46). In 5 cases, in this group, angina pectoris on effort became increasingly disabling before the development of myocardial infarction, (Cases 2, 26, 39, 54, 77), and in 7 cases, the angina pectoris

/pectoris on effort was followed by angina pectoris occurring at rest. (Cases, 2, 15, 16, 26, 39, 54, 77).

In 3 cases, (Cases 8, 17, 42a), an episode of chest pain which, by its character and radiation suggested angina pectoris at rest, occurred in the week before the onset of myocardial infarction while, in Case 84., a short attack of crushing retrosternal pain which did not radiate, occurred a fortnight before the probable onset of myocardial infarction.

It is well known that premonitory chest pain is common before the development of acute myocardial infarction e.g., Mounsey (1951); Harris (1955). In this small series, the incidence of prodromal pain was higher than that observed by Harris (1955), who found that 23 out of 75 cases of acute myocardial infarction had premonitory chest pain which he classified into three groups:-

1) Angina of effort of recent onset which had recently increased in severity; 2) constant sternal pain, roughly simulating angina in its site and radiation and 3) attacks of sternal pain unrelated to exertion or emotion. The first two groups were common in the present series. Symptoms prodromal to acute myocardial infarction are of great potential value in the prophylaxis of the illness and are obviously of primary importance in its diagnosis.

b) Angina Pectoris at Rest, without Electrocardiographic Evidence of Acute Myocardial Infarction.

Cases of acute myocardial infarction, presenting with characteristic pain seldom give rise to diagnostic errors but typical and severe symptoms may be due to coronary artery atherosclerosis without myocardial infarction. (Paton, 1957). In such cases, electrocardiographic aid in diagnosis is essential. This is well illustrated in the present investigation in which, in 23 attacks of angina pectoris at rest, the differentiation between acute myocardial infarction and myocardial ischaemia could only be made after examination, often serial, of the electrocardiogram.

c) Determination of Time of Onset of Acute Myocardial Infarction.

In 46 out of 67 attacks of acute myocardial infarction there was no difficulty in determining the time of onset of acute myocardial infarction on clinical grounds but, in 21 attacks, the exact time of onset could not be determined on clinical grounds alone. In 10 of these 21 attacks, the

/the clinical picture had been unusual (Cases 19a,84) or angina had been present on effort or at rest before the patient's admission to hospital (11a, 15, 35, 39, 42a, 48, 54, 71). After examination of the electrocardiogram in these 10 attacks, it was felt that a fairly accurate estimation of the time of onset could be reasonably made.

In the remaining 11 attacks, which were all characterised by repeated severe praecordial pain over a period of several days, the exact time of onset could not be determined even after examination of the electrocardiogram. (Cases 14, 16, 28, 29, 43, 47a, 49, 51, 55, 56, 59).

These findings show that,in an appreciable number of attacks of acute myocardial infarction, the exact time of onset of the lesion cannot be determined because of the presence of premonitory or post infarction chest pain. The importance of this will become apparent in subsequent discussion.

d) Cases of Acute Myocardial Infarction presenting with breathlessness and other signs,but without pain.

Pain may not be a prominent symptom in acute myocardial infarction and, in 11 attacks in this series, there was no complaint of pain in the chest.

i) Left Ventricular Failure.

In 7 attacks the presenting symptom was acute and severe dyspnoea due to left ventricular failure.(Cases 10,19a, 19b, 36b, 37, 69, 84).

In 2 cases (10, 84) the patients described a sensation of retrosternal constriction during the attack of dyspnoea but, in Case 10., the history was considered unreliable as the symptoms of left ventricular failure and of cerebral thrombosis came on simultaneously. In Cases 69, and 36b., the gravity of the patients' illness probably accounts for the failure to elicit a history of chest pain. In 3 attacks, however, although dyspnoea was severe, there was no evidence of mental confusion and the patients denied having felt chest pain when directly questioned. (Cases 19a, 19b, 37). It should be noted also that signs of congestive cardiac failure were present in 5 of these 7 attacks of acute myocardial infarction, (Cases 19a, 19b, 37, 36b, 69).

ii) Cerebral Thrombosis.

In 2 attacks, acute myocardial infarction presented with signs of cerebral thrombosis and without chest pain. (

/pain. (Cases 10 and 22). In Case 22., vertigo was the earliest symptom and this was succeeded by the development of signs of cerebral thrombosis. There was no complaint of chest pain or dyspnoea but the history was considered unreliable because of the patient's disability and low intelligence.

iii) Marked Peripheral Vascular Failure.

In Case 13b., the patient did not complain of pain during an attack of myocardial infarction which proved fatal. The presenting signs and symptoms were those of progressive peripheral vascular failure and increasing mental confusion. The patient was extremely ill and it was considered that the history was unreliable under these circumstances. In Case 20b., the onset of acute myocardial infarction was marked by the sudden development of dyspnoea and marked peripheral vascular failure. The patient complained of paraesthesiae in his left hand,but not of pain. The severity of his illness, however, made accurate history-taking difficult. It is evident that chest pain is not an invariable accompaniment to acute myocardial infarction and that the illness may present with acute dyspnoea, profound circulatory failure or a cerebrovascular accident.

Therefore, in 11 out of 67 attacks of acute myocardial infarction, the patient did not complain of pain. In 2 of these attacks, a sensation of retrosternal constriction was described and,in one case, disagreeable paraesthesiae were felt in the left hand,and such symptoms should probably be regarded as pain equivalents. The commonest type of painless myocardial infarction was that in which the onset of the infarction was related to dyspnoea and was found in 7 out of the 67 attacks of infarction studied. Congestive cardiac failure was a common finding in this group of cases. East and his colleagues (1928) described 8 cases of this sort and Papp (1952) reported 3 similar cases in which orthopnoea, cyanosis and severe distress were present. It seems probable that chest pain is overshadowed by dyspnoea in such cases. Severe peripheral circulatory failure masked pain in 2 out of these 11 attacks of infarction. Disturbance of consciousness due to cerebral ischaemia accounts for the absence of pain in the remaining 2 attacks e.g., Papp (1952) described 5 cases, in whom myocardial infarction occurred without pain whose predominant symptom was faintness due to complete heart block. This short review of the history and clinical findings in 67 attacks of acute myocardial infarction reveals that the diagnosis of acute myocardial infarction on clinical grounds alone without the help of the electrocardiogram may be difficult especially in cases of severe myocardial ischaemia without accompanying myocardial infarction and in cases presenting without characteristic pain.

e) Cases in which Acute Myocardial Infarction was diagnosed on clinical grounds only.

While the inaccuracy inherent in the clinical diagnosis of acute myocardial infarction is recognised, in 7 out of the 67 attacks of infarction the diagnosis was considered to be certain on the basis of the history and clinical findings and electrocardiograms were not recorded. (Cases, 2, 4, 13b, 20b, 36b, 38, 77). Confirmation of the presence of myocardial infarction was obtained at post mortem examination in 4 of the 7 cases. (Cases, 2, 4, 36b, 77). In 3 of the 7 attacks (13b, 20b, 36b) the patients were being treated in hospital,having sustained acute myocardial infarction which had been confirmed electrocardiographically, when they developed fresh infarctions or extensions of previous myocardial infarctions. In the remaining attack (Case 38) the history, clinical findings were typical of acute myocardial infarction.

Therefore, there is good evidence that the clinical diagnosis in these 7 attacks of infarction was soundly based. In each of these attacks, the time of onset of the infarction could be accurately determined.

CLASSIFICATION OF THE CASES OF ACUTE MYOCARDIAL INFARCTION UNDER CONSIDERATION ACCORDING TO THE ELECTROCARDIOGRAPHIC FINDINGS AND A COMMENT ON THE ACCURACY OF ELECTROCARDIOGRAPHIC DIAGNOSIS.

The electrocardiogram was examined in 60 out of 67 attacks of acute myocardial infarction. The electrocardiographic findings and the maximal serum transaminase activity demonstrated in each case are presented in Tables XV., XVI., & XVII in Appendix III.

1) Transmural Myocardial Infarction (Table XV.)

In 45 out of 60 attacks the electrocardiogram showed changes diagnostic of acute transmural myocardial infarction.

2) Intramural Myocardial Infarction (Table XVI).

In 9 out of the 60 attacks the electrocardiogram was typical of acute intramural myocardial infarction.

3) Attacks in which the Electrocardiogram, though grossly abnormal, was at no time diagnostic of Acute Myocardial Infarction (Table XVII).

In 6 cases in which the diagnosis of acute myocardial infarction was considered certain, the electrocardiogram failed to show patterns diagnostic of acute myocardial infarction. (Cases, 6, 10, 11b, 18, 19b, 24). In all attacks, however, the electrocardiogram was abnormal and it is generally accepted that a multiple chest lead electrocardiogram does not remain normal after acute infarction. (Wood, 1955). Katz (1942) and Hill (1950) have stressed the need for serial electrocardiograms and multiple chest leads if the greatest accuracy in the electrocardiographic diagnosis of infarction is to be attained.

Three instead of the usual six praecordial leads were employed in this study and this practice led, in attack 19b., to uncertainty in the electrocardiographic diagnosis of extension of a previous infarction. It is very probable that, if the electrocardiogram had been repeated using the customary number of praecordial leads, no diagnostic doubt would have remained. In attack 11b., the electrocardiogram was technically unsatisfactory although suggestive of a recent posterior myocardial infarction and diagnostic of supra-ventricular tachycardia, and should have been repeated on the cessation of arrhythmia. In attack 18., the electrocardio-

/gram showed changes diagnostic of acute coronary insufficiency and an old anterior myocardial infarction but the patient died before further electrocardiograms were recorded. In attack 6., serial electrocardiograms showed changes highly suggestive of an extensive intramural myocardial infarction and widespread myocardial ischaemia, and diagnostic of heart block (2:1) but again the patient died before further electrocardiographic studies were made. In 2 attacks, (10 and 24) the electrocardiographic patterns of left bundle branch block were present. It is recognised that the electrocardiographic diagnosis of acute myocardial infarction may be difficult or impossible in the presence of such patterns.(Goldberger, 1953). For example, in Case 10., only minor sequential changes, possibly indicative of acute myocardial infarction were present while, in Case 24., there was no electrocardiographic evidence of acute myocardial infarction. Three of these six attacks proved fatal (, 6,11 18) and the presence of acute myocardial infarction was confirmed on post mortem examination in two caaes.(6 and 11).

Therefore, in 54 out of 60 attacks of acute myocardial infarction in which electrocardiograms were recorded the electrocardiogram showed changes diagnostic of acute myocardial infarction i.e., in 90% of the attacks. The degree of accuracy of electrocardiographic diagnosis is probably greater than is represented in this study. In two attacks, in which the electrocardiogram failed to confirm the diagnosis of infarction,the fault probably lay with the clinician in omitting to perform further adequate electrocardiographic studies, rather than with the electrocardiogram. This degree of electrocardiographic accuracy found, however, is of a similar order to that reported by Paton (1957) who, in a study of 97 necropsies on patients dying of acute myocardial infarction in whom electrocardiographic observations had been made, found the electrocardiogram to be accurate in 94% of cases. However, it is clear that in a small percentage, the electrocardiogram,although abnormal, does not become diagnostic of acute myocardial infarction and in such cases additional objective diagnostic help would be valuable.

THE RESULTS OF SERUM TRANSAMINASE ASSAY IN ACUTE MYOCARDIAL INFARCTION.

The results of serum transaminase assays following 67 attacks of acute myocardial infarction are presented below.

1) The Period of delay before Serum Transaminase Activity rises following Acute Myocardial Infarction.

In 17 attacks of acute myocardial infarction in which the exact time of onset had been established serum transaminase activity was determined within 6 hours of the onset of the attack and in all instances was found to be normal. Two of these attacks (Cases, 4 and 18) proved fatal before a rise in serum transaminase activity was demonstrated and, in Case 4., the diagnosis of acute myocardial infarction was confirmed at post mortem examination. In those attacks of myocardial infarction in which the time of onset of the infarction had been established with certainty the earliest increases in serum transaminase activity were found in Cases 20a and 71, 7 hours after the onset of the attack.

2) High levels of Serum Transaminase Activity following Acute Myocardial Infarction.

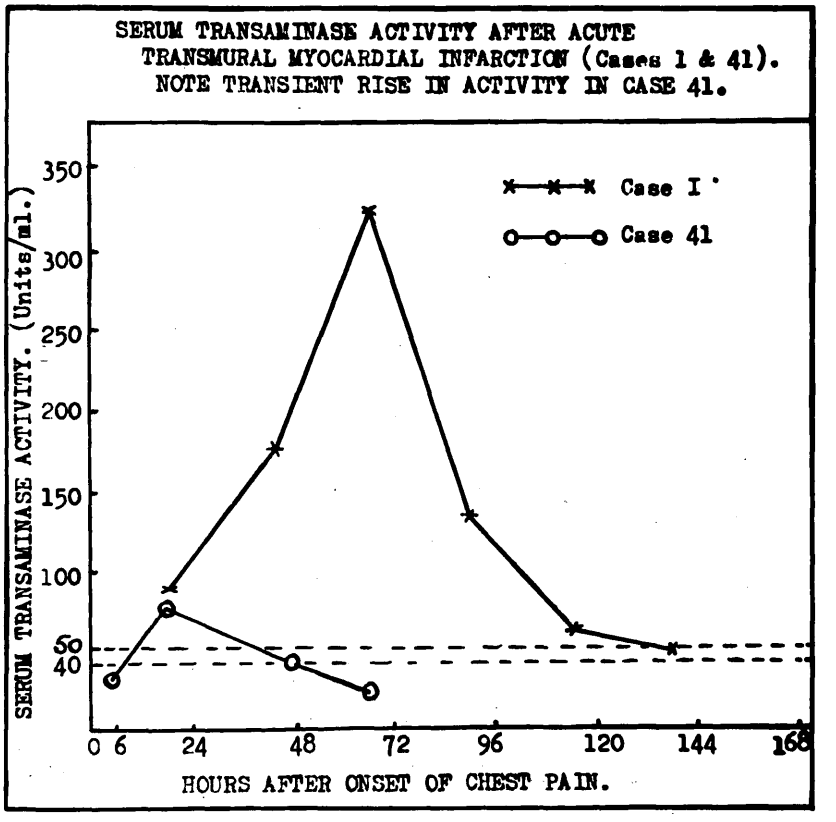
Attacks in which the diagnosis was based on the History, Clinical Findings and Electrocardiographic Patterns of Acute Myocardial Infarction.

---

a) In Acute Transmural Myocardial Infarction.

In 39 out of 45 attacks of acute transmural infarction, high levels of serum transaminase activity were demonstrated. (Table II, Appendix III). In 3 out of the 39 attacks only single specimens of serum were examined for transaminase activity 6 - 24 hours after the onset and in each of these attacks high levels of activity were found. In the remaining 36 attacks, serial assays were performed and peak levels of serum transaminase activity were reached 6 - 24 hours after the onset of illness in 10 attacks, 24 - 48 hours after the onset in 17 attacks and 48 - 72 hours after the onset in 4 attacks. In 5 attacks the first specimens of serum examined were withdrawn 72 - 144 hours after the onset of the illness and increased transaminase activity was demonstrated in these specimens. (Cases, 3, 9, 13a, 28, 40). In 13 attacks in which the assay was performed one week following the onset of the illness, high levels of transaminase activity were not found, although borderline levels of activity were found in 2 attacks.(Cases 1, 28). In 3 attacks, high levels of serum transaminase activity were demonstrated only in the 6 - 24

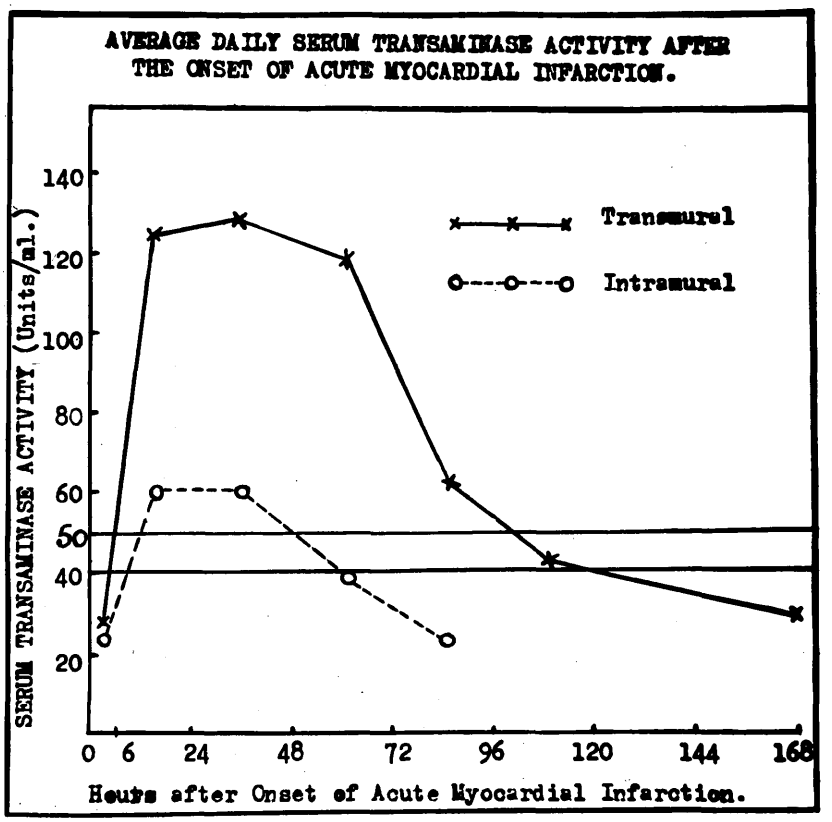
FIGURE I.


SERUM TRANSAMINASE ACTIVITY AFTER ACUTE TRANSMURAL MYOCARDIAL INFARCTION (Cases 1 & 41). NOTE TRANSIENT RISE IN ACTIVITY IN CASE 41.
SERUM TRANSAMINASE ACTIVITY. (Units/ml.)
350
300
250
200
150
100
50
40
Case I
Case 41
0 6 24 48 72 96 120 144 168
HOURS AFTER ONSET OF CHEST PAIN.

/6 - 24 hour period following the onset of infarction, subsequent assays showing borderline or normal levels of transaminase activity. (Cases 41, 42b, 47b). In one attack, (Case 48) serum transaminase activity was normal 6 - 24 hours after the onset of the illness but rose to high levels 24 - 48 hours after the onset of the illness. Figure I illustrates the variability of the duration of the rise in serum transaminase activity following acute transmural myocardial infarctions. It is seen that,in Case 1., peak levels of activity were reached 72 - 96 hours after the onset of the illness and that high levels were still present 5 days after the onset. In contrast, high levels of serum transaminase activity were found in Case 41, 6 - 24 hours after the attack, normal serum transaminase activity being found thereafter. High levels of serum transaminase activity were found in each of 33 attacks of acute transmural infarction in which serial assays were performed 6 - 24 hours and 24 - 48 hours after the onset of the attack. High levels of serum transaminase activity may persist for 6 days following acute transmural infarction, but it should be noted that high levels of activity were found in less in half the cases in whom the assay was performed 72 - 96 hours after the onset of the illness. (Table XVIII, Appendix III). The range of maximum serum transaminase activity in these attacks of acute transmural infarction was 62 - 493 units/ml. In 26 out of 39 attacks serum transaminase activity was found to be above 100 units/ml. In the other 13 attacks, serum transaminase activity did not rise above 100 units/ml.but., in 5 of these attacks, the first specimen of serum examined for transaminase activity was withdrawn at least 72 hours after the onset of the illness and it is, therefore, probable that maximum levels of activity were not present at this time. Therefore, in 8 attacks of transmural infarction, in which serum transaminase activity was estimated within 48 hours of the onset of the attack serum transaminase activity failed to rise above 100 units/ml.

The average daily serum transaminase activity in the 39 attacks of transmural infarction showing high levels of activity is illustrated in Figure II. The average transaminase activity was at normal levels in the period 0 - 6 hours following the onset of infarction and then quickly rose to high levels,which were maintained for 72 - 96 hours before falling to borderline levels in the period 96 - 120 hours after the onset of the infarction. By the end of the first week, the average activity had fallen to normal. The highest average serum transaminase activity was 130 units/ml. and was present 24 - 48 hours after the onset of infarction.

FIGURE II.

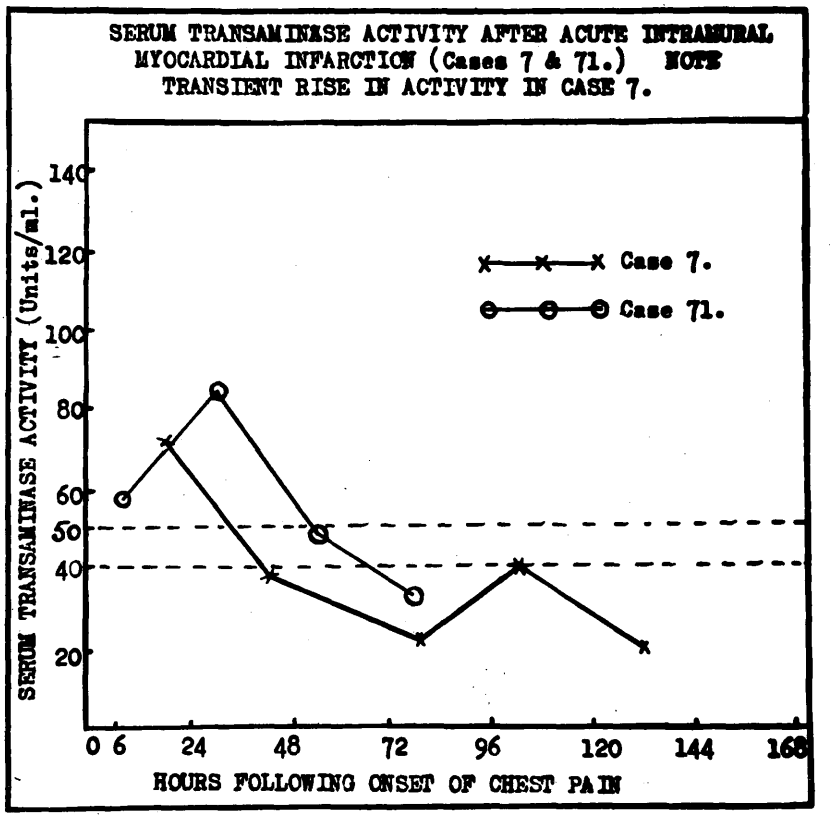

AVERAGE DAILY SERUM TRANSAMINASE ACTIVITY AFTER THE ONSET OF ACUTE MYOCARDIAL INFARCTION.
SERUM TRANSAMINASE ACTIVITY (Units/ml.)
140
120
100
80
60
50
40
20
Transmural
Intramural
0
6
24
48
72
96
120
144
168
Hours after Onset of Acute Myocardial Infarction.

b) In Acute Intramural Myocardial Infarction.

In 6 out of 9 attacks of acute intramural myocardial infarction serum transaminase activity rose to high levels. In these 6 attacks, serial assays of transaminase activity were performed. The results are presented in Table III, Appendix III.

The results of serial estimations of the transaminase activity in these attacks demonstrate the importance of performing the assay in the periods 6 - 24 hours and 24 - 48 hours after the onset of the attack, since high levels of activity were reached in each of the 6 attacks during these times. In 2 attacks (Cases 7, 25a), high serum transaminase activity was found 6 - 24 hours after the onset of the attack only, subsequent assays of transaminase activity showing normal levels. High levels of serum transaminase activity were not found more than 48 hours after the onset of these attacks, (Table XIX, Appendix III), although borderline levels of activity were demonstrated in 3 attacks 48 - 72 hours following the onset of illness. (Cases 25b, 39, 71). Figure III illustrates the short duration of increased serum transaminase activity found following acute intramural myocardial infarction. In Case 71., high levels of transaminase activity fell to borderline levels 48 - 72 hours after the onset. In case 7., high levels of activity were demonstrated 17 hours after the onset only. The range of maximum serum transaminase activity in the 6 attacks in this group was 55 - 85 units/ml. Serum transaminase activity did not rise above 100 units/ml. in any case, but peak levels may not have been detected in 2 attacks (Cases 39, 43), in which the assay was not performed in both the 6 - 24 hour and 24 - 48 hour periods after the onset of the illness. The maximum levels of transaminase activity observed were lower than those found in most cases of acute transmural myocardial infarction, but resembled those found in 8 cases of the latter group in which serum transaminase activity failed to rise above 100 units/ml. The average daily serum transaminase activity in attacks of acute intramural myocardial infarction, which showed a rise in serum activity, is illustrated in Figure II., which shows that serum transaminase activity was at normal levels 0 - 6 hours after the onset of infarction, quickly rose to high levels which were maintained for 24 - 48 hours following the onset of the illness, returned to normal levels 48 - 72 hours after the onset of myocardial infarction and thereafter remained normal. The highest average daily levels were 60 units/ml. and these were present in both the 6 - 24 and 24 - 48 hour periods following infarction.

FIGURE III.


SERUM TRANSAMINASE ACTIVITY AFTER ACUTE INTRAMURAL MYOCARDIAL INFARCTION (Cases 7 & 71.) NOTE TRANSIENT RISE IN ACTIVITY IN CASE 7.
SERUM TRANSAMINASE ACTIVITY (Units/ml.)
140
120
100
80
60
50
40
20
Case 7.
Case 71.
0 6 24 48 72 96 120 144 168
HOURS FOLLOWING ONSET OF CHEST PAIN

c) In Acute Myocardial Infarction in which the diagnosis was based on the history, clinical findings and electrocardiographic patterns which, though grossly abnormal, were at no time diagnostic of Acute Myocardial Infarction.

In 6 attacks of acute myocardial infarction the electrocardiogram, although abnormal, was at no time diagnostic of acute myocardial infarction. In 5 out of these 6 attacks, serum transaminase activity rose to high levels. The results of serial serum transaminase estimations in these 5 attacks are shown in Table IV,(Appendix III). The time/transaminase curve in these attacks resembled that already described in those attacks in which the electrocardiogram confirmed the diagnosis of acute myocardial infarction. The importance of performing assays of serum transaminase activity 6 - 24 hours following the onset of the attack is emphasised since, in Case 10., the only high level of activity demonstrated occurred in this period. The range of maximum serum transaminase activity was 60 - 220 units/ml.

d) Attacks in which the diagnosis of Acute Myocardial Infarction was based on the history and clinical findings only.

These 7 attacks of acute myocardial infarction have already been described. In 6 out of these 7 attacks high levels of serum transaminase activity were demonstrated and the results of transaminase assay in attacks, showing increased transaminase activity, are presented in Table V, Appendix III. Serial assays over a period of days were performed in only one attack (Case 20b). In 5 out of these attacks, high levels of transaminase activity were found 6 - 24 hours following the onset of the attack. In the remaining attack,a high level of activity was demonstrated 24 - 48 hours after the onset of the illness. The exact time of onset was known in each attack. The range of maximum serum transaminase activity observed was 73 - 620 units/ml. The highest level of transaminase activity recorded in 67 attacks of acute myocardial infarction was 620 units/ml. and was found in Case 13b.

3) Normal or Borderline Serum Transaminase Activity following Acute Myocardial Infarction.

In 11 out of 67 attacks of acute myocardial infarction high levels of serum transaminase activity were not detected following the onset of the attacks. (Cases, 4, 8, 16, 18, 19a., 29, 49, 51, 54, 56, 84). The results of transaminase assay in these attacks are presented in Table VI, Appendix III. It is emphasised that the time after the onset of severe symptoms which occasioned the patient's admission to hospital recorded in Table VI., is not identical with the time after the onset of

/of acute myocardial infarction. In all except 2 attacks, which proved rapidly fatal, (Cases 4 and 18)., serial and duplicate transaminase assays were made. These attacks will now be considered and the probable reasons for failure to demonstrate increased serum transaminase activity in them discussed.

In 2 attacks (Cases 4, 18) serum transaminase assay was performed within 6 hours following acute myocardial infarction that is, in the period before a rise in serum transaminase activity could be expected. These attacks proved quickly fatal and serial estimations could not be performed.

In 5 out of 45 attacks of acute transmural myocardial infarction, failure to demonstrate increased serum transaminase activity following myocardial infarction was considered to be due to late sampling of the patient's serum following the attack. (Cases 19a, 29, 51, 56, 84). In 2 of these 5 attacks, (19a, 84) the patients had not been admitted to hospital until 72 hours after the onset of the illness. In the remaining 3 attacks, it was impossible to determine the time of onset of acute myocardial infarction with certainty, (Cases 29, 51, 56) but, after consideration of all available clinical and electrocardiographic evidence, it was thought probable that acute myocardial infarction had occurred 4, 5 and 6 days respectively before the patient's admission to hospital. It was considered that attacks of angina pectoris at rest following acute myocardial infarction had prompted the patient's admission to hospital. In one attack of acute transmural myocardial infarction borderline levels of serum transaminase activity were found shortly after the patient's admission to hospital. (Case 49). Acute transmural myocardial infarction was presumed to have occurred four days before the patient's admission to hospital, and the borderline levels of serum transaminase activity to represent previously high levels of activity which were falling to normal. An equally valid explanation of the borderline increase in serum transaminase activity is that it was the result of a severe attack of angina pectoris at rest which occurred 13 hours before serum transaminase activity was measured since, as will be shown later, borderline levels of activity may occasionally follow such attacks. An error in technique in the performance of the test can probably be excluded since other tests performed on the same day on specimens of serum from other patients suffering from acute myocardial infarction revealed high levels of transaminase activity.

In 3 out of 9 attacks of acute intramural myocardial infarction normal transaminase activity was found. (Cases 8, 16, 54). In 2 of these 3 attacks of intramural myocardial infarction failure to detect increased serum transaminase

/transaminase activity was ascribed to late sampling of the patient's serum after the onset of the illness. In Case 8., the first serum transaminase assay was performed 54 hours and, in Case 54., 6 days after the onset of intramural myocardial infarction.

In the remaining attack (Case 16), normal serum transaminase activity was found although the assay had been performed 6 and 28 hours following the probable onset of myocardial infarction. The peak level of serum transaminase activity may have been missed since the first assay was performed at a time when a rise in activity could not be expected and the second assay was delayed until 28 hours after the onset of the illness. The other explanation which is equally likely is that serum transaminase activity failed to rise to high levels following acute intramural myocardial infarction. Technical errors in the performance of the assays in this case are considered unlikely since high levels of serum transaminase activity were demonstrated in other cases on the same day.

THE RESULTS OF POST MORTEM AND HISTOLOGICAL EXAMINATION IN CASES OF ACUTE MYOCARDIAL INFARCTION AND ANGINA PECTORIS AT REST.

It is obviously of great importance to obtain autopsy confirmation of the presence of acute myocardial infarction in the cases studied, especially those cases in which normal transaminase activity was found or in which the electrocardiogram failed to show patterns diagnostic of acute myocardial infarction and also in which the diagnosis had been made on clinical grounds alone. It is equally important in cases of angina pectoris at rest to demonstrate, at autopsy, the absence of a related acute myocardial infarction. Ideally, this latter aspect of serum transaminase activity should be studied in patients who have had symptoms of severe angina pectoris at rest and who have died from intercurrent disease shortly after serum transaminase assays have been performed. Such an opportunity did not arise in this investigation,but three patients who died of acute myocardial infarction had had attacks of severe angina pectoris at rest,following which serum transaminase activity had been studied. (Cases 2, 11, 77).

21 out of 57 patients died as a result of acute myocardial infarction. (Cases 1, 2, 3, 4, 6, 11, 12, 13, 15, 18, 20, 34, 35, 36, 38, 48, 50, 54, 59, 69, 77). In Cases 1 and 3., the electrocardiogram was diagnostic of acute transmural myocardial infarction and high levels of serum transaminase activity were demonstrated. The presence of acute myocardial infarction was confirmed at autopsy and microscopic examination of the myocardium showed changes diagnostic of acute myocardial infarction. In Case 4, acute myocardial infarction was diagnosed on clinical grounds. The patient died 4 hours after the onset of the attack and serum transaminase activity was normal 1¼ hours after the onset. Post mortem examination revealed a recent thrombus in the posterior coronary artery and histological examination of the myocardium supplied by this vessel revealed the earliest changes of acute myocardial infarction. This is an important observation since it shows that normal serum transaminase activity may be expected in the first hours following acute myocardial infarction.

In Case 36., the patient had sustained two attacks of acute myocardial infarction, there being an interval of 6 days between the attacks. After the first attack (36a) the electrocardiogram was diagnostic of acute transmural myocardial infarction and high levels of serum transaminase activity were present following this attack, which fell to normal levels 84 hours after the onset of this illness. The second attack (36b) was followed by a rise in serum transaminase activity to high levels, but an electrocardiogram was not

/not performed. Post mortem examination revealed two areas of fresh myocardial infarction of ages appropriate to the rises in transaminase activity observed.

In Case 11, two attacks of acute myocardial infarction were studied. In the first attack (11a) the electrocardiogram showed changes typical of an acute transmural anterior myocardial infarction and an old posterior myocardial infarction, and serum transaminase activity was increased to high levels. In the second attack (11b) which occurred 4 days after the first attack, when serum transaminase levels had returned to normal, the electrocardiogram was suggestive but not diagnostic of a recent acute posterior myocardial infarction, and serum transaminase activity following the onset of this illness rose from normal to high levels. Post mortem examination confirmed the presence of recent infarction, of several days' duration, of the anterior and posterior walls of the left ventricle and of the interventricular septum. An attack of angina pectoris at rest occurred in this case less than 2 days before death and lasted for 1½ hours but was not followed by increased serum transaminase activity. Unfortunately, electrocardiograms were not recorded following this attack of chest pain. There was no autopsy evidence of a very recent infarction which might be related in time to this attack of angina pectoris.

In Case 2., acute myocardial infarction was diagnosed on clinical grounds alone. High levels of serum transaminase activity were present following the attack. Post mortem examination revealed a recent acute infarction of the myocardium with acute pericarditis. In this case, very severe attacks of angina pectoris at rest had occurred 18 days before the onset of the acute myocardial infarction demonstrated at autopsy. Following these severe attacks of pain there was no electrocardiographic evidence of recent acute myocardial infarction, although there was evidence of an old anterior myocardial infarction. Serum transaminase activity was increased to borderline levels following these frequent attacks of angina pectoris at rest. There was no histological evidence of acute myocardial necrosis which could be related to the rise in transaminase activity found after angina pectoris at rest but an area of recent myocardial necrosis might be easily overlooked in a heart showing gross atheroma of the coronary arteries and gross ischaemic fibrosis of the myocardium, since the whole myocardium was not examined histologically.

In Case 6., the history and clinical findings were typical of acute myocardial infarction but serial electrocardiograms did not show changes typical of acute myocardial infarction, although they were very suggestive of acute posterior myocardial infarction. High levels of serum transaminase activity were demonstrated following the onset of the illness and post mortem examination confirmed the presence of acute myocardial infarction.

In Case 77., the diagnosis of acute myocardial infarction was made on clinical grounds only and high levels of serum transaminase activity were found after the onset of the illness. Post mortem examination confirmed the presence of acute myocardial infarction of about 24 hours' duration. 11 days before the onset of this acute myocardial infarction, the patient had suffered an attack of angina pectoris at rest which lasted for eight hours. The electrocardiogram following this attack showed the changes of acute coronary insufficiency but no evidence of acute myocardial infarction and serum transaminase activity was demonstrated to be normal 36 and 60 hours after this attack of chest pain. Although fibrosis of the posterior wall of the left ventricle was noted on autopsy, there was no evidence, on macroscopic examination of the heart, of a myocardial infarction which might be related to this attack of angina pectoris at rest. Unfortunately, histological examination of the myocardium was not made. The liver was examined histologically in 7 out of these 8 cases. No abnormality of liver structure was found in Case 4 in which the disease had proved fatal, within 4 hours. In 5 cases, histological changes indicative of moderate chronic venous congestion of the liver were present.(Cases 1, 3, 6, 11, 36). In 1 case, (Case 2) the histological changes were those of severe chronic venous congestion. There was no evidence of centrilobular necrosis of liver in any of the cases examined.

Therefore, pathological confirmation of the occurrence of acute myocardial infarction was obtained in 10 attacks of acute myocardial infarction. In 2 of these attacks, the electrocardiogram had not been diagnostic of acute myocardial infarction. (Attacks 6, 11b) and in 3 attacks the diagnosis had been made on clinical grounds alone. (Attacks 2, 36b, 77). In 9 of these 10 attacks high levels of serum transaminase activity were present following their onset. In one attack, serum transaminase activity was normal 1¼ hours after the onset confirming that a delay occurs before serum transaminase activity increases and that the assay is unlikely to be of diagnostic help if performed in the first hours after acute myocardial infarction. There was, therefore, good agreement between the results of serum transaminase assay and autopsy findings.

The post mortem findings in cases of angina pectoris at rest suggest that myocardial ischaemia unaccompanied by myocardial infarction does not result in high levels of serum transaminase activity. The autopsy evidence in this group of cases is not as convincing as that found in acute myocardial infarction. The unsuitability of the cases of angina pectoris at rest studied has already been discussed. The significance of borderline levels of transaminase activity demonstrated in Case 2., following frequent attacks of anginal pain is not clear but it is pointed out that myocardial necrosis was not finally excluded. Chronic venous congestion

/congestion of the liver was found in 7 out of the 8 cases of acute myocardial infarction examined at autopsy. Centrilobular necrosis of the liver was not found in any case.

EVIDENCE OF HEPATIC DYSFUNCTION IN ACUTE MYOCARDIAL INFARCTION AND AN INVESTIGATION INTO THE RELATIONSHIP BETWEEN HEPATIC DYSFUNCTION AND SERUM TRANSAMINASE ACTIVITY.

Evidence has been presented that serum transaminase may possibly be excreted by the biliary route and that chronic venous congestion of the liver is a commonautopsy finding in acute myocardial infarction. It was, therefore, decided to examine hepatic function in acute myocardial infarction to see if there was any relationship between hepatic dysfunction and serum transaminase activity in this disease. In 19 attacks of acute myocardial infarction, tests of the liver function and serum transaminase assays were performed on the same specimens of blood. (Attacks 1, 3, 5, 7, 8, 10, 11a, 11b, 12, 15, 16, 17, 25b, 26, 27, 31a, 31b, 48, 69).

Four attacks of acute intramural myocardial infarction were studied (7, 8, 16, 25b), and the results of liver function and serum transaminase assays are presented in Table XI, (Appendix III). There was no evidence of hepatic dysfunction in two of these four attacks (Attacks, 7 and 8). In Attack 8., serum transaminase activity was normal, due to late sampling of the serum following the attack while, in Attack 7., a transient rise of serum transaminase activity to high levels was observed. In the other two attacks, (16 and 25b), there was evidence of hepatic dysfunction, serum bilirubin and zinc turbidity levels being elevated in both attacks. In Attack 16., serum transaminase activity was normal although there was evidence of liver dysfunction. The probable reasons for failure to demonstrate increased serum transaminase activity in this attack have already been discussed. In Attack 25b., high levels of serum transaminase activity were demonstrated for 36 hours after the onset of the illness when there was no evidence of hepatic dysfunction. These high levels of activity fell to normal 84 hours after the onset of the illness when the results of tests of liver function were abnormal. These results suggest that increase in serum transaminase activity in acute intramural myocardial infarction is not the result of hepatic dysfunction.

Serial assays of liver function and serum transaminase activity were performed in 2 attacks of acute myocardial

/myocardial infarction, in which the electrocardiogram was at no time diagnostic of acute myocardial infarction, (Attacks 10, 11b). The results of these examinations are presented in Table XII, (Appendix III). In attack 10., a transient rise in serum transaminase activity to high levels was demonstrated in the absence of evidence of hepatic dysfunction and, in Attack 11b., serum transaminase activity rose to high levels although a positive Van den Bergh reaction was the only abnormality found in serial tests of liver function. These findings suggest that in these attacks increased serum transaminase activity was not due to disorder of the liver.

Tests of liver function and serum transaminase assays were performed in 13 attacks of acute transmural myocardial infarction and the results of these examinations are presented in Table X, (Appendix III). In 3 out of these 13 attacks there was no evidence of hepatic dysfunction. (13, 48, 69). In attacks 48 and 69., zinc turbidity levels were increased which, in the absence of other abnormalities in tests of liver function, were interpreted as evidence of an increase of the gamma globulin fraction of the plasma proteins, which may be due to lesions other than hepatic. In these 3 attacks, high levels of serum transaminase activity were demonstrated. In the remaining 10 attacks of acute transmural myocardial infarction, hyperbilirubinaemia was found which was accompanied in 2 attacks by high levels of zinc turbidity. (Attacks 5, 27). In 9 out of these 10 attacks serial assays of liver function and serum transaminase activity were performed. High levels of serum transaminase activity were demonstrated in 5 out of 9 attacks before there was evidence of liver dysfunction. (Attacks 3, 11a, 12, 27, 31b). Normal serum transaminase activity was found in the presence of abnormalities of liver function in 2 attacks. (5, 17). It is inferred from these findings that increased serum transaminase activity following acute transmural myocardial infarction is not the result of hepatic dysfunction.

The possibility that impaired excretion of serum transaminase consequent to liver damage might account for the longer duration of high levels of serum transaminase activity following acute transmural myocardial infarction is next considered since it was noted that, in those cases in which hyperbilirubinaemia and high levels of serum transaminase activity were found, serum transaminase levels tended not to fall to normal as rapidly as in those cases in which increased serum transaminase activity was demonstrated without hyperbilirubinaemia. Maximum serum transaminase activity was found when abnormality in tests of liver function was most marked in 3 attacks, (5, 12, 31a) but in 4 attacks serum transaminase activity was falling from peak levels when abnormalities in the tests of liver function had become more marked. (3, 26, 27, 31b). There is, therefore, no constant

/constant relationship between maximum serum transaminase activity and maximum disorder of hepatic function. However, in one patient in whom repeated bromsulphalein tests of liver function were performed, interesting results relevant to this problem were obtained. (Case 26). In this case, a bromsulphalein test was performed with normal result following an attack of angina pectoris at rest when serum transaminase activity was normal. Three days later, the patient developed acute transmural myocardial infarction. High levels of serum transaminase activity and marked retention of the dye, indicative of severe liver impairment, were demonstrated 30 hours after this attack. On the 7th.day after the attack, when signs of mild congestive cardiac failure were present, serum transaminase activity had returned to normal although a bromsulphalein test revealed moderate retention of the dye, indicative of continuing hepatic insufficiency. These results suggest that hepatic impairment, although not the cause of increased serum transaminase activity following acute myocardial infarction, may possibly impede the excretion of the enzyme through the liver and, in this way, contribute to the maintenance of high levels of serum transaminase activity for several days.

THE CORRELATION BETWEEN THE DEGREE OF PERIPHERAL VASCULAR FAILURE AND THE LEVEL OF SERUM TRANSAMINASE ACTIVITY FOUND FOLLOWING ACUTE MYOCARDIAL INFARCTION.

The degree of peripheral vascular failure, using clinical criteria, was assessed in 67 attacks of acute myocardial infarction. These assessments are included in individual case histories in Appendix II. There was no evidence of peripheral vascular failure during the period of observation in 20 out of 67 attacks of acute myocardial infarction. (Attacks 8, 9 11b, 14, 16, 19a, 25a, 25b, 28, 29, 37,41,42b, 43, 47a,49,51, 54, 56, 84). A minimal degree of peripheral vascular failure was present in 25 attacks of acute myocardial infarction.(Attacks 2, 7, 10, 11a, 15, 19b, 22, 24, 25c, 31b,36a, 36b, 39, 40,42a, 44, 45, 46, 47b, 48, 55, 69, 71, 77, 122). A minimal to moderate to extremely marked degree of peripheral vascular failure was present in the remaining 22 attacks. (Attacks 1, 3, 4, 5, 6, 12, 13a, 17, 18, 20a, 20b, 21, 23, 26, 27, 31a, 34, 35, 38, 50, 59). Therefore, in 45 out of 67 attacks of acute myocardial infarction there was either no evidence of peripheral vascular failure, or it was present to a minimal degree. A minimal to moderate to extremely marked degree of peripheral

/peripheral vascular failure was present in the remaining 22 attacks.

In 23 attacks of acute transmural infarction in which peripheral vascular failure was absent or present only to a minimal degree and in which a rise of serum transaminase activity was demonstrated, the average maximum serum transaminase activity was 116 units/ml., the range of maximum activity being 57 - 313 units/ml.(Attacks 9, 11a, 14, 15, 22, 25c, 28, 31b, 36a, 37, 40, 41, 42a, 42b, 44, 45, 46, 47a,47b, 48, 55, 69,122.) In 16 attacks of acute transmural myocardial infarction in which a minimal to extremely marked degree of peripheral vascular failure was present and in which a rise in serum transaminase activity was recorded, the average maximum serum transaminase activity was 214 units/ml., the range of maximum activity being 80 - 493 units/ml. (Attacks 1, 3, 5, 12, 13, 17, 20a, 21, 23, 26, 27, 31a, 34, 35, 50, 59).

In 6 attacks of acute intramural infarction in which a rise in serum transaminase activity was demonstrated peripheral vascular failure was absent in 3 attacks,(25a,25b, 43), and present to a minimal degree in 3 attacks, (7,39,71). More severe degrees of peripheral vascular failure were not observed. In this small number of attacks, the average minimum serum transaminase activity was 68 units/ml., the range of maximum activity being 55 - 185 units/ml.

In 11 out of 13 attacks of acute myocardial infarction in which the diagnosis was based either on clinical findings alone or on clinical findings together with electrocardiographic patterns which, although abnormal, were at no time diagnostic of acute myocardial infarction, high levels of serum transaminase activity were demonstrated. In 7 of these 11 attacks, peripheral vascular failure was absent or present to a minimal degree only. (Attacks 2, 10, 11b, 19b, 24, 36b, 77). In these 7 attacks, the average maximum serum transaminase activity was 101 units/ml., the range of maximum activity being 60 - 220 units/ml. In 4 out of 11 attacks, in this group, marked to extremely marked peripheral vascular failure was present and the average maximum serum transaminase activity in these cases was 248 units/ml., the range of maximum activity being 90 - 620 units/ml.

Therefore, in 36 attacks of acute myocardial infarction in which peripheral vascular failure was absent or present to a minimal degree and in which increased serum transaminase activity was found, the average maximum serum transaminase activity was 95 units/ml. In 20 attacks of acute myocardial infarction in which a rise of serum transaminase activity was demonstrated and in which a moderate to extremely marked degree of peripheral vascular failure was present, the average maximum serum transaminase activity was 231 units/ml. These figures must be accepted with reserve since the number of attacks studied was small and in several attacks it was not

/not certain that peak transaminase activity was measured, due either to late sampling of the patient's serum or to the early death of the patient. It is suggested , however, that they provide evidence of statistical correlation of serum transaminase activity to the degree of peripheral vascular failure developing after acute myocardial infarction, although it is clear that, in individual cases, the level of serum transaminase activity cannot be accepted as evidence of the degree of peripheral vascular failure present.

THE RESULTS OF SERUM TRANSAMINASE ASSAY AND ELECTROCARDIOGRAPHIC EXAMINATION IN CASES OF ANGINA PECTORIS AT REST.

Serial assays of transaminase activity were performed following 25 attacks of angina pectoris at rest occurring in 20 patients. The results of these assays are presented in Table VII, (Appendix III).

In each of these attacks the site, character and radiation of the chest pain was typical of angina pectoris. In 12 out of 25 attacks, chest pain was present for periods varying from 10-45 minutes. (Attacks, 7, 8, 26, 30a, 52, 57, 58a, 58b, 60, 61, 65). In 12 out of the 25 attacks, chest pain lasted for an hour or more.(Attacks 2, 11, 25d, 25e, 25f, 32, 33, 62, 67, 68a, 68b, 77). In the remaining attack, (30b), the duration of anginal pain was not recorded but the pain was severe and presumably prolonged since it required morphine sulphate for its relief. Acute myocardial infarction was suspected in these cases.

In 3 attacks the diagnosis of angina pectoris without myocardial infarction was made on clinical grounds. (Attacks 7, 11, 61. In attacks 7 and 11., electrocardiograms were not performed. In attack 11, paroxysmal auricular fibrillation was present. In attack 61., the electrocardiogram did not finally exclude a fresh myocardial infarction but, in the absence of serial electrocardiograms, the diagnosis of angina pectoris was made on clinical grounds. In the remaining 22 attacks, adequate electrocardiographic studies were made and in these attacks there was no electrocardiographic evidence of fresh myocardial infarction following the onset of anginal pain.

High levels of serum transaminase activity were not found following these 25 attacks of angina pectoris and serum transaminase activity remained normal in 22 out of the 25 attacks. However, in 3 out of the 25 attacks, borderline levels of transaminase activity were demonstrated following the onset of pain. (Attacks 2, 25e, 68b).

In attacks 2 and 25e., an increase in serum transaminase activity to borderline levels followed repeated and severe attacks of chest pain and it was impossible to relate the rise in transaminase activity to one particular attack of pain. In both these attacks there was electrocardiographic evidence of previous myocardial infarctions, but there was no evidence of a fresh myocardial infarction on serial examination of the electrocardiogram following the onset of severe chest pain. In attack 68b., borderline levels of serum transaminase activity were demonstrated following anginal pain of 3 hours' duration, the rise occurring 24 hours after the onset of the pain. The electrocardiogram following this attack showed no gross abnormality or evidence of myocardial infarction, although electrocardiographic changes, suggestive of myocardial fibrosis, were present. These 3 attacks belong to the group in which chest pain lasted for more than one hour but there seems to be no clear relationship between the duration of chest pain and a borderline increase in serum transaminase activity since normal serum transaminase activity was demonstrated in attacks 25d, and 77, in which anginal pain lasted for 8 hours, and in attack 32, in which pain was present for 14 hours.

Electrocardiographic observations were made following 23 attacks of angina pectoris and a high incidence of abnormality in the electrocardiogram was found.

In 9 out of 23 attacks there was electrocardiographic evidence of previous myocardial infarction, (2, 8, 25d, 25e, 25f, 30a, 30b, 32, 33), and the presence of a previous myocardial infarction was suspected in attacks 57 and 62. It is generally agreed that the electrocardiographic diagnosis of acute myocardial infarction may be very difficult in the presence of electrocardiographic changes due to previous myocardial infarction. The failure to demonstrate high levels of serum transaminase activity in these 9 attacks and the presence of normal transaminase activity in 7 out of the 9 attacks is of great interest and potential practical importance. The demonstration of borderline levels of activity in 2 attacks in this group has already been reported. (Attacks 2, and 25e).

The electrocardiographic patterns of acute coronary insufficiency were found in 6 out of 23 attacks of angina pectoris. (Attacks 53, 58a, 61, 65, 77). Normal serum transaminase activity was demonstrated following each of these attacks. In 7 out of 23 attacks of angina pectoris electrocardiographic changes indicative of myocardial ischaemia were present. (Attacks 26, 30a, 30b, 32, 33, 52, 60), but were associated in each instance with normal serum transaminase activity. Normal serum transaminase activity was also associated with the electrocardiographic patterns of left ventricular strain in attack 52 and with those of left ventricular hypertrophy and strain in attacks 58a, 58b, and 60..

THE RESULTS OF SERUM TRANSAMINASE ASSAY, ELECTROCARDIOGRAPHIC EXAMINATION, POST MORTEM AND LIVER FUNCTION TESTS IN CARDIOVASCULAR CONDITIONS OTHER THAN ACUTE MYOCARDIAL INFARCTION OR ANGINA PECTORIS AT REST.

The detailed results of serum transaminase assays, electrocardiographic examinations, post mortem examinations and liver function tests in the cardiovascular conditions considered below are included in individual case histories in Appendix II.

1) Acute left ventricular and congestive cardiac failure due to ischaemic heart disease.

It has been shown that acute myocardial infarction not uncommonly presents with signs of left ventricular failure and that congestive cardiac failure may accompany or follow acute myocardial infarction. It is important, therefore, to examine serum transaminase activity in cases of left ventricular and congestive cardiac failure which are unrelated to acute myocardial infarction or complicated by other lesions such as cardiac arrhythmias or thrombo-embolic phenomena etc., which may, as will be demonstrated later, be associated with increased transaminase activity.

4 cases of left ventricular failure were studied (Cases 64, 70, 72, 74). The causal lesion in each case was considered to be ischaemic heart disease, hypertension being a complicating factor in Cases 64 and 70. Serum transaminase activity was demonstrated to be normal in these 4 cases. There was no electrocardiographic evidence of acute myocardial infarction in any of the cases. Electrocardiographic patterns diagnostic of left ventricular strain were present in two cases (64 and 70), and could not be excluded in Case 74., where the effect of digitalis therapy made interpretation of the electrocardiogram difficult. In Case 64., changes in the electrocardiogram were diagnostic of antero-lateral ischaemia and, in Case 72., suggested chronic coronary artery disease. In Case 64., essential hypertension had entered the malignant phase and this diagnosis was confirmed on post mortem examination. It should be noted that, while gross coronary atherosclerosis was demonstrated at autopsy, there was no evidence of acute myocardial infarction.

3 cases of congestive cardiac failure due to ischaemic heart disease were studied (cases 72, 73, 114), and serum transaminase activity was normal on serial examination in each case. The findings in case 72., in which left ventricular failure was also present, have already been discussed. There was no clinical or electrocardiographic evidence of acute myocardial infarction in these cases. The electrocardiograms, in case 73., showed changes diagnostic of an old posterior

/posterior myocardial infarction and left ventricular strain. Electrocardiographic patterns, diagnostic of left bundle branch block, were present in case 114. These results suggest that left ventricular and congestive cardiac failure, when not associated with cardiovascular lesions known to result in increased serum transaminase activity, are associated with normal levels of serum transaminase activity.

2) Ischaemic Heart Disease.

Serum transaminase activity was normal on repeated examination in 7 patients who suffered from ischaemic heart disease (cases 64, 70, 72, 73, 74, 75,114). In these cases, there was no clinical or electrocardiographic evidence of recent myocardial infarction and there had been freedom from attacks of angina pectoris at rest before the assays were performed. In case 75., there was electrocardiographic evidence of antero-septal myocardial ischaemia. Signs of heart failure were present in the remaining 6 cases and the results in these cases were discussed in the preceding section. These results suggest that normal serum transaminase activity is present in patients suffering from ischaemic heart disease if there has been no recent acute myocardial infarction or attack of angina pectoris at rest.

3) Essential Hypertension.

Serum transaminase activity was demonstrated to be normal on repeated examination in four patients in whom essential hypertension was found. (cases 64, 70, 98, 131). The diastolic blood pressure in these cases was above 110 mm.Hg. There was no clinical or electrocardiographic evidence of acute myocardial infarction. The results of examinations in cases 64 and 70 have already been discussed in sections 1 and 2 while those in cases 98 and 131 are presented in section 8., since there was evidence, in both cases, of acute cerebrovascular disease. The results of serum transaminase assay in hypertension suggest that this condition is associated with normal serum transaminase activity.

4) Chronic Cor Pulmonale.

Serum transaminase assays were performed in 4 cases of chronic cor pulmonale in which there was no clinical or electrocardiographic evidence of acute myocardial infarction. (cases 63, 101, 102, 128). Congestive cardiac failure was present in cases 63 and 128 and marked bronchospasm in cases 101 and 102. An electrocardiogram was not performed in case 63. Electrocardiographic patterns of right ventricular strain were present in cases 101 and 128, In Case 102., electrocardiographic changes diagnostic of acute

/acute coronary insufficiency and lateral myocardial infarction of indeterminate age were observed. Serum transaminase activity was normal on repeated examination in these cases during the acute phase of the illness which suggests that cardiac disease of this origin and severe bronchospasm are associated with normal serum transaminase activity.

5) Acute Rheumatic Fever.

Serum transaminase activity was normal on repeated examination during the acute phase of 2 cases of acute rheumatic fever and in the first days of aspirin therapy of the disease. (Cases 85 and 86). There was no clinical or electrocardiographic evidence of acute myocardial infarction or of pericarditis, the electrocardiogram showing no significant abnormality.

6) Chronic Rheumatic Valvular Disease of the Heart.

Valvular disease of the heart was present in 2 cases of acute myocardial infarction (Cases 17, and 21). In Case 17., the lesion present was aortic incompetence of luetic origin and in Case 21., mitral stenosis of rheumatic origin and auricular fibrillation. Therefore, in 8 cases of rheumatic heart disease in which there was no clinical or electrocardiographic evidence of acute myocardial infarction, serum transaminase assays were performed to ensure that the rise in serum transaminase in cases 17 and 21 was not due to the valvular lesions present.(Cases 60, 66,87,88,89,90,129,130). The opportunity of performing serum transaminase assays in cases of syphilitic disease of the aorta and its valve, uncomplicated by acute myocardial infarction, did not arise. In 5 out of these 8 cases, no rise in serum transaminase activity was detected. (Cases 60, 66, 87, 129, 130).Rheumatic disease had affected the aortic valves in cases 60 and 66., the mitral valve in cases 87 and 129 and both of these valves in case 130. Auricular fibrillation, in which the heart rate at the apex was not more than 100 beats/min., was noted in cases 66, 87 and 130 and,in case 130., embolism of the renal artery had occurred before serum transaminase assays had been performed. These results suggested that rheumatic heart disease is associated with normal serum transaminase activity in the presence of auricular fibrillation of slow rate and systemic arterial embolism. However, increased serum transaminase activity was found in the 3 remaining cases of rheumatic heart disease.(Cases 88,89,90). In cases 88 and 90., rapid auricular fibrillation was present and in case 89., systemic arterial embolism had occurred. These findings led to the investigation of the effect of cardiac arrhythmias and thrombo-embolic lesions on serum transaminase activity and the results of this investigation are presented in sections 10 & 12.

7) Uraemic Pericarditis.

In case 94., pericarditis due to uraemia was mistaken for acute myocardial infarction before the patient's admission to hospital.

Biochemical examination revealed hyperkalaemia and uraemia and the electrocardiogram was grossly abnormal, showing changes diagnostic of hyperkalaemia and pericarditis. Serum transaminase activity was normal on repeated examination in this case.

8) Cerebral Infarction.

It has already been shown that acute myocardial infarction may present with signs of cerebral thrombosis. (Cases 10 and 22). In both of these cases, high levels of serum transaminase activity were found. It was, therefore, decided to investigate the effect of cerebral thrombosis and infarction, not associated with acute myocardial infarction, on serum transaminase activity, and four such cases were studied. (Cases 95, 98,110,131). In cases 95 and 98., cerebral infarction was due to cerebral embolism. In case 95., the site of origin of the embolus was presumed to be mural thrombus in the left ventricle of the heart since there had been clinical and electrocardiographic evidence of recent, extensive anterior myocardial infarction 14 days before the development of the acute cerebro-vascular accident. In case 98., the diagnosis on the patient's admission to hospital was one of cerebral thrombosis in association with essential hypertension, occurring in a patient who had previously sustained a myocardial infarction, since serial electrocardiograms showed changes diagnostic of left ventricular hypertrophy and strain and of an old antero-septal myocardial infarction. Post mortem examination, however, revealed that embolism of cerebral arteries had been the cause of the extensive cerebro-vascular lesion. The embolus was presumed to have arisen from mural thrombus at the site of a healed myocardial infarction. There was no evidence of recent acute myocardial infarction at autopsy. In cases 110 and 131., the diagnosis of cerebral thrombosis was made on clinical grounds. In case 110., the electrocardiogram showed no significant abnormality and in case 131., the electrocardiographic changes were indicative of left ventricular strain without evidence of myocardial infarction. In each of these 4 cases, serum transaminase activity was normal when repeatedly examined following the onset of the cerebro-vascular accident.

9) Acute Pulmonary Infarction.

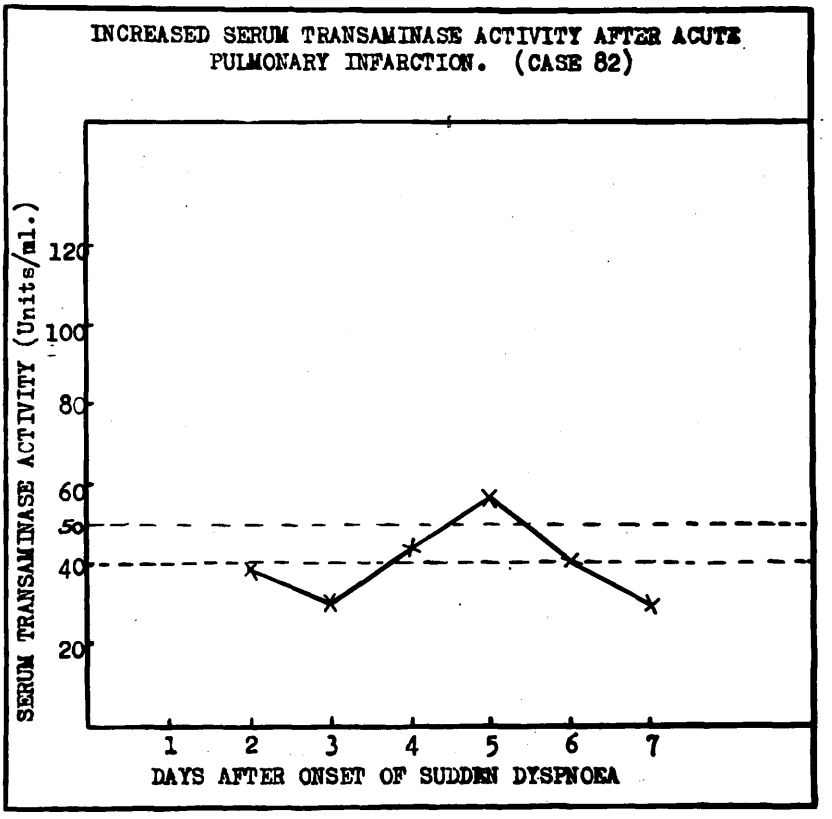
It may be very difficult to differentiate between acute myocardial infarction and acute pulmonary embolism with infarction on clinical or electrocardiographic grounds and it

/it seemed important to establish whether or not acute pulmonary infarction results in increased serum transaminase activity since, if normal serum transaminase activity was invariably found following acute pulmonary infarction, then serum transaminase assay might be of very great value in differentiating between the two conditions. Therefore, serum transaminase activity was measured in 6 cases of acute pulmonary infarction in which there was no electrocardiographic or autopsy evidence of acute myocardial infarction. (Cases 76, 80,81,82,83,108.) In case 76., pulmonary infarction was probably due to local pulmonary vessel thrombosis. In the remaining 5 cases acute pulmonary infarction was due to pulmonary artery embolism.

In 2 out of these 6 cases, normal levels of serum transaminase activity were found following the onset of the illness. (Cases 83, 108). In case 83., phlebothrombosis of the deep veins of the calf muscles of the left leg was present and this lesion was the site of origin of the pulmonary embolus. The electrocardiogram showed no significant abnormality. The patient suffered from rheumatic heart disease, aortic incompetence being the dominant lesion, but there was no evidence of heart failure or cardiac arrhythmia. In case 108., the pulmonary embolus probably originated from the right auricular appendage, there being no evidence of another source of embolus. The patient suffered from ischaemic heart disease. The electrocardiogram showed changes diagnostic of acute coronary insufficiency, auricular fibrillation and digitalis effect but there was no evidence of acute myocardial infarction. It should be noted that digitalis therapy before the onset of acute pulmonary infarction, had resulted in good control of the auricular fibrillation. (apex rate approximately 90/min.)

In 2 of these 6 cases, borderline levels of serum transaminase activity were detected following the onset of acute pulmonary infarction. (Cases 80, 81). In case 80., serum transaminase activity was increased to borderline levels 24 hours after the onset of acute pulmonary infarction. Rapid auricular fibrillation (apex rate 170-180 beats/min.) was present when serial transaminase assays were performed. There was no electrocardiographic evidence of acute myocardial infarction, the changes in the electrocardiogram being diagnostic of auricular fibrillation and suggestive of chronic coronary artery disease. The clinical diagnosis of acute pulmonary embolism with infarction and ischaemic heart disease was confirmed at post mortem examination, the pulmonary embolus having arisen from thrombus in the right auricular appendage. Atherosclerosis of the coronary arteries with myocardial fibrosis was found at autopsy but there was no evidence of acute myocardial infarction. The patient suffered repeated embolism of systemic arteries during the period of observation and the results of serum transaminase assay following these

FIGURE IV.


INCREASED SERUM TRANSAMINASE ACTIVITY AFTER ACUTE PULMONARY INFARCTION. (CASE 82)
SERUM TRANSAMINASE ACTIVITY (Units/ml.)
120
100
80
60
50
40
20
1
2
3
4
5
6
7
DAYS AFTER ONSET OF SUDDEN DYSPNOEA

/these incidents are presented in section 10. In case 81., borderline levels of serum transaminase activity were found 41 and 55 hours following the onset of acute pulmonary embolism with infarction. Mitral stenosis of rheumatic origin and auricular fibrillation were present and the embolus probably arose from thrombus in the right auricular appendage. There was no electrocardiographic evidence of acute myocardial infarction but the electrocardiogram confirmed the diagnosis of rapid auricular fibrillation, the heart rate being 170-180/min., and revealed changes of partial right bundle branch block or right ventricular strain.

In 2 out of the 6 attacks, high levels of serum transaminase activity were demonstrated following the onset of acute pulmonary infarction. (Cases 82, 76). In case 82., high levels of serum transaminase activity were detected on the fifth day following the onset of acute pulmonary embolism with infarction. (cf.Figure IV). The embolus originated from phlebothrombosis of the deep veins of the leg. The patient suffered from ischaemic heart disease, essential hypertension and congestive cardiac failure. There was no clinical or electrocardiographic evidence of arrhythmia or acute myocardial infarction. The electrocardiogram was diagnostic of left ventricular strain and also showed changes suggestive of right ventricular enlargement on serial examination. In case 76., serum transaminase activity rose to high levels 8 hours after the onset of symptoms very suggestive of left ventricular failure and the presence of an acute myocardial infarction was strongly suspected, since the electrocardiograms showed that changes of acute coronary insufficiency noted 3 days before the onset of acute symptoms had become more obvious and prolongation of the P-R interval had developed. The clinical diagnosis of left ventricular and congestive cardiac failure, aortic valve disease and ischaemic heart disease was made. At autopsy, however, there was no evidence of acute myocardial infarction on macroscopic or histological examination of the myocardium although the myocardium showed patchy areas of ischaemic fibrosis. (Plate I, Appendix IV). The clinical diagnosis of aortic valve and ischaemic heart disease was confirmed. However, an alveolar cell carcinoma of the lung, which had been unsuspected during life, was discovered. It was situated at the periphery of the lung. Histological examination of the lung revealed not only the appearance of carcinoma but also small areas of pulmonary infarction in close relationship to the tumour. (Plate II, Appendix IV). There was no evidence of centrilobular necrosis of the liver on histological examination, although the changes of severe chronic venous congestion of the liver were present. (Plate III, Appendix IV).

Therefore, out of 6 cases of acute pulmonary infarction, normal serum transaminase activity was demonstrated in 2 cases, borderline levels of activity in 2 cases in which

/which rapid auricular fibrillation was present and high levels of activity in 2 cases.

10). Thrombo-embolic conditions other than Acute Pulmonary Infarction.

Thrombo-embolic conditions other than acute pulmonary infarction may arise during the course of acute myocardial infarction and,therefore, serum transaminase assays were performed in such lesions occurring in the absence of acute myocardial infarction. It has been shown that phlebothrombosis of the deep veins of the lower limbs may be associated with normal serum transaminase activity (Case 83). In case 116., thrombosis of the inferior vena cava, the common iliac, internal and external iliac veins was present when serum transaminase activity was normal. The cause of this extensive phlebothrombosis was an adenocarcinoma of the pelvic colon found at post mortem examination. The electrocardiogram showed changes diagnostic of antero-septal myocardial ischaemia but there was no evidence of myocardial infarction. Post mortem examination confirmed that acute myocardial infarction had not occurred.

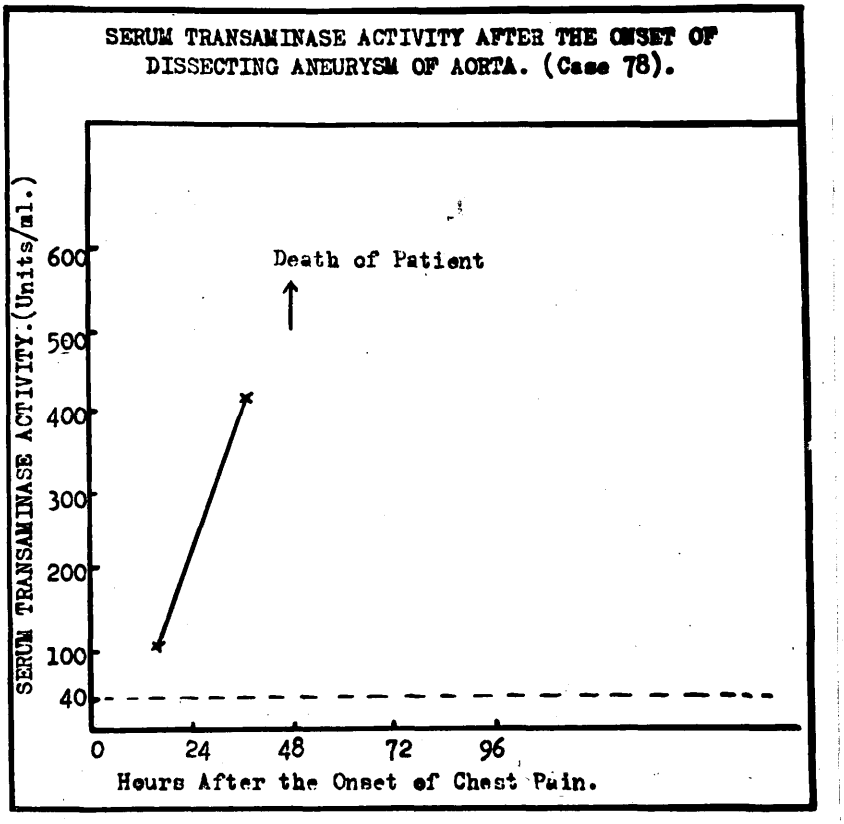
In case 130., serum transaminase activity was normal on repeated examination 12 and 36 hours following the onset of embolism of the renal artery with infarction of the kidney. This case has already been described in section 6. In case 75., serum transaminase activity was normal 48 and 72 hours following the onset of gangrene of the foot, due to peripheral arterial thrombosis. The patient suffered from ischaemic heart disease and the electrocardiographic findings have already been presented in section 2.

In case 80., serum transaminase activity was demonstrated to be at borderline levels of activity 7 days after the onset of saddle embolism of the aorta. When serum transaminase assays were performed, the patient had derived benefit from digitalis therapy, (the rate of auricular fibrillation being 90-110/min.). The electrocardiographic and post mortem findings in this case have already been presented in section 9.

In case 89., serum transaminase activity reached high levels 12 hours after the onset of embolism of the left middle cerebral, left brachial and left renal arteries. At autopsy, mitral stenosis of rheumatic origin was found and in the left atrium there was a pedunculated ball thrombus which had been the source of the emboli. There was no evidence of acute myocardial infarction. Auricular fibrillation and congestive cardiac failure were present when high levels of serum transaminase activity were detected but it should be noted that the rate of auricular fibrillation was not unduly rapid. (heart rate at apex, 90-100 beats/min.)

Therefore, normal serum transaminase activity was found in 4 out of 6 cases of thrombo-embolic disease.

FIGURE V.


SERUM TRANSAMINASE ACTIVITY AFTER THE ONSET OF DISSECTING ANEURYSM OF AORTA. (Case 78).
SERUM TRANSAMINASE ACTIVITY.(Units/ml.)
600
500
400
300
200
100
40
Death of Patient
0
24
48
72
96
Hours After the Onset of Chest Pain.

Borderline levels of serum transaminase activity were found in one case and high levels in the remaining case in which multiple emboli had occurred.

11) Dissecting Aneurysm of the Aorta.

Serum transaminase assays were performed in 2 cases of dissecting aneurysm of the aorta. (Cases 78 and 79). In case 78., high levels of serum transaminase activity were demonstrated 17 and 36 hours after the onset of the illness. (cf. Figure V). The history and clinical findings were very suggestive of acute myocardial infarction. The electrocardiogram showed changes diagnostic of left ventricular strain, although posterior myocardial infarction could not be finally excluded. This divergence between the history and clinical findings and the electrocardiographic changes observed led to the decision to avoid therapy with anticoagulant drugs, although the diagnosis of dissecting aneurysm of the aorta was not suspected until a few hours before the death of the patient when haematemesis occurred. Post mortem examination revealed rupture of a dissecting aneurysm of the first part of the aorta and haemopericardium which had given rise to cardiac tamponade. Severe calcifying atherosclerosis of the aorta and coronary arteries was present but there was no evidence of acute myocardial infarction on macroscopic or microscopic examination of the heart, although ischaemic fibrosis of the chordae tendiniae was noted. However, histological examination of the liver revealed the presence of marked centrilobular necrosis. (Plate IV, Appendix IV). In case 79., the history and clinical findings were very suggestive of acute myocardial infarction but the electrocardiogram, on serial examination, showed no evidence of acute myocardial infarction although electrocardiographic changes indicative of acute coronary insufficiency and digitalis effect were present. 5 days after the patient's admission to hospital, the tentative clinical diagnosis of dissecting aneurysm of the aorta was made. Post mortem examination 12 days after the onset of the illness confirmed this diagnosis. Haemopericardium was present. There was evidence of a very recent posterior myocardial infarction which was estimated to be of 24 - 48 hours' duration. High levels of serum transaminase activity were demonstrated for 5 days following the onset of dissecting aneurysm of the aorta. Serum transaminase activity fell to normal levels on the 6th day after the onset of the illness. The recent acute posterior myocardial infarction discovered at autopsy was considered to be a terminal event in this case and to be unrelated to the high levels of serum transaminase activity demonstrated. An attack of auricular fibrillation (heart rate at the apex 120-130 beats/min.) was observed, when high levels of serum transaminase activity were found.

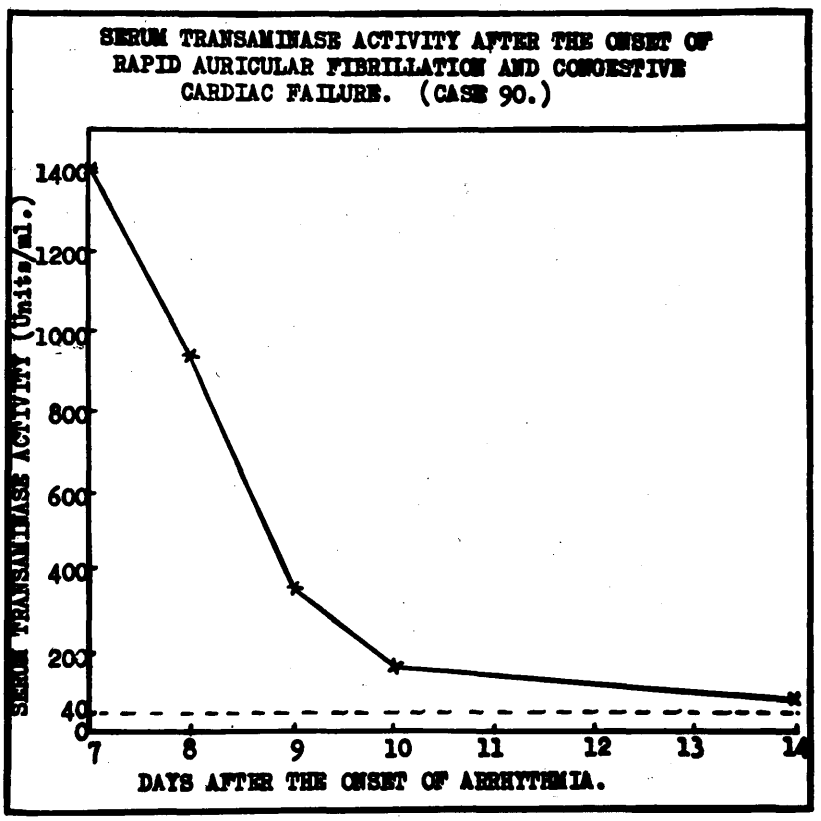
Unfortunately, the liver was not examined histologically in this case and so the presence of centrilobular necrosis of the liver was not excluded. Therefore, high levels of serum transaminase activity may be associated with dissecting aneurysm of the aorta.

12) Supraventricular Tachycardia and Auricular Fibrillation.

4 attacks of paroxysmal supraventricular tachycardia were observed in 3 cases of acute myocardial infarction. (Cases 11, 25, 34). In case 34., rapid supraventricular tachycardia (rate 140 beats/min.) was present when high levels of serum transaminase activity were found. In case 11., serum transaminase activity had returned to normal levels following acute myocardial infarction, but rose again to borderline levels following an attack of supraventricular tachycardia, although there was no clinical evidence of a fresh myocardial infarction. In case 25., 2 attacks of supraventricular tachycardia were observed. (Attacks 25g, 25h.) In attack 25g., supraventricular tachycardia (rate 160 beats/min.) lasted for 16 hours and was associated with angina pectoris at rest. There was no clinical or electrocardiographic evidence of fresh myocardial infarction, but serum transaminase activity rose to high levels following the onset of the arrhythmia. The suspicion that supraventricular tachycardia may have caused the increase in serum transaminase activity in attack 25g. was strengthened when, in attack 25h., serum transaminase activity rose to borderline levels 30 hours after the onset of rapid supraventricular tachycardia. Again, there was no electrocardiographic evidence of fresh myocardial infarction.

Auricular fibrillation was present in 3 cases of acute myocardial infarction. (Cases 11, 21, 35). In case 21., the arrhythmia had been present for many years and the heart rate was controlled by digitalis therapy, being 80-90 Beats/min. Following acute myocardial infarction, serum transaminase activity rose to high levels in this case but fell to normal levels although the abnormal rhythm continued. In case 35., auricular fibrillation (rate 130-140 beats/min.) developed as a complication of acute myocardial infarction and was present when high levels of serum transaminase activity were demonstrated following the infarction. It was impossible to decide whether the increase in serum transaminase activity was due to acute myocardial infarction or to rapid cardiac arrhythmia. In case 11.,paroxysmal auricular fibrillation, (rate 120-130 beats/min.) accompanied by angina pectoris at rest was diagnosed on clinical grounds. This attack of fibrillation lasted for 1½ hours but normal serum transaminase activity was demonstrated following it.

FIGURE VI.


SERUM TRANSAMINASE ACTIVITY AFTER THE ONSET OF RAPID AURICULAR FIBRILLATION AND CONGESTIVE CARDIAC FAILURE. (CASE 90.)
SERUM TRANSAMINASE ACTIVITY (Units/ml.)
1400
1200
1000
800
600
400
200
40
0
7
8
9
10
11
12
13
14
DAYS AFTER THE ONSET OF ARRHYTHMIA.

These findings suggested that the effect of rapid cardiac arrhythmia on serum transaminase activity was worthy of further study in conditions other than acute myocardial infarction. Therefore, serum transaminase assays were performed in 10 cases of auricular fibrillation, in which there was no clinical or electrocardiographic evidence of acute myocardial infarction. (Cases 66, 80, 81,87, 88, 89,90, 108, 117, 130).

In 5 out of these 10 attacks, normal serum transaminase activity was demonstrated. (Cases 66, 87, 108,117, 130). The arrhythmia was associated with chronic rheumatic valvular disease of the heart in 2 cases (Cases 66 and 87), and with thyrotoxicosis and congestive cardiac failure in case 117. In case 108., ischaemic heart disease was the underlying lesion and acute pulmonary infarction had occurred. In case 130., chronic rheumatic valvular disease of the heart and acute renal infarction had occurred. In this small group of cases, the rate of auricular fibrillation varied from 80-100 beats/min. These results show that slow auricular fibrillation (rate 8o-100 beats/min.) is compatible with normal serum transaminase activity.

However, in 5 out of 10 cases of auricular fibrillation, increased serum transaminase activity was found. (Cases 80, 81, 88, 89, 90). In 2 out of these 5 attacks, high levels of serum transaminase activity were found. (Cases 88 and 90). In case 90., the highest levels of serum transaminase activity detected in this study were demonstrated. (cf. Figure VI). These very high levels of serum transaminase activity (1,400 units/ml.) were found 7 days after the onset of congestive cardiac failure and auricular fibrillation due to mitral stenosis and incompetence of rheumatic origin and they fell gradually to normal during the succeeding 8 days. When these very high levels of activity were found the heart rate was approximately 190/min., and severe congestive cardiac failure was present. As the auricular fibrillation and congestive cardiac failure were controlled by digitalis therapy, serum transaminase activity fell to normal levels. High levels of serum bilirubin were present, although jaundice was absent, suggesting hepatic dysfunction when high levels of serum transaminase activity were noted, but serum bilirubin levels did not fall to normal coincidentally with serum transaminase activity. The electrocardiogram showed changes diagnostic of auricular fibrillation and suggestive of acute coronary insufficiency or left ventricular strain, but there was no evidence of acute myocardial infarction on serial examination.

In case 88., high levels of serum transaminase activity were demonstrated from the 6th to the 12th day following the onset of severe congestive cardiac failure and rapid cardiac arrhythmia due to varying supraventricular tachycardia

/tachycardia and auricular fibrillation. There was no electrocardiographic evidence of acute myocardial infarction on repeated examination of the electrocardiogram. When high levels of serum transaminase activity were found, the heart rate was more than 160 beats/min., and, as the heart rate slowed with treatment, serum transaminase activity fell towards normal levels. High levels of activity were present for 6 days but it was noted that there was no secondary rise in activity following short attacks of ventricular tachycardia. Convincing evidence of hepatic damage was found on serial examination of liver function although jaundice was absent. There was, however, no close correlation between the degree of liver dysfunction,as revealed by the tests employed,and the level of serum transaminase activity. Post mortem examination confirmed the presence of congestive cardiac failure, mitral stenosis and chronic bronchitis and emphysema. There was no evidence of acute myocardial or other infarction, or of gallbladder or pancreatic disease. Histological examination of the liver revealed the changes of centrilobular necrosis of the liver. (Plate V, Appendix IV). It should be noted that the time of onset of cardiac arrhythmia in cases 88 and 90 could not be accurately determined. The time of onset of symptoms of cardiac failure was taken as the probable time of onset of the arrhythmia. This arbitrary method of deciding the time of onset led to the conclusion that high levels of serum transaminase activity probably persisted for a longer time following auricular fibrillation and congestive cardiac failure than following acute myocardial infarction. For example, in case 90., high levels of serum transaminase activity were demonstrated 14 days and, in case 88., 12 days after the probable time of onset of rapid cardiac arrhythmia and congestive cardiac failure.

In 3 out of the 5 attacks, in which increased serum transaminase activity was demonstrated, serum transaminase activity rose to borderline levels (Cases 80, 81, 89). In case 81., acute pulmonary infarction and rapid auricular fibrillation (rate 170-180 beats/min.)were present when borderline levels of serum transaminase activity were found. Digitalis therapy was started on the patient's admission to hospital and resulted in less rapid rates of auricular fibrillation within 24 hours. Since serum transaminase activityhas been shown to rise to high levels in cases of rapid cardiac arrhythmia, (cases 88, 90), it is possible that the borderline levels of serum transaminase activity resulted from rapid auricular fibrillation of about 2 days' duration rather than from acute pulmonary infarction. The electrocardiographic findings in this case have been presented in section 9. In cases 80 and 89.,thrombo-embolic lesions and auricular fibrillation were present. In both cases, the rate of auricular fibrillation was approximately 100 beats/min., as in the cases of auricular fibrillation in which normal serum

/serum transaminase activity was found. This suggests that the borderline rise in serum transaminase activity in these two cases was more likely to be the result of thromboembolic damage than of cardiac arrhythmia. The findings in these cases have already been presented in section 10.

THE RESULTS OF SERUM TRANSAMINASE ASSAY, ELECTRO-CARDIOGRAPHIC EXAMINATION, POST MORTEM EXAMINATION AND LIVER FUNCTION TESTS IN DISEASES OUTWITH THE CARDIO-VASCULAR SYSTEM.

The results,in detail, of serum transaminase assays, electrocardiographic examination, post mortem examination and of liver function tests in the diseases considered below are included in Appendix II.

1) Diseases of the Alimentary Tract.

a) Peptic Ulcer.

7 out of 57 patients, suffering from acute myocardial infarction had had symptoms suggestive of peptic ulceration. (Cases 12, 13, 15, 35, 39, 50, 71). In 3 of these 7 patients the clinical diagnosis of peptic ulceration had been confirmed on radiological examination of the stomach and duodenum. (Cases 12, 15, 35). In case 15., the combined operation of gastro-enterostomy and vagotomy had been performed. In case 71., perforation of a duodenal ulcer had occurred and had been repaired surgically. In 2 patients, there was a history of haematemesis (cases 13 and 39). In case 13., radiological investigation of the stomach and duodenum had revealed no abnormality. The results of such examination in case 39 were not known. In case 50., symptoms suggestive of a peptic ulcer had been present intermittently for 20 years, and acute dyspepsia and haematemesis were present shortly after the patient's admission to hospital and anticoagulant therapy was stopped because of this. The results suggest that evidence of peptic ulceration is not uncommonly found in patients suffering from acute myocardial infarction, and so it was decided to study the effect of peptic ulceration on serum transaminase activity in cases in which there was no evidence of acute myocardial infarction especially in those cases in which perforation of a peptic ulcer had occurred. Therefore, in 6 cases of peptic ulcer, serum transaminase assays were performed. (Cases 91, 92, 93, 103, 104, 105).

In case 105., serum transaminase activity was normal when severe symptoms of acute dyspepsia due to duodenal ulcer were present. Acute myocardial infarction was suspected at this time but serial electrocardiograms showed no evidence of acute myocardial infarction and radiological examination confirmed the presence of a duodenal ulcer. Normal serum transaminase activity was present in the remaining 5 cases in which perforation of a peptic ulcer had occurred. In 3 of these 5 cases, serum transaminase activity was measured before the operation of laparotomy was performed, (Cases 91, 92, 103), and the diagnosis of perforated peptic ulcer was confirmed at operation in each of these cases. Serum transaminase assay

/assay was performed 4 hours, 6 hours and 7½ hours after the onset of symptoms in case 103., case 92 and case 91 respectively. In cases 93 and 104., the patients' admission to hospital had been unduly delayed and operative treatment was contra-indicated. Serum transaminase assay was performed with normal results 24 hours after the onset of symptoms in case 93, and 48 hours after the onset of symptoms in case 104. Acute myocardial infarction was not suspected in any of these 5 cases of perforated peptic ulcer and electrocardiograms were not examined. A post mortem examination was performed in case 104. The diagnosis of perforated stomal ulcer was confirmed and low-grade generalised peritonitis was present. An annular carcinoma of the transverse colon was also found. There was, however, no evidence at autopsy of acute myocardial infarction. Therefore, in 6 cases of peptic ulcer in which acute myocardial infarction was not suspected, there was no evidence of increased serum transaminase activity.

b) Hiatus Hernia.

Normal serum transaminase activity was found on repeated examination in 2 cases in which there was radiological evidence of hiatus hernia. (Cases 30 and 75). In both cases the hiatal lesion was an incidental finding. In case 75., ischaemic heart disease in association with diabetes mellitus were the source of disability while, in case 30., attacks of angina pectoris at rest had determined the patient's admission to hospital. However, in case 30., there seemed to be a relationship between attacks of angina pectoris at rest, accompanied by the electrocardiographic changes of myocardial ischaemia, and changes in the size and position of the hiatus hernia. When the hernia was large and situated behind the heart attacks of angina pectoris and the electrocardiographic patterns of myocardial ischaemia were observed. When the hernia was reduced in size, the electrocardiographic changes of myocardial ischaemia were no longer apparent and no attacks of angina pectoris occurred. There was no doubt that severe atherosclerosis of the coronary arteries was present in this case and these observations suggest that the changes in position of the heart, caused by the varying size and position of the hernia, had induced attacks of myocardial ischaemia.

c) Steatorrhoea.

Serum transaminase activity was normal in 2 cases in which steatorrhoea had been shown to be present by fat balance studies.(Cases 112 and 135). In case 112., steatorrhoea had followed partial pancreatectomy for carcinoma of the Ampulla of Vater. In case 135., steatorrhoea had been present for many years when hyperparathyroidism had developed, which had been cured by parathyroidectomy. When serum

/serum transaminase assay was performed the steatorrhoea was being treated with a gluten-free diet. Electrocardiograms were not performed in these cases.

2) Diseases of the Respiratory System.

The results of serum transaminase assay in chronic bronchitis have already been presented.

a). Pulmonary Tuberculosis.

Normal serum transaminase activity was found in 2 cases of pulmonary tuberculosis.(Cases 94 and 96). In case 94., uraemia and hyperkalaemia were present and,in case 96., amyloid disease of the kidneys.

b) Bronchopneumonia and Pleurisy.

Normal serum transaminase activity was found on repeated examination in bronchopneumonia (cases 85 and 133) and in pleurisy of the left diaphragmatic pleura.(case 109). Acute rheumatic fever was also present in case 85 and the electrocardiographic findings have been presented. In case 133., there was no suspicion of acute myocardial infarction and electrocardiograms were not performed. In case 109., acute myocardial infarction was suspected on clinical grounds but there was no electrocardiographic evidence of acute myocardial infarction, although electrocardiographic studies were incomplete.

c) Neoplasm of Lung.

In case 73., bronchial neoplasm which had caused obstruction of the superior vena cava was present in addition to ischaemic heart disease. Normal serum transaminase activity was repeatedly demonstrated in this case.

3) Diseases of the Endocrine Glands.

a) Diabetes Mellitus.

In one case of acute myocardial infarction in which high levels of serum transaminase activity were present, diabetes mellitus, requiring insulin for its control was present. (Case 37). Serum transaminase assays were,therefore, performed in 2 cases of diabetes mellitus in which there was

/was no clinical or electrocardiographic evidence of recent acute myocardial infarction. (Cases 75 and 131). In case 75., there was evidence of ischaemic heart disease and in case 131., recent cerebral artery thrombosis had occurred. The results of assays in these cases were within normal limits.

b). Thyrotoxicosis.

In 2 cases of thyrotoxicosis normal serum transaminase activity was demonstrated. (Cases 117 and 121). In case 117., a large nodular goitre, thyrotoxicosis, auricular fibrillation and congestive cardiac failure were found. In case 121., exophthalmic goitre was present. There was no clinical or electrocardiographic evidence of acute myocardial infarction in either case.

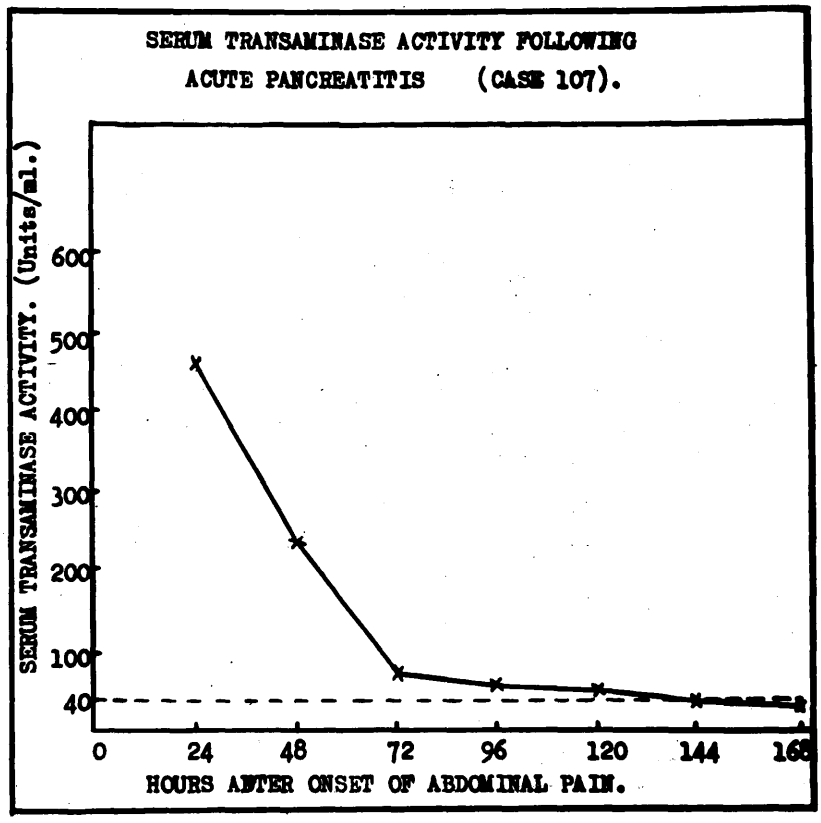
4) Cholelithiasis.

Serum transaminase assays were performed in 2 cases of cholelithiasis in which there was no evidence of acute myocardial infarction or acute pancreatitis. (Cases 99 and 100). In case 99., serum transaminase activity was normal before and after the operation of cholecystectomy was performed. Acute cholecystitis had developed. At operation, gallstones were present in the gallbladder and cystic duct but were not found in the common bile duct. There was no evidence,on clinical examination,of jaundice or acute myocardial infarction. In case 100., borderline levels of serum transaminase activity were demonstrated before the operation of cholecystectomy was performed. Chronic cholecystitis was found at operation and gallstones were present in the common bile duct. There was no evidence of jaundice on clinical examination, although the urine contained a trace of bile and the results of liver function tests indicated biliary obstruction. The electrocardiogram showed no significant abnormality. Cholelithiasis was demonstrated at laparotomy in 3 cases of acute pancreatitis. Therefore, in 2 out of 5 cases in which gallstones were found at operation, increased serum transaminase activity was demonstrated. (Cases 100 and 107).

5) Acute Pancreatitis.

Serum transaminase assays were performed in 3 cases of acute pancreatitis. (Cases 106, 107, 132). In case 106., normal serum transaminase activity was found 24 and 48 hours after laparotomy had been performed. The operation had been delayed until the acute symptoms of the disease had settled.

FIGURE VII.


SERUM TRANSAMINASE ACTIVITY FOLLOWING
ACUTE PANCREATITIS (CASE 107).
SERUM TRANSAMINASE ACTIVITY. (Units/ml.)
600
500
400
300
200
100
40
0
24
48
72
96
120
144
168
HOURS AFTER ONSET OF ABDOMINAL PAIN.

/settled. At operation, the pancreas showed no evidence of haemorrhage or necrosis but its appearance was consistent with the diagnosis of acute relapsing interstitial pancreatitis. There was no obstruction of the common bile duct although gallstones were present in the gallbladder and tests of liver function showed no abnormality. Acute myocardial infarction was not suspected and electrocardiograms were not performed. In case 132., serum transaminase activity was normal when examined 24 hours after the onset of acute pancreatitis. Laparotomy in this case revealed more acute changes in the pancreas than those observed in case 106. The pancreas was oedematous and indurated and there were a few areas of fat necrosis in the surrounding peritoneum. Gallstones were present in the gallbladder and cystic and common bile ducts. Neither tests of liver function nor electrocardiograms were performed in this case. In case 107., high levels of serum transaminase activity were found 24 hours after the onset of acute haemorrhagic pancreatitis and high levels of activity were present for 6 days following the onset of the illness (cf. Figure VII). At operation, areas of necrosis and haemorrhage were found in the pancreas and fat necrosis of the omentum was present. Gallstones were found both in the gallbladder and in the common bile duct and serial tests of liver function revealed abnormalities suggestive of liver dysfunction. The electrocardiographic changes of acute coronary insufficiency were shown to be present for 15 hours but further electrocardiographic observations were not made. Therefore, in one out of 3 cases of acute pancreatitis, high levels of serum transaminase activity were found.

6) Jaundice.

a) Obstructive Jaundice due to Neoplastic Conditions.

Serum transaminase activity was studied in 4 cases of obstructive jaundice due to neoplastic disease. (Cases 116, 118, 119, 127).In 3 out of these 4 cases, serum transaminase activity was normal. (Cases 116, 118, 119). In case 116., post mortem examination revealed adenocarcinoma of the pelvic colon with many secondary tumours of the liver. There was no evidence of acute myocardial infarction. In case 118., the jaundice was shown,at laparotomy, to be due to carcinoma of the gallbladder which had extended locally to obstruct the biliary passages. In case 119., adenocarcinoma of the head of the pancreas was found at operation. In each of these cases, the results of liver function tests suggested that extra-hepatic biliary obstruction was the cause of the jaundice. In the remaining case, high levels of serum transaminase activity were found. (Case 127). In this case, jaundice was due to a massive tumour of liver which histological examination showed to be a primary hepatoma. Tests of liver function showed changes characteristic of obstructive jaundice. There was no evidence /

/evidence of acute myocardial infarction on clinical examination. Therefore, in one out of 4 cases of jaundice due to neoplastic conditions, high levels of serum transaminase activity were demonstrated.

b) Jaundice due to Hepatic Cirrhosis.

Serum transaminase activity was studied in 4 cases of jaundice due to cirrhosis of the liver. (Cases 97, 115, 124, 126). There was no evidence on clinical examination of acute myocardial infarction in any of these cases. In each case, the results of liver function tests supported the diagnosis of hepatic cirrhosis. Normal serum transaminase activity was demonstrated in case 124 in which bleeding had occurred from oesophageal varices. In case 115., borderline levels of serum transaminase activity were found in the presence of post-hepatitis cirrhosis. In 2 cases, high levels of serum transaminase activity were demonstrated. (Cases 97 and 126). In case 97., the diagnosis of advanced hepatic cirrhosis and haemorrhage from oesophageal varices was confirmed on post mortem examination. There was no evidence of acute myocardial infarction at autopsy. The illness was characterised by episodes of hepatic failure and the results of serial liver function tests showed increasing jaundice of hepatogenous origin. In case 126., hepatic cirrhosis and peripheral neuropathy due to chronic alcoholism were present. Therefore, out of 4 cases of jaundice due to cirrhosis of the liver, high levels of serum transaminase activity were found in 2 cases, and borderline levels of activity in one case. In only one case was serum transaminase activity normal.

c) Jaundice due to Haemolytic Anaemia.

Serum transaminase activity was normal on repeated examination in case 125 in which jaundice due to severe haemolytic anaemia was present.

7) Lymphadenoma with Hepatic Involvement.

Serum transaminase activity was normal on repeated examination in a case of lymphadenoma in which there was clinical evidence of involvement of the liver in the disease process, although jaundice was not present. (Case 111).

8). Metabolic Disease of Bone.

Normal serum transaminase activity was demonstrated

/demonstrated in 3 cases of metabolic disease of bone. (Cases 113, 120, 134). In case 113., the assay was performed 6 days after the surgical removal of a simple adenoma of the parathyroid gland which had caused hyperparathyroidism. In case 120., osteomalacia had followed parathyroidectomy and mild attacks of carpo-pedal spasm were occurring when the assay was performed. In case 134., vitamin D resistant rickets was not fully controlled by treatment, the plasma alkaline phosphatase being increased when the assays were performed.

9). Uraemia and Oliguria.

In 3 cases of uraemia, normal serum transaminase activity was found. (Cases 64, 94, 123). The causal lesion in case 64 was malignant hypertension, and in case 123., prostatic hypertrophy. In case 94.,uraemia was probably due to bilateral renal tuberculosis but post mortem confirmation of this diagnosis was lacking. In case 96., amyloid disease of the kidney, secondary to chronic tuberculous empyema,was diagnosed on clinical grounds. Severe oliguria was present when normal serum transaminase activity was demonstrated.

SERUM TRANSAMINASE ACTIVITY COMPARED WITH PYREXIA AS AN INDEX OF ACUTE MYOCARDIAL INFARCTION.

The body temperature was recorded in all cases of acute myocardial infarction and the results of these examinations are included in the individual case histories in Appendix II.

In 29 out of 67 attacks of acute myocardial infarction, no rise in body temperature was recorded following the attack. In 2 of these 29 attacks, the patient died within 8 hours of the onset of acute myocardial infarction, death occurring before a pyrexial reaction could develop. (Cases 4 and 18). In 8 of the 29 attacks, acute myocardial infarction was judged to have occurred more than 3 days before temperatures were recorded. Therefore, in these attacks, the temperature had not been recorded at the ideal time i.e., within 48 hours of the onset of acute myocardial infarction. (Attacks 13a, 19a,29,49, 51,54,56,84). However, in the remaining 19 attacks, observations of body temperatures were made within 30 hours of the onset of illness and pyrexia was not found. These results compare unfavourably with

/with those of serum transaminase assay which failed to demonstrate high levels of serum transaminase activity in 11 out of the 67 attacks of acute myocardial infarction but in only one of 57 attacks in which the assay was considered to have been performed 6 - 24 hours after the onset of the attack. It is suggested, therefore, that transaminase assay is a more reliable index of the occurrence of acute myocardial infarction than pyrexia.

SERUM TRANSAMINASE ACTIVITY COMPARED WITH ERYTHROCYTE SEDIMENTATION RATE AS A DIAGNOSTIC AID IN ACUTE MYOCARDIAL INFARCTION AND ANGINA PECTORIS AT REST.

The erythrocyte sedimentation rate (E.S.R.) was measured in 54 out of 67 attacks of acute myocardial infarction and the results of these examinations are presented in the individual case histories in Appendix II. In 13 out of 54 attacks of acute myocardial infarction, the E.S.R. was normal. In 5 of these 13 attacks, only a single estimation of the E.S.R. was performed. (Attacks 3, 4, 6, 35, 47a). In case 4., both the E.S.R. and serum transaminase activity were normal 1¼ hours following the onset of the attack but, in the remaining 4 attacks, the E.S.R. was normal at intervals varying from 8½ - 53 hours after the onset of acute myocardial infarction, while high levels of serum transaminase activity were found. In 8 of these 13 attacks, the E.S.R. was normal on serial examination, (attacks 7, 8, 16, 19a, 25a, 25b, 39, 43), and in 5 of these 8 attacks, high levels of serum transaminase activity were found.

In 41 out of 54 attacks of acute myocardial infarction, the E.S.R. reached abnormally high levels. However, in 10 of these 41 attacks, the E.S.R. was normal within 24 hours of the onset of the attacks, later rising to abnormal levels. (Attacks 1, 5, 10, 11a, 25c, 27, 41, 44, 50, 71). In 9 of these attacks, high levels of serum transaminase activity were demonstrated within 24 hours of the onset of the attack, the exception being attack 11a., in which serum transaminase activity was not examined until 24 - 48 hours after the onset of the attack.

In 5 attacks of acute transmural myocardial infarction, the E.S.R. was abnormally high when normal or borderline levels of serum transaminase activity were present, due to late sampling of the serum. (Cases 29,49,51,56,84). It

/ It was also noted that, in 6 cases of angina pectoris at rest, the E.S.R. was elevated to abnormal levels, no extra-cardiac lesion being found to account for this elevation, whereas high levels of serum transaminase activity were not demonstrated following angina pectoris. (Cases 32, 33, 53, 58, 62, 77).

Therefore, the E.S.R. was abnormally high in 72% of attacks of acute myocardial infarction compared with the demonstration of high levels of serum transaminase activity in 84% of attacks. High levels of serum transaminase activity were found in 9 out of 13 attacks of acute myocardial infarction in which the E.S.R. was normal, and in 9 out of 10 attacks in which the E.S.R. was normal within 24 hours of the onset of acute myocardial infarction. These results suggest that serum transaminase assay is a more reliable early diagnostic index of acute myocardial infarction than the E.S.R. which, however, may be a very useful ancillary test when performed several days after the onset of acute myocardial infarction, when serum transaminase activity can be expected to be normal. In differentiating between acute myocardial infarction and myocardial ischaemia, serum transaminase assay would seem to be a more reliable guide as to whether or not acute myocardial infarction has occurred.

DISCUSSION OF RESULTS.

The spectrophotometric method of serum transaminase assay has been shown to be rapid, simple and accurate although it suffers the disadvantage of requiring expensive apparatus and reagents, which are unstable and need careful handling. (Appendix I).

The enzyme has been shown to be stable at room temperature and at freezing point for periods which facilitate its use as a diagnostic test. It has been shown that haemolysis of the red blood cells significantly alters serum transaminase activity and, consequently, that only clear specimens of serum should be used for the test if serious error is to be avoided.

The normal range of serum transaminase activity found in this series agrees quite closely with that of other workers. The serum transaminase activity of normal people appears to be fairly constant, to be unaffected by the state of digestion and hard physical exertion and to be independent of sex or age. Normal, borderline and high levels of serum transaminase activity have been arbitrarily defined. The source of transaminase in normal human serum remains uncertain but there is convincing experimental evidence that necrosis of any tissue with a high content of the enzyme may result in a significant rise in serum transaminase activity. Evidence has been obtained from experimental studies which suggests that rapid disappearance of the enzyme is due to its diffusion into the interstitial fluid, but little is known about the disposition of transaminase released into, or present in, the serum. Inhibition or inactivation of the enzyme in serum is unlikely as free transaminase has been demonstrated in all specimens of human sera examined. It has been shown that, while small amounts of the enzyme may be present in urine, significant amounts of transaminase are not excreted into the urine even when serum transaminase activity is abnormally high and also that oliguria and azotaemia can be associated with normal serum transaminase activity. This evidence and that of other workers, from both experimental and clinical studies, suggests that excretion of transaminase by the kidneys is not significant. On the other hand, it has been shown that bile, obtained at operation from diseased biliary tracts, contained significantly higher amounts of transaminase than the serum and other investigators have obtained convincing experimental evidence, which has been presented, that both damage to the liver cells or obstruction to the flow of bile may result in high levels of serum transaminase activity. These results support the conception of the biliary tree as a normal route for transaminase excretion.

In this study of 67 attacks of acute myocardial

/myocardial infarction, high levels of serum transaminase activity were demonstrated in 56 attacks. (84%). High levels of serum transaminase activity were not found within 6 hours after the onset of acute myocardial infarction and the earliest rises of serum activity to high levels were demonstrated 7 hours after the onset of the illness. Following this period of delay, serum transaminase activity reaches a peak level 24 - 48 hours after the onset of acute myocardial infarction. In attacks of acute transmural myocardial infarction, high levels of serum transaminase activity are maintained, on the average, for 3 or 4 days after the onset of the illness and then gradually fall to normal levels 6 - 7 days after the onset of the lesion. In these attacks, the highest average serum transaminase activity was 130 units/ml., and was present 24 - 48 hours after the onset of infarction. It was also noted that the peak level of transaminase activity was above 100 units in the majority of cases in which the assay had been performed within 48 hours of the onset of the infarction. In attacks of acute intramural myocardial infarction, the time/transaminase curve was similar to that found in acute transmural myocardial infarction. However, high levels of serum transaminase activity were not detected when the assay was performed more than 48 hours after the onset of acute intramural infarction and,in each attack,the maximum level of serum transaminase activity was less than 100 units/ml. The average daily serum transaminase activity was shown to be much lower in these attacks than in acute transmural myocardial infarction, being 60 units/ml. It was also observed that,in 3 attacks of acute transmural myocardial infarction and in 2 attacks of acute intramural myocardial infarction, high levels of serum transaminase activity were detected 6- 24 hours following the onset of infarction only, subsequent assays of activity showing normal results. These observations emphasise that increased serum transaminase activity following acute myocardial infarction may be of short duration and that acute transmural and intramural myocardial infarction cannot be differentiated by the levels of serum transaminase activity attained. It is generally agreed that, following acute myocardial infarction in dogs or human beings, serum transaminase activity starts to rise in 4 - 6 hours and reaches a peak in 18 - 36 hours and returns to normal in 4 - 6 days e.g., La Due et al (1954), and Kattus et al, (1956). La Due and Wroblewski (1955) in a study of 50 cases of acute transmural infarction reported that serum transaminase activity returned to normal by the 7th.day in all cases and by the 3rd.day in 20% of cases. Ostrow et al (1956) in a study of 60 cases of acute transmural myocardial infarction suggested that a single assay would most likely be positive if performed 24 - 48 hours after the onset of symptoms and Gutteridge and McKean (1958)

/make similar recommendations. On the other hand, Kattus et al (1957) permitted greater latitude in the time of withdrawal of serum for the assay since they did not observe a case of myocardial infarction in which serum transaminase activity failed to rise provided serial blood samples were examined during the first 4 days of the disease. It is pointed out that these recommendations are based on studies of acute transmural myocardial infarction while, in this investigation, both acute transmural and intramural myocardial infarctions have been observed. My observations suggest that, unless serum transaminase assays are performed 6 - 24 hours and 24 - 48 hours after the onset of acute myocardial infarction, high levels of serum transaminase activity may escape detection. For example, in each of the 33 attacks of acute transmural myocardial infarction in which the time of onset was accurately known and in which this procedure was followed, high levels of serum transaminase activity were found. Thus, in this group of cases, there was 100% correlation between the diagnosis of acute myocardial infarction and the results of serum transaminase assay whereas, in the whole series, normal or borderline transaminase activity was found in 11 out of 67 attacks of acute myocardial infarction. (16%). In 10 of these 11 attacks of myocardial infarction (14.5%)., failure to demonstrate high levels of serum transaminase activity was ascribed to sampling of the serum outwith the recommended times. When the reasons for failure to comply with the recommended procedure in these 10 attacks are examined, it is clear that many of them are unavoidable in routine hospital practice. For example, in 2 attacks the patient died within 6 hours of the onset of acute myocardial infarction and in another 4 attacks the patients were not admitted to hospital until at least 50 hours after the onset of symptoms. The difficulty in determining the exact time of onset of acute myocardial infarction in cases characterised by premonitory of post-infarction chest pain has already been pointed out and this difficulty was encountered in the remaining 4 attacks of myocardial infarction, in which serum transaminase assay gave normal or borderline results. In these 4 attacks, after full consideration of all the evidence, acute myocardial infarction was judged to have occurred 4 or more days before serum transaminase assay was performed. In each attack, the assay had been performed following an attack of angina pectoris and acute myocardial infarction had been suspected. In 3 of these attacks serum transaminase activity was normal while in one attack it reached borderline levels, which were interpreted as representing falling levels of activity following acute myocardial infarction or a borderline increase in activity following severe angina pectoris at rest. In one of the 11 (1.5%) attacks of acute myocardial infarction, normal transaminase activity was demonstrated 6 and 28 hours following the probable time of onset of the illness, although

/although the exact time of onset of the infarction could not be determined. In this attack a transitory increase in serum transaminase activity may have been missed. Alternatively, for reasons unknown, there was no increase in transaminase activity following the onset of the illness.

The results are similar to those reported by other workers but are, on the whole, not so favourable to the test. For example, La Due and Wroblewski (1955) found high levels in 74 out of 75 cases of unequivocal acute transmural infarction (98.6%). In the one case in which no rise of serum transaminase activity was observed the serum had been stored for over 3 weeks and this was thought to explain the false negative result. Chinsky et al,(1956) followed 400 patients, 117 of whom had had acute myocardial infarctions. In 113 patients of this group serum transaminase activity was increased (92%) and only 4 patients had fals e negative results. Of these 4 patients, 2 had their first assay performed 3 days after the onset of symptoms, 1 died within an hour and a half and one had no assay performed between 6 and 60 hours after the infarction. The study of Denney et al (1956) of 150 patients included 77 with unequivocal myocardial infarction, 63 of whom had elevated levels, (82%).Of the 14 cases which failed to show increased serum transaminase activity 5 patients had the assay performed more than 3 days after the onset of their illness, 6 had only one sample of serum examined. However, 3 patients who had early and serial transaminase assays performed showed normal transaminase activity, (4.75%). Steinberg and Ostrow (1955) reported elevated levels of activity in 22 out of 24 cases of unequivocal acute myocardial infarction,(91%). In both cases which failed to show a ris e of serum transaminase activity, the assay had been performed on samples of serum withdrawn within 48 hours of the onset of the attack. Rudolph and Lyons (1955) described 39 cases of acute myocardial infarction, in 32 of which increased transaminase activity was found (82%); of the 7 patients with false negative results of serum transaminase assay, 1 patient died within 3 hours, 4 had their first assay performed after 3 days and only 2 had had serial assays performed within 48 hours of the onset of the attack.(2.5%). Kattus and his co-workers (1956) observed increased serum transaminase activity in 13 of 14 patients following acute myocardial infarction (93%), and that the patient with normal activity died within 3 hours of the onset of the infarction. Merrill and his colleagues (1956) found high levels of serum transaminase activity in each of 9 cases of acute myocardial infarction.(100%). Kattus and his associates (1957) demonstrated high levels of serum transaminase activity in 110 out of 111 cases of acute transmural myocardial infarction. (99.1%). The patient in whom the assay gave a normal result died within 4 hours

/hours of the onset of symptoms. Nydick and his co-workers (1957) reported that they had demonstrated high levels of serum transaminase activity in 297 out of 300 patients suffering from acute myocardial infarction (99%), but gave no explanation of the 3 false negative results. Ratner and Sacks (1957) in their study of 64 cases of unequivocal myocardial infarction found high levels of serum transaminase activity in 59 cases (92%), 1 case showing borderline values and 4 cases normal values. Of the 4 cases with normal serum transaminase activity, 3 were inadequately studied while the 4th had serial assays performed at appropriate times. There are many more descriptions in the literature of the results of serum transaminase assay which agree in substance with those already presented e.g., Biorck and Hanson (1956, Hanson and Biorck (1957), Walsh et al (1957), Losner et al (1957), Seligson et al (1957), Hoevenaars and Overholt (1957), Moore et al (1957) and Durant et al (1958). On review of the present findings and those of other workers, it is obvious that accurate timing of the withdrawal of blood samples for the serum transaminase assay is very important and that, in those cases of acute myocardial infarction, in which this is possible, the assay is found to show a high level of diagnostic accuracy. When the assay is performed as a routine procedure in unselected cases of acute myocardial infarction, as in the present series, these stringent conditions cannot be met, the diagnostic accuracy and value of the test fall and the number of serum transaminase assays giving normal results rises. These observations suggest that, unless acute myocardial infarction is thought to have occurred within 2 days of the performance of the test, the absence of high levels of serum transaminase activity cannot be used as evidence against the occurrence of acute myocardial infarction and that the use of the test as a routine procedure under such conditions is unrewarding. It should be noted also that in a very small percentage of cases, less than 5%., serum transaminase activity remains normal although serially examined at the recommended times following acute myocardial infarction. Failure to demonstrate increased transaminase activity, although uncommon, has also been observed following acute myocardial infarction, experimentally produced.(Rudolph et al (1957). Agress et al (1955) suggest that such exceptional findings may result from very small myocardial infarctions which involve less than 5% of the heart muscle. Whatever the true explanation may be these observations emphasise that great caution should be exercised in the interpretation of normal results of serum transaminase assay.

It is very important to establish the diagnosis of

/of acute myocardial infarction with certainty in order to evaluate this new diagnostic procedure. Pathological confirmation of the occurrence of acute myocardial infarction was obtained in 10 attacks of acute myocardial infarction and high levels of serum transaminase activity were demonstrated following 9 of these attacks. In the single case of acute myocardial infarction in which increased transaminase activity was not demonstrated death had occurred within 4 hours of the onset of the disease and the assay had been performed in the 0 - 6 hour-period following the onset of symptoms. Walsh et al (1957) reported a similar case of acute myocardial infarction, confirmed at autopsy, in which serum transaminase activity was normal 2½ hours after the onset. This confirms that there is a period of delay following acute myocardial infarction before a rise in serum transaminase activity occurs. Therefore, in this study, there was good agreement between the demonstration of high levels of serum transaminase activity during life and of acute myocardial infarction at autopsy. Ostrow et al (1956) have also demonstrated excellent correlation between serum transaminase activity and the findings at autopsy in 18 cases. 12 of their cases showed recent myocardial infarction at post mortem examination and all had shown high levels of serum transaminase activity in the period immediately after the onset of symptoms. 5 of these cases showed no evidence of recent myocardial infarction at autopsy and in none of these cases was there an increase in serum transaminase activity. Hence, in 17 out of 18 cases of acute myocardial infarction the diagnosis, as indicated by the results of serum transaminase activity, was corroborated by the results of post mortem examination. In the remaining case in which there was no evidence of recent myocardial infarction at autopsy and in which high levels of serum transaminase activity were demonstrated, Fiedler's myocarditis was found, indicating that any type of acute myocardial necrosis may result in elevated levels of activity. Kattus et al (1957) reported that 28 cases of uncomplicated acute myocardial infarction confirmed at post mortem examination had all shown high levels of serum transaminase activity. Ratner and Sacks (1957) found that in 15 out of 16 fatal cases in which acute myocardial infarction had been confirmed at autopsy, high levels of serum transaminase activity had been detected. In the remaining case, borderline levels of activity had been found on the second day following infarction, when the patient died of rupture of the heart. Durant and his associates (1957) obtained pathological confirmation of the presence of acute myocardial infarction in 6 cases in which serum transaminase activity had been high. It has been shown that,under experimental conditions,acute myocardial

/myocardial infarction almost invariably results in a rise in serum transaminase activity and that there appears to be a rough correlation between this rise, the size of the infarcted area of the myocardium and the diminution of tissue concentration of the enzyme. These experimental observations, together with those in fatal human cases, strongly suggest that increased transaminase activity in cases of acute myocardial infarction is the result of necrosis of heart muscle.

When the present investigation was begun, La Due and Wroblewski (1955) had already reported that high levels of serum transaminase activity may be found in the presence of liver disease. In 1951., Sherlock, in her study of the liver in heart failure, showed that the most constant histological finding, in liver biopsy material, was centrilobular necrosis of the liver and obtained positive biochemical evidence of impaired liver function. An unexpected finding, in view of the great functional reserve of the liver, was that evidence of impairment of liver function was obtained in many cases with only trivial histological lesions. In 1952., Evans and his associates demonstrated impaired hepatic function in congestive cardiac failure using tests which included bromsulphalein excretion, serum bilirubin, thymol turbidity and serum albumin and globulin. It is well known that congestive cardiac failure is common in acute myocardial infarction and in 6 out of 7 fatal cases of acute myocardial infarction in this series there was histological evidence of varying degrees of chronic venous congestion of the liver, although there was no evidence of centrilobular necrosis of liver. It is recognised that post mortem hepatic autolysis is particularly rapid in heart failure, (Popper 1948): (Sherlock,1951): and that the histological appearances of liver may be misleading in these cases but patients who had suffered an acute myocardial infarction were not considered to be suitable subjects for liver biopsy. It was decided, therefore, to examine hepatic function in cases of acute myocardial infarction by serum analysis since this was the most convenient and least disturbing method, to find out if the rise in serum transaminase activity in this condition was due to associated liver dysfunction. The results of serial examinations of liver function and serum transaminase activity have been presented and the conclusion has been drawn from them that increased serum transaminase activity in acute myocardial infarction is not the result of liver dysfunction although impairment of liver function may possibly contribute to the persistence of high levels of serum transaminase activity for several days after the onset of the infarction. I have been unable to find reference

/reference in the literature to a similar investigation of the possible relationship between hepatic impairment and increased transaminase activity following acute myocardial infarction in human beings although Rudolph and his associates reported that pathological study of the liver in 10 dogs, selected at random, in which acute myocardial infarction had been induced, revealed no abnormalities. Although centrilobular necrosis of the liver was not found at autopsy in cases of acute myocardial infarction it has been found that this condition may arise in rapid cardiac arrhythmia or dissecting aneurysm and result in high levels of serum transaminase activity. In these cases of centrilobular necrosis of liver the enzyme is probably derived from the liver as a result of liver cell damage. Hepatic cell necrosis supervening in acute myocardial infarction could conceivably result in high levels of serum transaminase activity to which enzyme released from both heart and liver contributed and this aspect of hepatic function in acute myocardial infarction merits further study.

The nature of the pathological examination, in this study, did not permit investigation of a quantitative relationship between peak levels of serum transaminase activity and the amount of infarcted heart muscle, such as has been described in experimental studies, and insufficient data has been collected to permit even tentative conclusions to be drawn about the value of transaminase activity in the prognosis of acute myocardial infarction. La Due and Wroblewski (1955) in their study of 50 patients with unequivocal acute myocardial infarction were unable to find any correlation between the height of serum transaminase activity and the presence or absence of shock. Chinsky and Sherry (1957) in a study of 222 acute myocardial infarctions reported that their data was still insufficient to correlate serum transaminase activity with the size of myocardial infarction or prognosis, but their results seemed to show a relationship between the height of serum activity and morbidity and mortality. Of 214 patients who survived the first day of their illness, 48 developed serum transaminase levels of more than 200 units/ml. Of these 48 patients, 25 died (52%) and 10 were in a state of severe shock for protracted periods of time. Of 166 patients in whom serum transaminase activity did not reach levels of 200/units/ml., only 22 died (13%) and the incidence of shock was lower. Kattus and his associates (1957) reported that their findings in fatal cases strongly suggested that serum transaminase levels above 350 units/ml were an indication of a grave prognosis and probably indicated extensive myocardial infarction. They also observed that very high levels of serum transaminase activity above

/above 1,000 units/ml. were associated with profound shock but also that shock did not always produce extremely high levels of activity. In my study of serum transaminase activity and the degree of peripheral vascular failure, as estimated by clinical criteria, following acute myocardial infarction, the average maximum serum transaminase activity in attacks in which a moderate to extremely marked degree of peripheral vaacular failure was present, was 231 units/ml. while the average maximum serum transaminase activity in those attacks in which peripheral vascular failure was absent or present only to a minimal degree was 95 units/ml. Although these averages are based on a relatively small number of assays, they provide evidence that suggests statistical correlation of serum transaminase activity to the degree of peripheral vascular failure in acute myocardial infarction. However, it has been pointed out that, in individual cases, the level of serum transaminase activity cannot be accepted as evidence of the degree of peripheral vascular failure since there is an overlap in the ranges of serum transaminase activity found in the various degrees of failure.

Prodromal angina pectoris at rest has been shown to be common in acute myocardial infarction and the differentiation of severe angina pectoris from acute myocardial infarction to depend upon examination of the electrocardiogram. The electrocardiographic diagnosis may be difficult or delayed especially in those cases in which the electrocardiogram shows changes indicative of a previous myocardial infarction, of acute coronary insufficiency or of myocardial ischaemia since, in these circumstances, the final electrocardiographic diagnosis depends upon serial examination of the electrocardiogram. Evidence has been obtained from experimental work that acute myocardial ischaemia in dogs does not result in increased serum transaminase activity unless ischaemia of heart muscle has been so prolonged that necrosis of this tissue has resulted. In view of these observations, it was decided to investigate the effect of acute myocardial ischaemia on the serum transaminase activity in human subjects. 25 attacks of angina pectoris at rest occurring in 20 patients were studied. The severity of symptoms, in each attack, had been of sufficient degree to raise suspicion of the development of acute myocardial infarction. In 22 out of these 25 attacks of angina pectoris, there was no electrocardiographic evidence of fresh myocardial infarction following the onset of the attack. In the remaining 3 attacks, the diagnosis of angina pectoris without myocardial infarction was made on clinical grounds. Serial serum transaminase assays were performed within 48 hours of the onset of symptoms in 24 out of the 25 attacks and,in the remaining attack, serial assays were performed 24 - 48 hours and 48 - 72 hours after the onset.

High levels of serum /2

/serum transaminase activity were not demonstrated in any of these attacks of angina pectoris. Normal serum transaminase activity was found in 22 out of 25 attacks of angina pectoris even in the presence of electrocardiographic abnormalities, diagnostic of previous myocardial infarction, acute coronary insufficiency, myocardial ischaemia and of left ventricular hypertrophy and strain. Borderline levels of serum transaminase activity were demonstrated in 3 attacks of angina pectoris. 2 of these attacks had been characterised by repeated and severe attacks of chest pain and had occurred in patients whose electrocardiograms showed changes indicative of previous myocardial infarction. However, in the remaining attack, in which an increase of serum transaminase activity to borderline levels was detected, the attack had been of shorter duration than in 3 attacks in which normal activity had been found and was accompanied by non-specific changes in the electrocardiogram suggestive of myocardial fibrosis which suggests that the increase in transaminase activity is unrelated both to the duration of symptoms and to particular electrocardiographic patterns. These findings confirm those found in experimental myocardial ischaemia. When serum transaminase assay is performed at the recommended times the contrast between the high levels of serum transaminase in attacks of acute myocardial infarction and the normal or borderline levels of activity in attacks of acute myocardial ischaemia without myocardial infarction is so striking as to suggest that the test might be of help in the differentiation of these conditions. In the attacks of angina pectoris under consideration, the time of onset of the attacks could be estimated with accuracy and there was no evidence of complicating disease, known to be associated with increased transaminase activity, except in one attack in which a short paroxysm of auricular fibrillation was observed. Under these circumstances, it is presumed, on the basis of experimental work, that the borderline increases of serum transaminase activity observed are due to myocardial necrosis, the result of prolonged myocardial ischaemia. The failure to confirm the presence of such necrosis electrocardiographically may be due to the presence of pre-existing patterns of myocardial infarction or to the microscopic size of the area of infarcted muscle. These results and their interpretation have been confirmed by several workers. For example, Chinsky and Sherry (1957) in a study of 109 cases of angina pectoris found normal serum transaminase activity in 99 cases and borderline activity in 10 cases. In no instance was a high level observed. Nydick and his associates (1957) in a study of 50 patients suffering from "clinical" coronary insufficiency found normal levels of serum transaminase activity in 34 patients and increased activity in 16. All these patients had had constant praecordial

/praecordial pain of at least 30 minutes' duration and their electrocardiograms showed definite T wave abnormalities, but without evidence of fresh myocardial infarction although, in some cases, there were changes of previous myocardial infarction. These workers comment that these patients frequently showed ST-T abnormalities in the electrocardiogram which suggests that examples of acute intramural myocardial infarction, as defined in this investigation, may be included in their studies. This may account for the much higher incidence of increased serum transaminase observed. Rafner and Sacks (1957) found normal levels of serum transaminase activity in 32 out of 33 patients who had suffered short and typical bouts of angina pectoris and found high levels of transaminase activity in the remaining case. They also investigated 47 patients whose anginal pain was severe and prolonged but who had no clinical or electrocardiographic stigmata of acute myocardial infarction and found normal serum transaminase activity in 41 of these patients, the remaining 6 showing high levels of activity. The presence of normal serum transaminase activity in a high percentage of cases of angina pectoris has been reported by other workers and they attribute, as I have done, borderline or high levels of activity in this clinical setting to myocardial necrosis following prolonged myocardial ischaemia e.g., La Due and Wroblewski (1955); Losner et al, (1957); Hoevenaars and Overholt,(1957) and Walters and Littlejohn (1958). In the human subject proof of this conception depends upon the demonstration at autopsy of the absence of acute myocardial infarction in those patients suffering from angina pectoris, in whom normal serum transaminase activity was found and also upon obtaining pathological confirmation of the presence of acute myocardial necrosis in those cases of angina pectoris without clinical or unequivocal electrocardiographic evidence of infarction in which increased serum transaminase activity had been demonstrated. Ideally, pathological proof should be sought in cases of angina pectoris, dying of intercurrent diseases, shortly after the attack of chest pain which was followed by normal serum transaminase activity. Such an opportunity did not arise in this study but 3 fatal attacks of acute myocardial infarction which had been preceded by attacks of angina pectoris associated with normal or borderline levels of serum transaminase activity were studied at post mortem. There was no evidence in these cases of acute myocardial infarction, related in time to the period during which normal or borderline serum transaminase activity had been observed following angina pectoris. It has already been noted that in the attack of angina pectoris which was followed by an increase of

/of serum transaminase activity, microscopic areas of heart cell necrosis, related to the rise in transaminase activity, may have escaped detection at autopsy. The observations of Ostrow and his associates (1957) to which I have already referred, are also relevant to this problem. They performed autopsies on 5 patients in whom normal serum transaminase activity had been demonstrated. 2 of these 5 patients had been considered to have sustained an acute myocardial infarction, the electrocardiogram, in each case, showing serial T wave inversions, but no myocardial infarction was demonstrated by gross and microscopic examination of the myocardium. In the remaining 3 cases, although electrocardiographic changes of "ST-T type" were present, the illness was not considered to be due to acute myocardial infarction and at autopsy no acute myocardial infarctions were found. Therefore, although pathological proof is lacking, there is pathological evidence, albeit scanty, which suggests that high levels of serum transaminase activity are not found following angina pectoris without acute myocardial necrosis. In this regard, the importance of accurately estimating the time of withdrawal of serum samples for the assay is obvious.

The results of serum transaminase assay in cardiovascular conditions other than acute myocardial infarction or angina pectoris at rest have already been presented and will now be discussed.

In this study, normal serum transaminase activity was demonstrated in cases of left ventricular and congestive cardiac failure due to ischaemic heart disease and in one case the absence of acute myocardial infarction was confirmed at autopsy. Similar findings have been reported by La Due and Wroblewski (1955), Steinberg and Ostrow (1955) and Kattus et al (1956). However, Chinsky and Sherry (1957) in a study of 27 cases of acute pulmonary oedema in which acute myocardial infarction was not the precipitating cause, found normal levels of serum transaminase activity in 19 cases and borderline levels in 7. Liebermann and his associates (1957b) studied 14 patients suffering from moderate to severe congestive cardiac failure and found normal serum transaminase activity in 11 out of the 14 cases, (78.6%), but in 2 of the 14 cases serum transaminase activity was high and in the remaining case, borderline. They suggested that sudden passive congestion of a liver already damaged by chronic heart failure may promote further damage to the liver cells with consequent rise in serum transaminase activity. I have already suggested, from my study of hepatic function in acute myocardial infarction, such a possibility. On the other hand, Chinsky and Sherry (1957) observed normal serum transaminase activity in 26 cases of congestive cardiac failure. These observations suggest that serum transaminase activity is not

/not ordinarily significantly affected by left ventricular or congestive cardiac failure and that, if increased serum transaminase activity is found in these conditions, the diagnosis of acute myocardial infarction in such circumstances should depend upon the history and the electrocardiogram.

Normal serum transaminase activity was found in 7 cases of ischaemic heart disease, in 4 cases of essential hypertension and in 4 cases of chronic cor pulmonale due to chronic bronchitis and emphysema. Many workers have confirmed these findings e.g., Denney et al (1956), and Chinsky et al (1956). These observations suggest that these conditions are unlikely to affect the diagnostic usefulness of the assay, unless complicated by other lesions known to be associated with increased serum transaminase activity.

In this study, normal serum transaminase activity was demonstrated in 2 cases of acute rheumatic fever in the first days of aspirin treatment of the disease. In 1955., Nydick and his associates,in a study of 64 patients with acute rheumatic fever, found 26 patients with acute rheumatic carditis. Elevated serum transaminase activity was found in 17 of these 26 patients. Histological examination of the heart was performed either at autopsy or during the operation of mitral commissurotomy on 15 patients. 10 of these 15 patients had evidence of active carditis and 5 of them had increased serum transaminase activity. Hence, they found that in rheumatic carditis 50% - 65% of patients show elevated levels of serum transaminase activity. However, Manso and his co-workers, (1956), found that serum transaminase activity was increased to abnormal levels in more than 50% of children, not suffering from acute rheumatic fever, to whom aspirin or sodium salicylate had been administered. The mechanism for this rise in transaminase activity is unknown but they suggested the possibility of increased release of the enzyme from the liver since Goodman and Gilman (1955) had shown that changes in hepatic function and morphology may follow aspirin administration. Whatever the explanation of these observations they suggest that serum transaminase assay cannot be relied upon to differentiate acute rheumatic fever, salicylate toxic hepatitis and acute myocardial infarction. Therefore, the test has no value as a means of assessing the degree of myocarditis in acute rheumatic pericarditis. The differentiation of acute rheumatic fever and acute myocardial infarction is rarely difficult. In such circumstances e.g., acute rheumatic pericarditis, the demonstration of normal serum transaminase activity, provided serum samples had been withdrawn at the appropriate times, would favour the diagnosis of acute rheumatism. It is generally agreed that uncomplicated,inactive rheumatic

/rheumatic heart disease is associated with normal serum transaminase activity and this was confirmed in a study of 5 such cases in the present series.

In cases of acute pericarditis, it may be difficult to decide whether or not the lesion is due to acute myocardial infarction. In this study, only one case of acute pericarditis was observed. In this case, the inflammation was due to uraemia and there was electrocardiographic evidence of acute pericarditis and hyperkalaemia but normal serum transaminase activity was found. Nydick and his associates (1957) demonstrated normal serum transaminase activity in 9 out of 11 cases of acute pericarditis. The group in which normal serum transaminase activity was found included 3 cases of idiopathic benign pericarditis, 3 cases of uraemia, one case of Hodgkin's Disease and one case of disseminated lupus erythematosus. In 2 cases intermittent elevations of serum transaminase activity were found and, in these cases, pericarditis was due to infective mononucleosis and leukaemia respectively. Several workers have reported normal serum transaminase activity in acute pericarditis. For example, Chinsky and Sherry (1957) reported normal serum transaminase activity in 5 cases of benign idiopathic pericarditis and Biorck and Hanson (1957) made similar observations on a single case of this condition. Evidence has been derived from a study of experimental pericarditis in dogs that normal serum transaminase activity is present unless damage to sub-epicardial heart muscle is found. These findings suggest that serum transaminase assay, as in acute rheumatic fever, might be a valuable ancillary diagnostic tool in differentiating acute pericarditis, due to acute myocardial infarction, from other forms of acute pericarditis. The demonstration of normal serum transaminase activity would favour the diagnosis of acute pericarditis without acute myocardial infarction provided the assay had been performed at the recommended times.

In this study, 2 cases of acute myocardial infarction presented with signs and symptoms of a cerebro-vascular accident and in one of these cases, the cerebro-vascular lesion was the only symptom of acute myocardial infarction. The simultaneous occurrence of a cerebro-vascular lesion and acute myocardial infarction has previously been reported by Bean and Read (1942) and by Bean and his associates (1949). They believed that cerebral involvement in such cases was secondary to the hypotension associated with acute myocardial infarction and observed that thrombosis of vessels was seldom found. It was thought that the neurological signs resulted from reduced circulation through cerebral vessels which were already rigid and narrowed from atherosclerosis. However, Paton

/Paton (1957) found cerebral haemorrhages or major cerebral thromboses in all cases observed by him, in which a cerebrovascular accident and acute myocardial infarction had occurred simultaneously. Both of the patients observed by me had severe residual paralysis of limbs, suggesting that a major cerebral thrombosis had occurred in each case. Normal serum transaminase activity was found in 4 cases of cerebral infarction not associated with acute myocardial infarction. In 2 cases cerebral infarction was due to cerebral embolism. In one of these cases, the diagnosis was confirmed at autopsy and the absence of acute myocardial infarction was demonstrated. In 2 cases the diagnosis of cerebral thrombosis was made on clinical grounds. Similar findings were reported by Green and his associates (1957) who observed normal serum transaminase activity in 11 patients suffering from cerebral infarction. It has already been shown that experimentally produced cerebral infarctions in dogs may result in increased serum transaminase activity. It is not surprising, therefore, to find that other workers have reported increased serum transaminase activity following cerebral infarction. For example, Fleisher and his colleagues (1957) showed that high levels of serum transaminase activity followed 8 out of 21 cases of cerebral infarction. Liebermann and his associates (1957b) observed high levels of serum transaminase activity in 12 out of 21 patients suffering from cerebral infarction. In 3 of these 12 patients, acute myocardial infarction was also present. In the 9 patients in whom there was no evidence of acute myocardial infarction, the time/ transaminase curve obtained following the cerebrovascular accident resembled the curve obtained in acute myocardial infarction, although the upslope was more gradual and the attainment of maximum serum transaminase activity was delayed for 48 - 72 hours following the onset of illness. They observed also that, while the levels of serum transaminase activity reached following cerebral infarction were, in general, not so high as those reached following acute myocardial infarction, the levels of activity overlapped. Myerson and his associates (1957) have also reported slight to moderate increases in serum transaminase activity in 11 out of 21 cases of cerebral infarction. These observations suggest that serum transaminase assay is of little value in the diagnosis of acute myocardial infarction when cerebral infarction co-exists.

The differential diagnosis between acute myocardial infarction and acute pulmonary infarction may be very difficult. (Hamman 1934). The electrocardiographic pattern of acute cor pulmonale which was originally described by McGinn and White in 1935 is found in only a few patients. (Sokolow et al, 1940). In view of these

/these difficulties serum transaminase assays were performed in 6 cases of acute pulmonary infarction since, if this condition were shown to be associated with normal serum transaminase activity, then the test might be of great value in the differentiation of acute pulmonary infarction from acute myocardial infarction which has been shown to be associated with high levels of serum transaminase activity. In 5 of the 6 cases of pulmonary infarction, infarction followed pulmonary embolism. In the remaining case, acute pulmonary infarction was due to local pulmonary vessel thrombosis. In 2 of these 5 cases of acute pulmonary embolism and infarction normal serum transaminase activity was found following the onset of the illness. In one of these cases, the electrocardiogram showed the changes of acute coronary insufficiency and auricular fibrillation but the ventricular rate was slow, approximately 90/min. In 2 of the 5 cases of pulmonary embolism serum transaminase activity reached borderline levels following the onset of the illness and in both cases there was electrocardiographic evidence of rapid auricular fibrillation with a ventricular rate of 170-180/min. In one of these cases, the diagnosis of acute pulmonary embolism and infarction was confirmed at autopsy and the absence of acute myocardial infarction demonstrated. In the remaining case of acute pulmonary embolism with infarction high levels of serum transaminase activity were demonstrated 5 days after the onset of symptoms. In this case, there was no electrocardiographic evidence of acute myocardial infarction or arrhythmia and the reason for the delay before the rise in serum transaminase activity is unknown. In the single case in which acute pulmonary infarction was due to local pulmonary vessel thrombosis high levels of transaminase activity were demonstrated. Although the electrocardiograms, in this case, showed the patterns of increasing acute coronary insufficiency, no evidence of acute myocardial necrosis was found on gross or microscopic examination of the heart at autopsy. Acute pulmonary infarction occurring in relation to an alveolar cell carcinoma of lung was found at autopsy together with left ventricular and congestive cardiac failure. In the absence of microscopic evidence of centrilobular necrosis of liver, the rise in serum transaminase activity was ascribed to release of enzyme from the acute pulmonary lesion although it may have been due to left ventricular or congestive cardiac failure, or to a microscopic area of acute myocardial necrosis which had escaped detection . It has been shown that rapid auricular fibrillation with ventricular rates above 160/minute can be associated with high levels of serum transaminase activity in cases in which there was no evidence of acute pulmonary infarction.

Therefore, in the 2 cases of acute pulmonary embolism and infarction showing borderline levels of serum transaminase activity this increase could not be attributed to acute pulmonary infarction with certainty. Of the 4 cases in which rapid cardiac arrhythmia was absent, 2 cases showed normal and 2 showed high levels of serum transaminase activity. Chinsky and Sherry (1957) observed 6 cases of acute pulmonary infarction. In 5 of them they demonstrated normal levels of serum transaminase activity but,in the remaining case, high levels of serum transaminase activity were detected before the patient succumbed to a massive pulmonary infarction. Goldstein and his associates (1956) reported that normal serum transaminase activity was found in 21 out of 26 cases of acute pulmonary infarction. In one of the 5 cases showing high levels of serum transaminase activity, jaundice was present from multiple pulmonary emboli and the rise in transaminase activity,which did not occur until the third day after the onset of illness,was ascribed to liver damage rather than directly to the pulmonary infarction. In the other 4 cases, in which high levels of serum transaminase activity were detected, lesions other than acute pulmonary infarction were present which could have accounted for the rise in transaminase activity viz., liver necrosis, portal cirrhosis, extensive third-degree burns and fractured femur with tissue injury. The series of Denney et al (1956)of 4 patients with acute pulmonary infarction included 2 patients with normal serum transaminase activity values and 2 with high values. Ostrow and his colleagues (1956) in a study of 15 cases of acute pulmonary embolism with infarction demonstrated normal serum transaminase activity in 8 cases. In 7 out of these 15 cases, serum transaminase activity was increased but the levels did not rise above 85 units/ml. They observed that the rise of serum transaminase activity did not occur, in most cases, until the fourth or sixth day after the onset of symptoms, unlike the sharp early rise in activity demonstrated following acute myocardial infarction,and also that the increase in transaminase activity often just preceded or accompanied jaundice, following pulmonary infarction. They attributed the rise in serum transaminase activity following acute pulmonary infarction to pulmonary necrosis, haemolytic reaction, hepatic dysfunction or a combination of these. Nydick and his associates demonstrated normal serum transaminase activity in 6 out of 7 cases of acute pulmonary infarction. In one of the 7 cases, serum transaminase activity reached a peak level of 50 units/ml.

These observations suggest that high levels of

/of serum transaminase activity may follow acute pulmonary infarction and that in some cases the rise in activity may be delayed compared with the rapid rise to high levels following acute myocardial infarction. They also suggest that there are many possible sources of the rise in serum transaminase activity following acute pulmonary infarction. The rise in activity may be due to release of the enzyme from necrotic lung tissue as suggested by the post mortem findings in one of my cases, or due to conditions which may precede, accompany or follow acute pulmonary infarction and which themselves may cause high levels of serum transaminase activity e.g., traumatic lesions, rapid auricular fibrillation and hepatic dysfunction secondary to pulmonary infarction. Seligson and his colleagues (1957) also suggest that the rise in serum transaminase activity following some cases of acute pulmonary infarction may be due to subendocardial necrosis of the myocardium, secondary to prolonged shock. Although such a sequence of events was not found in this small series, the presence of the electrocardiographic patterns of acute coronary insufficiency in 2 of my cases indicates that this suggestion merits further study. However, the frequent demonstration of normal serum transaminase activity following acute pulmonary infarction suggests that, in differentiating between acute myocardial and acute pulmonary infarction, the detection of normal serum transaminase activity 6 - 24 and 24 - 48 hours after the onset of symptoms is evidence in favour of the diagnosis of acute pulmonary infarction.

In a study of 6 patients suffering from thrombo-embolic conditions other than acute pulmonary infarction, normal serum transaminase was found in 4 patients, borderline levels of serum transaminase activity in one and high levels in one. In no instance, was there any clinical or electrocardiographic evidence of acute myocardial infarction. Phlebothrombosis of the deep veins of the lower limbs was associated with normal serum transaminase activity in 2 cases. In one case, embolism of the renal artery with infarction of the kidney was associated with normal serum transaminase activity and, in another case, gangrene of the foot, due to arterial thrombosis, was associated with normal activity. Borderline levels of serum transaminase activity were observed in one case, 7 days after the onset of saddle embolism of the aorta. In this case, there was no evidence, at autopsy, of acute myocardial infarction. The increase in serum transaminase activity observed was ascribed to release of the enzyme from necrotic skeletal muscle and other tissues. High levels of serum transaminase activity were found in one case of mitral stenosis in which multiple emboli of systemic arteries had occurred.

/occurred. In this case, there was no evidence of myocardial infarction on post mortem examination and the high levels of serum transaminase activity were ascribed to release of enzyme from the tissues damaged by the arterial emboli. In both cases in which increased serum transaminase activity was found, auricular fibrillation was present but the ventricular rate was relatively slow in each case and, therefore, the arrhythmia was unlikely to have resulted in the increased serum transaminase activity observed. Other workers have reported high levels of serum transaminase activity following thrombo-embolic lesions. For example, Chinsky and his colleagues, (1956) observed high levels of serum transaminase activity in a case of gangrene of the foot, and Merrill and his associates (1956) reported high levels of activity in a similar case. Kattus and his co-workers (1956) in a study of 2 cases of subclavian artery thrombosis found normal levels of serum transaminase activity in one patient and borderline levels of activity in the other. Evidence, obtained from animal experiments, suggests that arterial occlusion results in high levels of serum transaminase activity. These observations suggest that in the human subject increased transaminase activity may occasionally result from arterial occlusion and, therefore, that the presence of such lesions may detract from the usefulness of the assay in the diagnosis of acute myocardial infarction.

It may be very difficult to differentiate between acute myocardial infarction and dissecting aneurysm of the aorta. Serial serum transaminase assays were performed in 2 cases of dissecting aneurysm of the aorta and in each case high levels of serum transaminase activity were demonstrated. In each of these cases, the diagnosis was confirmed at autopsy. There was no evidence at autopsy, in either case, that acute myocardial necrosis was responsible for the high levels of transaminase activity found. In one case, histological examination revealed the presence of marked centrilobular necrosis of the liver and, since hepato-cellular damage is known to result in high levels of serum transaminase activity (Molander et al, 1955) the high levels of serum transaminase activity observed were probably due to the release of the enzyme from necrotic hepatic tissue. It is regretted that, through an oversight, microscopic examination of the liver was not performed in the other case, but it seems probable that, in this case too, liver damage resulted in elevated serum transaminase activity. Other workers have reported single cases of dissecting aneurysm of the aorta in which normal serum transaminase was observed e.g., Hoevenaars and Overholt (1957) and Seligson et al (1957). These observations indicate that high levels of serum transaminase

/transaminase activity may occur in acute dissecting aneurysm of the aorta and suggest that centrilobular necrosis of the liver may be the source of elevated serum transaminase activity in this condition. It is suggested that in the differentiation of acute myocardial infarction and dissecting aneurysm of the aorta, the demonstration of normal serum transaminase activity is in favour of the diagnosis of dissecting aneurysm of the aorta, if the assay is performed at the proper time.

It has been shown that supraventricular tachycardia and auricular fibrillation not uncommonly develop during the course of acute myocardial infarction and, therefore, serum transaminase assays were performed in 10 cases of auricular fibrillation in which there was no evidence of acute myocardial infarction. In 5 out of these 10 attacks normal transaminase activity was demonstrated and in these attacks the ventricular rate was relatively slow, approximately 80 - 100/min. In 3 out of these 10 attacks, serum transaminase activity rose to borderline levels,but this increased activity could not be confidently attributed to the cardiac arrhythmia because of the presence of other lesions known to be associated with increased serum transaminase activity viz., acute pulmonary infarction in one case, and systemic arterial embolism in 2 cases. In the 2 cases in which auricular fibrillation and systemic arterial embolism co-existed the ventricular rate was relatively slow, approximately 100/min. Since slow rates of auricular fibrillation have been shown to be compatible with normal serum transaminase activity, it was thought that the increased levels of serum transaminase activity observed in these 2 cases were probably due to release of the enzyme from tissues damaged by the arterial emboli. In the remaining case, acute pulmonary infarction was present at the time when very rapid auricular fibrillation (ventricular rate 170-180/min) was observed. Since high levels of serum transaminase activity have been demonstrated in both of these conditions, either lesion may have resulted in the increased levels of serum transaminase activity found. High levels of serum transaminase activity were found in 2 out of the 10 cases of auricular fibrillation and in one of these 2 cases the highest levels of serum transaminase activity demonstrated in this series were found. In both of these cases the arrhythmia was very rapid, the ventricular rate being over 160/min., and frank congestive cardiac failure was present. No other cardiovascular lesions, known to be associated with increased serum transaminase activity were found in either case. In both cases, serial examination of liver function revealed high levels of serum bilirubin, suggestive of liver dysfunction.

/dysfunction. Centrilobular necrosis of the liver was found at autopsy in one case and the absence of other lesions known to result in increased serum transaminase activity was confirmed. Although there was no close correlation between the degree of liver dysfunction, as revealed by the tests employed, and the level of serum transaminase activity demonstrated, these observations suggest that,in cases of auricular fibrillation in which the ventricular rate is above 160/min., centrilobular necrosis of liver may supervene with the release of the enzyme into the serum and the development of high levels of serum transaminase activity, since it is well established that hepato-cellular damage may result in very high levels of serum transaminase activity. Chinsky and Sherry (1957) observed 22 cases with various cardiac arrhythmias. Their group included 7 cases of paroxysmal supraventricular tachycardia, 4 cases of auricular fibrillation, 3 cases of auricular flutter, 2 cases of ventricular tachycardia, one case of nodal tachycardia and one case of Wolff-Parkinson-White syndrome. In 9 out of these 22 cases, high levels of serum transaminase activity were detected and,in these cases, the ventricular rate was usually above 180/minute. In one of the 9 cases, marked centrilobular necrosis was found at autopsy and there was no evidence of myocardial necrosis. They also reported another case, which had been observed at another institution, in which rapid arrhythmia had been associated with high levels of serum transaminase activity and in which extensive centrilobular liver cell necrosis had been found at autopsy. These observations suggest that high levels of serum transaminase activity may be observed in association with very rapid arrhythmias of any type. The number of cases studied is small and the mechanism of the rise in serum transaminase activity is uncertain. Chinsky and Sherry (1957) suggested that centrilobular liver cell necrosis secondary to the diminished cardiac output of very rapid cardiac arrhythmia was the cause of increased serum transaminase activity in these cases and my findings lend support to this conception. Therefore, it is suggested that the serum transaminase assay should be regarded as unreliable in the diagnosis of acute myocardial infarction when rapid arrhythmia is present, especially when the ventricular rate is 160/minute or more. In differentiating between acute myocardial infarction and angina pectoris, in the presence of arrhythmia, it is suggested that the demonstration of normal serum transaminase activity is evidence in favour of the diagnosis of angina pectoris. It should be noted that these suggestions are at variance with those of Krause and his colleagues (1957) who considered that the demonstration of elevated serum transaminase activity might confirm the diagnosis of acute myocardial infarction in the presence of

/of cardiac arrhythmia. Evidence has also been presented that high levels of serum transaminase activity due to rapid auricular fibrillation may persist for longer periods than those due to acute myocardial infarction but this difference in time/transaminase curves has no practical value.

The results of serum transaminase assay in diseases outwith the cardiovascular system have already been presented and will now be discussed.

It has been shown that evidence of peptic ulceration is not uncommonly found in patients suffering from acute myocardial infarction. The demonstration of normal serum transaminase activity in one case of severe duodenal ulcer dyspepsia in which acute myocardial infarction was suspected and in 5 cases of perforated peptic ulcer, suggests that the assay might be valuable in differentiating between acute myocardial infarction and peptic ulceration in that the demonstration of normal serum transaminase activity at the proper times following the onset of pain would lend support to the diagnosis of peptic ulceration as there is general agreement that peptic ulceration is associated with normal serum transaminase activity e.g., Pryse-Davies and Wilkinson, 1958. It is also suggested, however, that as serum transaminase activity may not rise to high levels until 6 hours have elapsed following acute myocardial infarction, the assay will prove of little practical value in the differentiation of perforated peptic ulcer from acute myocardial infarction, since the perforated viscus should be repaired surgically as soon as possible and certainly within 8 hours of its onset. Under these circumstances, the diagnosis should obviously depend upon the history and the clinical and electrocardiographic findings, rather than on the results of transaminase assay.

Gastro-oesophageal pain may resemble cardiac pain, (Evans, 1952). Whether reflexes from the alimentary tract affect the coronary circulation is uncertain since the exact action of the vagus and the sympathetic nerves on the heart in the intact animal is obscure.(Gregg,1950). Baylis and his associates (1955) have studied the oesophagus as a source of pain resembling angina pectoris, by distending a rubber bag in the lower oesophagus in 8 healthy people,and 3 patients with coronary artery disease. Distension of the bag was accompanied by pain which was similar in the healthy subjects and in the patients, who found that it differed from their angina pectoris but were unable clearly to define the difference. These workers found that such oesophageal distension did not produce electrocardiographic changes which could be confused with those of myocardial ischaemia and they concluded, like

/like Evans (1952), that the electrocardiogram was the most reliable method of distinguishing cardiac from oesophageal pain. It is obvious, however, if the electrocardiogram already shows the changes of a previous myocardial infarction, the differentiation between the pain of acute myocardial infarction and the pain of oesophageal origin may be very difficult. This diagnostic difficulty was encountered in a case in the present series in which there was electrocardiographic evidence of a previous myocardial infarction and in which severe attacks of angina pectoris, suggestive of acute myocardial infarction, were induced by changes in the size and position of a large hiatus hernia. It was uncertain whether these attacks of anginal pain and their accompanying electrocardiographic changes of myocardial ischaemia were due to alteration in the position of the heart caused by changes in the hiatus hernia, or to reflex effects of these changes upon the coronary circulation. In this case and in another, in which there was no suspicion of acute myocardial infarction, normal serum transaminase activity was demonstrated. Several workers have reported normal serum transaminase activity in hiatus hernia e.g., Chinsky and Sherry (1957); Sawyer and his colleagues (1958). These observations suggest that serum transaminase assay may be of value in differentiating between acute myocardial infarction and hiatus hernia since the demonstration of normal levels of serum transaminase activity at the proper times following the onset of symptoms would lend support to the latter diagnosis. They also suggest that the assay is of no value in differentiating between the pain of angina pectoris, unaccompanied by infarction and oesophageal pain.

Normal serum transaminase activity was demonstrated in 2 cases of steatorrhoea and this finding has been confirmed by Pryse-Davies and Wilkinson (1958), who examined 5 cases of this disease. These workers also observed normal serum transaminase activity in gastro-intestinal diseases provided there was no evidence of hepatic involvement e.g., argentaffinoma, gastric, rectal and colonic carcinoma and regional ileitis. Therefore, it is suggested that the presence of steatorrhoea will not affect the usefulness of serum transaminase assay in the diagnosis of acute myocardial infarction.

Acute bronchopneumonia, when accompanied by profound shock, may be mistaken for acute myocardial infarction, (Paton, 1957). Normal serum transaminase activity was found in 2 cases of bronchopneumonia and in one case of diaphragmatic pleurisy, in which acute myocardial infarction was suspected. These findings are in agreement with those of other workers e.g., Chinsky and Sherry (1956) although Biorck and Hanson (1956) expressed doubt as to whether

/whether severe infection of the respiratory tract might result in high levels of serum transaminase activity when associated with circulatory distress and suggested that such increased transaminase might occur primarily or be secondary to liver damage. These results suggest that, in the differentiation of acute myocardial infarction and acute pneumonia, the demonstration of normal serum transaminase activity, if the assay is performed at the proper times, is in favour of the latter diagnosis.

Normal serum transaminase activity was demonstrated in 2 cases of pulmonary tuberculosis. Of 2 cases of neoplasm of the lung, normal serum transaminase activity was found in one case and, in the other, high levels of activity were found in association with acute pulmonary infarction. There is general agreement that pulmonary tuberculosis is associated with normal serum transaminase activity, which suggests that the presence of this disease is unlikely to interfere with the rise of transaminase assay in the diagnosis of acute myocardial infarction. The differentiation between neoplasm of the lung and acute myocardial infarction is rarely difficult. The demonstration of high levels of serum transaminase activity in neoplasm of lung either due to acute pulmonary infarction, as in this investigation, or to metastatic spread of the tumour to the liver (Wroblewski and La Due, 1955b) suggests that, when acute myocardial infarction is suspected in a patient suffering from neoplasm of lung, normal results of serum transaminase assay,if performed at the proper times, would be evidence against the diagnosis of acute myocardial infarction.

At least 50% of all diabetics die as a result of cardiovascular complications and the relative incidence of this cause of death is increasing as other fatal complications of diabetes mellitus are eliminated. In diabetes mellitus, the most common fatal cardiovascular lesion is coronary occlusion (White, 1951). The combination of diabetes mellitus and acute myocardial infarction was observed in one case in this series. Normal serum transaminase activity was demonstrated in 2 cases of diabetes mellitus in this study, and there is general agreement that diabetes mellitus is associated with normal serum transaminase activity e.g., Gutteridge and McKean, (1958). These findings suggest that transaminase assay is reliable in the diagnosis of acute myocardial infarction when diabetes mellitus is present. Normal serum transaminase activity was also found in 2 cases of thyrotoxicosis. In one of these cases, auricular fibrillation of slow ventricular rate was present. Several workers have reported similar findings e.g., Gutteridge and McKean (1958), which suggests that the presence of

/of thyrotoxicosis is unlikely to interfere with the usefulness of serum transaminase assay in the diagnosis of acute myocardial infarction unless thyrotoxicosis is complicated by rapid arrhythmia, which is known to result in high levels of serum transaminase activity. Normal serum transaminase activity has been repeatedly observed by other workers in myxoedema, hypoparathyroidism, hyperparathyroidism and Simmond's Disease, e.g., Gutteridge and McKean, (1958). There is general agreement that endocrine diseases are associated with normal serum transaminase activity.

The incidental association of gallstones and coronary atherosclerosis of high degree and the occasional confusion in diagnosis between these conditions (White, 1951) led me to examine the effect of cholelithiasis on serum transaminase activity. Normal serum transaminase activity was found in a case of gallstones, complicated by acute cholecystitis in which there was no evidence of obstructive jaundice. Borderline levels of serum transaminase activity were detected in another case in which gallstones were associated with obstruction of the biliary tract and chronic cholecystitis. Gallstones were also demonstrated at laparotomy in 3 cases of acute pancreatitis and were associated with high levels of serum transaminase activity in one of these cases. Therefore, in this small series, 2 out of 5 cases in which gallstones were present showed increaaed serum transaminase activity and in both of these cases there was evidence of liver dysfunction. Other workers have studied serum transaminase activity in gallbladder disease. For example, Ostrow and his associates (1956) observed high levels of serum transaminase activity in one case of acute cholecystitis with gallstones, in which there was no evidence of hepatocellular involvement. They found normal serum transaminase activity in another 7 cases of acute cholecystitis, the majority of which also had cholelithiasis. Chinsky and Sherry (1956) studied 7 cases of acute cholecystitis and demonstrated normal serum transaminase activity in 6 cases. In the 7th.case, which had presented with right upper quadrant abdominal and substernal pain, high levels of serum transaminase activity were found. There was no electrocardiographic evidence of acute myocardial infarction, but the gallbladder, which showed no function on radiological examination, contained gallstones. Ratner and Sacks (1957) reported elevated transaminase activity in a case of acute cholecystitis associated with jaundice. These observations suggest that high levels of serum transaminase activity may occasionally be found in cholelithiasis which is not unexpected since it has been shown that obstructive jaundice may be associated with increased serum transaminase activity. However, they also

/also suggest that, in differentiating between acute myocardial infarction and gallstones, the demonstration of normal serum transaminase activity at the proper times following the onset of symptoms is evidence in favour of the diagnosis of gallstones.

The clinical picture of acute pancreatitis may be very similar to that of acute myocardial infarction and the electrocardiographic changes of acute coronary insufficiency may develop during acute pancreatitis. Under such conditions, the differentiation of these diseases may be difficult and usually depends upon the results of serum amylase determinations and serial examination of the electrocardiogram. It was decided to investigate the effect of serum transaminase activity in acute pancreatitis since, if normal levels of activity were consistently found in acute pancreatitis, serum transaminase assay would be of value in differentiating this disease from acute myocardial infarction, which has been shown to be associated with high levels of serum transaminase activity. 3 cases of acute pancreatitis were studied. Normal levels of serum transaminase activity were found in 2 cases of acute interstitial pancreatitis and high levels of serum transaminase activity in one case of acute haemorrhagic pancreatitis. In each of these cases, the diagnosis of acute pancreatitis was confirmed by examination of the pancreas at operation. In one of the cases in which normal serum transaminase activity was found, performance of the assay may have been unduly delayed but, in the other case, showing normal levels, the assay had been performed at the proper time. In the case of acute haemorrhagic pancreatitis in which high levels of serum transaminase activity were found, the electrocardiographic changes of acute coronary insufficiency were present for 15 hours and serial examination of liver function revealed abnormalities suggestive of liver dysfunction. The cause of the rise in serum transaminase activity in this case remains uncertain. The rise in activity may have been due to necrosis of pancreatic tissue with release of the enzyme into the blood stream but two other possible explanations of the rise must be considered. First, the electrocardiographic studies in this case were incomplete and the possibility of acute subendocardial myocardial infarction with release of the enzyme from this tissue was not excluded. Secondly, high serum transaminase levels may have been the result of release of the enzyme from areas of hepatic damage since there was evidence of liver dysfunction. Other workers have reported similar results of serum transaminase assay in acute pancreatitis. For example, Chinsky and Sherry (1957) studied 26 cases of

/of acute pancreatitis. The diagnosis of acute haemorrhagic pancreatitis was made in only one case and this diagnosis was confirmed at autopsy. The remaining 25 cases were considered to be suffering from acute interstitial pancreatitis. High levels of serum transaminase activity were demonstrated in 17 of these 26 patients. They observed high levels of serum transaminase activity in almost all jaundiced cases while the majority of cases in which jaundice was absent had normal levels of serum transaminase activity. In the case of acute haemorrhagic pancreatitis, they observed borderline levels of serum transaminase activity. They found no correlation between the level of serum diastase and serum transaminase activity and suggested that the rise of serum transaminase activity in patients with acute pancreatitis may not be due to pancreatic necrosis alone, but that biliary or hepatic factors may also be involved. Denney and his associates (1956) studied 10 cases of acute pancreatitis and found increased serum transaminase activity in 5 cases. These observations suggest that,in the differential diagnosis of acute pancreatitis and acute myocardial infarction, electrocardiographic examination and serum amylase estimations are of primary importance, although normal results of serum transaminase assay, if performed at the proper time, would lend support to the diagnosis of acute pancreatitis. Evidence derived from experimental work on animals has been presented which suggests that hepato-cellular necrosis and obstruction of the biliary tract may result in high levels of serum transaminase activity. Since there is rarely confusion in diagnosis between acute myocardial infarction and disease of the liver, an exhaustive study of serum transaminase activity in liver disease was not attempted. A few cases of liver disease of varying aetiology were investigated to confirm that increased serum transaminase activity may result from such lesions. In 3 out of 4 cases of obstructive jaundice, due to neoplasm affecting either the liver or the biliary passages, normal serum transaminase activity was demonstrated. In one of these 4 cases, high levels of serum transaminase activity were demonstrated. In 4 cases of jaundice due to cirrhosis of the liver, high levels of serum transaminase activity were found in 2 cases, borderline levels in one case and normal levels in one case. In one case of jaundice due to haemolytic anaemia, normal serum transaminase activity was found, although it should be noted that other workers have reported high levels of activity in this condition e.g., Ratner and Sacks (1957). These findings suggest that,in the presence of hepatogenous, haemolytic or obstructive jaundice, serum transaminase assay is unreliable in the detection of acute myocardial infarction, although they also suggest that the demonstration of normal

/normal serum transaminase activity if the assay is performed at the proper times is evidence against the diagnosis of acute myocardial infarction. In 1954, Wroblewski and La Due observed very high levels of serum transaminase activity in patients suffering from toxic jaundice due to carbon tetrachloride poisoning and from acute infective hepatitis. They also observed increased serum transaminase activity in cases of neoplastic invasion of the liver, cholangitis and cirrhosis of the liver. These observations suggested that serum transaminase assay might be of value as a test of liver function and several workers have studied the effect of liver diseases on serum transaminase activity. In 1956., Wroblewski and La Due and Wroblewski and his colleagues observed very high peak levels of serum transaminase activity, (400 - 2,500 units/ml) in 40 cases of infective hepatitis and 12 cases of homologous serum jaundice whereas much lower peak levels of activity were found in cases of jaundice due to extra-hepatic obstruction. They reported that, in infective hepatitis, relapses of the disease were accompanied by secondary rises in serum transaminase activity. They suggested that the assay permitted the early detection of infective hepatitis in the asymptomatic and/or prodromal phase in people who had been exposed to this infection, since they had observed increased serum transaminase activity (40- 100 units) in 9 out of 151 individuals who had been exposed to the infection and, in these cases, this rise in serum transaminase activity was the only indication of abnormal liver function. In 4 out of these 151 patients, serum transaminase values ranged from 100-350 units, and the conventional liver function showed increased thymol turbidity. Three out of the 151 patients developed infective hepatitis and serum transaminase values ranging from 390-1,800 units/ml. They suggested that serum transaminase assay, if performed on all contacts during an epidemic of infective hepatitis, would permit differentiation between those individuals who may develop non-icteric, sub-icteric or icteric infective hepatitis from those who are to remain well. They also observed high and fluctuating levels of serum transaminase activity in 20 out of 28 cases of multilobular cirrhosis of the liver and these rises in activity were related to the activity of the disease. Normal serum transaminase activity was demonstrated in the remaining 8 cases of hepatic cirrhosis. They reported increased serum transaminase activity (range, 45-250 units) in 75 out of 100 cases of primary hepatoma or metastatic tumour of the liver and suggested that serum transaminase assay might be a relatively sensitive index of spread of tumour to the liver, except in liver involvement due to lymphoma or leukaemia in which serum transaminase activity is usually found to be within the normal range.

/range. Normal serum transaminase activity was demonstrated in one case of lymphadenoma, with liver involvement, in this study. They also observed high levels of serum transaminase activity in 6 cases of infectious mononucleosis, complicated by liver involvement, and normal levels of activity in 10 uncomplicated cases of this diseaae. They suggested that serum transaminase assay might prove valuable in anticipating toxic hepatitis in patients who received potentially hepatotoxic drugs since they demonstrated that increased serum transaminase activity precedes the development of jaundice resulting from chlorpromazine. They observed that the results of serum transaminase assay did not necessarily correlate with other tests of liver function. These findings have been confirmed by other workers e.g., Molander et al, (1957).

The place of serum transaminase assay in the diagnosis of diseases of the liver and biliary tract has not been finally evaluated but, in recent studies, an attempt has been made to assess the value of the test in the differential diagnosis of various diseases of the liver and biliary tracts. Madsen and his associates (1958) found good correlation between the height of the serum transaminase levels and the severity of parenchymal disease of the liver, as judged clinically. They found that repeated assays were a valuable aid in the differential diagnosis between parenchymal and obstructive jaundice and suggested that, in the presence of severe jaundice, serum transaminase levels of over 600 units/ml. indicate hepatitis, whereas a moderate elevation of serum transaminase activity strongly suggests obstructive jaundice. Pryse-Davies and Wilkinson (1958) confirmed these findings and observed that serum transaminase levels of over 500 units/ml. were characteristic of infective hepatitis and carbon tetrachloride poisoning. Madsen et al (1958) suggested that, in multilobular cirrhosis and chronic hepatitis, serum transaminase assays might be of help in evaluating the activity of the necrotising process in the liver since they observed increased transaminase activity in cases which showed clinical deterioration and, in most cases of cirrhosis of liver, a rapid decrease in serum transaminase activity occurred with successful conservative treatment. Pryse-Davies and Wilkinson, (1958) made similar observations and O'Brien and his colleagues (1958) employed serial transaminase assays to determine the rate of liver cell necrosis in 5 patients with active chronic hepatitis. In 4 out of these 5 patients, they demonstrated a pronounced fall in serum transaminase activity which coincided with cortisone

/cortisone treatment. These results suggest that the test may prove of value in assessing the effect of therapy in chronic hepatic disorders. Madsen and his associates, (1958) in a study of an epidemic of acute infective hepatitis in a children's institution, confirmed that serum transaminase assay was of value in the diagnosis of anicteric hepatitis and in detecting asymptomatic contact cases, and observed that rises in serum transaminase activity were encountered two to eight days before the onset of clinical symptoms. They concluded that the test had not proved of assistance in distinguishing between different types of chronic liver disease as identical time/transaminase curves were obtained in cases of primary portal cirrhosis, biliary cirrhosis, chronic hepatitis and cancer of the liver. Pryse-Davies and Wilkinson (1958) showed variable increases in activity in similar cases and also in hepatitis, due to infectious mononucleosis and in toxic hepatitis and suggested that, in such cases, serum transaminase assay was unreliable when used alone but was valuable when assessed with the results of conventional tests of liver function. Therefore, serum transaminase assay may command a future place in the battery of tests presently used to examine liver function. These observations serve to emphasise the unreliability of the test as an index of acute myocardial infarction in the presence of acute or chronic disease of the liver or biliary system.

Normal serum transaminase activity was demonstrated in 3 cases of metabolic disease of bone and in one of these cases the plasma alkaline phosphatase was abnormally high. Wroblewski and La Due (1955b) have reported normal transaminase activity in most cases of non-malignant or malignant disease of bone. They observed high levels of serum alkaline phosphate in many of these cases, in the absence of evidence of hepatic disease. These observations suggest that serum transaminase assay may be of value in distinguishing elevations in plasma alkaline phosphatase, due to bone disease, from those due to liver disease, since transaminase activity is not raised in bone disease. They also suggest that the test can be used as an index of acute myocardial infarction when there is evidence of accompanying bone disease.

In 3 cases of uraemia, one of which was characterised by severe oliguria, normal serum transaminase activity was demonstrated. Chinsky and Sherry (1957) observed normal serum transaminase activity in 12 cases of uraemia. In 8 cases the uraemia was secondary to chronic renal disease and in 4 cases acute renal disease was the precipitating cause. Similar findings have been reported

/reported by other workers e.g., Steinberg and Ostrow,(1955). However, Seligson and his associates (1957) suggested that acute renal tubular necrosis might possibly be associated with high levels of serum transaminase activity and Walsh and his colleagues (1957) observed high levels of activity, which remained unexplained after autopsy, in a case of uraemia. These observations suggest that, although normal serum transaminase activity is usually associated with uraemia, serum transaminase assay should be interpreted with caution in the diagnosis of acute myocardial infarction in the presence of uraemia.

The difficulty in diagnosing acute myocardial infarction following a surgical operation has long been recognised. (Master et al, 1938). It has been shown that surgical operations on dogs resulting in skeletal muscle injury, are usually associated with a rise in serum transaminase activity. Nickel and Allbritten (1957) in a study of the post-traumatic response of serum transaminase activity in 81 patients found high levels of serum transaminase activity, although the level did not rise above 70 units following thoracic, cardiovascular and biliary tract surgery and observed that there appeared to be a rough correlation between the degree of surgical trauma and the consequent rise in serum transaminase activity. Other abdominal surgery and retroperitoneal surgery resulted in minor elevations of serum transaminase activity in most instances. Their data did not permit conclusions to be drawn about the part played by anaesthesia in the post-operative increases in serum transaminase activity observed. On the other hand, Chinsky and Sherry (1957) in a study of 11 patients undergoing abdominal laparotomy found normal serum transaminase activity in 10 of these patients and borderline levels of activity in one case. The operations performed included 6 cholecystectomies, 2 hysterectomies, one subtotal gastrectomy, one colostomy and one lysis of small bowel adhesions. Steinberg and Ostrow (1955) have also observed only minor changes in serum transaminase activity following surgical procedures in man. These observations suggest, however, that serum transaminase assay is an unreliable aid in the diagnosis of acute myocardial infarction following a surgical operation. The demonstration of normal serum transaminase activity, when acute myocardial infarction is suspected following an operation, would be evidence against the occurrence of acute myocardial infarction, provided the assay had been performed at the proper times. Similar caution in the interpretation of the results of serum transaminase assay is also advised in cases of traumatic injury since Liebermann and his associates (1957a) in a study of 51 injured patients found high levels of serum transaminase activity in 37

/37 patients (72.5%), and normal levels in only 14 patients, (27.5%). They reported that elevation of serum transaminase levels was likely to occur in individuals subjected to moderate or severe injury and concluded that the assay cannot be used as a specific test of cardiac injury in accident victims. The highest levels of serum transaminase activity were observed following heart, brain, liver and kidney injuries.

Significant increases in serum and spinal fluid transaminase activity have been reported by Fleisher and his associates (1957) in cerebrovascular diseases without cerebral infarction, head injury, degenerative disease of the central nervous systems and in convulsive disorder. It is suggested, therefore, that when such neurologic disorders are present, the assay is not a reliable index of acute myocardial infarction.

de Moragas and his colleagues (1957) studied 17 patients suffering from dermatomyositis and classified them as active or inactive according to clinical criteria. Three patients in the inactive phase of the disease were found to have normal serum transaminase activity while the remaining 14 patients, who were in the active phase of the disease, had high levels of activity which in some cases were extreme.(10 x normal.) They observed that clinical improvement in the disease was accompanied by decreasing values of serum transaminase activity. These workers also described high serum transaminase activity in 2 cases of lupus erythematosus and one case of acrosclerosis. Siekert and Fleisher (1956) also observed that serum transaminase activity was quite consistently elevated in a group of muscle disorders including dermatomyositis, polymyositis and muscle dystrophy, although they found normal serum transaminase activity in disease of the peripheral nerves and of the neuro-muscular junction. Ritter and Seligson (1957) in a study of four children suffering from pseudohypertrophic muscular dystrophy found increased serum transaminase activity in each case and also increased urinary coproporphyrins. These results suggest that the assay may be of value in the diagnosis of these diseases and in the assessment of their activity and also that the assay cannot be used as an index of myocardial infarction in the presence of these diseases.

In this study, increased serum transaminase activity was demonstrated in 6 cases in which there was no evidence of acute myocardial infarction at autopsy. These observations clearly show that increased serum transaminase activity is not specific to acute myocardial infarction and may occur in association with lesions which may co-exist with, complicate, or be mistaken for acute myocardial infarction.

/infarction. My results and those of other workers suggest that necrosis of any tissue, rich in the enzyme, may result in increased serum transaminase activity and that diseases other than acute myocardial infarction may not uncommonly cause increased serum transaminase activity by the production of liver or skeletal muscle or subendocardial myocardial damage. This suggests that, in the differential diagnosis of acute myocardial infarction, the demonstration of normal serum transaminase activity lends supporting evidence against the diagnosis of acute myocardial infarction provided the assay has been performed at the recommended times. It is emphasised, however, that great caution should be observed in the interpretation of normal results of transaminase assay and that, in such clinical situations, the assay is ancillary to the electrocardiogram and other well established diagnostic techniques.

It is, therefore, suggested that serum transaminase assay is most usefully employed in the differentiation of acute myocardial infarction from acute myocardial ischaemia. The value of the assay in such circumstances will now be discussed and a comparison made between the assay and other methods of diagnosis.

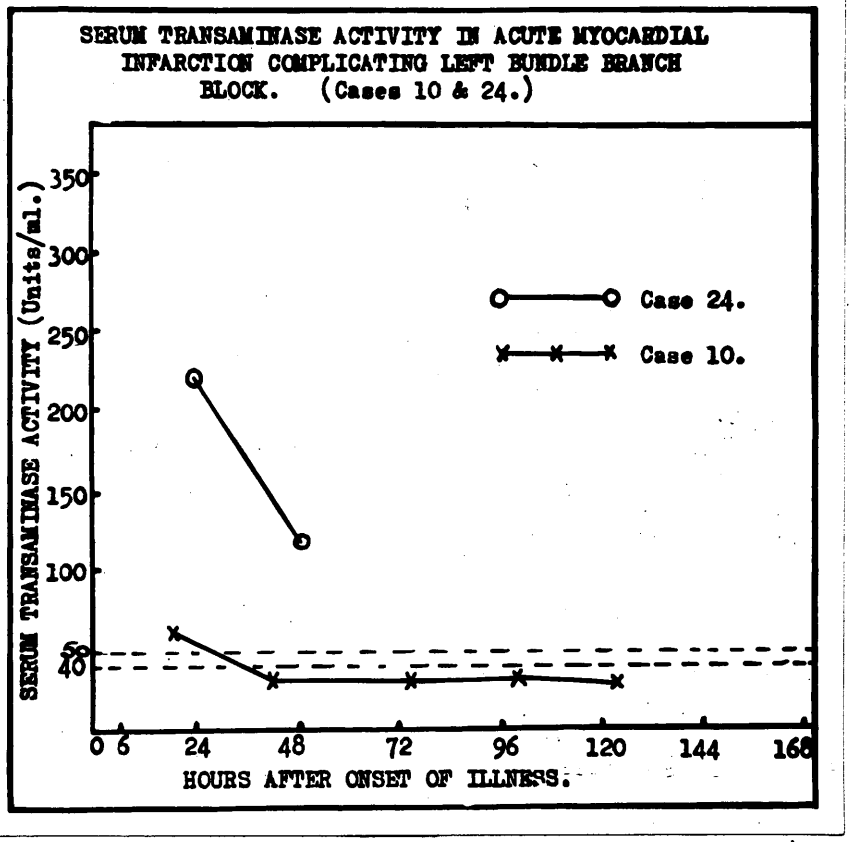
In this investigation, the electrocardiogram was diagnostic of acute myocardial infarction in 54 out of 60 attacks i.e., in 90% of attacks, whereas high levels of serum transaminase activity were found in 84% of the attacks studied. The electrocardiogram may be diagnostic of acute myocardial infarction before a rise in serum transaminase activity occurs e.g., in Cases 37 and 84. The transience of the rise in serum transaminase activity in some cases of acute myocardial infarction has been emphasised and it has been demonstrated that high levels of serum transaminase activity may not be detected following acute myocardial infarction if the assay has not been performed on serum withdrawn 6-24 and 24-48 hours after the onset of the illness. The assay was performed either too early or too late after the onset of acute myocardial infarction in 10 out of 11 attacks and this accounted for my failure to detect high levels of serum transaminase activity in these cases. It has been shown that in certain cases the exact time of onset of acute myocardial infarction may be impossible to determine and also that, in hospital practice, the patient's admission to hospital may have been so delayed that the assay cannot be performed at the proper time. In addition, the assay even when performed at the proper times as in Case 16., may fail inexplicably to reveal high levels of serum transaminase activity. Although such

/such an occurrence is not common enough to be regarded as a serious defect of the test, it remains a defect. The electrocardiogram has demonstrably fewer defects as a diagnostic technique since in 9 of the 11 attacks of acute myocardial infarction which were associated with normal or borderline serum transaminase activity, the electrocardiogram was diagnostic of acute myocardial infarction. (Attacks 8, 16, 19a, 29, 49, 51, 54, 56 and 84). In one of the remaining 2 attacks, the electrocardiogram showed changes diagnostic of acute coronary insufficiency and of an old anterior infarction (case 18) and in the other, an electrocardiogram was not performed (case 4). The electrocardiogram may also provide information not obtainable by other methods of investigation. For example, it may show changes diagnostic of old myocardial infarction, or of conduction defects in the heart, or of the various types of cardiac arrhythmia. The unreliability of the assay in the presence of rapid cardiac arrhythmia has been demonstrated. These observations clearly show that serum transaminase assay cannot replace the electrocardiogram in the diagnosis of acute myocardial infarction.

This suggestion receives further support when cases of acute myocardial infarction which present atypically with breathlessness or other signs, but without characteristic pain, are considered. Paton (1957) suggests that errors in the clinical diagnosis of acute myocardial infarction are most likely to occur in such cases. It has been shown, in this study, that acute myocardial infarction presented without pain in 11 out of 67 attacks. In 7 of these 11 attacks, acute myocardial infarction presented with signs of left ventricular failure and, in 5 of these attacks, congestive cardiac failure was also present. In 2 of these 11 attacks, the clinical picture was dominated by signs of cerebral thrombosis and, in the remaining 2 attacks, by profound circulatory failure. It has been pointed out that each of these presenting conditions may occasionally be associated with high levels of serum transaminase activity in the absence of acute myocardial infarction. Therefore, in atypical cases of acute myocardial infarction, the results of serum transaminase assay may be misleading and electrocardiograms should be examined in such cases.

There are varying reports of the accuracy of purely clinical diagnosis in acute myocardial infarction. Paton, in 1957, reported that the clinical diagnosis of acute myocardial infarction, unaided by the electrocardiogram, was correct in only 13 out of 37 cases of acute myocardial infarction i.e., 35%. Zinn and Cosby (1950) reported an accuracy rate of 70% for purely clinical diagnosis. These observations suggest that the diagnosis of acute myocardial infarction on clinical grounds alone

FIGURE VIII.

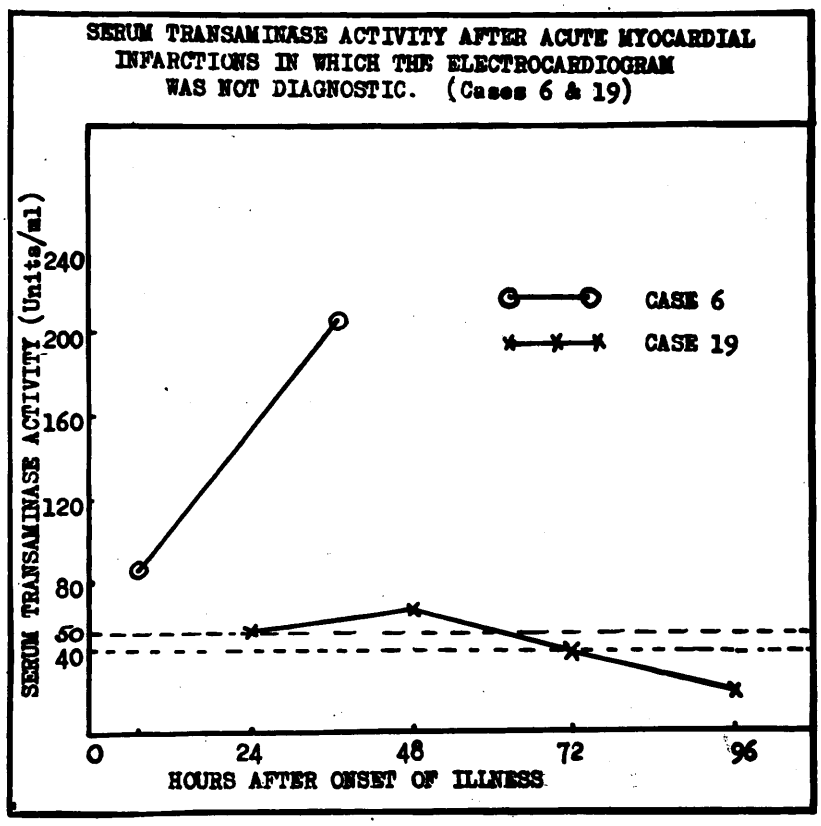

SERUM TRANSAMINASE ACTIVITY IN ACUTE MYOCARDIAL INFARCTION COMPLICATING LEFT BUNDLE BRANCH BLOCK. (Cases 10 & 24.)
SERUM TRANSAMINASE ACTIVITY (Units/ml.)
350
300
250
200
150
100
50
40
Case 24.
Case 10.
0 6 24 48 72 96 120 144 168
HOURS AFTER ONSET OF ILLNESS.

/alone is inaccurate. In 7 out of 67 attacks of acute myocardial infarction, in this series, a clinical diagnosis was made unsupported by electrocardiographic study and, in 6 out of these 7 attacks, high levels of serum transaminase activity which lent support to the clinical diagnosis, were demonstrated. The remaining attack (case 4) proved fatal within 4 hours of its onset and consequently normal serum transaminase activity was found. Evidence has been presented that the clinical diagnosis in these attacks was soundly based, but it should be noted that, in 3 of the 6 attacks in which high levels of serum transaminase activity were demonstrated, the mode of presentation of the illness had been atypical. (Attacks 13b., 20b., 36b). These observations suggest that serum transaminase assay may be of value in the diagnosis of attacks of acute myocardial infarction in which the electrocardiogram is not available, provided the attack studied has been characteristic and not associated with other lesions known to result in high levels of serum transaminase activity.

Although serum transaminase assay cannot replace the electrocardiogramin the diagnosis of myocardial infarction, my observations suggest that it may be a valuable diagnostic aid when the electrocardiographic findings are equivocal.

It has been shown that, in 6 out of 67 attacks of acute myocardial infarction, the electrocardiogram, though grossly abnormal, was at no time diagnostic of acute myocardial infarction. In these attacks, the diagnosis was based on the history, clinical findings and electrocardiographic changes. In 5 out of these 6 attacks, high levels of serum transaminase activity were found. (Attacks 6, 10, 11b., 19b., 24). The remaining attack, proved fatal within a few hours and consequently normal serum transaminase activity was demonstrated. Therefore, in 5 out of 6 attacks of acute myocardial infarction, serum transaminase assay provided valuable aid in the diagnosis of acute myocardial infarction, although it should be noted that, in case 10., cerebral thrombosis may have made some contribution to the increase in serum transaminase activity. The demonstration of high levels of serum transaminase in attacks 10 and 24 is of particular interest since it is well recognised that the electrocardiographic diagnosis of acute myocardial infarction may be difficult, if not impossible, in the presence of the electrocardiographic patterns of left bundle branch block, (Goldberger, 1953), and suggests that serum transaminase assay is of great diagnostic value in such cases. (cf. Figure VIII). Several workers have commented favourably on the value of serum transaminase assay in the diagnosis of acute myocardial

FIGURE IX.


SERUM TRANSAMINASE ACTIVITY AFTER ACUTE MYOCARDIAL INFARCTIONS IN WHICH THE ELECTROCARDIOGRAM WAS NOT DIAGNOSTIC. (Cases 6 & 19)
SERUM TRANSAMINASE ACTIVITY (Units/ml)
240
200
160
120
80
50
40
CASE 6
CASE 19
0
24
48
72
96
HOURS AFTER ONSET OF ILLNESS

/myocardial infarction in the presence of left bundle branch block e.g., Krause et al (1957) and Moore et al, (1957). The electrocardiographic diagnosis of extension of a previous myocardial infarction may be very difficult since the electrocardiographic changes of fresh infarction may be obscured by the pre-existing patterns. The demonstration of high levels of serum transaminase activity in attack 19b suggests that serum transaminase assay is a valuable diagnostic aid in such circumstances.(cf.Figure IX). Several workers have reported that serum transaminase assay is of particular value in confirming the extension of myocardial infarction e.g., Sawyer et al (1958). These observations suggest that serum transaminase assay is helpful in the diagnosis of acute myocardial infarction when the electrocardiogram fails to show diagnostic changes, or when the interpretation of the electrocardiogram is difficult because of the presence of the electrocardiographic changes of previous myocardial infarction or of left bundle branch block.

In 40 attacks of acute myocardial infarction, the first electrocardiogram examined after the onset of symptoms showed changes diagnostic of an acute transmural myocardial infarction. It is suggested that, in such cases, the performance of serum transaminase assay is superfluous. However, it is not always possible to make a confident electrocardiographic diagnosis of acute myocardial infarction on examination of the first electrocardiogram recorded following the onset of symptoms. The importance of left bundle branch block and previous myocardial infarction in this regard has already been mentioned but the most common cause of uncertainty in electrocardiographic diagnosis is delay in the evolution of diagnostic electrocardiographic patterns e.g., attack 47b.

The electrocardiographic diagnosis of acute intramural myocardial infarction depends upon observing sequential changes in serial electrocardiograms, although an experienced observer may consider the changes observed in the initial electrocardiogram strongly suggestive of the diagnosis. In 6 out of 9 attacks of acute intramural myocardial infarction early and v aluable confirmation of the diagnosis was obtained by serum transaminase assay which revealed high levels of serum transaminase activity. The value of the assay in the diagnosis of this type of infarction was particularly well illustrated in attacks 7 and 25b. In these attacks, the electrocardiographic diagnosis depended upon serial examination of the electrocardiogram and in attack 25b., was rendered difficult by the presence of a recent previous acute intramural infarction. In both of these attacks, serum transaminase assay revealed high levels of activity, confirming the diagnosis before the

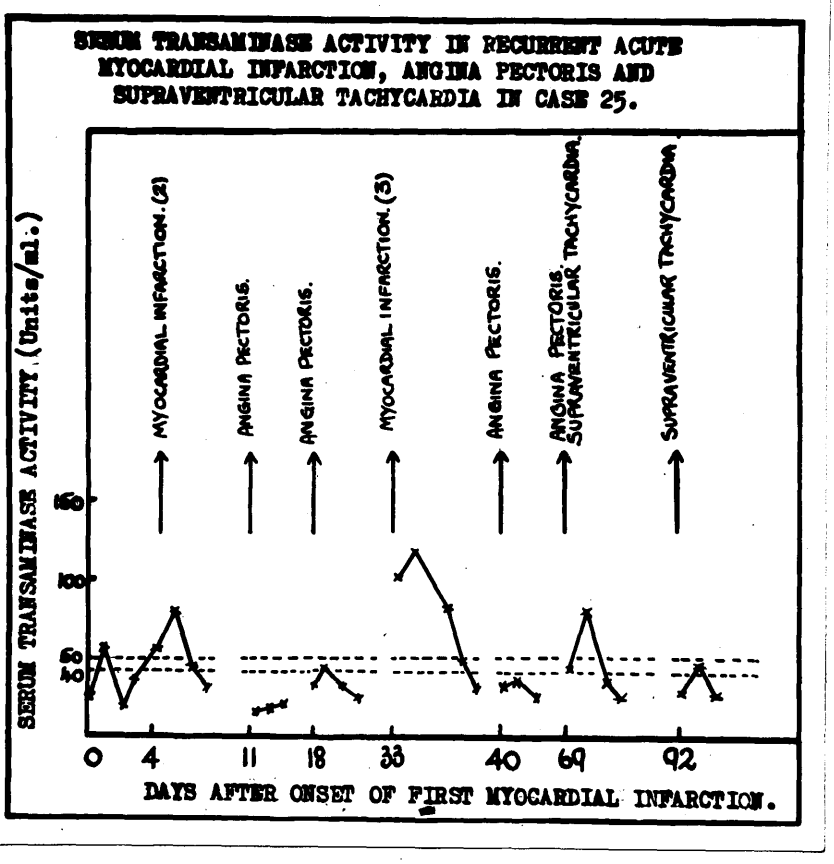
/the electrocardiogram developed diagnostic patterns. These observations suggest that serum transaminase assay is a valuable diagnostic aid in the diagnosis of acute intramural myocardial infarction.

The first electrocardiogram examined after the onset of symptoms was not diagnostic of infarction in 5 attacks of acute transmural myocardial infarction and serial electrocardiograms were needed for electrocardiographic confirmation of the diagnosis. (Attacks 17, 31a, 34, 41, 47b). In 4 out of these 5 attacks, the presence of the electrocardiographic changes of previous myocardial infarction made interpretation of the electrocardiogram difficult. (Attacks 17, 31a, 41, 47b). In attack 17., the first electrocardiogram, examined 2 hours after the onset of symptoms, showed changes diagnostic of acute coronary insufficiency and of an old transmural posterior myocardial infarction, whereas serum transaminase assay showed high levels of activity 22 hours after the onset of symptoms, providing confirmation of the diagnosis of infarction before a second electrocardiogram was examined. In attack 31a., the first electrocardiogram examined 15 hours after the onset of symptoms showed patterns diagnostic of an antero-septal myocardial infarction of indeterminate age, whereas serum transaminase assay performed at the same time as this electrocardiogram, provided confirmatory evidence of the occurrence of acute myocardial infarction. A second electrocardiogram showed that the myocardial infarction had been recent. In attack 34., the first electrocardiogram was examined 14 hours after the onset of symptoms and showed changes suggestive of intraventricular conduction defect and of acute myocardial infarction, although they were not diagnostic of the latter condition. Serum transaminase assay revealed high levels of activity 16 hours after the onset of symptoms providing early confirmation of the diagnosis. A second electrocardiogram, performed 43 hours after the onset of symptoms was diagnostic of acute transmural antero-septal myocardial infarction and probably of supraventricular tachycardia. The arrhythmia was not present before the initial rise in serum transaminase activity and, therefore, did not contribute to this rise. In attack 41., the first electrocardiogram examined 3½ hours following the onset of symptoms was very suggestive, but not diagnostic, of acute posterior myocardial infarction, whereas serum transaminase assay revealed high levels of activity 17 hours after the onset of symptoms, providing early confirmation of the diagnosis of acute myocardial infarction. A second electrocardiogram, performed 21 hours after the onset of symptoms, was diagnostic of acute antero-septal myocardial infarction. Confusion, as to the site of acute

/acute myocardial infarction, had arisen because of pre-existing electrocardiographic changes of a previous unsuspected posterior myocardial infarction. In case 47b., serum transaminase assay revealed high levels of activity 24 hours after the onset of symptoms, providing early confirmation of the diagnosis of acute myocardial infarction. The first electrocardiogram was not performed, in this attack, until 9 days after the onset of symptoms and showed the changes of anterior myocardial ischaemia only. The evolution of electrocardiographic patterns typical of acute myocardial infarction was long delayed and was found in an electrocardiogram performed 28 days after the onset of symptoms. This attack of acute myocardial infarction coincided with the onset of infarction of the kidney, and so it is possible that this lesion may have made some contribution to the rise in serum transaminase activity demonstrated. These observations suggest that serum transaminase assay, if performed at the proper times, is of great value in establishing the diagnosis of acute myocardial infarction early in the illness in cases of acute intramural myocardial infarction, and in those cases of acute transmural myocardial infarction in which the final electrocardiographic diagnosis depends upon the examination of serial electrocardiograms.

Chest pain not uncommonly recurs following acute myocardial infarction. In such cases, the differentiation between the pain of acute myocardial infarction and that of severe myocardial ischaemia is often impossible on clinical grounds and usually depends upon electrocardiographic examination. The demonstration of normal or borderline levels of serum transaminase activity following attacks of severe myocardial ischaemia suggests that serum transaminase assay might prove a useful diagnostic aid in these cases, since electrocardiographic diagnosis is difficult in the presence of electrocardiographic changes of previous myocardial infarction. 8 patients in this study suffered a recurrence or extension of acute myocardial infarction and serum transaminase assay revealed high levels of activity following each recurrence. (Attacks 11b., 13b., 19b., 20b., 31b., 36b., 42b., 47b). In 4 patients recurrent chest pain following acute myocardial infarction was due to severe myocardial ischaemia and in each attack of anginal pain studied, was associated with either normal or borderline serum transaminase activity. (Cases, 7, 8, 11, 25). The results of serum transaminase assay in case 25 merit more detailed consideration since they illustrate the merits and defects of serum transaminase assay in the differentiation of acute myocardial infarction from myocardial ischaemia. The serum transaminase curves obtained in this case are illustrated

FIGURE X.


SERUM TRANSAMINASE ACTIVITY IN RECURRENT ACUTE MYOCARDIAL INFARCTION, ANGINA PECTORIS AND SUPRAVENTRICULAR TACHYCARDIA IN CASE 25.
SERUM TRANSAMINASE ACTIVITY (Units/ml.)
MYOCARDIAL INFARCTION. (2)
ANGINA PECTORIS.
ANGINA PECTORIS.
MYOCARDIAL INFARCTION. (3)
ANGINA PECTORIS.
ANGINA PECTORIS. SUPRAVENTRICULAR TACHYCARDIA.
SUPRAVENTRICULAR TACHYCARDIA.
100
40
0
4
11
18
33
40
69
92
DAYS AFTER ONSET OF FIRST MYOCARDIAL INFARCTION.

/illustrated in Figure X. The patient had sustained an acute myocardial infarction shortly before his admission to hospital. An electrocardiogram,performed 3 hours after the onset of symptoms, showed the changes of a recent antero-lateral intramural myocardial infarction and high levels of serum transaminase activity were demonstrated 15 hours after the onset of symptoms, providing confirmation of the diagnosis. (Attack 25a). 4 days after this first infarction, the patient complained of retrosternal pain and serum transaminase activity, which had fallen to normal, rose again to high levels 12 hours after the onset of symptoms, suggesting that a second acute myocardial infarction had occurred. Serial electrocardiograms revealed changes diagnostic of an acute antero-septal intramural myocardial infarction, (25b). Following this, serum transaminase assay was performed following two severe attacks of chest pain in which the electrocardiogram showed no evidence of fresh myocardial infarction. In the first attack of myocardial ischaemia (25d) normal serum transaminase activity was found following the pain. In the second attack (25e) borderline levels of activity were demonstrated 20 hours after the onset of the pain. After an interval of 14 days,during which the patient was free from pain, he again complained of retrosternal pain. The electrocardiogram showed changes diagnostic of an acute transmural antero septal myocardial infarction (25c). Serum transaminase activity reached peak levels 36 hours after the onset of symptoms and had fallen to normal levels on the sixth day, when the patient again complained of severe chest pain. There was no electrocardiographic evidence of fresh myocardial infarction following this pain, which was considered to be due to myocardial ischaemia, and serum transaminase activity remained at normal levels (25f). Four weeks after this, the patient again complained of severe chest pain, which,on this occasion, was associated with supraventricular tachycardia,(25g). The electrocardiogram confirmed the diagnosis of supraventricular tachycardia but serial electrocardiograms showed no evidence of fresh myocardial infarction. It was evident that the cause of this attack of pain had been myocardial ischaemia which had been provoked by paroxysmal tachycardia of rapid ventricular rate (210-220/minute). Serum transaminase activity rose to high levels 31 hours after the onset of rapid tachycardia illustrating once again the unreliability of serum transaminase assay in the diagnosis of acute myocardial infarction in the presence of rapid arrhythmia. Three weeks later, the patient suffered another attack of paroxysmal supraventricular tachycardia (25h). On this occasion, there was no complaint of chest pain and no electrocardiographic evidence of fresh myocardial infarction. Serum transaminase activity rose to borderline levels of

/of activity following this paroxysm of supraventricular tachycardia which was of shorter duration than the previous attack. These observations suggest that serum transaminase assay is a valuable diagnostic aid in the diagnosis of recurrent acute myocardial infarction and in the differential diagnosis of chest pain following acute myocardial infarction, provided the results of the assay are cautiously interpreted with regard for other conditions which may be associated with increased serum transaminase activity.

In this study, serum transaminase assay proved a valuable diagnostic supplement to the electrocardiogram in 3 attacks of acute myocardial infarction in which the diagnosis was made on purely clinical grounds, in 5 attacks in which the electrocardiogram failed to show changes diagnostic of infarction, in 6 attacks of acute intramural myocardial infarction and in 5 attacks of acute transmural myocardial infarction in which the diagnosis depended upon serial examination of the electrocardiogram. Therefore, the test provided early and useful confirmation of the diagnosis in 19 out of 67 attacks of acute myocardial infarction i.e., in 28% of attacks studied.

Serum transaminase assay compares favourably with both pyrexia and the erythrocyte sedimentation rate as an index of acute myocardial infarction. It has been shown that pyrexia followed 48 out of 67 attacks of acute myocardial infarction i.e., 72% of attacks. In these attacks temperatures had been recorded at the ideal time viz., within 48 hours of the onset of symptoms. In contrast, it has been shown that in 56 out of 57 attacks in which serum transaminase assay was performed at the ideal times, high levels of serum transaminase activity were demonstrated i.e., in 98.3% of attacks. It is also clear that temperature as a sign of acute myocardial infarction is even less specific than serum transaminase assay. These observations suggest that the assay is a more reliable and specific index of acute myocardial infarction than pyrexia. Several workers have reported similar findings. For example, Ratner and Sacks (1957) found pyrexia in only 72% of acute myocardial infarction compared with the demonstration of increased serum transaminase activity in 92% of attacks.

The E.S.R. was found to be abnormally high in 41 out of 54 attacks of acute myocardial infarction i.e., in 87% of attacks, whereas serum transaminase activity rose to high levels in 56 out of 67 attacks of acute myocardial infarction i.e., in 84% of attacks. In 18 out of 23 attacks of acute myocardial infarction in which the E.S.R.

/E.S.R. was normal throughout the course of the illness, or in the first 24 hours after the onset of symptoms, serum transaminase activity rose to high levels. This suggests that serum transaminase assay is a more reliable diagnostic index of acute myocardial infarction than measurement of the E.S.R., in the early phase of the illness. It has been shown, however, that the E.S.R. was abnormally high following 5 attacks of acute transmural myocardial infarction in which serum transaminase assay revealed normal or borderline levels of activity because of late sampling of the serum. These results suggest that the E.S.R. is a more useful anxillary test in the diagnosis of acute myocardial infarction than serum transaminase assay in those cases in which several days have elapsed since the onset of symptoms. The E.S.R. was also found to be abnormally high following 6 attacks of angina pectoris due to myocardial ischaemia. In these cases, there was no electrocardiographic evidence of acute myocardial infarction or evidence of an extracardiac lesion, which could account for the elevation of the E.S.R. High levels of serum transaminase activity were not demonstrated in any of these 6 attacks of myocardial ischaemia. These results suggest that, in differentiating between acute myocardial infarction and myocardial ischaemia, serum transaminase activity is a more reliable index of acute myocardial infarction than the E.S.R. These findings have been corroborated by other workers. For example, Ratner and Sacks found the E.S.R. elevated in 88% of their cases of acute myocardial infarction and increased serum transaminase activity in 92% of cases. Losner and his associates (1957) reported finding high levels of serum transaminase activity in 7 out of 25 cases of acute myocardial infarction, characterised by shock and haemoconcentration, in which the E.S.R. remained normal until the endoof the second week after the onset. They also observed considerable elevation of the E.S.R. following attacks of myocardial ischaemia which had been associated with normal serum transaminase activity. Nydick and his colleagues (1957) also observed elevation of the E.S.R. in 14 out of 34 cases of coronary insufficiency in which normal serum transaminase activity was found.

SUMMARY.

The assay of serum transaminase, by the spectrophotometric method, is accurate, reproducible and suitable for research purposes. The enzyme is of such stability as to facilitate its clinical usefulness. Only specimens of serum, without evidence of haemolysis should be used for the test. Normal, borderline and high levels of serum transaminase activity have been arbitrarily defined.

High levels of serum transaminase activity were demonstrated following 84% of attacks of acute myocardial infarction. The importance of performing the assay 6-24 and 24-48 hours after the onset of acute myocardial infarction is emphasised since, in 14.5% of attacks, too early or too late sampling of the serum accounted for the failure to demonstrate high levels of serum transaminase activity. In those attacks of acute myocardial infarction in which the assay was performed at the recommended times, high levels of serum transaminase activity were detected in 98.2%.

There was no evidence that the rise of serum transaminase activity following acute myocardial infarction was due to damage to the liver. Evidence has been presented which suggests that there is a statistical correlation between the level of serum transaminase activity and the degree of peripheral vascular failure developing after acute myocardial infarction, although serum transaminase activity cannot be used as an index of the degree of peripheral vascular failure in the individual case.

High levels of serum transaminase activity are not found in myocardial ischaemia, although an increase of activity to borderline levels may be demonstrated.

Increased serum transaminase activity may be detected in lesions other than acute myocardial infarction. High levels of serum transaminase activity were demonstrated in diseases of the liver, but this matters less than the detection of increased serum transaminase activity in conditions which may be confused with, or complicate, acute myocardial infarction e.g., in dissecting aneurysm of the aorta, acute pulmonary infarction, acute pancreatitis, chronic cholecystitis, arterial embolism and thrombosis and in rapid cardiac arrhythmias. The probable sources of increased serum transaminase activity

/activity in conditions other than acute myocardial infarction have been discussed. In differentiating between acute myocardial infarction and other diseases, the demonstration of normal serum transaminase activity at the recommended times after the onset of illness is supporting evidence against the diagnosis of acute myocardial infarction.

Serum transaminase assay cannot replace the electrocardiogram in the diagnosis of acute myocardial infarction. It is a diagnostic aid rather than a substitute for any of the existing diagnostic procedures, although it has been shown to be superior to pyrexia and the E.S.R. as an index of acute myocardial infarction in the early stages of the illness.

The assay should not be performed as a routine procedure when the initial electrocardiogram is diagnostic of acute myocardial infarction. If serum can be withdrawn for transaminase assay at the recommended times, it is suggested that the most practical and economic method of using the test is in the following situations:-

1). In cases of suspected acute myocardial infarction in which the electrocardiogram is not available, but in which the mode of presentation of the illness is characteristic.

2). In cases of acute myocardial infarction in which the electrocardiographic changes of this lesion are not observed at any time following the onset of symptoms, the assay being especially valuable in cases showing the electrocardiographic changes of left bundle branch block.

3). In cases of acute intramural and transmural myocardial infarction in which serial electrocardiograms are required for final electrocardiographic diagnosis.

4). In cases of acute myocardial infarction in which the diagnosis of extension or recurrence of infarction is difficult because of the presence in the electrocardiogram of changes diagnostic of myocardial infarction.

5). In cases in which the differentiation between acute myocardial infarction and acute myocardial ischaemia is difficult.

When employed in this way, serum transaminase assay is a valuable diagnostic aid in the diagnosis of acute myocardial infarction.

ACKNOWLEDGMENTS.

I wish to thank Dr. J. Gibson Graham for permission to pursue this study in patients under his care. I am indebted to Dr. I. A. Anderson for his permission to work in his laboratory, where a spectrophotometer was available, and for his advice and encouragement. I am grateful to Dr. A. J. V. Cameron for his interpretations of the electrocardiograms, used in this study, and to Dr. W.P.Weir, who performed the autopsies and permitted me to use his reports of histological examinations.

R E F E R E N C E S.

AGRESS, C.M., GLASSNER, H.F., BINDER, M.J. (1956) Proc. Soc. exp. Biol., 92, 826.

AGRESS, C.M., GLASSNER, H.F., JACOBS, H.I. (1956) Circulat. Res., 4, 220.

AGRESS, C.M., JACOBS, H.I., GLASSNER, H.F., LEDERER, M.A., CLARK, W.G., WROBLEWSKI, F., KARMEN, A., La DUE, J.S. (1955) Circulation, 11, 711.

AGRESS, C.M., ROSENBURG, M.J., JACOBS, H.I., BINDER, M.J., SCHNEIDERMAN, A., CLARK, W.G., (1952) Amer. J. Physiol., 170, 536.

AMES, S.R., ELVEHJEM, C.A. (1946) J.biol. Chem., 166, 81.

AWAPARA, J., SEALE, B. (1952) J. biol.Chem., 194, 497.

BARON, D.N., BELL, J., OAKLEY, C. (1956) Association of clinical biochemists. Newsletter, No.12, p.12.

BAYLIS, J.H., KAUNTZE, R., TROUNCE, J.R. (1955) Quart. J. Med., 24, 143.

BEAN, W.B., FLAMM, G.W., SAPADIN, A. (1949) Amer. J. Med., 7, 765.

BEAN, W.B., READ, C.T. (1942) Amer.Heart J., 23, 362.

BIÖRCK, G., HANSON, A. (1956) Acta med.Scand., 155, 317.

BRAUNSTEIN, A.E., KRITZMANN, M.G. (1937) Enzymologia, 2,129.

BRITISH CARDIAC SOCIETY. (1949) Report of the committee on Multiple unipolar leads. Brit.Heart J., 11, 103.

CAMMARATA, P.S., COHEN, P.P. (1950) J. biol.Chem., 187, 439.

CAMMARATA, P.S., COHEN, P.P. (1951a) J. biol.Chem., 193, 45.

CAMMARATA, P.S., COHEN, P.P. (1951b) J. biol.Chem., 193, 53.

CHINSKY, M., SHERRY, S. (1957) A.M.A. Arch.intern.Med., 99, 556.

CHINSKY, M., SHMAGRANOFF, G.L., SHERRY, S. (1956) J.Lab. clin. Med., 47, 108.

COHEN, P.P. (1939) Biochem. J., 33, 1478.

COHEN, P.P. (1940) J. biol.Chem., 136, 565.

DAVIDSON, C.S., LEWIS, J.H., TAGNON, H.J., ADAMS, M.A., TAYLOR, F.H.L. (1946) New Engl. J.Med., 234, 279.

DENNEY, J.L., McAULEY, C.B., MARTIN, H.E., WARE, A.G., SEGALOVE, M. (1956) J. Amer.med. Ass., 161, 614.

DUNN, M., MARTINS, J., REISSMANN, K.R. (1958) J. Lab. clin. Med., 51, 259.

DURANT, J.R., BOWERS, G.N., TWADDLE, P. H. (1958) Amer. J. med.Sci., 235, 644.

EAST, C.F.T., BAIN, C.W.C., CARY, F.L. (1928) Lancet, 2, 60.

EVANS, J.M., ZIMMERMAN, H.J., WILMER, J.G., THOMAS, L.J., ETHRIDGE, C.B. (1952) Amer.J. Med., 13, 704.

EVANS, W. (1952) Lancet, 2, 1091.

FLEISHER, G.A., WAKIM, K.G., GOLDSTEIN, N.P. (1957) Proc. Mayo Clin., 32, 188.

FRIEND, C., WROBLEWSKI, F., La DUE, J.S. (1955) J. exp.Med., 102, 699.

GOLDBERGER, E., (1953). Unipolar lead electrocardiography. 3rd. ed. London, H. Kimpton.

GOLDSTEIN, F., ISRAEL, H.L., SELIGSON, D. (1956) New Engl. J. Med., 254, 746.

GOODMAN, L.S., GILMAN, A. (1955) The pharmacological basis of therapeutics. 2nd ed. London, Macmillan. p.286.

GREEN, D.E., LELOIR, L.F., NOCITO., V.(1945) J. biol.Chem., 161, 559.

GREEN, J.B., O'DOHERTY, D.S., OLDEWURTEL, H.A., FORSTER, F.M. (1957) New Engl. J. Med., 256, 220.

GREGG, D.E., (1950) Coronary circulation in health and disease. London, H.Kimpton.

GUTTERIDGE, N.M., McKEAN, C.J. (1958) Med. J. Aust., 1,528.

HAMMAN, L. (1934) Ann. intern. Med., 8, 417.

HANGER, F.M., PATEK, A.J., (1941) Trans. Ass. Amer. Phycns., 56, 372.

HANSON, A., BIÖRCK, G. (1957) Acta med. scand., 157, 493.

HARRIS, K. (1955) Brit. med. J., 2, 874.

HELM, J.D., MACHELLA, T.E. (1942) Amer. J. dig.Dis., 9, 141.

HILL, I.G.W. (1950) Lancet, 1, 1027, 985.

HOEVENAARS, H.A.M., OVERHOLT, B.M. (1957) J. Tenn. med. Ass., 50, 95.

HSIEH, K.M., BLUMENTHAL, H.T. (1956). Proc. Soc. exp. Biol., 91, 626.

KARMEN, A., WROBLEWSKI, F., LaDUE, J.S. (1955) J. clin. Invest., 34, 126.

KATTUS, A.A., WATANABE, R., SEMENSON, C. (1957) Circulation, 15, 502.

KATTUS, A.A., WATANABE, R., SEMENSON, C., DRELL, W., AGRESS, C. (1956) J. Amer. med. Ass., 160, 16.

KATZ, L.N., GOLDMAN, A.M., LANGENDORF, R., KAPLAN, L.G., KILLIAN, S.T. (1942) Amer. Heart J., 24, 627.

KING, E.J. (1946) Micro-analysis in medical biochemistry. London, J.& A. Churchill.

KING, E.J., ARMSTRONG, A.R. (1934) Canad. med.Ass. J., 31, 376.

KRAUSE, S., HECKERT, E.W., SOLINAS, P., BOGARD, I.M. (1957) Dis. Chest, 31, 512.

KUNKEL, H.G. (1947) Proc. Soc. exp. Biol., 66, 217.

LaDUE, J.S., WROBLEWSKI, F. (1955) Circulation, 11, 871.

LaDUE, J.S., WROBLEWSKI, F., KARMEN, A. (1954) Science, 120, 497.

LIEBERMAN, J., LASKY, I.I., DULKIN, S.I., LOBSTEIN, O.E. (1957a) Ann. intern. Med., 46, 485.

LIEBERMAN, J., LASKY, I.I., DULKIN, S.I. LOBSTEIN, O.E. (1957b) Ann. intern. Med., 46, 497.

LOSNER, S., VOLK, B.W., ARONSON, S.M. (1957) Amer. Heart J., 54, 225.

McGINN, S., WHITE, P.D. (1935) J.Amer. med. Ass., 104, 1473.

MACLAGAN, N.F. (1944) Brit. J. exp. Path., 25, 15.

MADSEN, S., BANG, N.U., IVERSEN, K. (1958) Brit. med. J., 1, 543.

MAGALINI, S.I., STEFANINI, M. (1956) Proc. Soc. exp. Biol., 91, 404.

MANSO, C., TARANTA, A., NYDICK, I. (1956) Proc. Soc. exp. Biol., 93, 84.

MASTER, A.M., DACK, S., JAFFE, H.L. (1938) J. Amer. med. Ass., 110, 1415.

MERRILL, J. M., STONE, J.L., GRACE, J.T., MENEELY, G.R. (1955) Clin. Res. Proc. 3, 113.

MERRILL, J.M., LEMLEY-STONE, J., GRACE, J.T. MENEELY, G.R. (1956) J. Amer. med. Ass., 160, 1454.

MOLANDER, D.W., FRIEDMAN, M.M. (1956) Clin.Res.Proc., 4, 39.

MOLANDER, D.W., SHEPPARD, E., PAYNE, M.A. (1957) J. Amer. med. Ass., 163, 1461.

MOLANDER, D.W., WROBLEWSKI, F., LaDUE, J.S. (1955) J. Lab. clin. Med. 46, 831.

MOORE, C.B., BIRCHALL, R., HORACK, H.M., BATSON, H.M. (1957) Amer. J. med. Sci., 234, 528.

MORAGAS, J.M. de., PERRY, H.O., FLEISHER, G.A. (1957) J. Amer. med. Ass., 165, 1936.

MOUNSEY, P. (1951) Brit. Heart J., 13, 215.

MYERSON, R.M., HURWITZ, J.K., SALL, T. (1957) New Engl.J. Med., 257, 273.

NICKEL, W.K., ALLBRITTEN, F.F. Jr. (1957) Surgery, 42, 240.

NYDICK, I., RUEGSEGGER, P., WROBLEWSKI, F., LaDUE, J.S. (1957) Circulation, 15, 324.

NYDICK, I., TANG, J., STOLLERMAN, G.H., WROBLEWSKI, F., LaDUE, J. S. (1955) Circulation, 12, 795.

NYDICK, I., WROBLEWSKI, F., LADUE., J.S. (1955) Circulation, 12, 161.

O'BRIEN, E.N., GOBLE, A.J., MACKAY, I.R. (1958) Lancet, 1, 1245.

O'KANE, D.E., GUNSALUS, I.C. (1947) J. biol. Chem., 170, 425.

OSTROW, B.H., STEINBERG, D., TICKTIN, H.E., POLIS, G.N., EVANS, J.M. (1956) Circulation, 14, 790.

PAPP, C. (1952) Brit. Heart J., 14, 250.

PARKINSON, J., BEDFORD, D.E. (1928) Lancet, 1, 4.

PATON, B.C. (1957) Amer. J. Med., 23,761.

POPPER, H. (1948) Arch. Path., 46, 132.

PRYSE-DAVIES, J., WILKINSON, J. H., (1958) Lancet, 1, 1249.

RATNER, J.T., SACKS, H.J. (1957) Canad. med.Ass. J., 76, 720.

RITTER, J.A., SELIGSON, D. (1957) Amer. J. med. Sci., 233,559

RUDOLPH, L.A., DUTTON, R., SCHAEFER, J.A. (1955) J. clin. Invest., 34, 960.

RUDOLPH, L.A., LYONS, R.H. (1955) Clin. Res. Proc., 3, 113.

RUDOLPH, L.A., SCHAEFER, J.A., DUTTON, R.E., LYONS, R.H. (1957) J. Lab. clin. Med., 49, 31.

RUSSEK, H.I., ZOHMAN, B.L., WHITE, L.G., DOERNER, A.A. (1951) J. Amer. med.Ass., 145, 390.

SAWYER, K.C., ROBB, W.C., KONEMAN, E. (1958) Rocky Mtn. med. J., 55, 47.

SELIGSON, D., ZINGESSER, L.H., GOLDSTEIN, F. (1957) Penn. med. J., 60, 728.

SHERLOCK, S. (1951) Brit. Heart J., 13, 273.

SIEKERT, R.G., FLEISHER, G.A. (1956) Proc. Mayo Clin., 31, 459.

SOKOLOW, M., KATZ., L.N., MUSCOVITZ, A.N. (1940). Amer. Heart J., 19, 166.

STEINBERG, D., OSTROW, B.H. (1955) Proc. Soc. exp. Biol., 89, 31.

TONHAZY, N.E., WHITE, N.G., UMBREIT, W.W. (1950). Arch. Biochem., 28, 36.

WAKIM, K.G., FLEISHER, G.A. (1956) Proc. Mayo Clin., 31, 391.

WALSH, J.R., HUMOLLER, F.L., GILLICK, F.G., (1957) Ann. intern. Med., 46, 1105.

WALTERS , M.N.I., LITTLEJOHN, P.G. (1958) Med. J. Aust., 1, 76.

WESTERGREN, A. (1926) Amer. Rev. Tuberc., 14, 94.

WHITE, P.D. (1951) Heart Disease. 4th ed. New York, Macmillan Co.

WOOD, P. (1956) Diseases of the heart and circulation. 2nd ed. London, Eyre and Spottiswoode.

WROBLEWSKI, F. (1957) Amer. Heart J., 54, 219.

WROBLEWSKI, F. JERVIS., G., LaDUE, J.S.,(1956) Ann. intern. Med., 45, 782.

WROBLEWSKI, F., LaDUE, J.S. (1954) J. Lab. clin. Med., 44,958

WROBLEWSKI, F., LaDUE, J.S. (1955a) Ann. intern. Med., 43, 345.

WROBLEWSKI, F., LaDUE, J.S. (1955b) Cancer (Philad.), 8,1155.

WROBLEWSKI, F., LaDUE, J.S. (1956) J. Amer. med. Ass., 160, 1130.

ZINN, W.J., COSBY, R.S. (1950). Amer. J. Med., 8, 177.

V O L U M E II.

APPENDIX I.

APPENDIX I.

THE SPECTROPHOTOMETRIC METHOD OF GLUTAMIC OXALACETIC TRANSAMINASE ASSAY IN SERUM, BILE AND URINE.

(Karmen,1955).

---

1. Historical Introduction.

The process of transamination was first discovered by Braunstein and Kritzmann in 1937 and the presence of transaminases was demonstrated in pigeon breast muscle. Their substance contained several transaminases and it was further purified by Cohen (1939, 1940) who thought it capable of catalyzing the reaction with two or three amino acids only. Further work, however, has indicated that 25 amino acids undergo transamination and that each probably has a specific transaminase. (Cohen, 1940; O'Kane and Gunsalus,1947; Cammarata and Cohen,1950). It had also been shown that transaminase activity was not confined to pigeon breast muscle and, in 1952, transaminase activity was demonstrated in eight organs of the rat. Maximal transaminase activity was present in heart homogenates and the enzyme was demonstrated in decreasing order of activity in skeletal muscle, lung, brain, liver, spleen, prostate and testes.(Awapara and Seale, 1952). Later observations showed that the organ distribution of the enzyme was species specific and that,in man, the enzyme was present in heart, liver, skeletal muscle and kidney in decreasing order of activity. (Nydick et al, 1955; Nydick et al, 1957; Wroblewski, 1957). The first determinations of transaminase activity were tedious and inaccurate. (Cohen,1939; Green et al, 1945; Ames and Elvehjem, 1946; Tonhazy et al, 1950; Cammarata and Cohen, 1950; Awapara and Seale,1952). In 1951, a spectrophotometric technique similar to the one used in this study was devised. (Cammarata and Cohen, 1951(a), 1951(b).)

In 1955., an accurate and reproducible method of transaminase assay employing paper chromatography was described by Karmen et al, but this was still a long procedure requiring over thirty-six hours for its completion. At the same time, Karmen et al described a spectrophotometric method of transaminase assay which they had found rapid, simple, accurate and extremely reproducible. This was the method used in this study.

2. MATERIALS USED IN THE PROCEDURE AND THEIR PREPARATION.

0.1 M. Phosphate Buffer pH 7.4.

Add 96 ml. of anhydrous KH_2PO_4 (13.6 gm./l litre) to 404 ml. anhydrous $Na_2H.PO_4$, (14.2 gm./l litre) and adjust to pH 7.4 by addition of small quantities of either solution.

0.2 M. Aspartate Solution pH 7.4.

Dissolve 2.652 gm. aspartic acid in 80 ml. of the 0.1 M phosphate buffer solution. Bring the pH back to 7.4 by the dropwise addition of 10% NaOH and make up to 100 ml. with phosphate buffer.

0.1 M. Alpha-keto-glutarate solution pH 7.4.

Dissolve 1.461 gm. of alpha-keto-glutaric acid in 80 ml. of 0.1 M phosphate buffer solution. Bring the pH back to 7.4 by the dropwise addition of 10% NaOH and make up to 100 ml. with phosphate buffer.

Purified Malic Dehydrogenase Solution.

This enzyme is obtained commercially. A solution of it in a strength of 50 micrograms of enzyme protein/1 ml. is prepared.

Reduced Diphosphopyridine Nucleotide Solution.

This solution must be made up fresh just before the test in a strength of 1 mgm. of DPNH/1 ml.of 0.1 M. phosphate buffer solution. The substance is obtained commercially.

The malic dehydrogenase and α ketoglutarate solutions should be stored, frozen, in a deep freeze cabinet.

/3 - over.

3. DESCRIPTION OF PROCEDURE FOLLOWED.

From 0.1 - 1.0 ml. of serum (or bile or urine) 1 ml. of 0.1 M phosphate buffer (pH 7.4), 0.5 ml. of 0.2 M. aspartate in buffer (pH 7.4), 0.2 ml. of reduced diphosphopyridine nucleotide (1 mgm.perml), and 0.1 ml. of a solution of purified malic dehydrogenase are mixed and brought to a final volume of 2.8 ml. in a cuvette having a 1cm. light path. A blank of the same volume is also prepared which contains all the reagents except that 0.2 ml. of phosphate buffer replaces reduced diphosphopyridine nucleotide. After 10 minutes, 0.2 ml. of 0.1 M alpha-keto-glutarate in buffer (pH 7.4) is added and the optical density at wavelength 340 mu is followed for 5 minutes in a Unicam S.P. 500 spectrophotometer at room temperature. The rate of decrease of optical density due to the oxidation of reduced diphosphopyridine nucleotide is taken as a measure of the transaminase activity of the serum, bile or urine and the activity is expressed in units of enzyme activity of the serum, bile or urine.

As in the original method, no correction was made for variations in temperature.

4. COMMENTS ON THE PROCEDURE.

a) Practical Considerations.

In their study of serum transaminase activity and substrate concentration, Karmen and his associates (1955) found that maximal activity was obtained when the 3 ml.reaction mixture, described above, was employed. In this study, 0.2 ml. of serum was used routinely and, in the presence of abnormally high serum activities, the serum was diluted as indicated.

The omission of malic dehydrogenase from otherwise complete transamination mixtures results in a variable decrease in the observed rate of oxidation of diphosphopyridine nucleotide. Karmen and his associates suggested that this was evidence either of the presence of malic dehydrogenase in serum or the decarboxylation of oxalacetic to pyruvate and subsequent oxidation of diphosphopyridine nucleotide by lactic dehydrogenase. The addition of excess malic dehydrogenase to any serum

/serum transaminase assay results in no further increase in the measured rate of reaction, indicating that the enzyme is present in excess in the assay mixture. It was found that malic dehydrogenase retained its activity for at least three months when kept in the frozen state.

The delay of 10 minutes advised before adding alpha-ketoglutarate is very important since, when reduced diphosphopyridine nucleotide is added to serum without the addition of substrates, the optical density of the mixture decreases for 6 - 7 minutes indicating the oxidation of a finite quantity of diphosphopyridine nucleotide. Early in the present study, it was found that a longer period than 10 minutes was often required before alpha keto-glutarate could be added and that occasionally a further 0.2 ml. of reduced diphosphopyridine nucleotide had to be added to the reaction mixture before a suitable optical density was recorded, prior to adding alpha-keto-glutarate. The specimens of blood showing these unusual features were found to be those which had been kept for some hours before the serum and plasma had been separated. Karmen and his associates (1955) suggested that the oxidation of diphosphopyridine nucleotide by serum alone depended upon the presence of pyruvate and lactic dehydrogenase in the serum and that the reaction stops when all the pyruvate in the serum has been enzymatically reduced to lactate by reduced diphospho-pyridine nucleotide. In 1956., Hsieh and Blumenthal, when studying serum lactic dehydrogenase activity in various disease states, found that lactic dehydrogenase activity increased by 25% if separation of the serum or plasma from venous clotted blood at room temperature was delayed for an hour, which presumably explains the above-mentioned difficulty with blood which had not been separated quickly. Therefore, in the present study, the practice of separating serum and plasma from the blood at the earliest opportunity was followed and the products were stored at 0 - 4°C. in a refrigerator and the tests performed within four days. When this procedure was followed, the difficulty described was no longer encountered.

b) The Accuracy, Reproducibility, and Simplicity of the Method.

The spectrophotometric method of transaminase assay is usually described as accurate and simple to perform. The accuracy of the test is not in doubt. Karmen and his associates (1955) compared the results of spectrophotometric assay of transaminase activity with those obtained using a

/a quantitative paper chromatographic technique and they closely agreed. However, the test can be regarded as simple to perform only in a well equipped laboratory as instruments capable of making serial meaasurements in the ultra-violet region of the spectrum are very expensive and available in only a few laboratories. In addition, the enzymatic reagents are expensive.

A single estimation usually takes 20 - 30 minutes to perform when all the reagents are available. In the present study it was found that reduced diphosphopyridine nucleotide did not retain its activity in solution for more than 12 hours even in the frozen state, which meant that the substance had to be weighed in the dry state before each batch of sera was tested, a tedious and time-consuming procedure, especially if the result of assay is urgently required. To obviate this difficulty a stock of tubes containing approximately 2 mgm. of DPNH, accurately weighed was held in the dry state in the deep freeze and was readily available.

It is concluded that the spectrophotometric method of transaminase assay is suitable for research purposes in well equipped laboratories but that, for routine studies of transaminase activities, one of the many reasonably accurate colorimetric methods of assay may be found satisfactory.

VOLUME II.

APPENDIX II.

CASE NO. 1.

History of Present Illness.

An unmarried woman, aged 62 years, a retired thread winder, was admitted to hospital on 2nd February, 1957, complaining of severe retrosternal pain of seven hours' duration. The pain was of sudden onset, constricting in character and radiated down the left arm. The pain came on shortly after a heavy meal and was ascribed to indigestion, but it gradually increased in severity during the day and the patient began to vomit and then to cough, producing blood-stained frothy sputum. This was the first time that the patient had experienced such pain although she had complained of indigestion and flatulence for years.

There was no relevant past or social history.

Clinical Findings on Admission.

The patient was stuporose, confused and orthopnoeic. She coughed continuously, the sputum being blood-stained and frothy.

Cardiovascular System: The B.P. could not be recorded. The neck veins were congested. There was no oedema. The patient sweated profusely and her extremities were very cold and mottled. The pulse could not be felt at the wrist. The apex beat was neither visible nor palpable. The heart sounds were barely audible, being heard with difficulty because of constant coughing. The heart rate was 120 beats per minute.

Respiratory System: The breathing was rapid and gasping. Examination was limited by the patient's distress. On auscultation moist, bubbling râles were heard throughout the lung fields and mild bronchospasm was present.

No abnormality was found on examination of the alimentary or central nervous systems.

Treatment and Progress.

Immediate treatment with oxygen, intramuscular morphine sulphate, intramuscular heparin and penicillin was given. Within an hour, the pulse could be felt, the blood pressure was 50/30 mm. Hg., dyspnoea was less severe and the extremities were warmer.

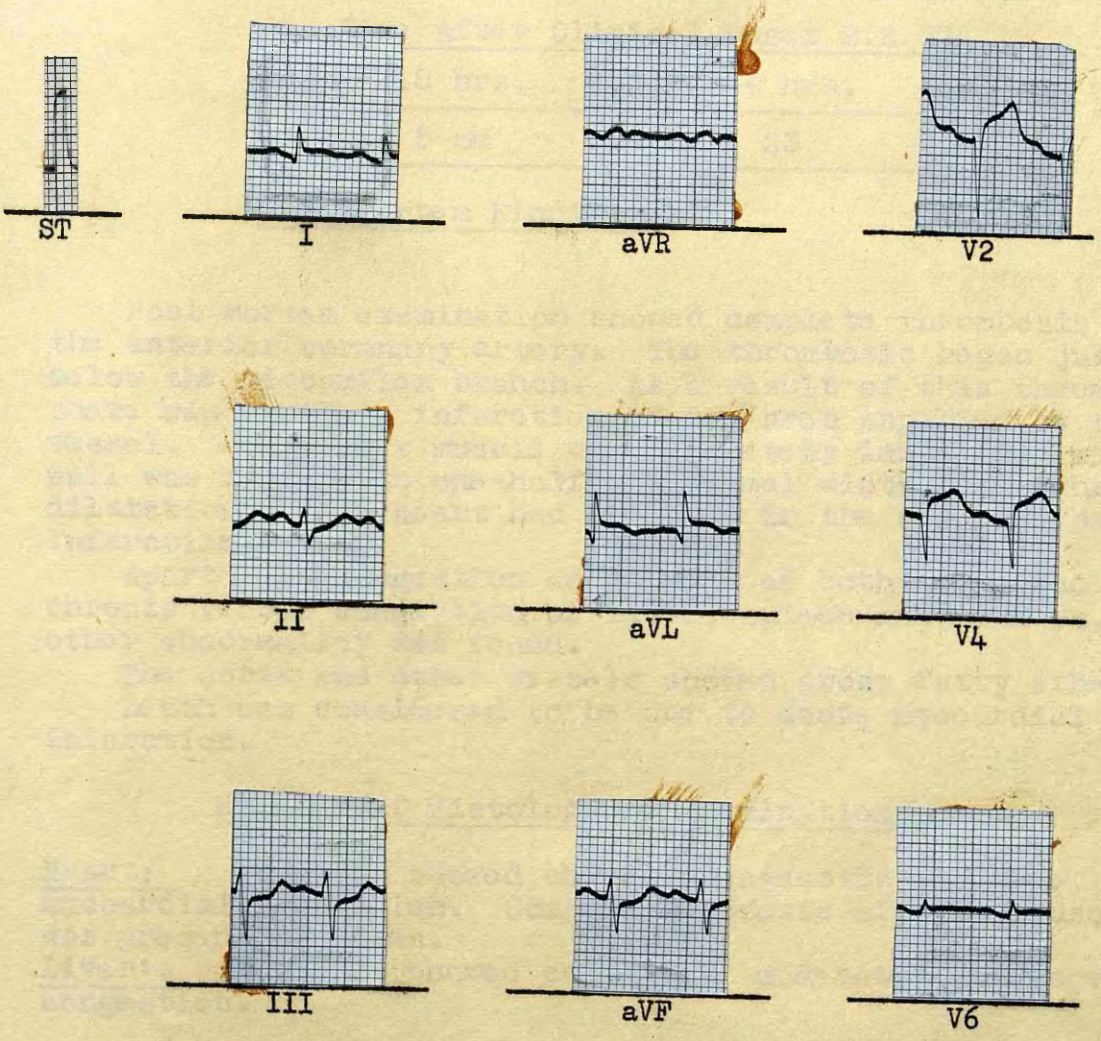
3.2.57. Treatment with Dindevan was started. Dyspnoea was less, the respiration rate was 28/min. Hypotension persisted - B.P. 50/30 mm. Hg. Patient remained stuporose.

Continued therapy resulted in little improvement in the condition and on 7th. February, 1957, the patient was still confused, although dyspnoea and cyanosis had improved. Blood pressure was 85/60 mm. Hg. The prognosis was regarded as poor and the patient died on 10th February, 1957.

Electrocardiographic Findings.

I. 3.2.57, 18 hours after onset of pain, an electrocardiogram showed changes diagnostic of an extensive transmural antero-septal infarction.

ELECTROCARDIOGRAM CASE NO. 1



Temperature Record: T. 100°F. eight hours after admission.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Clinical Onset 2.2.57.

18 hrs.	44 hrs.	65 hrs.	89 hrs.	113 hrs.	137 hrs.
90	176	328	135	66	50

Erythrocyte Sedimentation Rate (Westergren.)

Time After Clinical Onset 2.2.57.

18 hrs.	44 hrs.
5 mm	23

Post Mortem Findings.

Post mortem examination showed complete thrombosis of the anterior coronary artery. The thrombosis began just below the circumflex branch. As a result of this thrombosis there was complete infarction of the area supplied by this vessel. The heart muscle was completely infarcted, and the wall was reduced to one-half its normal width. Slight dilatation of the heart had occurred in the area of the infarction.

Apart from congestion and oedema of both lungs and chronic venous congestion of liver, spleen and kidneys, no other abnormality was found.

The aorta and other vessels showed gross fatty atheroma.

Death was considered to be due to acute myocardial infarction.

Results of Histological Examination.

Heart: Sections showed changes diagnostic of acute myocardial infarction. Complete necrosis of heart muscle was present in areas.

Liver:- Sections showed changes of moderate chronic venous congestion.

COMMENT:

The history and clinical findings were very suggestive of a poor risk myocardial infarction and the electrocardiograms showed changes diagnostic of transmural myocardial infarction. Pyrexia and a marked - extremely marked degree of peripheral vascular failure was present. Serum transaminase levels reached high levels before the E.S.R. was elevated and rose to very high levels, but were

/ were not considered to have contributed to the diagnosis of infarction. The diagnosis of myocardial infarction was confirmed at post mortem examination.

CASE NO. 2.

History of Present Illness.

A male, aged 55 years, a labourer, was admitted to hospital on the 20th.March, 1957, complaining of attacks of constricting retrosternal pain which was referred down the left arm. These attacks had begun two days after his dismissal from hospital in January, 1957. Initially, the attacks were related to exertion but then they started to come on at rest, notably during the night. The attacks were relieved by trinitrin (gr. 1/150). During the days before admission, he had been suffering attacks of agonising anginal pain at rest lasting from ten minutes to half an hour, approximately every hour. Whilst waiting in the Out-Patient Department on the morning of admission, he had been seized by a very severe pain which failed to respond to trinitrin. The pain came on at 10.45 a.m., and lasted until 2.45 p.m., being allayed by morphine sulphate gr.1/4, subcutaneously. For seven years he had complained of bouts of epigastric pain and discomfort occurring half an hour after food and relieved by taking alkaline powders.

Past History.

May 1950 - Posterior Myocardial Infarction.
January, 1955 - Postero-lateral myocardial infarction successfully treated by anticoagulants.
December, 1956 - The patient had suffered an attack of acute coronary insufficiency following development of angina of effort in July, 1956, which had forced him to stop work. There was no evidence of infarction on electrocardiographic examination. He was treated by anticoagulants, glyceryl trinitrate and mycardol tablets, which were continued after discharge in January, 1957.

Clinical Findings on Admission.

The patient was a middle-aged male with cyanosed lips. The neck veins were slightly engorged. Clubbing of the fingers was present. No oedema was found.

Cardiovascular System: Blood pressure 110/80 mm. Hg. Pulse regular in rate and rhythm. Apex beat was not felt. Heart sounds were pure but very soft.

Alimentary System: The liver was enlarged 3" below the costal margin.

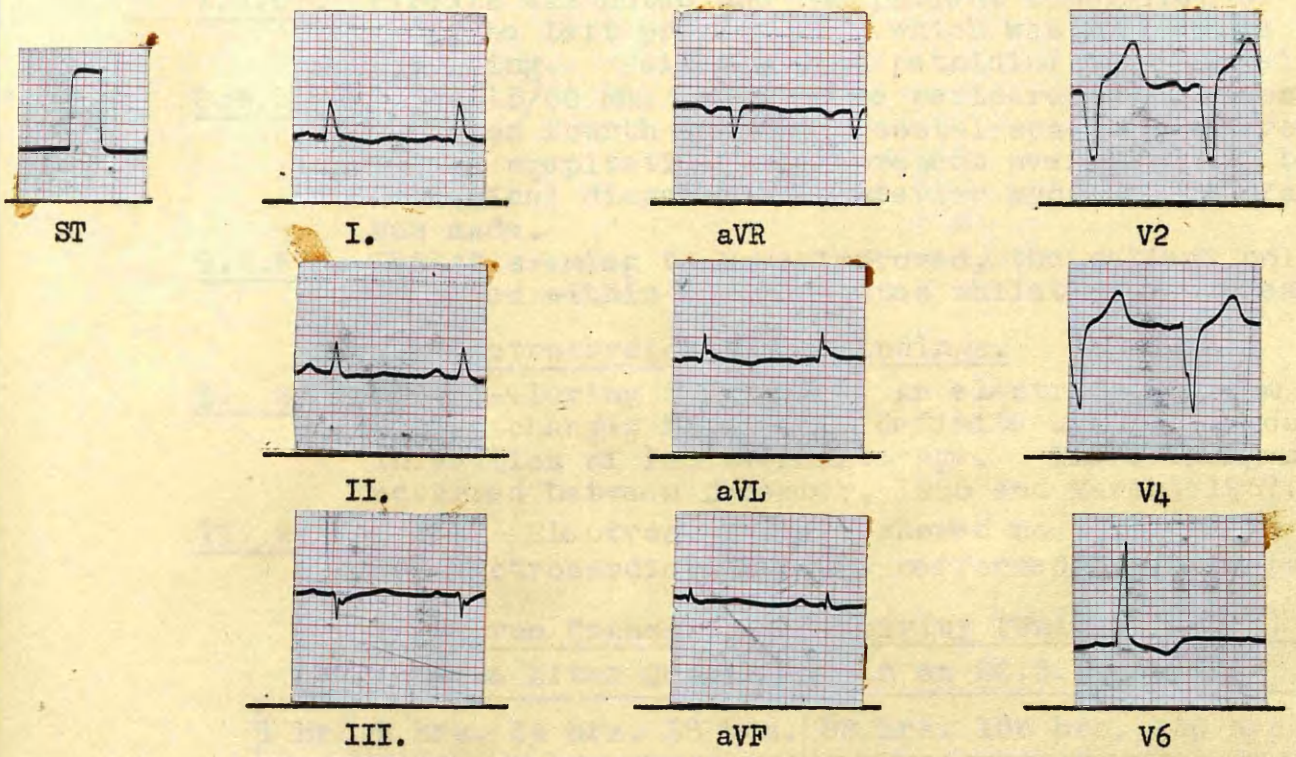
Respiratory System: Fine crepitations were heard at the bases of both lungs.

No other abnormality was discovered on examination.

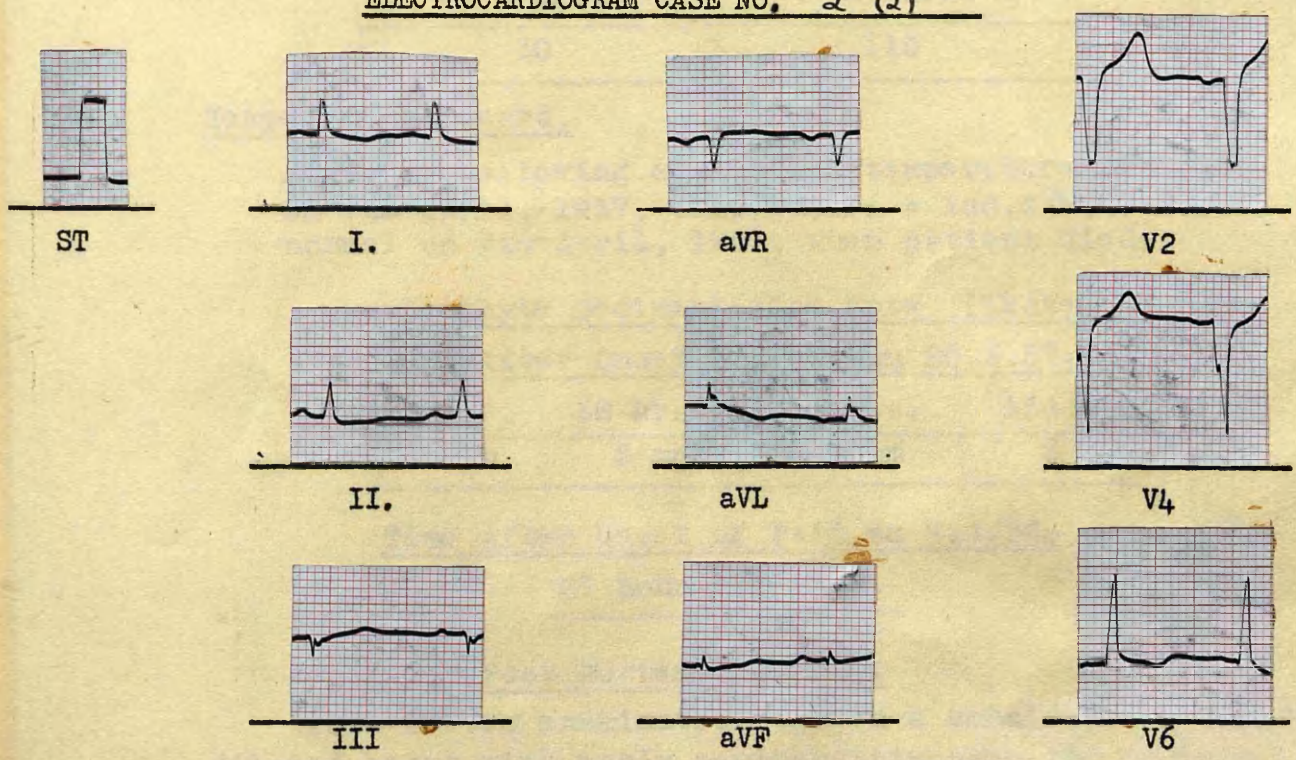
Treatment and Progress.

Treatment with anticoagulants was continued, but frequent attacks of nocturnal angina pectoris continued despite the use of vasodilators. The long continued pain had given rise to severe anxiety symptoms and these were somewhat relieved by treatment with sodium amytal and meprobamate. Eventually, methyl thiouracil 400 mgm. daily was given on the 1st. April, 1957, in the hope that the reduction of the basal metabolic rate would /

ELECTROCARDIOGRAM CASE NO. 2 (1)



ELECTROCARDIOGRAM CASE NO. 2 (2)



/ would relieve his symptoms.

7.4.57. Pyrexia was noted and the patient complained of pain over the left praecordium, which was made worse by breathing. Pain required pethidine for its relief.

8.4.57. B.P. 115/60 mm. Hg. Coarse pericardial friction was heard on fourth left intercostal space. Numerous medium crepitations were present over the lung bases. A clinical diagnosis of anterior myocardial infarction was made.

9.4.57. Whilst seeming to have improved, the patient collapsed and died within a few minutes whilst eating breakfast.

Electrocardiographic Findings.

I. 20.3.57. -(During the pain). An electrocardiogram showed changes indicating definite anterior myocardial infarction of indeterminate age. These changes had occurred between December, 1956 and March, 1957.

II. 26.3.57. - Electrocardiogram showed no significant change. No electrocardiograms were performed during fatal attack.

Serial Serum Transaminase Activity (Units/ml/min.)

a) Time After Onset of Pain on 20.3.57.

1 hr.	9 hrs.	34 hrs.	58 hrs.	82 hrs.	106 hrs.	130 hrs.	154 hrs
29	31	22	22	43	26 un.	25	25

b) Time After Onset of Pain on 7.4.57.

3 hrs.	27 hrs.
30	110

Temperature Record.

24 hours following admission, temperature = 99°F. On 7th April, 1957, temperature = 100.6°F, but fell to normal on 9th April, 1957, when patient died.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Pain on 20.3.57.

1 hour.	58 hrs.	82 hrs.	154 hrs.
6 mm	5 mm	6 mm	5 mm

Time After Onset of Pain on 7.4.57.

27 hours / 13 mm.

Post Mortem Findings.

Post-mortem examination showed a considerably enlarged and dilated heart with early pericarditis over the surface of the left ventricle. The left auricular appendage was also covered /

/covered with early fibrinous deposit. At this point the heart was adherent to the pericardial sac. No abnormality was seen in the valves or chambers of the heart apart from the left ventricle. The coronary arteries all showed severe calcifying atheromatous degeneration and each vessel was equally affected. There was virtually no lumen existing in either vessel. Examination of the heart muscle showed two old areas of fibrosis of the posterior wall. The segment supplied by the anterior descending vessel showed recent acute infarction of 12 or more hours' duration.

No other abnormality was seen in any of the organs of the body apart from basal congestion in the lungs and well marked "nutmeg" change in the liver.

Death was considered to be due to acute myocardial infarction and atherosclerosis of the coronary vessels.

Results of Histological Examination.

Heart: Sections showed gross ischaemic fibrosis of the heart muscle with pericarditis and endocardial mural thrombus. Acute myocardial infarction with marked polymorphic infiltration was also present.

Liver: Sections showed changes characteristic of severe chronic venous congestion.

COMMENT:

An attack of severe angina pectoris at rest and one of acute myocardial infarction were studied in this case.

The history of attacks of angina pectoris at rest of gradually increasing severity together with the development of severe anginal pain, which lasted for four hours after the patient's admission to hospital, and signs of early congestive cardiac failure were very suggestive of a poor risk acute myocardial infarction. Serial electrocardiograms, however, while they showed changes diagnostic of infarction of indeterminate age, showed no evidence of a fresh infarction. Pyrexia was noted but there was no evidence of peripheral vascular failure. The erythrocyte sedimentation rate was normal despite continued attacks of pain. Serum transaminase activity rose to borderline levels 82 hours after a severe attack of chest pain. Whether this rise of transaminase activity was associated with the attack of angina pectoris which occasioned the patient's admission to hospital, or with one of the frequent attacks of angina pectoris which followed his admission, it is impossible to say but it was concluded that severe angina pectoris at rest can cause a rise of serum transaminase activity to borderline levels.

On 7.4.57., the history and clinical findings were typical of a poor risk myocardial infarction. Electrocardiograms /4

/ Electrocardiograms were not performed. Pyrexia and minimal peripheral vascular failure followed this attack and the erythrocyte sedimentation rate was slightly elevated. Serum transaminase activity reached high levels 27 hours after the onset of the illness. Post-mortem examination confirmed the presence of a very recent anterior myocardial infarction. The assay was considered, in the absence of electrocardiographic evidence, to have contributed early confirmatory evidence of the occurrence of acute myocardial infarction.

CASE NO. 3.

History of Present Illness.

A male, aged 62 years, a chauffeur, developed sudden severe retrosternal pain at rest on the 27th February, 1957 at 9 a.m. The pain was severe, constant and crushing and radiated into the neck and down both arms. He was admitted to hospital on the 1st. March, 1957, i.e., 53 hours following the onset of pain. For two years, he had complained of angina and dyspnoea on effort, and of a winter cough, productive of a white spit. For many years he had complained of epigastric pain two hours after meals, which was relieved by alkalis. These dyspeptic symptoms, which were sometimes accompanied by vomiting, lasted only for a few days, there being long remissions. There was no relevant past or social history.

Clinical Findings on Admission.

The patient was complaining of pain and he was in a state of mild to moderate shock.

Cardiovascular System:- Blood Pressure 100/80 mm. Hg. Tachycardia 110/min.; pulse regular in rate and rhythm. The heart sounds were pure but distant, and the first sound at apex very soft.

No abnormality was found on clinical examination of respiratory, central nervous or alimentary systems.

Treatment and Progress.

On admission, morphine sulphate, gr. 1/4 relieved the pain and the condition of the patient remained stationary until 1 a.m. on the 2nd March, 1957 (12 hours after admission), when the patient suddenly collapsed. There was no precordial or other pain. Following this, the patient became hypotensive, B.P., 70/60 mm. Hg., and he was obviously suffering from severe peripheral circulatory failure. Meteorism was noted. Attempts to raise the blood pressure by the use of intravenous nor adrenaline failed and the patient's condition remained unchanged until 4.45 p.m. on the 2nd March, 1957, when he complained of excruciatingly severe retrosternal pain which persisted despite morphine therapy until he died at 5.25 p.m. Anticoagulant therapy had been started on admission.

Electrocardiographic Findings.

I.. 1.3.57: (53 hours after the onset of pain). The electrocardiogram showed changes diagnostic of a moderately extensive antero-septal myocardial infarction. Serial electrocardiograms were not taken.

Serial Serum Transaminase Activity(Units/ml/min.)

Time After Clinical Onset.

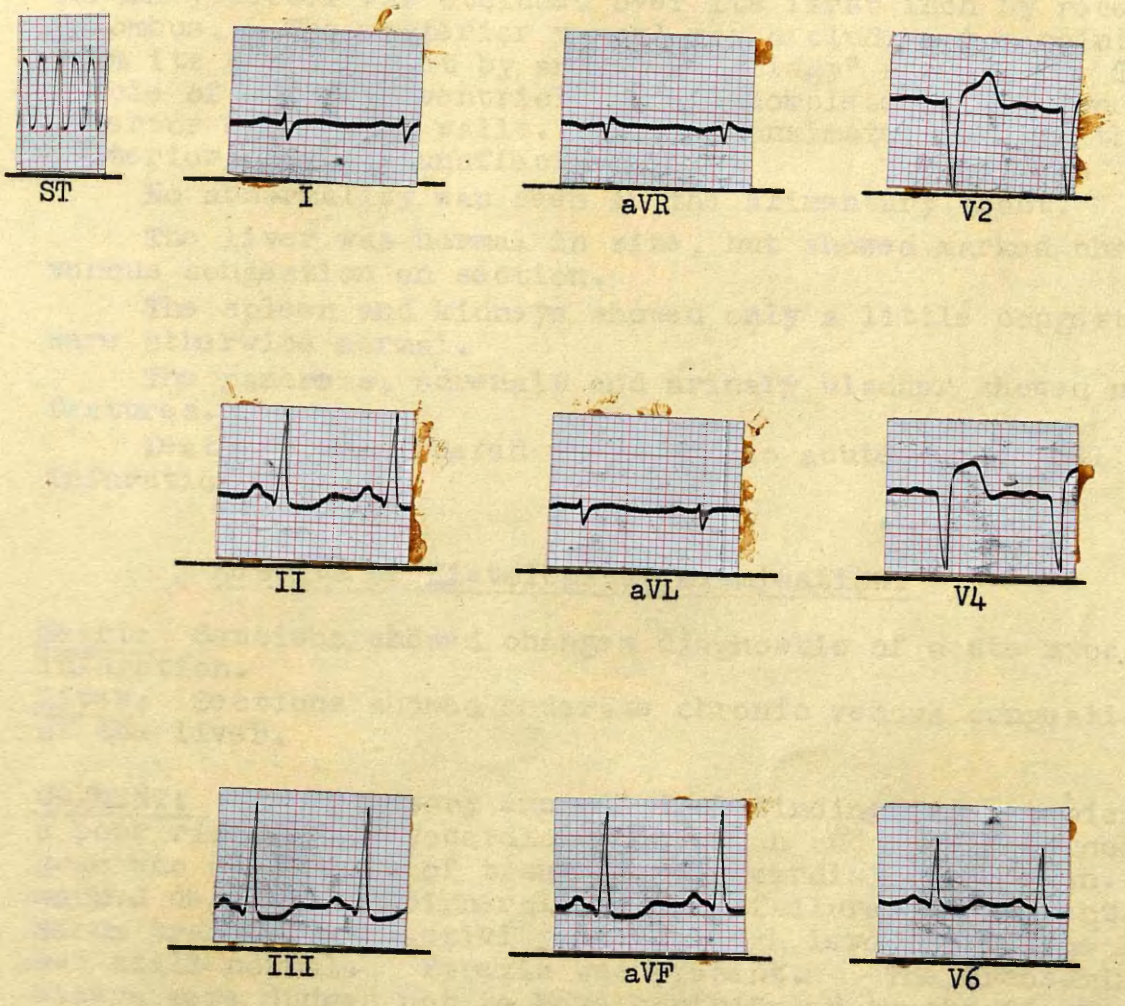
53 hrs.	64 hrs.	72 hrs.	80 hrs.
179	238	199	147

Temperature Record.

Eleven hours after admission, i.e., 63 hours after onset, the patient's temperature was 99°F.

/2

ELECTROCARDIOGRAM CASE NO. 3



Erythrocyte Sedimentation Rate (Westergren).

53 hours following the onset of pain = 5 mm. in first hour.

Post-Mortem Findings.

The post-mortem examination was carried out on March 4th., 1957. This showed the right lung to be lightly adherent to the chest wall. The left lung lay free. Both lungs on section showed moderate congestion and considerable œdema.

The heart was larger in size than normal due to dilatation of the left ventricle. The valves and other chambers of the heart were normal. The coronary arteries were extensively diseased throughout by calcifying atheroma. The anterior coronary vessel was occluded over its first inch by recent thrombus. The posterior vessel was occluded at a point 2½" from its commencement by an old "porridgy" atheroma. The heart muscle of the left ventricle showed complete infarction of the anterior and septal walls. Only approximately 1½" of the posterior wall was unaffected.

No abnormality was seen in the alimentary tract.

The liver was normal in size, but showed marked chronic venous congestion on section.

The spleen and kidneys showed only a little congestion but were otherwise normal.

The pancreas, adrenals and urinary bladder showed no special features.

Death was considered to be due to acute myocardial infarction.

Results of Histological Examination.

Heart: Sections showed changes diagnostic of acute myocardial infarction.
Liver: Sections showed moderate chronic venous congestion of the liver.

COMMENT: The history and clinical findings were typical of a poor risk acute myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction. A marked degree of peripheral vascular failure was present. Serum transaminase activity was at high levels when the E.S.R. was still normal. Pyrexia was present. The transaminase assays were judged not to have contributed to the diagnosis. The diagnosis of myocardial infarction was confirmed at post mortem examination.

CASE NO. 4.

History of Present Illness.

A male, aged 55 years, a foreman trucker, was admitted to hospital on the 11th March, 1957, having been seized with severe retrosternal pain whilst sitting in a bus. The pain was referred down the left arm and had begun at 7.30 a.m., on the morning of admission. There was no relevant past or social history.

Clinical Findings on Admission.

The patient was a heavy, middle-aged man of good colour. He was mildly shocked.

Cardiovascular System: Blood pressure 110/70 mm. Hg. Pulse (90 beats per minute) was regular in rate and rhythm. Apex beat was not felt. The heart sounds were pure, but distant. No abnormality was found on examination of other systems.

Treatment and Progress.

The pain complained of on admission responded to morphine sulphate gr. 1/4 subcutaneously. The patient's condition was unchanged when, at 11.45 a.m.,(3 hours 45 minutes after admission) his respirations became gasping in character and he lost consciousness. The blood pressure could not be recorded and the pulse was impalpable. Treatment with intravenous aminophyline and nor adrenaline was without effect and the patient died at noon, approximately 4 hours after the onset of his illness. Anticoagulant therapy was started one hour after admission.

Electrocardiographic Findings.

An electrocardiogram was not performed.

Serum Transaminase Activity (Units/ml/min).

23 units/ml/min. 1¼ hours following onset of pain.

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren)

3 mm/ 1st.hour, 1¼ hours following pain.

Post Mortem Findings.

Post-mortem examination showed marked pulmonary oedema. Both lungs were also moderately congested but showed no other pathological features.

The heart was normal in size and the valves and chambers showed no disease. The coronary arteries, however, were markedly atheromatous, and a recent clot was found in the posterior vessel 1½ inches from its commencement. No infarctions were found in the heart muscle, but a portion of the posterior wall of the left ventricle was taken for histological examination. /

No abnormality was seen in the alimentary tract.

The viscera were congested but otherwise normal.

Death was considered to be due to coronary artery thrombosis.

Results of Histological Examination.

Heart: Sections showed the early signs of myocardial infarction with increased polymorph myocardial infiltration and oedema between the muscle bundles.

Liver: No abnormality was seen in the sections examined.

COMMENT:

The history and clinical findings were typical of a poor risk myocardial infarction. Extremely marked peripheral vascular failure developed and the patient died before an electrocardiogram was performed. The temperature and erythrocyte sedimentation rate were normal and serum transaminase activity was normal 1¼ hours following the onset of the illness. The clinical diagnosis was confirmed at post-mortem examination at which thrombosis of the posterior coronary vessel was demonstrated.

This case illustrates that, in the early period (0-6 hours) following myocardial infarction, transaminase activity may be normal.

CASE NO. 5.

History of Present Illness.

A male, aged 59 years, a works manager, was admitted to hospital on the 2nd. April, 1957, having been seized at 3 a.m., by a severe cramp-like pain in the left arm which radiated into the chest. This pain persisted as a heavy discomfort felt retrosternally in spite of a dose of morphine sulphate, gr. 1/4, given intramuscularly at 4.20 a.m.

Five weeks previously, he had a similar, less severe retrosternal pain, which came on when he was walking and lasted for twenty minutes. At this time, mild diastolic hypertension had been noted. (B.P. 160/110 mm. Hg). He had returned to work only one week prior to this acute attack.

Past History.

In 1937, the patient was in bed for fourteen days suffering from "nephritis".

Clinical Findings on Admission.

The patient was a pale, middle-aged, obese man, who complained of continuing retrosternal pain and who was moderately shocked.

Cardiovascular System: B.P. 105/80 mm. Hg. Pulse was regular in rate and rhythm. Apex beat was not felt. The heart sounds were pure but very distant.

No other abnormality was found on full clinical examination.

Treatment and Progress.

Anticoagulant therapy was started on admission. Despite repeated intramuscular doses of pethidine, mgm. 100., the patient still had fairly severe retrosternal pain on admission.

2.4.57:- (10 a.m.) Blood pressure 90/80 mm.Hg. Jugular venous congestion with mild superficial skin oedema were present.

Chest:- Fine crepitations at both bases.

The clinical diagnosis was one of severe myocardial infarction. Mild to moderate shock persisted.

4.4.57:- There had been no recurrence of pain, but haemoptysis was present.

Cardiovascular System: B.P. 90/50 mm. Hg. Pericardial friction was heard to the left of lower end of sternum, in the fifth intercostal space.

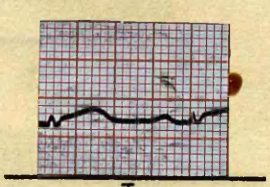
8.4.57:- The haemoptysis had cleared 48 hours after onset. There was no evidence of focal lung lesion on X-ray film of chest. Jugular venous congestion was still present. The pulse was irregular due to the presence of ventricular ectopic beats. B.P. 75/50.

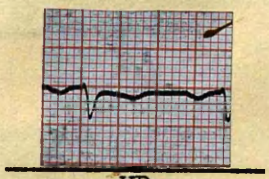
24.4.57:- The patient remained symptom-free but hypotension (B.P. 85/60) persisted, and there was evidence of mild congestive failure. Mersalyl therapy was started and resulted in a satisfactory diuresis with great improvement in the cardiac action.

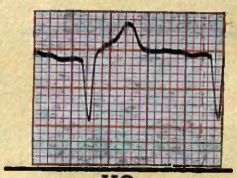
21.5.57:- The patient was fit for discharge. No evidence of

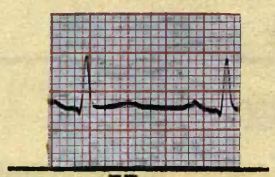
ELECTROCARDIOGRAM CASE NO. 5 (1)

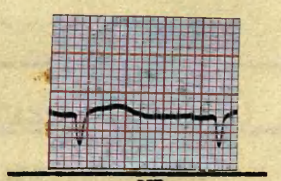

ST

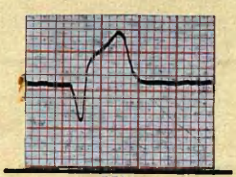

I

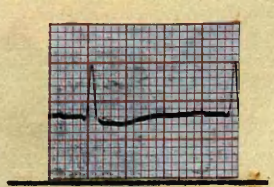

aVR

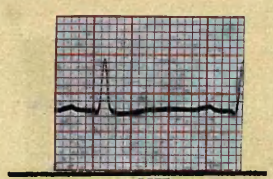

V2

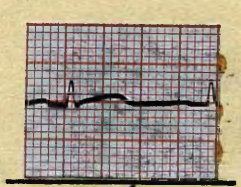

II


aVL

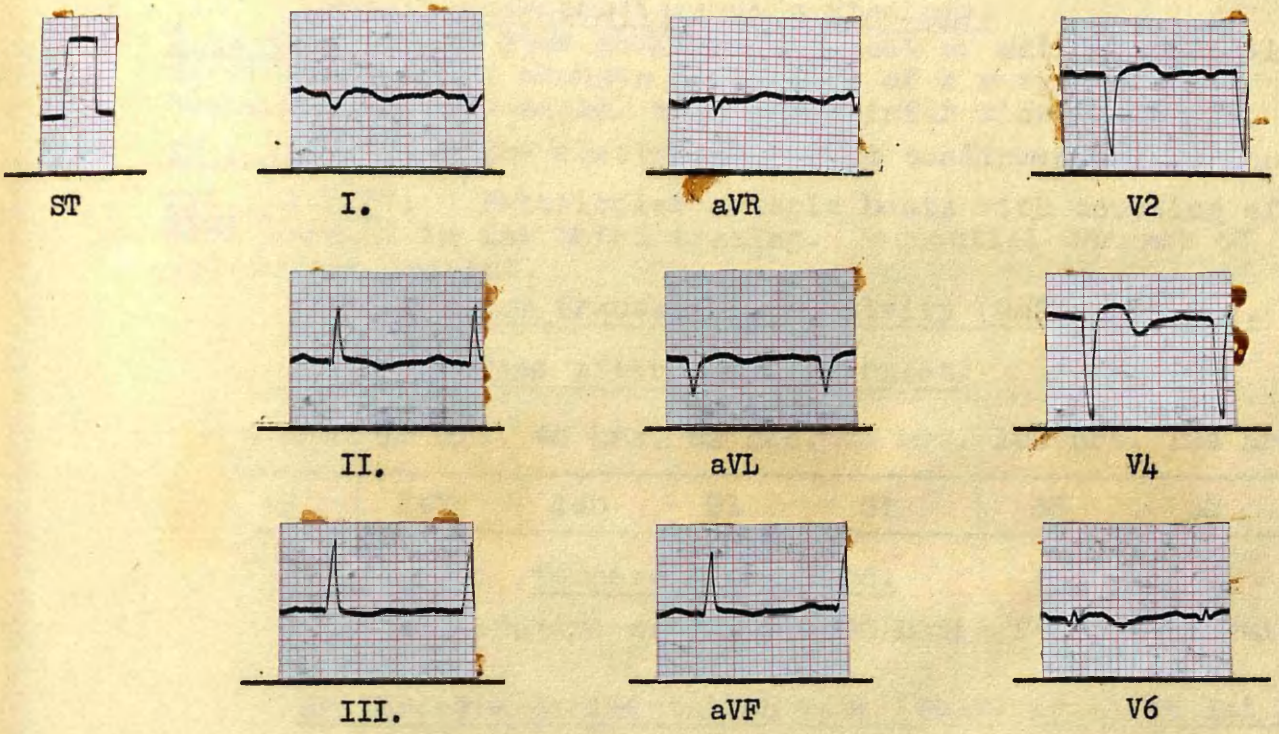

V4


III

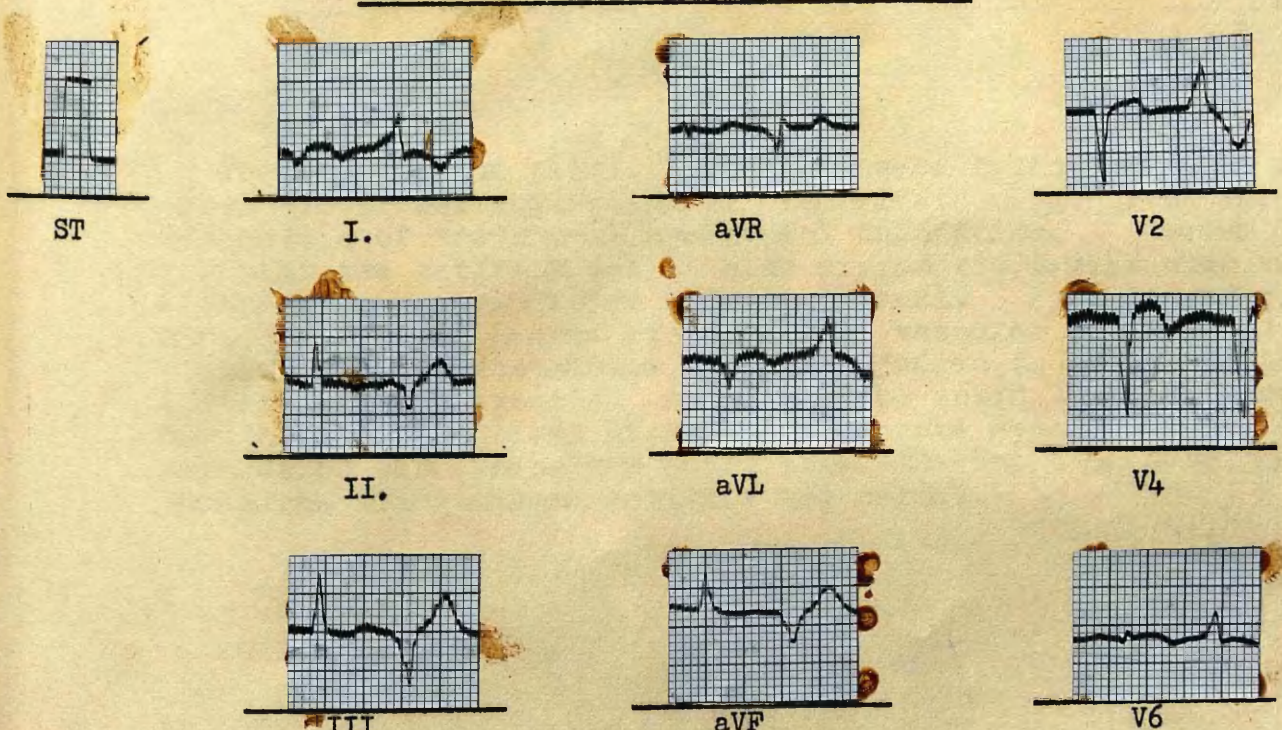

aVF


V6

ELECTROCARDIOGRAM CASE NO. 5 (2)



ELECTROCARDIOGRAM CASE NO. 5 (3)



/ of congestive cardiac failure. Symptom-free on exertion. Blood pressure 100/80 mm. Hg.

Electrocardiographic Findings.

I....2.4.57: (Four hours after onset of pain). The electrocardiogram showed changes diagnostic of a very extensive transmural antero-septal myocardial infarction.

II...15.4.57: The electrocardiogram confirmed the diagnosis.

III.. 1.5.57: Ventricular ectopic beats with coupling of beats were present in the third tracing. Sequential changes of infarction present.

Serial Serum Transaminase Activity (Units/ml/min).

Time After Clinical Onset.

4 hrs.	16 hrs.	40 hrs.	52 hrs.	76 hrs.	100 hrs.	124 hrs.	19th day.
17	247	140	91	51	35	30	21

Temperature Record.

The temperature was 99.6., 28 hours following admission.

Erythrocyte Sedimentation Rate (Westergren) in 1st.Hour.

Time After Clinical Onset.

16 hrs.	6th day.	13th day.	27th day.	35th day.	41st day.	48th day
9 mm	21	23	17	15	25	21

COMMENT:

The history and clinical findings were typical of poor risk acute myocardial infarction and the electrocardiograms were diagnostic of transmural myocardial infarction. Serum transaminase activity was at high diagnostic levels when the erythrocyte sedimentation rate was normal. Pyrexia and a minimal-moderate degree of peripheral vascular failure was present. The transaminase assay was judged to have contributed little to the diagnosis. It should be noted that electrocardiographic patterns diagnostic of acute myocardial infarction were present 4 hours after the onset of pain, when the serum transaminase activity was normal.

CASE NO. 6.

History of Present Illness.

A male, aged 75 years, a retired labourer, was admitted to hospital on the 30th. March, 1957, at 1 p.m. On the 29th. March, 1957, he had slight constricting pain in his chest whilst walking, which passed off in five minutes when he rested. On the 30th.March, 1957, at 9 a.m., he complained of very severe constricting retrosternal pain which did not radiate. The pain made him sweat and he was still complaining of mild retrosternal pain at 1 p.m.

Past History.

The patient had complained of dyspnoea on moderate exertion for five years.

Clinical Findings on Admission.

The patient was a pale, thin, elderly man with slightly cyanosed lips, who had a severe retrosternal pain whilst he was being examined.

Cardiovascular System: Blood pressure 100/70 mm. Hg. Pulse regular in rate (92/min.) and rhythm. The apex beat was impalpable. The heart sounds were pure but very faint.

Chest:- Numerous medium crepitations were present throughout the lung fields.

Alimentary System: The liver was enlarged two finger-breadths to percussion. Fullness and slight tenderness in epigastrium and right hypochondrium.

No other abnormality was found on the limited examination possible in a dangerously ill patient.

Treatment and Progress.

Anticoagulant therapy was started shortly after admission. During the night 30th March / 31st March, 1957, the patient required three injections of Omnopon, gr. 1/3., intramuscularly for recurrent pain and extreme restlessness.

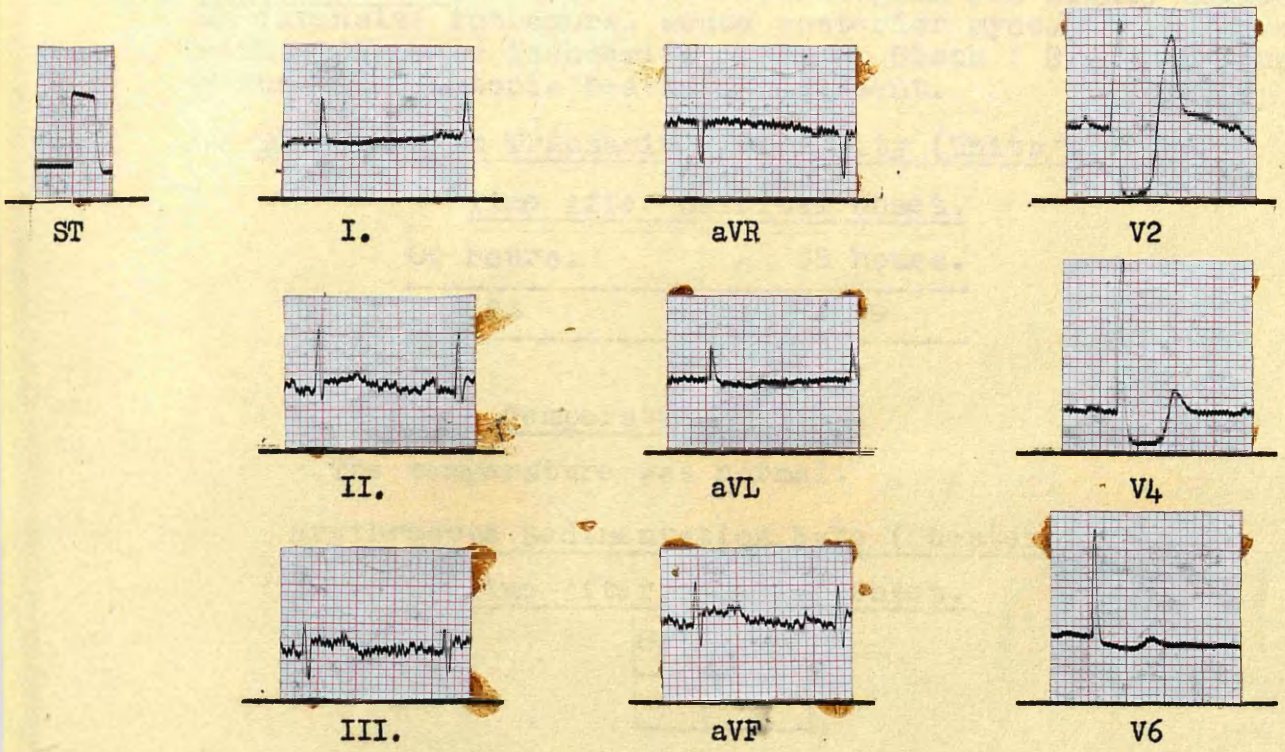
31.3.57: At 2 p.m., the patient collapsed and became unconscious for one hour. On recovering consciousness, he complained of mild anginal pain. On examination, the patient was pale, cold and sweating. The radial pulse was irregular. The heart rate at the apex was 68/min. The blood pressure was 40 mm. systolic pressure, the diastolic pressure being unrecordable. Signs of pulmonary oedema were present. Intravenous nor adrenaline was given in repeated doses without appreciable effect on the blood pressure. The shock phase persisted until the patient died at 11.45 p.m., on the 31st. March, 1957.

Electrocardiographic Findings.

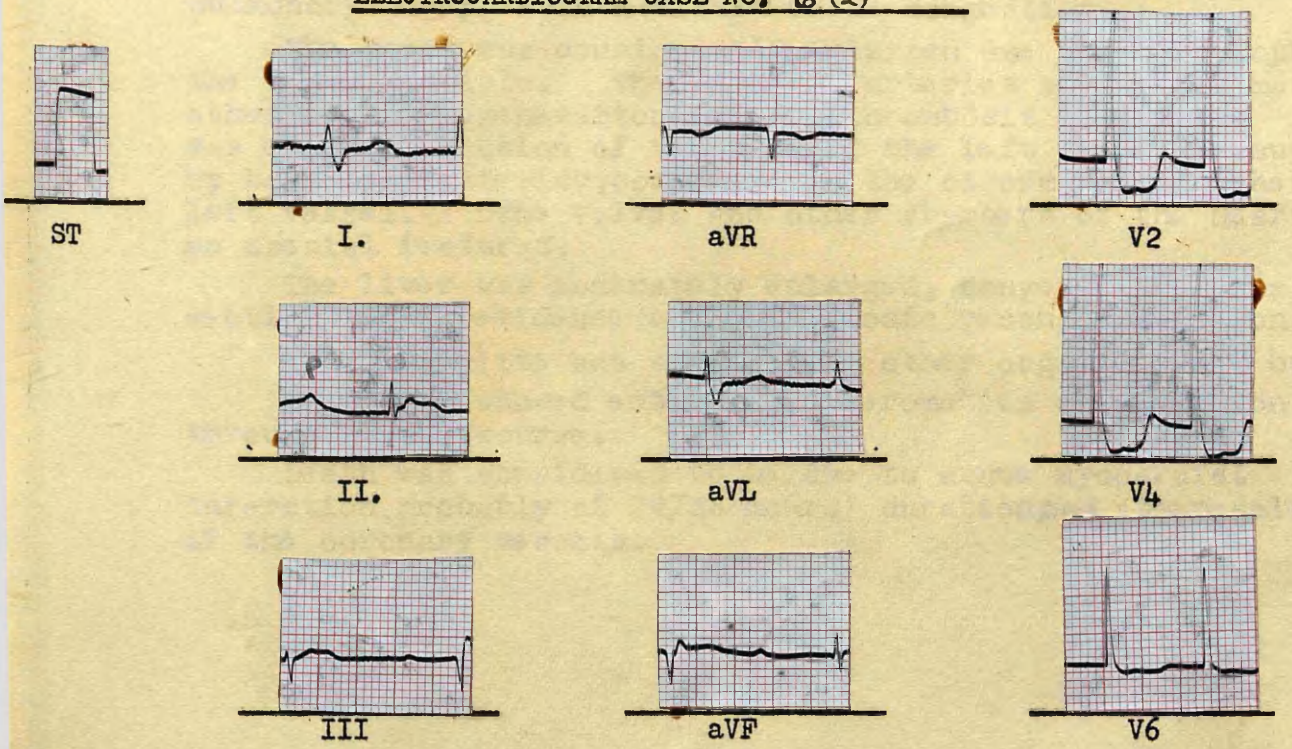
I... 30.3.57, at 3 p.m. (Seven hours after onset of pain). The electrocardiogram was not diagnostic but was very suggestive of an acute posterior myocardial infarction with widespread ischaemia.

/2

ELECTROCARDIOGRAM CASE NO. 6 (1)



ELECTROCARDIOGRAM CASE NO. 6 (2)



Electrocardiographic Findings (ctd.)

II... 31.3.57: The electrocardiogram was highly suggestive of an extensive intramural acute posterior myocardial infarction with widespread ischaemia. Heart Block (2:1) and supra-ventricular ectopic beats were present.

Serial Serum Transaminase Activity (Units/ml/min).

Time After Clinical Onset.

8½ hours.	38 hours.
83	209

Temperature Record.

The temperature was normal.

Erythrocyte Sedimentation Rate (Westergren).

Time After Clinical Onset.

8½ hours.
4 mm

Post-Mortem Findings.

Post-mortem examination, carried out on 2.4.57, showed small bilateral pleural effusions. Both lungs were lightly adherent to the thoracic cage. On section they showed some pulmonary oedema with a little basal congestion.

The heart was considerably enlarged due to hypertrophy of the left ventricle. The coronary arteries all showed marked atheromatous degeneration, but no thrombosis was found. There was early infarction of the area of the left ventricle supplied by both the posterior, coronary and the circumflex branches of the left vessel. The valves and other chambers of the heart showed no special features.

The liver was moderately enlarged, congested, and on section showed evidence of some chronic venous congestion.

No abnormality was seen in the other organs of the body.

The aorta showed extensive atheromatous degeneration throughout its course.

Death was considered to be due to acute myocardial infarction, probably of 24/36 hours' duration, and atherosclerosis of the coronary vessels.

/3

Results of Histological Examination.

Heart: Sections showed changes diagnostic of acute myocardial infarction with marked polymorphic infiltration.

Liver: sections showed moderate chronic venous congestion.

COMMENT: The history and clinical findings were very suggestive of a poor risk myocardial infarction. There was no pyrexia but extremely marked peripheral vascular failure developed. Serial electrocardiograms were highly suggestive of extensive intramural acute myocardial infarction and heart block (2 : 1) was present. The erythrocyte sedimentation rate was normal 8½ hours after the onset of the illness. The serum transaminase activity was at diagnostic levels 8½ hours after the onset of the illness and rose to high levels 38 hours after the onset of the illness.

When the history, clinical findings and electrocardiographic patterns were considered together, there was no doubt about the diagnosis of acute myocardial infarction but the assay was considered to have provided early and valuable confirmation of the occurrence of acute myocardial infarction before the onset of severe peripheral vascular failure.

Post mortem examination confirmed the presence of an acute myocardial infarction.

CASE NO. 7.

History of Present Illness.

A male, aged 62 years, an engineering inspector, was admitted to hospital on the 26th. February, 1957 at 8 p.m., complaining of severe retrosternal pain of three hours' duration. Three hours before admission, at 5 p.m., he had been seized with severe gripping retrosternal pain, which travelled into his throat, neck and jaw. The pain was very severe for an hour and then gradually eased. It was still present in a mild degree at 8 p.m. He had complained, for one year, of a feeling of constriction in his throat when exerting himself, which passed off in a few minutes when he rested. There had been no complaint of dyspnoea or ankle swelling.

Past History.

The patient had suffered from winter bronchitis since 1947.

Clinical Findings on Admission.

He was a well-built man, whose lips were slightly cyanosed. He was cold and sweating, and appeared slightly shocked.

Cardiovascular system: Blood Pressure was 120/80 mm.Hg. The pulse was regular (56 beats per minute) in rate and rhythm. The apex beat was not palpable. The heart sounds were faint, but pure.

Respiratory system: There were a few medium crepitations at both lung bases.

No other abnormality was discovered on full clinical examination.

Treatment and Progress.

The pain responded quickly to treatment with intramuscular morphine sulphate, gr.1/4., and anticoagulant therapy was started soon after admission.

27.2.57: (9 a.m.) His general condition had improved and he was considered to be out of shock phase. The B.P. remained unchanged i.e., 125/80 mm.Hg.

4.3.57. Having been symptom-free since admission, the patient complained of an attack of mild but constricting pain in his throat and lower jaw, lasting for thirty minutes. The pain began at 12.10 p.m. In the following week, the patient suffered several similar attacks of pain in the throat but these responded to treatment with trinitrin gr.1/150 and cleared spontaneously on the 11th. March, 1957.

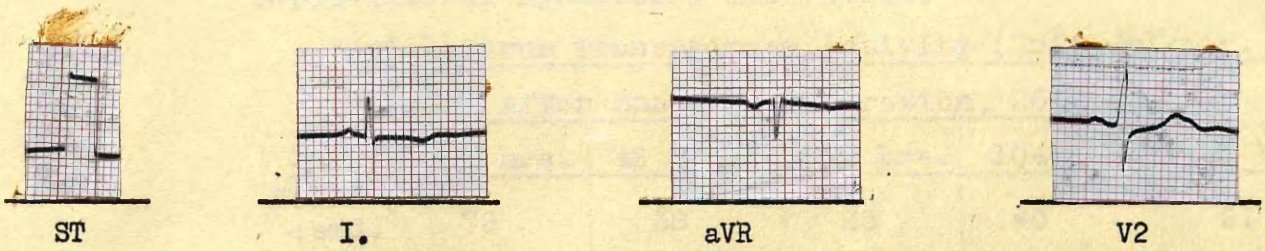
5.4.57: Symptom-free, fit for discharge home.
Blood pressure - 110/75 mm. Hg.

Electrocardiographic Findings.

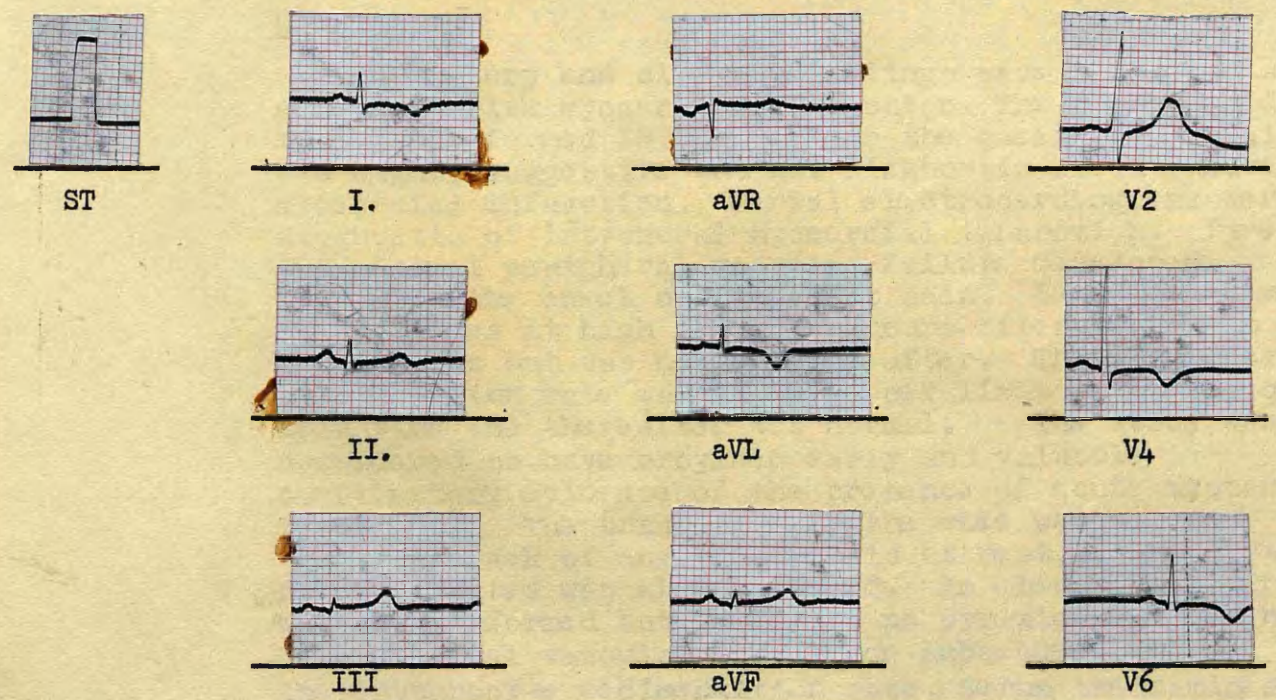
I. 27.2.57: (18 hours after the onset of chest pain). The electrocardiogram showed changes highly suggestive, but not diagnostic, of an extensive intramural antero-septo-lateral infarction.

II. 1.3.57: /2

ELECTROCARDIOGRAM CASE NO. 7 (1)



ELECTROCARDIOGRAM CASE NO. 7 (2)



II. 1.3.57. The electrocardiogram showed progressive ST-T changes, diagnostic of an extensive intramural antero-septo-lateral myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Infarction, 26.2.57.

3 hrs.	18 hrs.	42 hrs.	80 hrs.	104 hrs.	131 hrs.
Haemoly):sed.	73	38	23	40	21

Time After Onset of Post-Infarction Angina, 4.3.57.

During pain.	21 hrs.	45 hrs.	69 hrs.
21	20	20	22

Temperature Record.

Temperature 99°F., 24 hours following admission.

Erythrocyte Sedimentation Rate (Westergren).

Time After Clinical Onset.

	18 hrs.	42 hrs.	131 hrs.	9th day.	16th day.	23rd day.	30th day.
mm/1st.hr.	10.	5	8	7	3	7	9

COMMENT:

The history and clinical findings were very suggestive of a good risk myocardial infarction. The electrocardio-:gram,, performed 18 hours after the onset of the pain, was highly suggestive but not diagnostic of intramural myocardial infarction. Serial electrocardiograms were diagnostic of intramural myocardial infarction. Pyrexia and minimal peripheral vascular failure developed following the onset of the chest pain. Serum transaminase activity was at high levels 17 hours after the onset of the illness but was normal thereafter. The erythrocyte sedimentation rate was at the upper limit of normal at this time and thereafter was normal. The assay was considered to have provided early and valuable confirmatory evidence of the presence of acute myocardial infarction. The transience of the rise was noted.

An attack of angina pectoris at rest, which lasted for 30 minutes was also observed. An electrocardiogram was not performed but there was no pyrexia, no evidence of peripheral vascular failure or subsequent rise in the erythrocyte sedimentation rate. Serum transaminase activity was normal following this attack of anginal pain.

CASE NO. 8.

History of Present Illness.

A male, aged 44 years, a spirit merchant, was admitted to hospital on the 27th. February, 1957. He had previously been in hospital from the 16th September, 1956 to the 29th. September, 1956, at which time he had complained of a sudden attack of burning pain at the back of his neck, which spread into the front of his chest and down both arms. Five days previously, after skipping, he had experienced sharp pain in the right calf muscles, and the right lower leg had become swollen and painful. The calf muscles were acutely tender on admission and it was thought that he had a deep venous thrombosis, probably associated with a minor muscle tear. The electrocardiogram showed no abnormality and it was considered that his symptoms had been due to pulmonary embolism without pulmonary infarction. He was treated with anticoagulants for a fortnight and the leg was supported by viscopaste. He was discharged from hospital on the 29th September, 1956, and was seen as an out-patient on the 10th October, 1956 and the 7th November, 1956, when he appeared to have made a good recovery except for a complaint of discomfort at the back of his neck, which was not suggestive of angina pectoris.

On the 27th December, 1956, he was seen again because of two transient episodes of stabbing chest pain. The history was not suggestive of angina pectoris. Full clinical examination revealed no abnormality and the electrocardiogram showed no significant abnormality.

On the 26th. February, 1957, he was again examined, having felt generally unwell for two months. For two weeks he had complained of short lasting attacks of weakness and paraesthesia affecting his arms and, on the 24th February, 1957, he had complained of acute burning pain in the right shoulder and arm and in the chest to the right of the sternum, lasting fifteen minutes. He vomited once.

On the 26th February, 1957, at 3.a.m., he was awakened by severe chest pain felt to the right of the sternum, which was burning in character. The pain was felt also in his right shoulder and down the right arm, passing between the shoulder blades. It was very severe and lasted for six hours and caused him to vomit several times. He was admitted to hospital on the 27th February, 1957.

Clinical Findings on Admission.

The patient was a middle-aged man, who was in no distress.

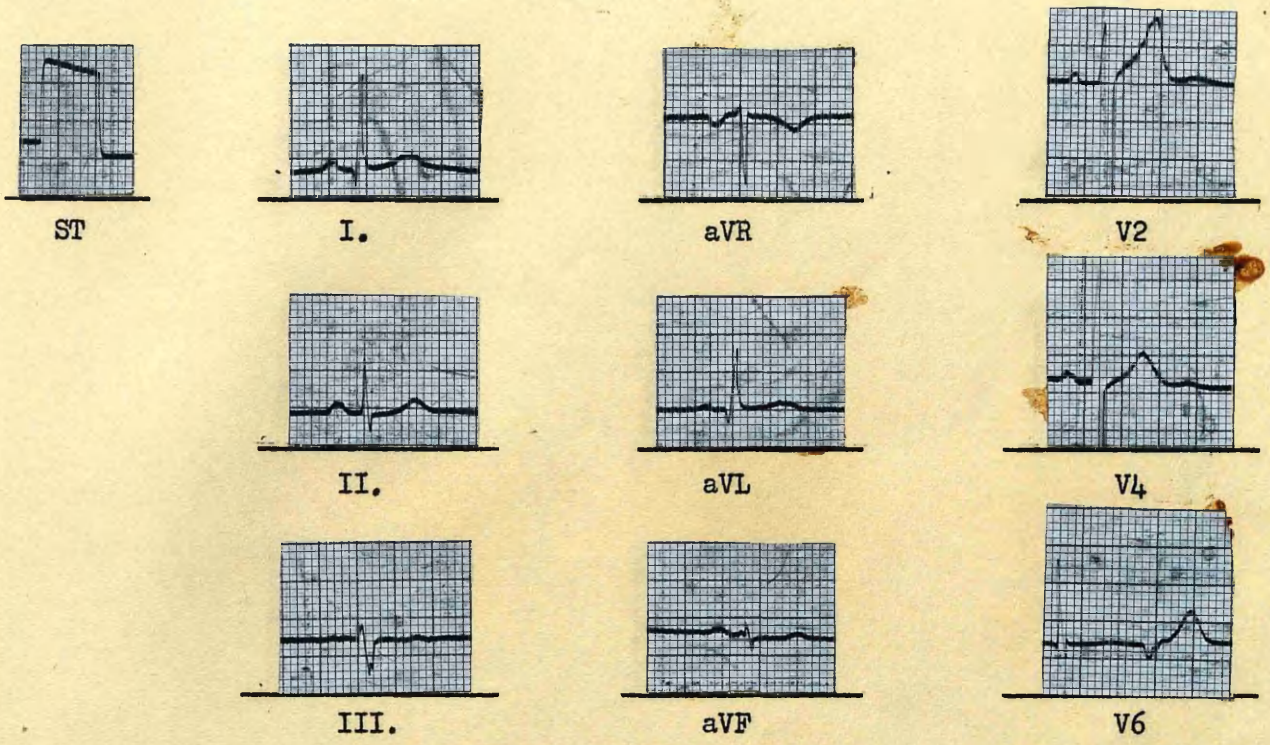
Cardiovascular system: Blood pressure 140/85 mm.Hg. The pulse was regular in rate (90/min.) and rhythm. The apex beat was not felt. The heart sounds were pure and of good quality. The second aortic sound was accentuated. No abnormality was found on full examination of other systems.

Treatment and Progress.

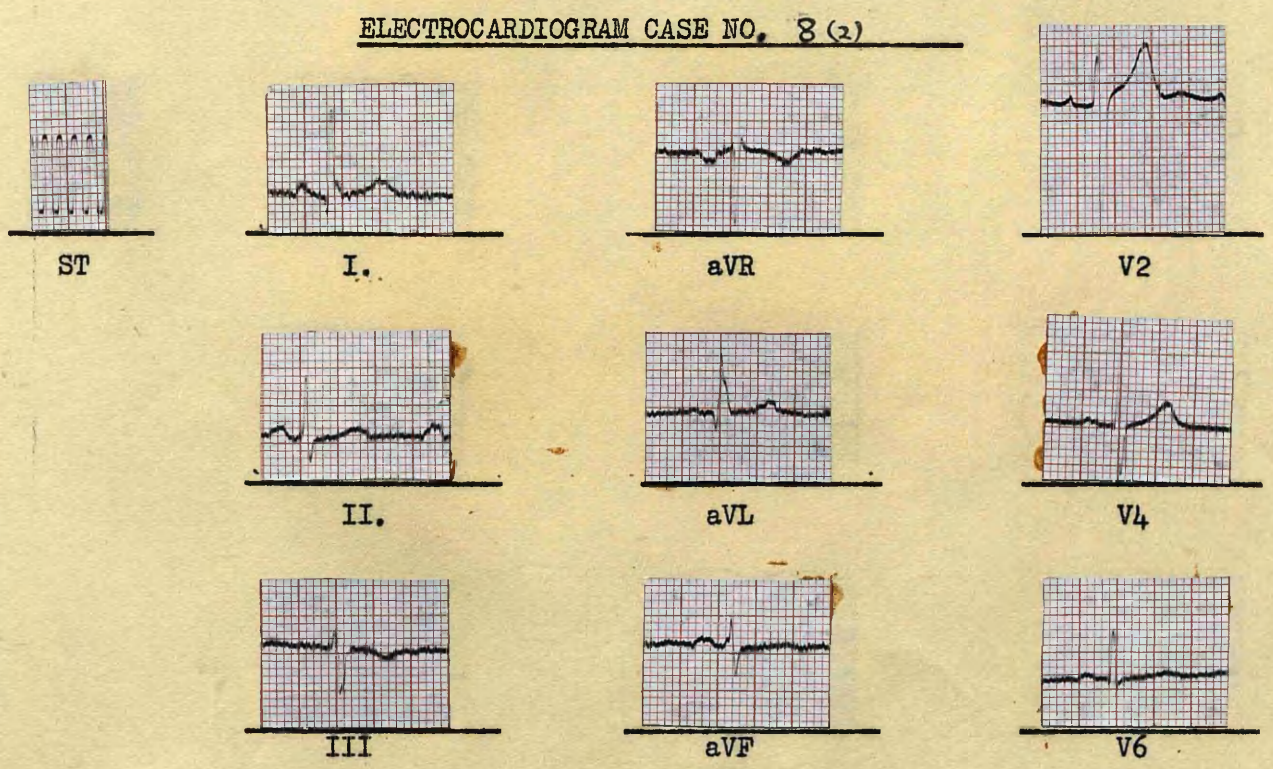
Anticoagulant therapy was started on the 28th February, 1957 and continued for 28 days.

/2

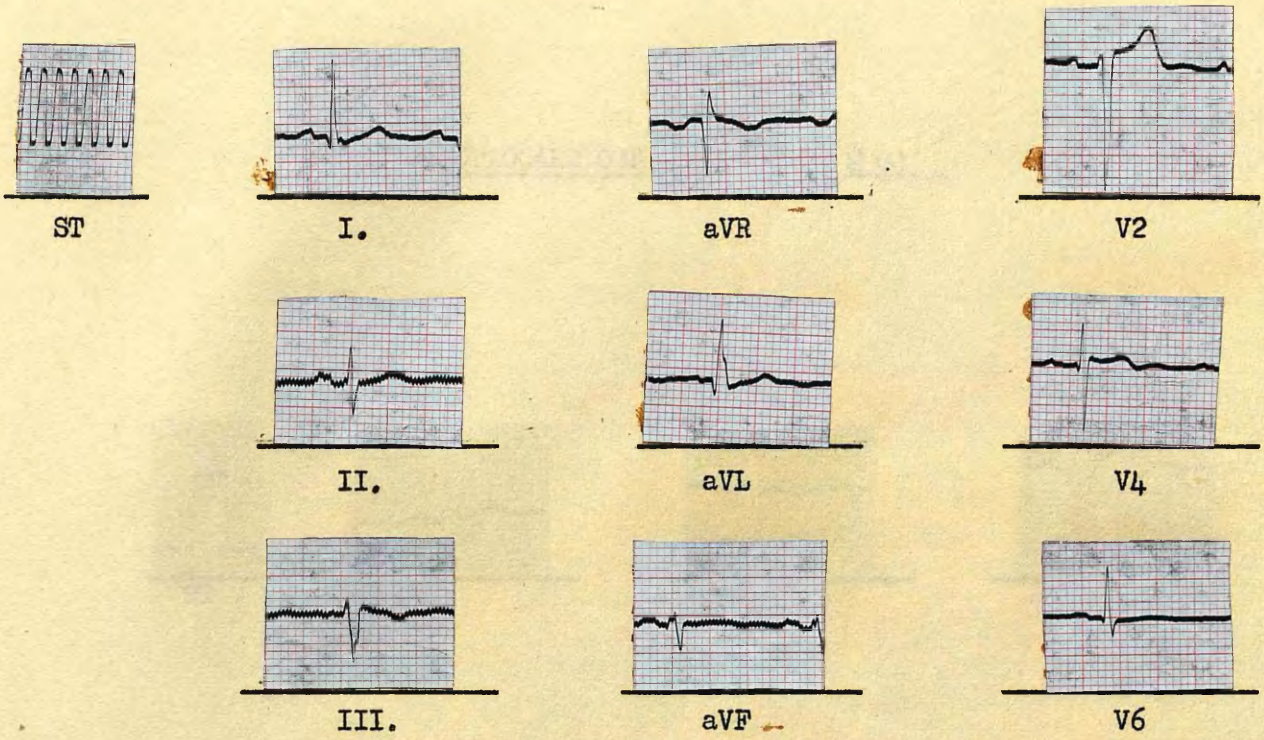
ELECTROCARDIOGRAM CASE NO. 8 (1)



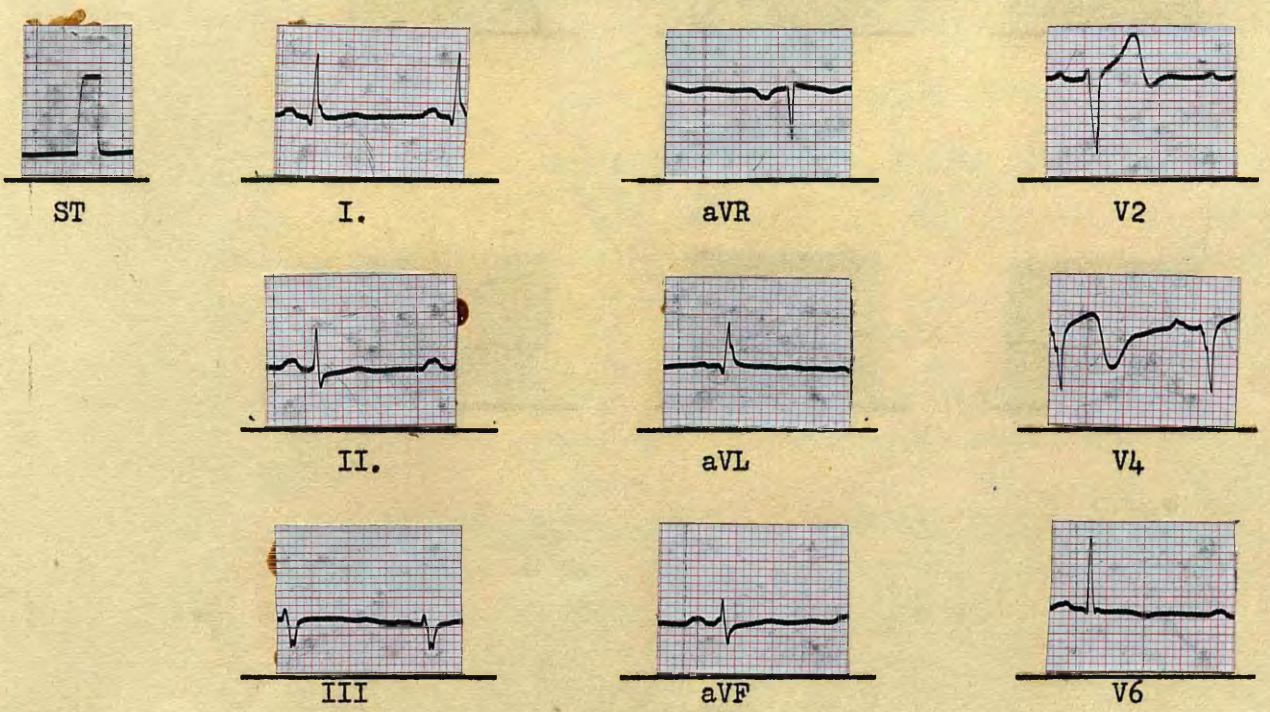
ELECTROCARDIOGRAM CASE NO. 8 (2)



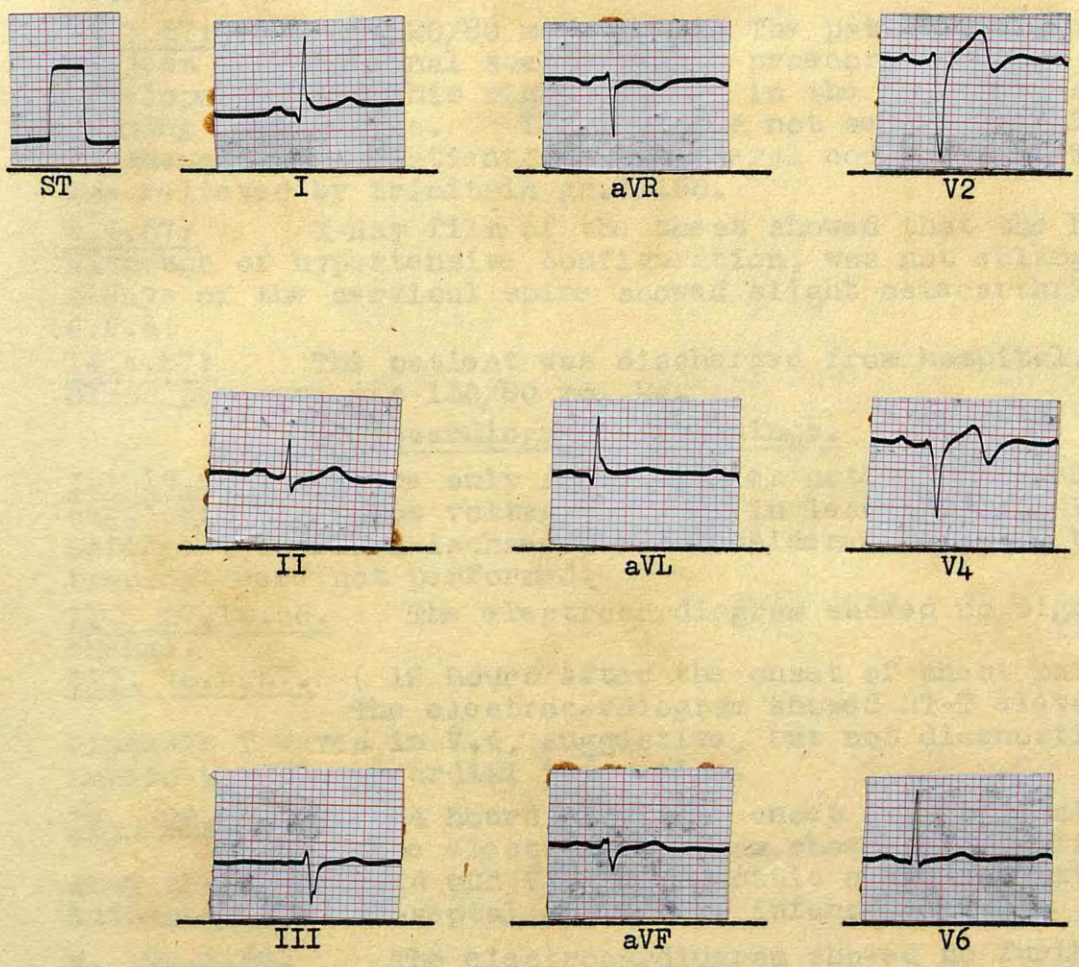
ELECTROCARDIOGRAM CASE NO. 8 (3)



ELECTROCARDIOGRAM CASE NO. 8 (4)



ELECTROCARDIOGRAM CASE NO. 8 (s)



Treatment and Progress (ctd.)

1.3.57: Severe numbing pain, felt above the right elbow and referred down into the inside of the arm and into the fourth and fifth fingers of the right hand, began whilst the patient was at rest and lasted in severe form for 20 minutes, but responded within a minute to trinitrin gr.1/150. He had similar, but less severe attacks of pain on the 28th February, 1957, at 2.30 p.m., and 7.45 p.m.

2.3.57: B.P. 95/50/0 mm. Hg. The patient complained of a feeling of tightness in the left praecordium.

4.3.57: B.P. 110/80 mm. Hg. There had been no recurrence of pain. The heart sounds were distant and difficult to hear.

20.3.57: B.P. 120/80 mm. Hg. The patient had been subject to occasional stabbing left praecordial pains when he developed pain in his right arm and in the back of his neck lasting three hours. The pain was not severe and there was no change in the patient's good general condition. The pain was relieved by trinitrin gr.1/150.

2.4.57: X-Ray film of the chest showed that the heart, although of hypertensive configuration, was not enlarged. X-Rays of the cervical spine showed slight osteoarthritis of C.V.5.

14.4.57: The patient was discharged from hospital. His blood pressure was 130/80 mm. Hg.

Electrocardiographic Findings.

I. 17.9.56. The only abnormalities noted in the electrocardiogram were low voltage T waves in leads III and V.6. Lateral myocardial ischaemia was considered possible but serial tracings were not performed.

II. 27.12.56. The electrocardiogram showed no significant change.

III. 26.2.57. (12 hours after the onset of chest pain.) The electrocardiogram showed ST-T elevation with biphasic T waves in V.4, suggestive, but not diagnostic of antero-septal myocardial infarction.

IV. 28.2.57 (54 hours after the onset of chest pain). The electrocardiogram showed progressive ST-T changes in V.4 and V.6., diagnostic of fairly extensive intramural antero-septal myocardial infarction.

V. 24.3.57. The electrocardiogram showed no further change.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Clinical Onset on 26th. February, 1957 at 3 a.m.

54 hrs.	78 hrs.	102 hrs.	126 hrs.	150 hrs.	174 hrs.
35	40	35	35	29	20

Note that there was no rise in S.G.O.T. levels following /3

/following severe pain on the 1st. March, 1957, (78 hours following onset of pain on the 26th February, 1957.

Temperature Record.

99.6°F. (4 days after admission.)

Erythrocyte Sedimentation Rate (Westergren.)

Time After Clinical Onset on 26th.February, 1957.

5 days.	14 days.	31 days.
6 mm.	4 mm	3 mm.

COMMENT:

The history and clinical findings were very suggestive of a good risk myocardial infarction and serial electro-:cardiograms showed changes diagnostic of intramural myocardial infarction. Following the patient's admission to hospital, pyrexia was noted but there was no evidence of peripheral vascular failure and the erythrocyte sedimentation rate was normal on repeated examination. Serum transaminase activity was first estimated 54 hours following the onset of chest pain and normal results were obtained then and on succeeding days. It was considered that the peak transaminase activity had probably occurred before the patient's admission and that activity had fallen to normal levels before estimations were performed. The alternative explanation is that transaminase activity had failed to rise for reasons unknown. That faulty technique was not the explanation of the findings was suggested by the finding of high serum transaminase activity in other sera on the same day.

An attack of angina pectoris at rest lasting for 20 minutes was observed 78 hours following the pain which accompanied myocardial infarction. There was no electro-:cardiographic evidence of a fresh myocardial infarction. Serum transaminase activity did not rise above normal levels and the erythrocyte sedimentation rate remained normal.

CASE NO. 9.

History of Present Illness.

A male, aged 62 years, a welfare officer, was admitted to hospital on the 6th.February, 1957, complaining of dyspnoea and angina pectoris on exertion, of six months' duration. For six months he had been breathless on moderate exertion and had noted a burning pain in the left upper praecordium and shoulder. This pain cleared in about a minute if he stopped to rest.

On the 31st. January, 1957, when climbing stairs, a similar pain occurred which lasted for ten minutes after resting and, on the morning of the 1st. February, 1957, whilst dressing, the patient suffered a burning pain in the left upper praecordium which radiated down the left arm and lasted for 24 hours despite rest in bed. The pain settled spontaneously and did not recur. He became breathless on the slightest exertion thereafter and, two or three times each day, he had short attacks of dyspnoea with a sensation of choking, lasting three minutes. His body weight had been increasing.

Past History.

The patient had right lobar pneumonia in November, 1955.

Clinical Findings on Admission.

He was an elderly, obese, anxious man whose lips were slightly cyanosed.

Cardiovascular System: Blood Pressure was 130/90 mm.Hg. The pulse was regular in rate, 100 per minute, and rhythm. The apex beat was not palpable. The left border of the heart was outwith the mid-clavicular line by percussion method. The heart sounds were distant, but pure. The second pulmonic sound was accentuated.

Respiratory System: The only abnormality detected was high-pitched rhonchi audible at all areas with fine crepitations at both lung bases. No other abnormality was discovered on full clinical examination.

Treatment and Progress.

The patient's anxiety was allayed by treatment with sodium phenobarbitone, gr. 1 t.i.d.

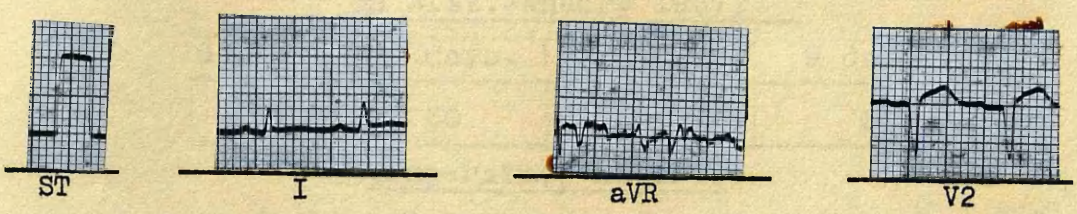
9.2.57: Dyspnoea had improved with rest but the liver was enlarged 2" below the right costal margin. Ascites and minimal sacral oedema with jugular vein congestion were present and Mersalyl therapy was started.

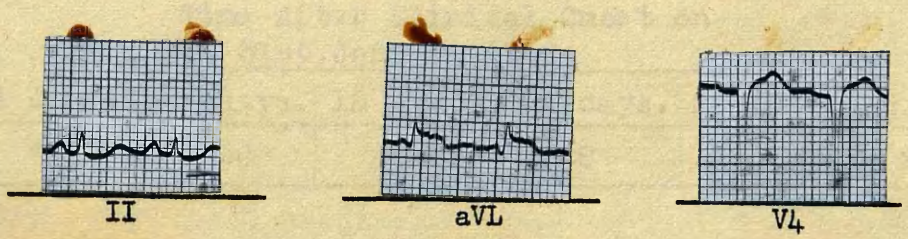
25.2.57: The signs of mild congestive cardiac failure had cleared with Mersalyl treatment and progress was uninterrupted.

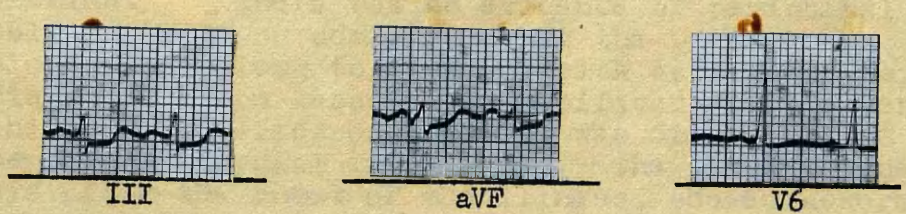
20.3.57: The patient was fit for discharge from hospital; ambulant without symptoms.

/2

ELECTROCARDIOGRAM CASE NO. 9







/symptoms. Blood Pressure = 145/ 95 mm.Hg. X-Ray film of chest, compared with previous films (November, 1957), showed enlargement of the left ventricle.

Electrocardiographic Findings.

I. 7.2.57:- (6 days after clinical onset). The electrocardiogram was diagnostic of an extensive transmural antero septal myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Clinical Onset on 31st.January 1957.

6 days.	7 days.	8 days.	9 days.
84	30	30	30

Temperature Record.

Low Grade Pyrexia was present. Temperature = 99° - 99.4°., for three days following admission.

Erythrocyte Sedimentation Rate (Westergren).

Time After Clinical Onset on 31st.January 1957.

6 days.	11 days.	18 days.	32 days.	39 days.	46 days.
40	60	39	28	22	25

COMMENT:

The history and clinical findings were very suggestive of left ventricular failure following acute myocardial infarction. There was no evidence of peripheral vascular failure on admission, but the patient was considered to belong to the poor risk category of myocardial infarction because of significant enlargement of the heart. The electrocardiogram was diagnostic of transmural myocardial infarction. The transaminase assay, 6 days after the onset of the illness, showed abnormally high transaminase activity but was judged not to have contributed to the diagnosis.

CASE NO. 10.

History of Present Illness.

A male, aged 69 years, a retired Naval Petty Officer, had been treated in hospital in April, 1952, when he was suffering from attacks of paroxysmal cardiac dyspnoea, due to severe ischaemic heart disease, the electrocardiogram showing changes characteristic of left bundle branch block. At that time, he was very obese but, after having lost three stones by strict dieting, he made a surprisingly good recovery, his only complaint being dyspnoea on moderate exertion. The B.P. was 160/80 mm.Hg. on discharge.

At 2 p.m., on the 27th February, 1957, whilst attending a funeral, he collapsed and was admitted to hospital within an hour of the onset of his illness.

Clinical Findings on Admission.

The patient was unconscious and could not be roused by painful stimuli. He was very cyanosed and pink, frothy sputum flecked his lips. He was extremely dyspnoeic.

Cardiovascular System: Blood Pressure was 210/120., pulse rate 64 beats per minute, irregular due to the presence of ventricular extrasystoles. The heart was enlarged, the apex beat being situated 6" from the mid-sternal line in the fifth interspace.

Respiratory System: Coarse râles were heard throughout the lung fields and the percussion note was diminished at the right lung base.

Treatment and Progress.

Oxygen, given by oxygen mask, resulted in a return to consciousness in 30 minutes and the severe gasping respirations responded to treatment with morphine sulphate, gr.1/4 intramuscularly. Treatment with anticoagulant drugs was started. Following resuscitation, further examination was possible.

Examination of the central nervous system revealed slurring of the speech, although the patient was rational, and there were signs of right hemiparesis, the plantar response on the right side being extensor. Ophthalmoscopic examination revealed doubtful papilloedema of the left optic disc with Grade III arteriosclerotic changes in both fundi.

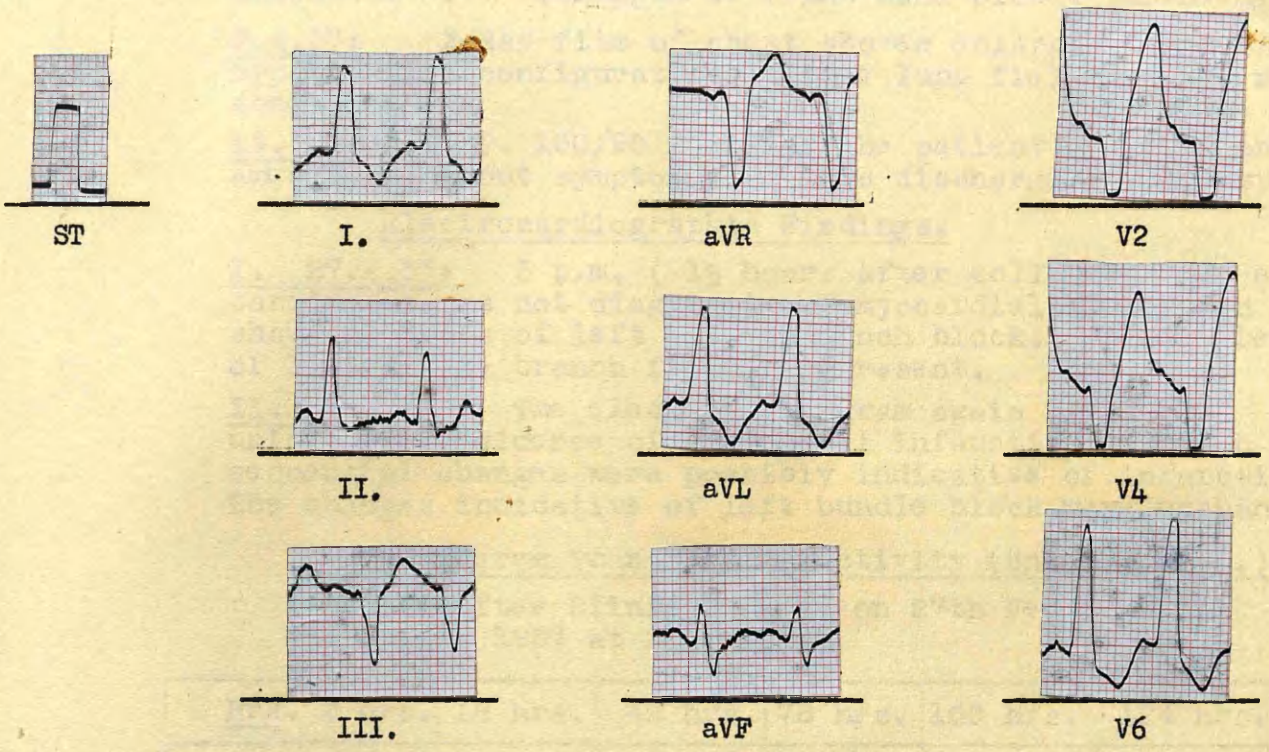
The acute dyspnoea lasted 8 hours.

28.2.57: Dyspnoea was no longer present. The right facial weakness had recovered, while the right plantar response was equivocal. Weakness of the right arm persisted. The B.P. was 115/80 mm.Hg. The patient could not remember the events of the previous day with clarity but recalled having a tight feeling in his chest before the incident.

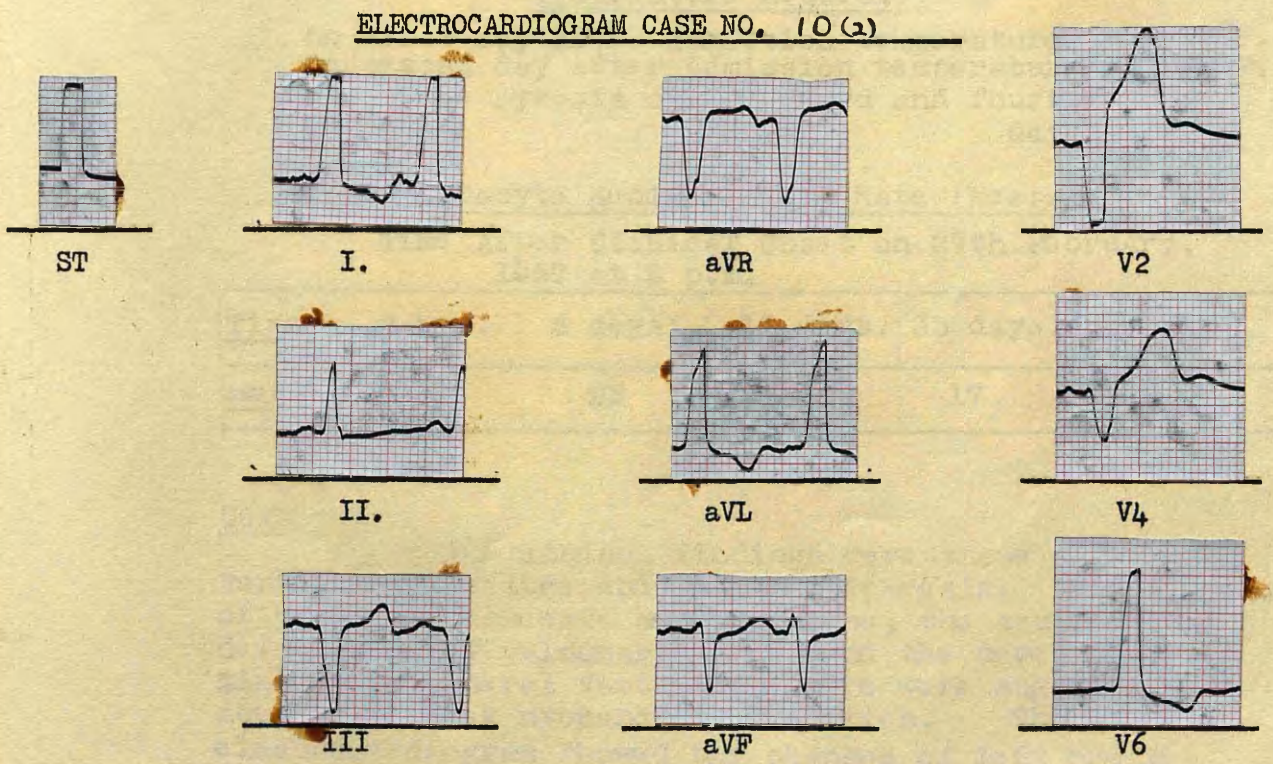
1.3.57: B.P. 135/80 mm.Hg. Numerous ventricular ectopic beats were present. Weakness of finger and wrist movements of right hand was noted.

15.3.57: /2

ELECTROCARDIOGRAM CASE NO. 10 (1)



ELECTROCARDIOGRAM CASE NO. 10 (2)



15.3.57: B.P. 140/80 mm.Hg. No further symptoms complained of. Strength of right hand slowly improving.

9.4.57: X-Ray film of chest showed enlarged heart of hypertensive configuration. The lung fields showed no abnormality.

14.4.57: B.P. 160/90 mm.Hg. The patient was well and ambulant without symptoms, and was discharged from hospital.

Electrocardiographic Findings.

I. 27.2.57: 3 p.m. (1½ hours after collapse) The electrocardiogram was not diagnostic of myocardial infarction but showed changes of left bundle branch block. Ectopic beats of left bundle branch form were present.

II. 5.3.57: The electrocardiogram again showed no uniquivocal evidence of myocardial infarction although minor sequential changes were possibly indicative of infarction. The changes indicative of left bundle block were unchanged.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Clinical Onset on 27th February 1957 at 2 p.m.

Hrs.	2 hrs.	18 hrs.	42 hrs.	76 hrs.	100 hrs.	124 hrs.
Units.	Haemolysed.	60	32	32	34	30

Temperature Record.

On first day after admission temperature = 100.6°F.
On second day after admission temperature = 100.8°F.
Low-grade pyrexia during third and fourth days = 99°F.

Erythrocyte Sedimentation Rate (Westergren.)

Time After Clinical Onset on 27th.February, 1957 at 2 p.m.

Time.	2 hrs.	5 days.	12 days.	33 days.	41 days.
mm/1st hr.	2.	23	19	17	20

COMMENT:

The clinical findings were those of left ventricular failure and right hemiparesis. The history of previous ischaemic heart disease, the acute development of pulmonary oedema and the development of minimal peripheral vascular failure were suggestive of acute poor risk myocardial infarction. The first electrocardiogram showed the changes of left bundle

/3

/ bundle branch block and there was no unequivocal evidence of myocardial infarction in the second electro-:cardiogram although there were minor sequential changes possibly indicative of myocardial infarction. The erythrocyte sedimentation rate was raised five days after the onset of the illness and pyrexia was noted.

Serum transaminase activity reached high levels 18 hours after the onset of the illness and this was the only abnormal estimation recorded on repeated examination. The rise in transaminase activity was transient. The presence of cerebral artery thrombosis, however, makes interpretation of the serum transaminase findings difficult. In this study, cerebral infarction has not been found to be associated with increased serum transaminase activity, but such an increase in activity has been reported by other workers so that, in this case, it is uncertain whether the rise in activity was due to acute myocardial infarction or acute cerebral infarction, or the combination of these conditions.

CASE NO. 11.

History of Present Illness.

A female, aged 69 years, a housewife, had been treated in hospital in April, 1956, for a myocardial infarction of considerable severity, which had been preceded by anginal pain on effort of eight months' duration. There was a history also of a mild myocardial infarction in July, 1954. During her stay in hospital in 1956 bouts of paroxysmal auricular fibrillation were observed. The heart was enlarged, an X-ray film of the chest shewing an enlarged heart of hypertensive configuration. The blood pressure was 135/70 mm.Hg.

After discharge from hospital, the patient remained well until August, 1956, when she began to suffer severe sharp pain in the left praecordium which spread into the throat and down the left arm to the elbow. These pains were induced by exertion, relieved by rest and prevented by the judicious use of trinitrin.

In January, 1957, the patient began to have the same pain on slight exertion. On the 10th February, 1957, she had an attack of palpitation lasting several hours, unaccompanied by pain. On the 11th.February, 1957, anginal pain came on at rest and lasted for one and a half hours. The patient went to bed. At 1.30 a.m., on the 15th February, 1957, she had an attack of angina pectoris at rest, which lasted until 8 a.m., on the same day. At 10.30 p.m., on the 17th February, 1957, the pain recurred and had been present until her admissionto hospital at noon on the 18th February, 1957.

Clinical Findings on Admission.

The patient was an elderly, obese woman, whose lips were cyanosed. Mild shock was also present.

Cardiovascular System: Blood pressure 160/100 mm.Hg. The pulse was regular in rate (112/min.) but occasional ectopic beats, probably auricular, were present. The apex beat was not defined but the heart was enlarged to percussion.

No abnormality was detected on full clinical examination of other systems.

Treatment and Progress.

19.2.57: Anticoagulant therapy was started, the chest pain having been controlled by repeated intramuscular doses of Pethidine, 100 mgm. The patient's general condition was good. The state of shock lasted for four hours after admission.

20.2.57: Blood pressure 105/55 mm.Hg. There was jugular congestion and painful hepatomegaly. Medium crepitations at both lung bases were heard on auscultation. The pain in the right hypochondrium was considered to be associated with congestion of the liver. There was no complaint of chest pain.

21.2.57: The patient complained of central chest pain, referred to the area between the shoulder blades. Dyspnoea at rest was noted. B.P. 110/80 mm.Hg. Pericardial friction was heard in the fourth left intercostal space, 2" from the mid-sternal line. The heart and pulse were irregularly irregular in beat (rate 120/min.) /2

On examination of the abdomen, liver tenderness was less marked. No abnormality was present on examination of the chest.

22.2.57: Marked tachycardia and pulsus alternans were present but the pulse was regular.

23.2.57: The patient complained of intermittent epigastric and substernal discomfort. The pulse was grossly irregular. Auricular fibrillation, probably paroxysmal in type, was diagnosed.

25.2.57: The pulse was regular in rate and rhythm. Bouts of tachycardia, during which the pulse and heart beats were totally irregular, were observed frequently. The episodes of irregularity were short, lasting from 10 minutes to 15 minutes. Paroxysmal auricular fibrillation was considered to be the most likely diagnosis but electrocardiographic confirmation was not obtained.

27.2.57: Extreme tachycardia was noted. The pulse was regular, the rate being 160 beats per minute. A test dose of Quindine sulphate, gr.3., was given. Following electrocardiograms:- The tachycardia subsided, the apex rate being 98 beats/minute.

1.3.57: Pulsus alternans was again noted. Slight sacral oedema was present.

4.3.57: Increasing dyspnoea, sacral oedema and jugular venous congestion were noted and congestive cardiac failure was diagnosed. Mersalyl therapy was started.

6.3.57: The patient's general condition was much improved. There had been no recurrence of pain.

7.3.57: A bout of paroxysmal auricular fibrillation associated with severe angina pectoris lasting for one and a half hours was observed. There was clinical evidence of bilateral pleural effusions. Congestive cardiac failure was still present and treatment with digitalis leaf was started. Heart rate during paroxysmal fibrillation was 120-130 beats/min.

9.3.57: The patient's condition steadily deteriorated and she died at 7.30 a.m.

Electrocardiographic Findings.

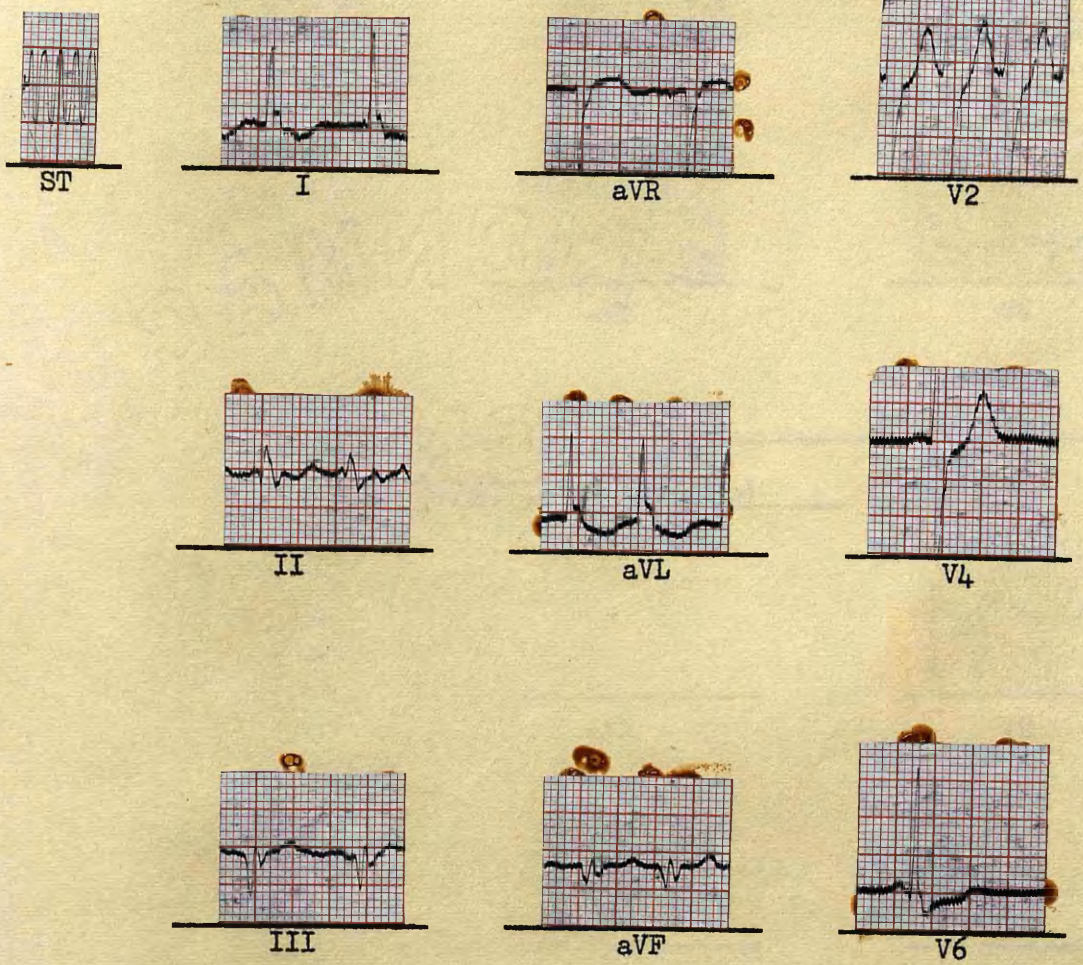
I. 23.4.56: Electrocardiographic changes were consistent with the diagnosis of old posterior myocardial infarction with left ventricular strain. Transient auricular fibrillation or supraventricular tachycardia was noted in lead V.2.

II. 18.2.57: (20 hours after the onset of pain on 17.2.57): The electrocardiogram showed changes diagnostic of a recent fairly extensive antero septal myocardial infarction and of an old posterior myocardial infarction. Ventricular ectopic beats were noted. The recent infarction is transmural.

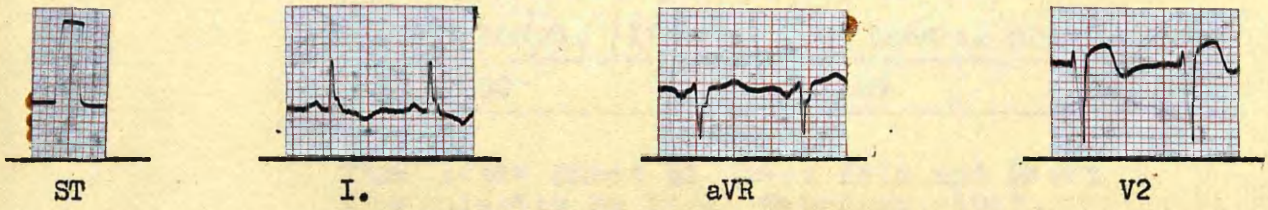
III. 27.2.57: The electrocardiogram showed changes suggestive of recent posterior myocardial infarction. Supraventricular tachycardia rate 160/min. was present. Full chest leads were not taken.

/3

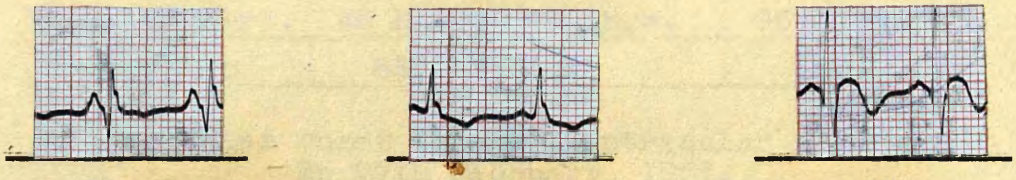
ELECTROCARDIOGRAM CASE NO. 11 (1)



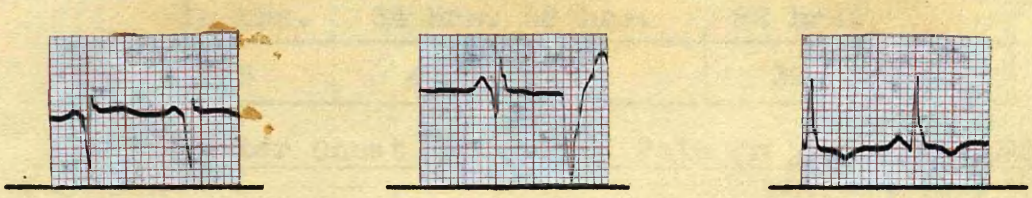
ELECTROCARDIOGRAM CASE NO. II (2)



ST I. aVR V2

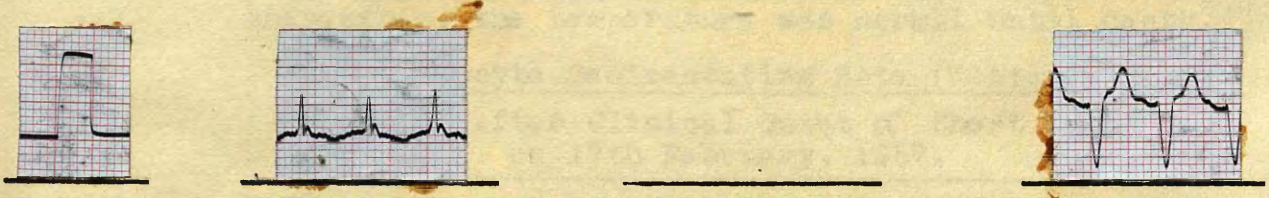


II. aVL V4

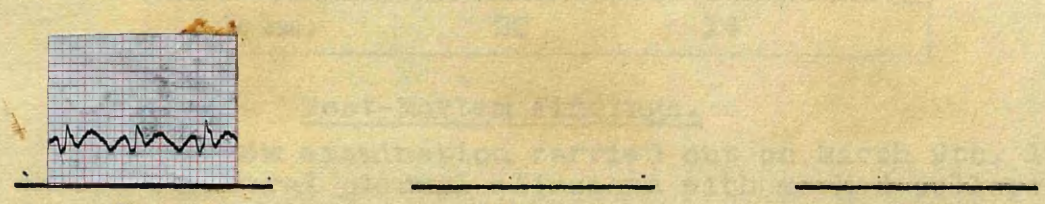


III. aVF V6

ELECTROCARDIOGRAM CASE NO. II (3)



ST I. aVR V2



II. aVL V4

III aVF V6

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Clinical Onset of Chest Pain on 17th February, 1957 (10.30 p.m.)

14 hours.	35 hours.	59 hours.	83 hours.
62	158	87	36

Time After Onset of Chest Pain and Heart Irregularity on 21st. February, 1957.

0.	24 hrs.	48 hrs.	72 hrs.	96 hrs.
36	60	86	40	34

Time After Onset of Supraventricular Tachycardia on 27th February, 1957.

10 hrs.	34 hrs.	58 hrs.	82 hrs.
46	48	48	32

Time After Onset of Anginal Pain on 7th March 1957.

7 hours.	31 hours.
18	20

Temperature Record.

99.2°F was recorded 24 hours after admission; thereafter, the temperature was normal until death.

Erythrocyte Sedimentation Rate (Westergren).

Time After Clinical Onset of Chest Pain on 17th February, 1957.

14 hrs.	8 days.	14 days.
9 mm.	20	14

Post-Mortem Findings.

Post-mortem examination carried out on March 9th. 1957, showed bilateral pleural effusions with marked collapse of both lungs. The lungs on section contained relatively little blood or air.

The heart was considerably enlarged due to dilatation of the anterior wall of the left ventricle. The coronary arteries all showed severe atheromatous degeneration. The anterior vessel was occluded by fairly recent clot and atheroma, at a point 2 inches from its commencement; the circumflex vessel was not occluded but was very narrow at several places. The posterior vessel showed old occlusion /

/occlusion at a point 3 inches from its commencement. The left ventricle showed two old small areas of healed infarction, one on the posterior wall and the other on the left lateral wall. There was recent complete infarction of the remainder of the posterior wall, the interventricular septal and a small part of the anterior wall. The infarction was of several days' duration, and the wall at this point showed early dilatation.

The alimentary tract showed no abnormality apart from three small gastric polyps.

The liver showed an extreme degree of congestion with early cardiac cirrhosis.

The spleen and other organs of the body showed only congestive changes.

Death was considered to be due to coronary artery thrombosis and left ventricular failure.

Results of Histological Examination.

Heart: Sections showed changes diagnostic of recent acute myocardial infarction, with widespread necrosis of heart muscle. Areas of ischaemic fibrosis of the muscle were also present.

Liver: Sections showed moderate chronic venous congestion.

COMMENT:

The patient was considered to have sustained myo-:cardial infarctions on 17.2.57 (11a) and on 21.2.57 (11b).

In the first attack (11a)., the history and clinical findings were typical of poor risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction . A minimal degree of peripheral vascular failure and pyrexia were present. Serum transaminase levels were significantly elevated while the E.S.R. was within normal limits and before the electro-cardiograms were performed. Transaminase assay was judged to have contributed early,valuable evidence of the occurrence of myocardial infarction.

In the second attack (11b)., the history and clinical findings were typical of poor risk acute myo-cardial infarction, the development of pericardial friction and paroxysmal auricular fibrillation being considered very significant. The electrocardiogram showed changes very suggestive but not diagnostic of recent posterior myocardial infarction. It is noted that these changes were observed 5 days following the onset of the myocardial infarction and, in addition, that full chest leads were not taken. Peripheral vascular failure was not noted during this attack. Serum transaminase levels of activity rose to high levels 24 hours after the onset and were

/ were considered to have been valuable in confirming the diagnosis. The bouts of paroxysmal auricular fibrillation were considered to be too evanescent to have affected the serum transaminase levels.

On 27.2.57., a bout of supraventricular tachycardia was followed by a borderline rise in serum transaminase levels. There was no clinical evidence of recurrence of myocardial infarction.

An attack of severe angina pectoris in association with paroxysmal auricular fibrillation on 7.3.57 did not result in significant rise in serum transaminase activity. There was no clinical evidence of recurrence of myocardial infarction, but no electrocardiograms were performed.

Post mortem examination confirmed the presence of myocardial infarctions.

CASE NO. 12.

History of Present Illness.

A male, aged 51 years, a watchmaker, was admitted to hospital on the 21st. January, 1957, having been seized with severe retrosternal pain,whilst working,at 10 a.m. The pain, which was crushing in character, was not referred and was still present on admission to hospital at 11 a.m., despite the administration of morphine sulphate, gr.1/4., intramuscularly, by the patient's family doctor.

Past History.

The patient had had symptoms suggestive of peptic ulceration for ten years and a duodenal ulcer was diagnosed after radiological examination in April, 1956. In January, 1956, the patient had an attack of similar severe praecordial pain, which was related to exertion, and he was confined to bed for six weeks and did not return to work for three months. Following this rest he still complained of anginal pain and breathlessness on undue exertion. At this time, hypertension had been noted.

Clinical Findings on Admission.

The patient was pale and frightened. His skin was cold and clammy and there was overfilling of the neck veins.

Cardiovascular System: Blood pressure was 200/140 mm.Hg. The pulse rate was regular in rate (110/min) and rhythm. The heart was enlarged, the apex beat being situated 5" from the mid sternal line in the fifth interspace. The heart sounds were well heard. There was a loud blowing systolic murmur, best heard at the apex of the heart. The second aortic sound was accentuated.

Respiratory System: No adventitiae were heard on auscultation over the anterior chest or axillary regions. No other abnormality was discovered on full clinical examination.

Treatment and Progress.

The retrosternal pain responded to treatment with Pethidine 100 mgm. given intravenously. Anticoagulant therapy was not started because of recent symptoms of dyspepsia.

22.1.57: B.P. 140/110 mm.Hg. Tachycardia was present, (120/min.) Jugular vein congestion was present and the patient remained pale and apprehensive.

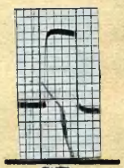
On examination of the abdomen, the lower abdomen was tense and distended, although there was no muscular rigidity or tenderness on palpation. This distension was ascribed to meteorism.

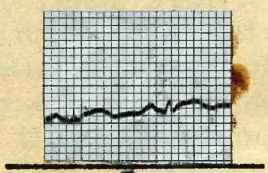
23.1.57: B.P. 125/90 mm.Hg. Tachycardia (110/min.) The patient was no longer shocked.

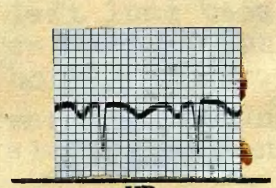
25.1.57: B.P. 110/60/zero (sounds did not disappear). General condition much improved.

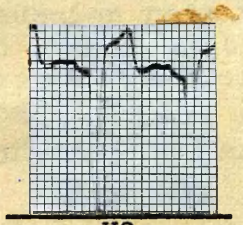
/2

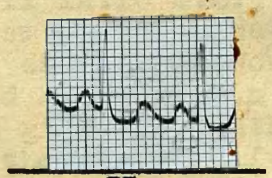
ELECTROCARDIOGRAM CASE NO. 12

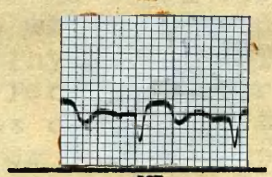


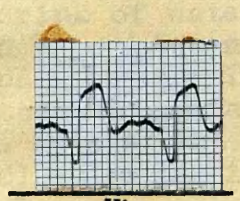


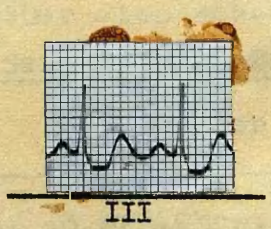


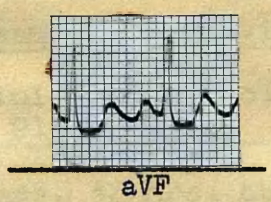


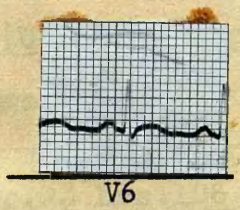












26.1.57: Blood pressure 125/90 mm.Hg.

28.1.57: Blood pressure 115/90 mm.Hg. There was no evidence of congestive cardiac failure.

29.1.57: The patient was feeling well. There was no recurrence of pain although he was still dyspnoeic on slight exertion.

Blood pressure was 120/90 mm.Hg. The apex beat was situated 4" from the mid-sternal line in the fifth interspace. Loud, creaking, systolic sound was heard over the mitral and pulmonic areas, conducted over the left lung anteriorly. The character of the sound suggested the diagnosis of pleuro-pericardial friction but there was no diastolic component to the sound.

On examination of the chest, the percussion note was diminished over the left lung base and the air entry was diminished in this area. Numerous crepitations were heard on auscultation over both lung bases posteriorly.

A ward film confirmed the presence of heart enlargement and there was lung field congestion.

31.1.57: The friction sound was no longer heard.

1.2.57: B.P.110/80 mm.Hg. The patient had no complaints except dyspnoea on slight exertion.

3.2.57: The patient's condition had been satisfactory until 12.15 a.m., when he asked for a drink of water. The nurse noticed that he was collapsed and breathing noisily and called the House Physician. The patient was found to be dead at 12.20 a.m. Permission for autopsy examination was not given. Death was considered to be due either to rupture of the heart or further massive myocardial infarction.

Electrocardiographic Findings.

I. 21.1.57: (7 hours after onset of chest pain). The electrocardiogram showed changes diagnostic of an extensive transmural acute antero septal myocardial infarction. No further electrocardiograms were taken.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Clinical Onset of Chest Pain on 21.1.57.

Hrs.	3 hrs.	9hrs.	21hrs.	45 hrs.	69 hrs.	93 hrs.	126 hrs.
Units.	10	86	186	164	82	24	32

Time After Friction Sound noted (29.1.57).

24 hrs.	48 hrs.	72 hrs.
16	20	20

Temperature Record.

A temperature of 99°F. was recorded 16 hours after admission and an irregular low-grade pyrexia was present for seven days after admission, the temperature ranging from 97.2°F., to 100.4°F. The temperature was elevated to 99.4°F. at 6 p.m., on the 31st. January, 1957.

Erythrocyte Sedimentation Rate (Westergren.)

9 hours after onset of pain (21.1.57) E.S.R = 20mm./1st.hr.

COMMENT:

The history and clinical findings were typical of a poor risk acute myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction. Pyrexia and a minimal - moderate degree of peripheral vascular failure were present. Serum transaminase activity reached high diagnostic levels but the assay was not considered to have contributed to the diagnosis, the electrocardiogram having provided the earliest confirmation of the diagnosis.

CASE NO. 13.

History of Present Illness.

A male, aged 52 years, a watchmaker, was admitted to hospital on the 10th December, 1956, complaining of severe burning retrosternal pain, which had begun on the 7th December, 1956 at 3 a.m., and which radiated to the left shoulder blade and into both arms. Since then, he had been breathless. The pain had been more or less constant although it varied in severity. It had eased since the 9th December, 1956.

Previously he had not experienced breathlessness, even on climbing stairs, and had not noticed any ankle swelling.

Past History.

For several years he had suffered from indigestion after meals, with epigastric pain going through to the back on occasions. This pain was always relieved by alkalis.

He had a haematemesis one year ago but barium meal examination showed no abnormality. Although he had vomited several times since the onset of pain on the 7th December, 1956, there had been no blood in the vomitus.

Clinical Findings on Admission.

The patient was an ill-looking, apprehensive man who was dyspnoeic at rest. There was neck vein congestion and peripheral coldness was noted. There was no cyanosis or oedema. Blood pressure was 80/65 mm.Hg.

Cardiovascular system: Pulse rate was 130 beats per minute, regular in rate and rhythm, thready in character. The apex beat was 1½" outwith the mid-clavicular line. The heart sounds were very distant. A pericardial friction rub was heard over the mid-sternal region.

Respiratory System: Coarse crepitations were heard on auscultation at both bases, being more marked on the right side.

Alimentary system: The liver was one finger's breadth palpable below the right costal margin and was tender on palpation. No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

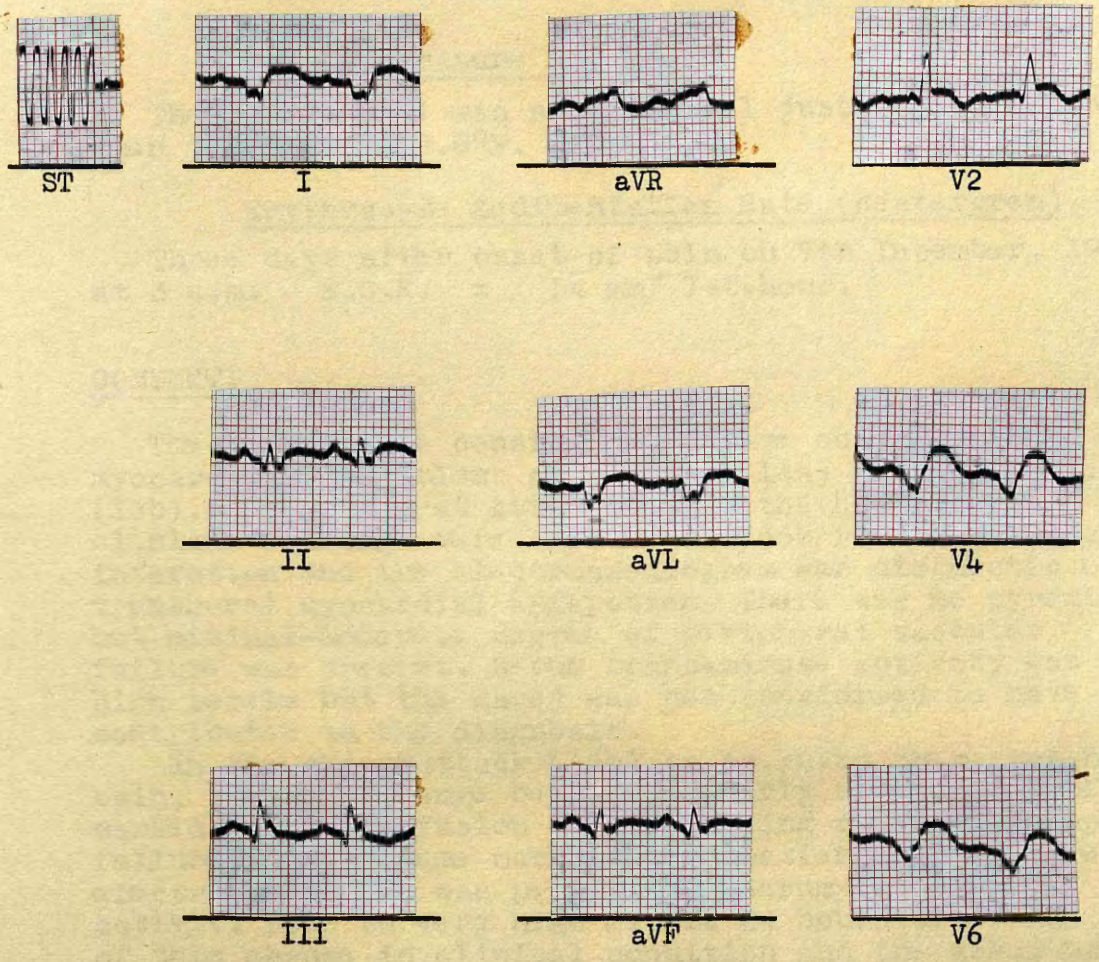
Morphine sulphate, gr.1/4., was given to control the pain. Anticoagulants were not used because of previous history of peptic ulcer. Penicillin (600,000 units Distaquaine daily) and Digitalis leaf, gr.ii. t.i.d., were administered.

12.12.56: B.P. 86/65 mm.Hg. Hypotension and congestive cardiad failure were present.

13.12.56: B.P. 75/55 mm.Hg. The patient had no complaints but he was obviously very ill and marked mental confusion was noted.

14.12.56: B.P. 85/30 mm.Hg. There was no recurrence of pain but the patient's condition deteriorated and he died suddenly. Unfortunately permission for post mortem exam. was refused. /2

ELECTROCARDIOGRAM CASE NO. 13



Electrocardiographic Findings.

I. 10.12.56: (Three days after onset of retrosternal pain). The electrocardiogram showed changes diagnostic of an acute and very extensive transmural myocardial infarction. (antero septo lateral,& posterior).

Serial Serum Transaminase Activity(Units/ml/min.)

Time After Clinical Onset at 3 a.m. on 7th December, 1956.

4 days.	5 days.	6 days.
80	60	620

Temperature Record.

The temperature was normal until just before death, when it rose to 99.8°F.

Erythrocyte Sedimentation Rate (Westergren).

Three days after onset of pain on 7th December, 1956 at 3 a.m., E.S.R. = 54 mm/ 1st.hour.

COMMENT:

The patient was considered to have sustained myocardial infarctions on 7.12.56 (13a) and on 13.12.56 (13b). In the first attack, (13a) the history and clinical findings were typical of poor risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction. There was no pyrexia but minimal-moderate degree of peripheral vascular failure was present. Serum transaminase activity was at high levels but the assay was not considered to have contributed to the diagnosis.

In the second attack (13b) on 13.12.56 there was no pain, the only change being the fairly rapid onset of marked mental confusion and increasing peripheral vascular failure which became marked. The patient died before an electrocardiogram was performed. Serum transaminase activity rose to very high levels 24 hours after the onset of this change in clinical condition and the assay was considered to have provided valuable evidence in support of the clinical diagnosis of poor risk myocardial infarction. In the absence of post mortem confirmation of the diagnosis the possibility of the rise in transaminase activity being due to centrilobular necrosis of liver cannot be finally excluded.

CASE NO. 14.

History of Present Illness.

A male, aged 65 years, a starch worker, was admitted to hospital on the 2nd. December, 1956, complaining of retrosternal pain. Whilst hurrying homewards on the 29th November, 1956, at 11 p.m., he was seized with severe epigastric pain which radiated into the substernal and left praecordial region of the chest and down the inner aspect of the Left arm, causing the fingers of the patient's left hand to tingle. The pain was very severe and constricting in character, and stopped him in his tracks. It remained fairly severe for three hours and then subsided, to be succeeded by a sensation of retrosternal tightness which was made worse by exertion. He continued to work, however, until the 1st. December, 1956, when a similar pain started at 5 p.m., and remained severe until he called his doctor on the 2nd. December 1956, who, after giving the patient Omnopon gr.2/3 intramuscularly, sent him to hospital. The pain lasted until 2.30 p.m., on the 2nd December, 1956.

Past History.

The patient had been unduly breathless on exertion for several years and he had also complained of a sensation of epigastric fullness, relieved only occasionally by alkali powders for two years. Mild symptoms of intermittent claudication affecting the right leg had been present since 1954. At this time, the blood pressure was 210/100 mm.Hg. The patient underwent an operation for prostatectomy in January, 1956, and he had no symptoms referable to urinary tract thereafter.

Clinical Findings on Admission.

The patient was overweight and apprehensive. Slight cyanosis of the lips and finger tips was noted.

Cardiovascular system: Blood pressure was 130/90 mm.Hg. The pulse was irregular due to the presence of ventricular ectopic beats, rate 92 beats per minute. The apex beat was situated 4½" from the mid-sternal line in the fifth interspace. The heart sounds were well heard. A systolic murmur was heard just medial to the apex beat.

Respiratory System: A few fine crepitations were heard on auscultation over both lung bases.
No other abnormality was found on full clinical examination of other systems.

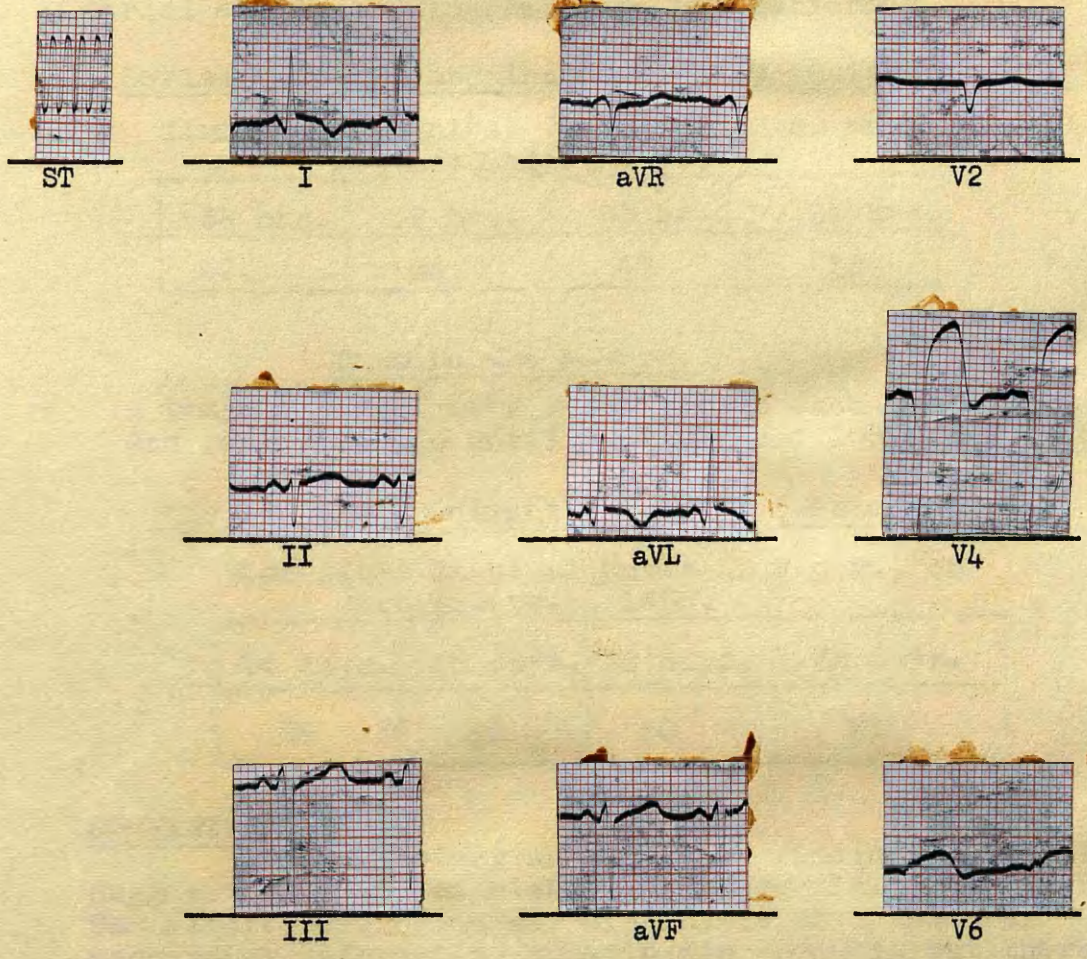
Treatment and Progress.

Anticoagulant therapy was started on admission and was continued for 28 days.

3.12.56: Blood pressure was 160/80 mm.Hg. The patient had an attack of praecordial pain associated with a sense of constriction, lasting for 15 minutes; this was relieved by Omnopon, gr.1/3 intramuscularly.

8.12.56: The patient developed diarrhoea which responded

ELECTROCARDIOGRAM CASE NO. 14



/responded within 5 days to treatment with phthalylsulphathiazole, despite failure to isolate organisms from the faeces.

A ward film of the chest showed enlargement of the heart but the lung fields were clear.

20.1.57: The patient made an uneventful recovery. He was ambulant without symptoms before discharge from hospital. Blood pressure was 150/80 mm.Hg.

Electrocardiographic Findings.

I. 3.12.56:- 6.30 a.m. (38 hours after onset of pain at 5 p.m., on the 1st.December, 1956.) The electrocardiogram showed changes diagnostic of an acute extensive, transmural, antero septo lateral myocardial infarction.

Serial electrocardiograms were not pefformed.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Clinical Onset at 5 p.m. on 1st. December, 1956.

38 hrs.	59 hrs.	83 hrs.	131 hrs.
62.	36	17	12

Temperature Record.

A temperature of 99°F was recorded each day from 2nd December 1956 until 5th December 1956.

Erythrocyte Sedimentation Rate (Westergren).

Time After Clinical Onset at 5 p.m., on 1st.December, 1956.

16 days.	21 days.	28 days.	35 days.
35	31	30	25

COMMENT:

The history and clinical findings were very suggestive of a good risk acute myocardial infarction. The electrocardiogram was diagnostic of transmural myocardial infarction. Pyrexia was present, but there was no evidence of peripheral vascular failure. Serum transaminase activity was significantly elevated but the assay was not considered to have contributed to the diagnosis.

CASE NO. 15.

History of Present Illness.

A male, aged 57 years, a storeman, was admitted to hospital on the 30th March, 1957, complaining of retrosternal pain. For one month he had had mild attacks of retrosternal pain and dyspnoea on exertion which subsided spontaneously when he rested. On the 26th March, 1957, he developed severe retrosternal pain, gripping in character, whilst at rest in bed. This pain spread into the upper arms and into the back of the neck. It eased gradually over a period of hours but the patient remained conscious of substernal unease until, on the day of admission, he suffered another attack of severe pain of similar nature at 10 a.m.

Past History.

In 1952, the patient underwent the combined operation of gastro-enterostomy and vagotomy for symptoms of duodenal ulcer. He had been symptom-free since this operation.

Clinical Findings on Admission.

The patient complained of moderately severe retrosternal pain but he was only mildly shocked.

Cardiovascular System: B.P. 100/70 mm.Hg. The pulse was regular in rate (90/min) and rhythm. The apex beat was not palpable. The heart sounds were faintly heard,but pure.

Respiratory System: A few rhonchi were heard on auscultation over both lung bases.

No other significant abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Retrosternal pain was quickly controlled by injection intramuscularly of Omnopon, gr.1/3 and anticoagulant therapy was started on day of admission.

2.4.57: B.P. 95/70 mm.Hg. There had been no recurrence of symptoms and the patient felt well.

9.4.57: B.P. 100/70 mm.Hg. His general condition was satisfactory.

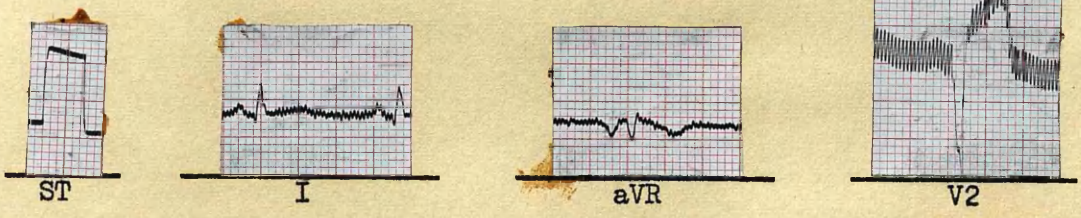
12.4.57: Whilst apparently making satisfactory progress, the patient collapsed and died suddenly. Permission for post-mortem examination was refused.

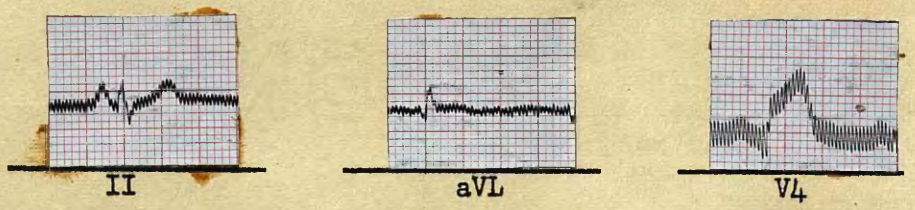
Electrocardiographic Findings.

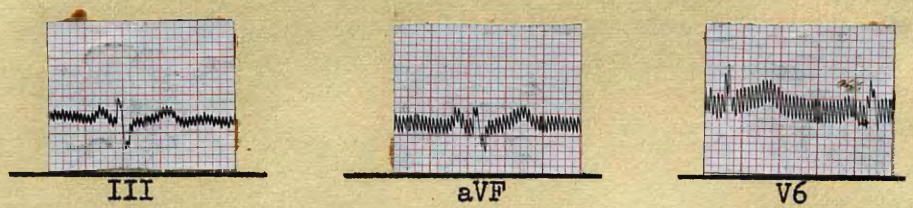
I. 30.3.57: 5 p.m. (7 hours after clinical onset.) The electrocardiogram was technically unsatisfactory because of electrical interference, but showed changes diagnostic of an acute, extensive, transmural, antero septo myocardial infarction. Serial electrocardiograms were not performed.

/2

ELECTROCARDIOGRAM CASE NO. 15







Serial Serum Transaminase Activity (Units/ml/min).

Time After Onset of Pain at 10 a.m. on the 30th March, 1957.

7 hrs.	24 hrs.	47 hrs.	74 hrs.	85 hrs.	109 hrs.
48	60	65	56	29	25.

Temperature Record.

20 hours after admission, a temperature of 99°F was recorded.

Erythrocyte Sedimentation Rate (Westergren).

Time After Clinical Onset at 10 a.m. on 30th March, 1957.

24 hrs.	6 days.	14 days.
52	20	14

COMMENT: The history and clinical findings were very suggestive of a good risk acute myocardial infarction, while the electrocardiogram was diagnostic of transmural myocardial infarction. Pyrexia and a minimal degree of peripheral vascular failure were present. Serum transaminase activity reached high levels but the assays were not considered to have contributed to the diagnosis. Despite the relatively low levels of serum transaminase activity recorded, the patient died suddenly presumably from another attack of myocardial infarction. It should be noted also that, whereas the electro-cardiogram was diagnostic of myocardial infarction, 7 hours after the onset of the illness, serum transaminase activity was at borderline levels.

CASE NO.16.

History of Present Illness.

A male, aged 54 years, a parks superintendent, was admitted to hospital on the 16th March, 1957, complaining of recurring attacks of retrosternal pain of fourteen days' duration.

On the 2nd March, 1957, he had complained of retrosternal pain on exertion which had lasted for fifteen minutes, despite resting.

On the 7th March, 1957, he had an attack of gripping retrosternal pain at rest which lasted for five minutes.

On the 12th March, 1957, and on 15th March, 1957, at 5 p.m., he suffered minor attacks of anginal pain at rest.

At 1 a.m., on the 15th March,1957, he was awakened from sleep by severe gripping retrosternal pain, which lasted for one hour and was accompanied by an attack of paroxysmal cardiac dyspnoea. At 8 a.m., on the morning of admission, the pain returned whilst at rest and remained fairly severe for three hours. There had been no radiation of the pain.

Past History.

In December, 1956, the patient was admitted to hospital for treatment of epistaxis arising from Little's area. No cardiovascular abnormality was present at this time. The Blood pressure was 120/65 mm.Hg.

Clinical Findings on Admission.

The patient was a well built man of ruddy complexion. There were no signs of shock or of congestive cardiac failure.

Cardiovascular System: Blood pressure was 125/85 mm.Hg. The pulse was regular in rate (68/min) and rhythm. The apex beat was situated in the mid-clavicular line in the fifth interspace. The heart sounds were well heard and were pure. The second aortic sound was accentuated.
No other abnormality was found on examination of other systems.

Treatment and Progress.

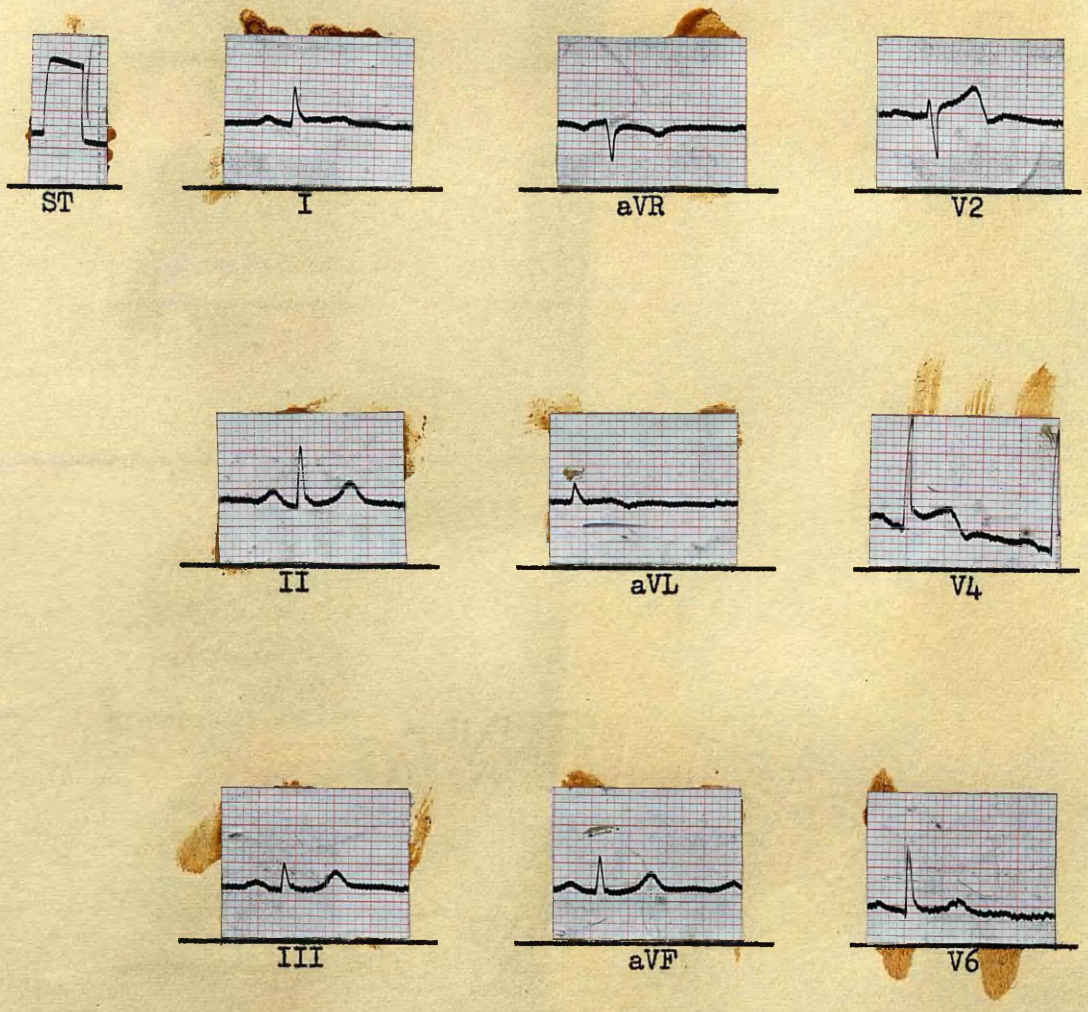
The pain, present on admission, was adequately treated by Omnopon, gr.1/3., administered intramuscularly. Treatment with anticoagulant drugs was started shortly after admission and continued for 21 days.

19.3.57: B.P. 110/75 mm.Hg. The patient complained of slight burning pain over the lateral aspect of his left upper arm, having been symptom-free since admission.

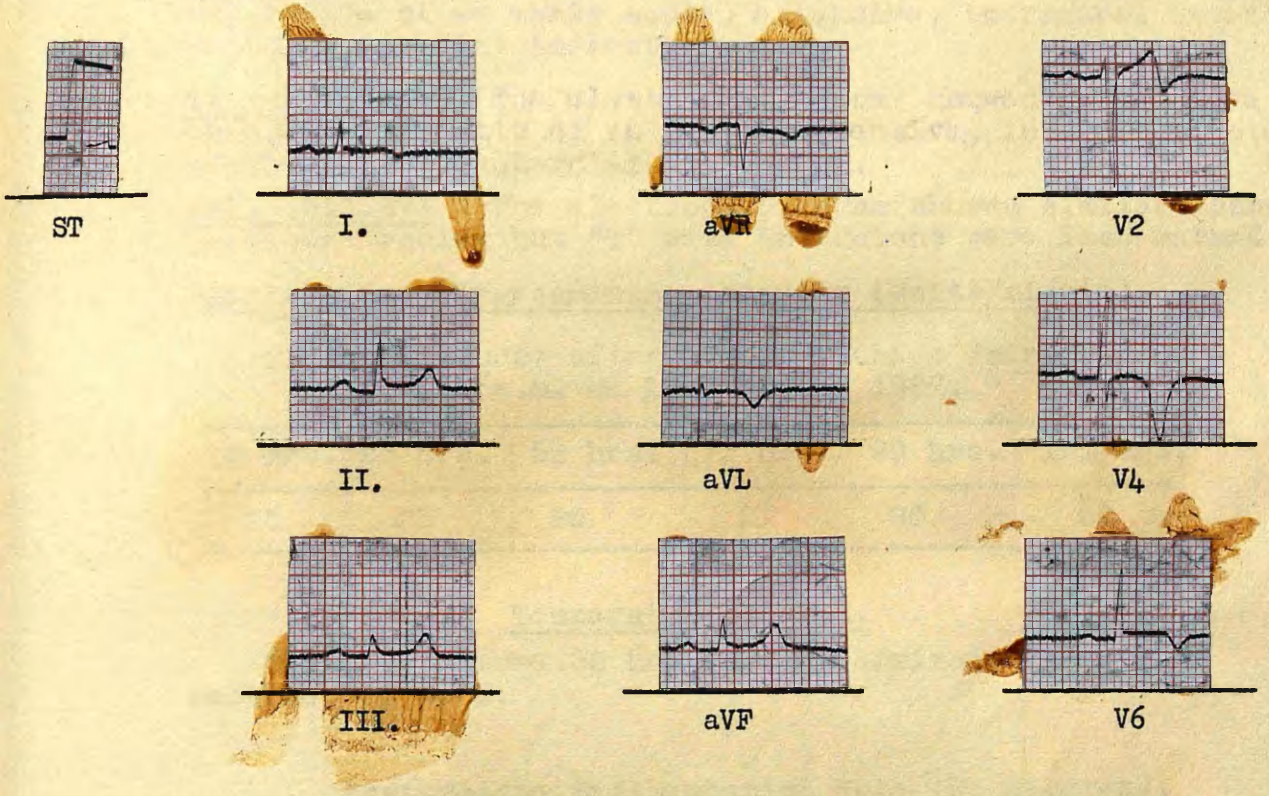
10.4.57: B.P. 115/80 mm.Hg. The patient was feeling well On examination of the cardiovascular system, the apex beat was situated 1/2" outwith the mid-clavicular line. The heart sounds were pure.

27.4.57: B.P. 125/85 mm.Hg. After uneventful progress, the patient was discharged from hospital, having been symptom-free whilst ambulant.

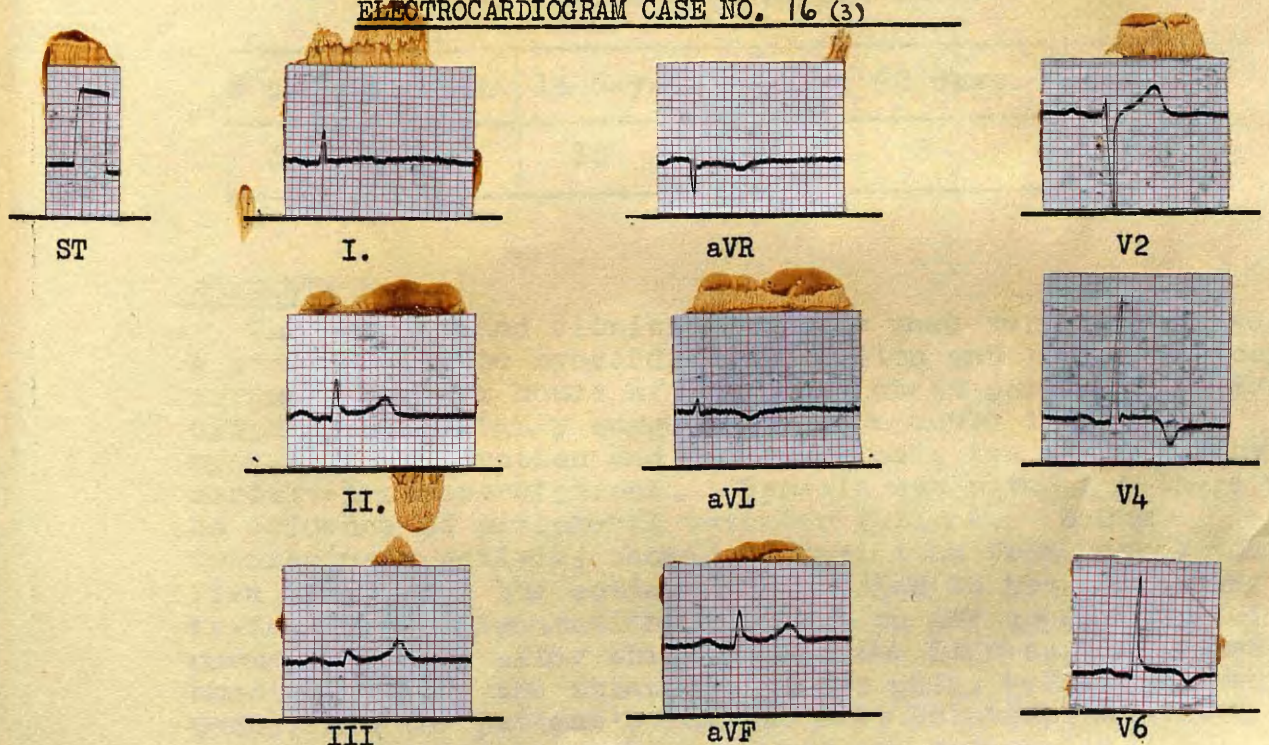
ELECTROCARDIOGRAM CASE NO. 16(1)



ELECTROCARDIOGRAM CASE NO. 16 (2)



ELECTROCARDIOGRAM CASE NO. 16 (3)



Electrocardiographic Findings.

I. 16.3.57: The electrocardiogram showed changes highly suggestive of an early acute, extensive, intramural antero septal myocardial infarction.

II. 28.3.57: The electrocardiogram showed progressive changes diagnostic of an acute, extensive, intramural antero septo lateral myocardial infarction.

III. 6.4.57: The electrocardiogram showed similar changes to previous tracing but "T" wave inversions were less marked.

Serial Serum Transaminase Activity (Units/ml/min).

Time (in hours) after onset of Chest Pain at 8 a.m. on 16th March, 1957.

6 hrs.	28 hrs.	52 hrs.	73 hrs.	99 hrs.	125 hrs.
25	23	26	21	23	20

Temperature Record.

The temperature, 30 hours after admission, was recorded as 99°F.

Erythrocyte Sedimentation Rate (Westergren).

Time After Clinical Onset of Chest Pain at 8 a.m. on 16th March, 1957.

6 hrs.	10 days.	14 days.	21 days.	28 days.	35 days.
3	10	10	10	8	8

COMMENT:

The history and clinical findings were very suggestive of a poor risk acute myocardial infarction and the electrocardiogram, taken six hours after severe chest pain accompanied by dyspnoea, was highly suggestive of an acute intramural myocardial infarction and this diagnosis was confirmed by serial electrocardiograms. Pyrexia was noted but there was no evidence of peripheral vascular failure. Serum transaminase activity showed no deviation from normal for five days after the patient's admission to hospital. The erythrocyte sedimentation rate rose to the upper limit of normal ten days after the onset of the illness. It was considered that the attacks of chest pain, before that which occasioned the patient's admission to hospital, had been angina pectoris and that the failure of

/3

/failure of transaminase activity to rise above normal was not due to late sampling of the serum, although a satisfactory explanation of the failure could not be found since the specimens of sera from the patient were repeatedly examined, with normal result. Also, the specimens of other sera examined on the same day showed abnormally high transaminase activity. The only alternative explanation is that a transient rise, which was not detected, occurred between 6 and 28 hours after the onset of the myocardial infarction.

CASE NO. 17.

History of Present Illness.

A male, aged 64 years, a labourer, was admitted to hospital at 2.45 p.m., on the 19th March, 1957, complaining of severe retrosternal pain. At 1.30 p.m., on the day of admission, he had been seized by severe retrosternal pain, constricting in character, which spread all over the front of the chest and into the neck and lower jaw. The pain was still present on admission. On the evening of the 18th March, 1957, he had suffered a minor attack of retrosternal pain whilst sitting in a chair. The pain had lasted for about ten minutes and settled on his retiring to bed.

Past History.

The patient was in hospital from the 31st. October, 1955, until the 14th December, 1955, following an attack of myocardial infarction, posterior in site, complicated by the development of mild failure of the left ventricle. Aortic incompetence of syphilitic origin, the blood Wasserman Reaction being positive, was also diagnosed and, following his recovery from the attack of myocardial infarction, he received two courses of treatment with potassium iodide orally, penicillin by intramuscular injection and bismuth by intramuscular injection. On discharge from hospital, his blood pressure was 140/75 mm.Hg. Following his discharge from hospital in December, 1955, he had been symptom-free.

Clinical Findings on Admission.

The patient was in great pain on admission and very distressed. He was dyspnoeic and slight cyanosis of the lips and finger tips was present. He was considered to be suffering from moderate, severe shock.

Cardiovascular System: B.P. 140/40 mm.Hg. The pulse was regular in rate (96 per minute) and rhythm. The apex beat was 1/2" outwith the mid-clavicular line. The heart sounds were well heard. A long, blowing diastolic murmur was present at the aortic area and was conducted down the left border of the sternum into the mitral area.

Respiratory System: Numerous rhonchi were heard on auscultation over both lung bases posteriorly and anteriorly.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

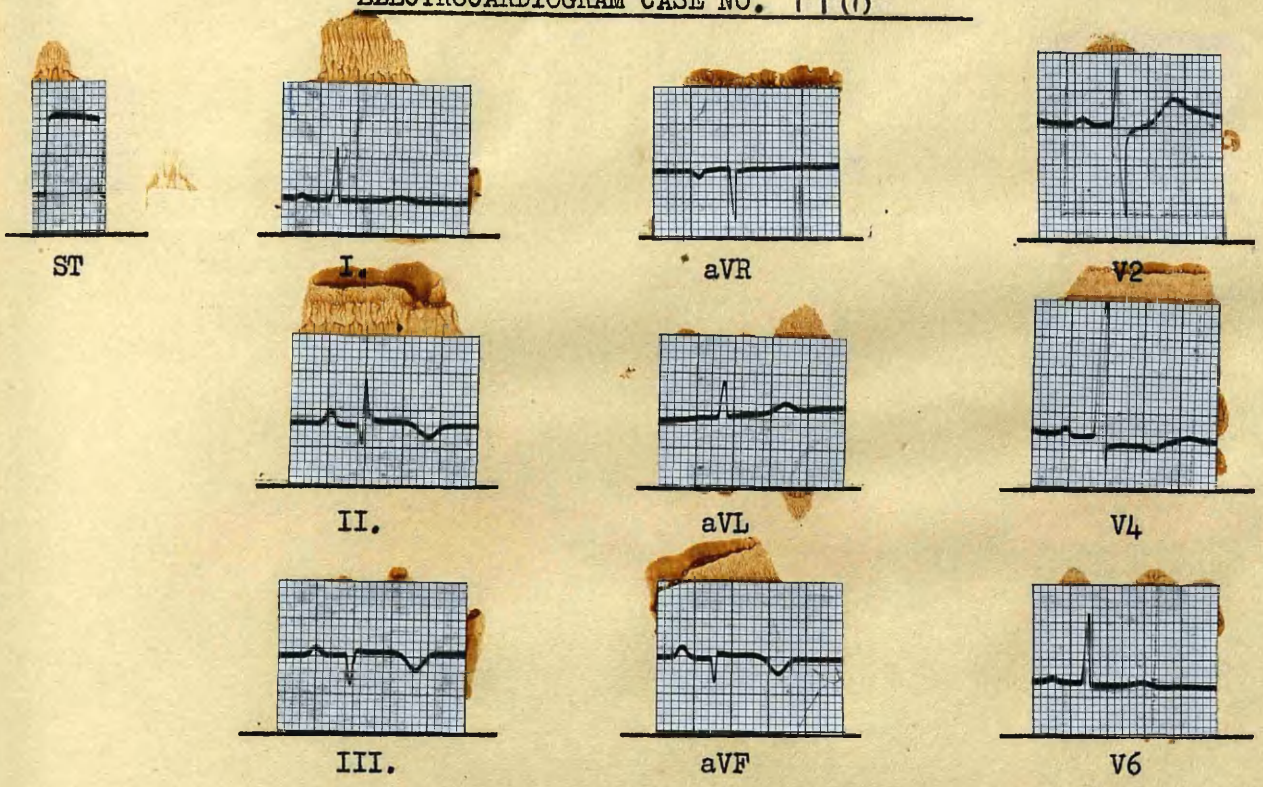
The chest pain responded to repeated injections of pethidine 100 mgm., intramuscularly and treatment with anti-coagulant drugs was started on the day of admission and continued for 28 days.

20.3.57: Blood pressure was 105/45 mm.Hg. No recurrence of pain or dyspnoea was noted.

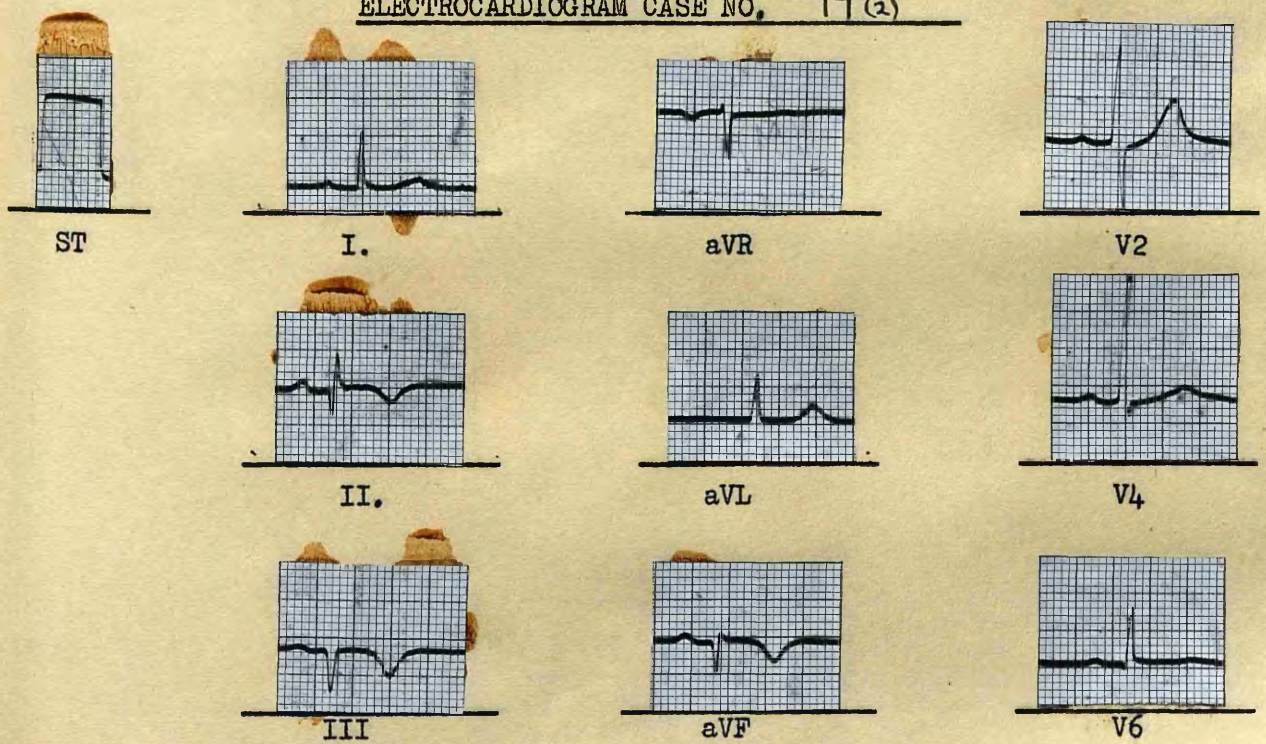
2.4.57: The patient remained symptom-free. Blood pressure 125/45 mm.Hg.

27.4.57: /2

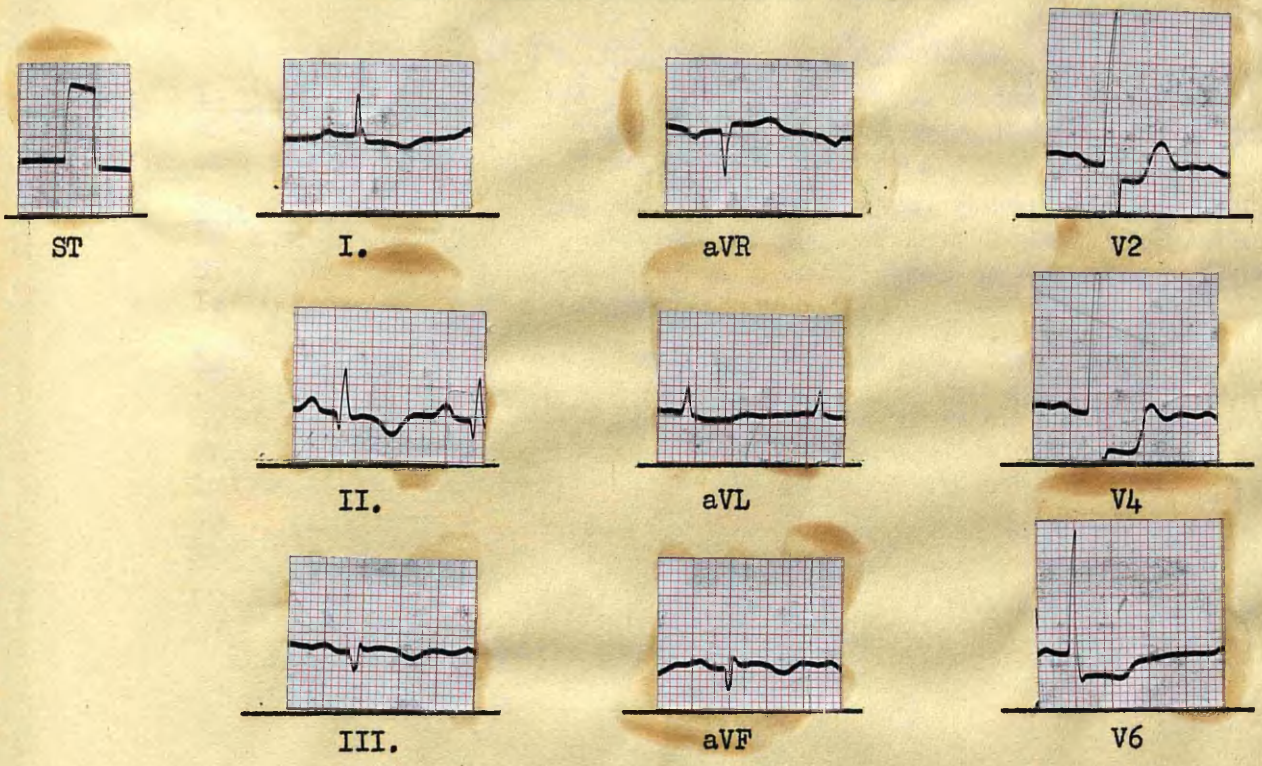
ELECTROCARDIOGRAM CASE NO. 17 (1)



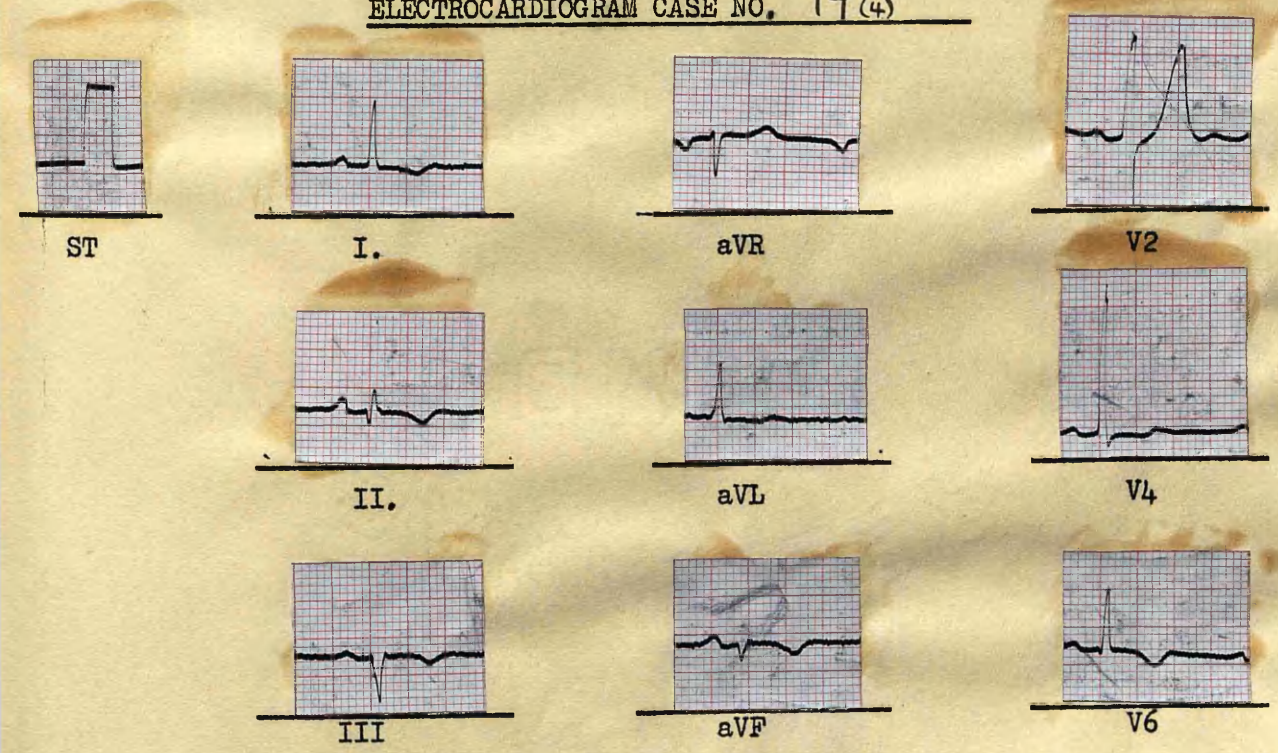
ELECTROCARDIOGRAM CASE NO. 17 (2)



ELECTROCARDIOGRAM CASE NO. 17 (3)



ELECTROCARDIOGRAM CASE NO. 17 (4)



27.4.57: The patient had been ambulant without symptoms and he was considered to be fit for discharge from hospital. Blood pressure was 140/60 mm.Hg.

Electrocardiographic Findings.

I. 31.10.55:- The electrocardiogram showed changes diagnostic of a transmural, posterior myocardial infarction and was suggestive of septal ischaemia.

II. 16.11.55:- The electrocardiogram showed changes as before of posterior, transmural myocardial infarction, but the ST-T change to normal in V.4., confirmed that antero septal ischaemia had been present.

III. 19.3.57:- (2 hours after onset of chest pain on 19th March, 1957). The electrocardiogram showed widespread ST-T depressions diagnostic of acute coronary insufficiency. Changes diagnostic of an old, transmural posterior myocardial infarction remained.

IV. 16.4.57:- The electrocardiogram showed changes consistent with the diagnosis of postero-lateral infarction, possibly an extension of old, posterior myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min).

Time (in hours) after onset of chest pain at 1.30 p.m. on 19th March, 1957.

2 hrs.	22 hrs.	46 hrs.	70 hrs.	94 hrs.	118 hrs.
33	171	93	60	25	25

Temperature Record.

The temperature was 99.8°F., 24 hours after admission.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Chest Pain at 1.30 p.m. on 19th March, 1957.

46 hrs.	9 days.	16 days.	23 days.	30 days.
11	9	15	8	14

COMMENT / 3

COMMENT:

The history and clinical findings were very suggestive of poor risk acute myocardial infarction. Serial electrocardiograms were diagnostic of transmural myocardial infarction. Pyrexia and peripheral vascular failure of a minimal - moderate degree were present. Serum transaminase activity reached high levels when the electrocardiographic pattern was not diagnostic of acute myocardial infarction, and when the erythrocyte sedimentation rate was just above normal levels and consequently was considered to have made a valuable contribution to the diagnosis. Aortic incompetence of syphilitic origin was not thought to have contributed to the rise in serum transaminase activity.

CASE NO. 18.

History of Present Illness.

A female, aged 56 years, a housewife, was admitted to hospital on the 26th. February, 1957, complaining of severe retrosternal pain of five hours' duration. Five hours before admission, whilst at rest, the patient developed severe gripping retrosternal pain, which disappeared within a few minutes of her taking a tablet of trinitrin,(gr.1/150.) The pain returned in severe degree half an hour later and the administration of trinitrin was without effect. The pain was gripping, steady and severe, and radiated down the inner aspect of the left upper arm. The patient had felt unusually breathless on exertion before the pain started. She had vomited several times before admission to hospital. Omnopon, (gr.1/3), had been administered intramuscularly by her family doctor.

Past History.

The patient had been in hospital from the 12th November, 1953, until the 16th January, 1954, for treatment of an anterior myocardial infarction. This illness had been preceded by attacks of anginal pain on exertion of ten days' duration and by symptoms of intermittent claudication in the left leg of three months' duration. She was successfully treated with anticoagulant drugs. The blood pressure on admission had been 220/110 mm.Hg., but had fallen to 120/70 mm. Hg., before discharge from hospital. Following her discharge from hospital, the patient's general condition was good but she had attacks of anginal pain on exertion and excitement, which responded to treatment with trinitrin. She was breathless on exertion following meals. The blood pressure during this period returned to hypertensive levels, e.g., 190/130 mm.Hg., 180/110 mm.Hg.

Clinical Findings on Admission.

The patient was pale, and her skin was cold and clammy. She was restless and, despite sedation, continued to complain of severe pain. There was no dyspnoea.

Cardiovascular System: Blood pressure 140/105 mm.Hg. The pulse was regular in rate (100/min.) and rhythm. The apex beat was neither visible nor palpable. The heart sounds were well heard and were pure.

Respiratory System: A few fine crepitations were heard on auscultation over the lung bases.

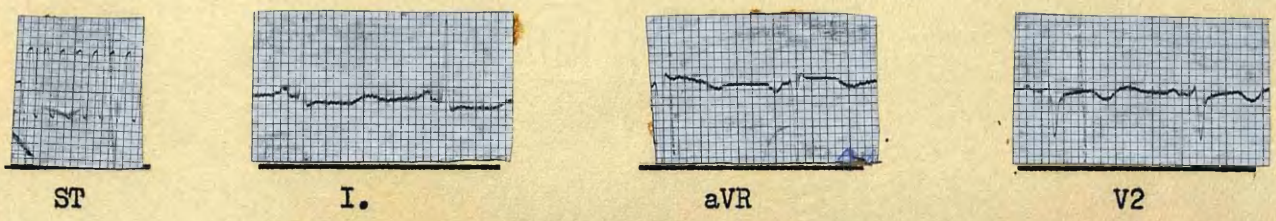
No other abnormality was discovered on full clinical examination of other systems.

Treatment and Progress.

Anticoagulant therapy was started shortly after admission, and repeated doses of pethidine, 100 mgm., intramuscularly, were given to alleviate the chest pain.

The blood pressure fell precipitously to 80/60 mm.Hg., and the patient died suddenly at 3 a.m., (8 hours after the onset of pain). Permission for a post-mortem examination was /2

ELECTROCARDIOGRAM CASE NO. 18 (1)

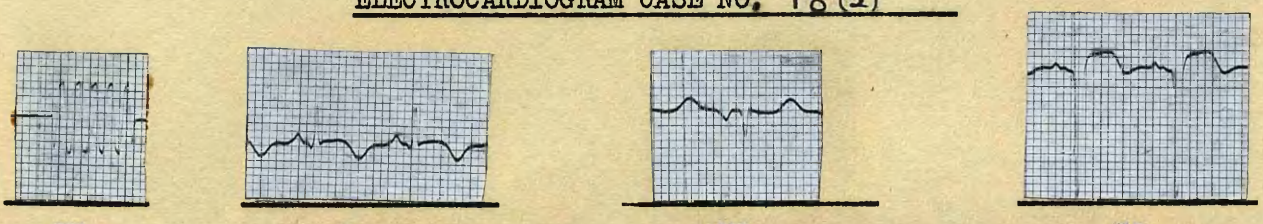


ST I. aVR V2

II. aVL V4

III. aVF V6

ELECTROCARDIOGRAM CASE NO. 18 (2)

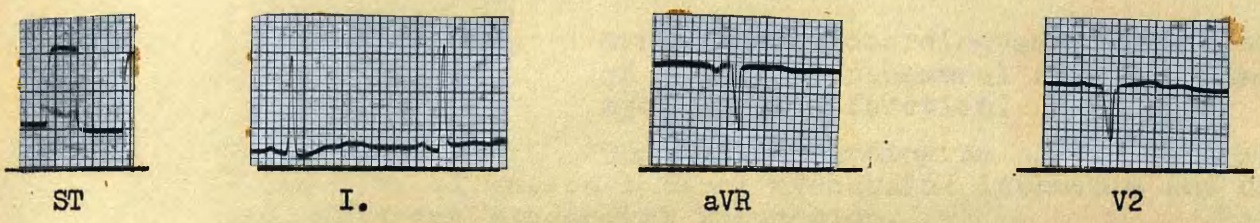


ST I. aVR V2

II. aVL V4

III aVF V6

ELECTROCARDIOGRAM CASE NO. 18 (3)

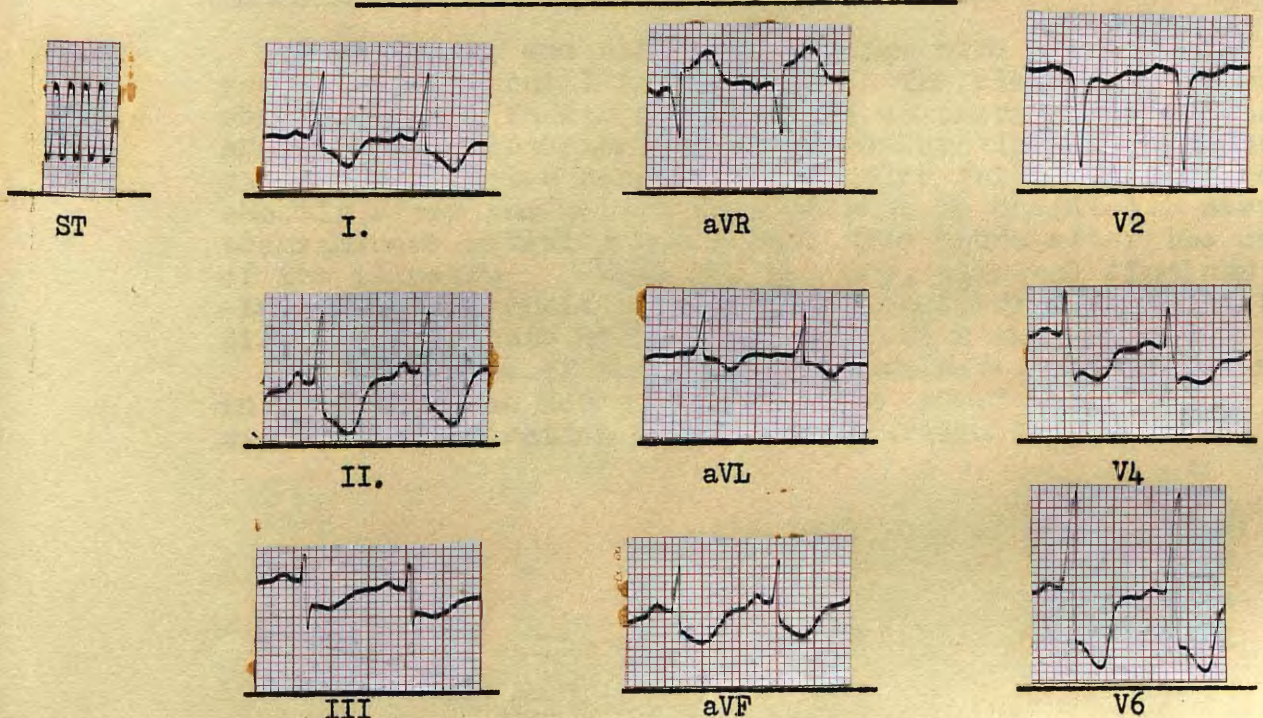


ST I. aVR V2

II. aVL V4

III. aVF V6

ELECTROCARDIOGRAM CASE NO. 18 (4)



ST I. aVR V2

II. aVL V4

III aVF V6

/ was refused.

Electrocardiographic Findings.

I. 12.11.53.)
II. 16.11.53.) - Serial electrocardiograms showed changes of an acute transmural antero septal myocardial infarction.

III. 28.1.57: The electrocardiogram showed changes indicative of antero-lateral myocardial ischaemia and of an old, anterior myocardial infarction.

IV. 26.2.57: (5 hours after onset of chest pain). The electrocardiogram showed changes indicative of acute coronary insufficiency and also changes consistent with diagnosis of an old myocardial infarction remained.

Serial Serum Transaminase Activity (Units/ml/min).

5 hours after onset of pain = 30 units.

Temperature Record.

The patient's temperature was normal throughout period of observation. -

Erythrocyte Sedimentation Rate (Westergren).

No examinations were performed.

COMMENT:

The history and clinical findings were typical of poor risk myocardial infarction. The electrocardiograms showed changes indicative of acute coronary insufficiency and of an old anterior myocardial infarction. There was no pyrexia but marked peripheral vascular failure developed shortly after the patient's admission to hospital. Serum transaminase activity was normal five hours after the onset of the illness. When the history, clinical findings and electrocardiographic changes were considered together, the diagnosis of acute myocardial infarction was made.

The failure of the serum transaminase activity to rise in the first few hours following the onset of an acute myocardial infarction is well illustrated in this case.

CASE NO. 19.

History of Present Illness.

A female, aged 68 years, a housewife, was admitted to hospital on the 20th February, 1957, complaining of attacks of breathlessness since the 17th February, 1957.

The patient, who had been subject to winter chest colds for many years, had developed a chest cold five weeks before admission to hospital. The chest infection took longer than usual to subside and she observed that, following this illness, she was unable to climb a flight of tenement stairs without marked breathlessness. This alarmed her, since such exertion previously had not induced such symptoms.

On the 17th February, 1957, she awoke during the night and was very breathless for fifteen minutes. Neighbours gave her brandy, which helped her greatly. Since then, although forced to do a certain amount of housework, as she lived alone, she had had frequent attacks of breathlessness which were most severe on first rising in the morning.

There was no relevant past history.

Clinical Findings on Admission.

The patient was an elderly, dyspnoeic female, whose lips were cyanosed. Slight jugular vein overfilling and minimal ankle oedema were present. There was no chest pain.

Cardiovascular System: B.P. 160/100 mm.Hg. The pulse was regular in rate (96/minute) and rhythm. The heart was enlarged, the apex beat being situated 1" outwith the mid-clavicular line. The heart sounds were well heard and pure, the second aortic sound being accentuated.

Respiratory System: The percussion note was diminished over the right lung base and, on auscultation, fine crepitations were heard over both lung bases.

Abdomen: The liver edge was palpable 1" below the costal margin in the right hypochondrium.

No other abnormality was found on full clinical examination of other systems.

The diagnosis of left ventricular and congestive cardiac failure, probably due to "silent" myocardial infarction, was made, and anticoagulant therapy was started.

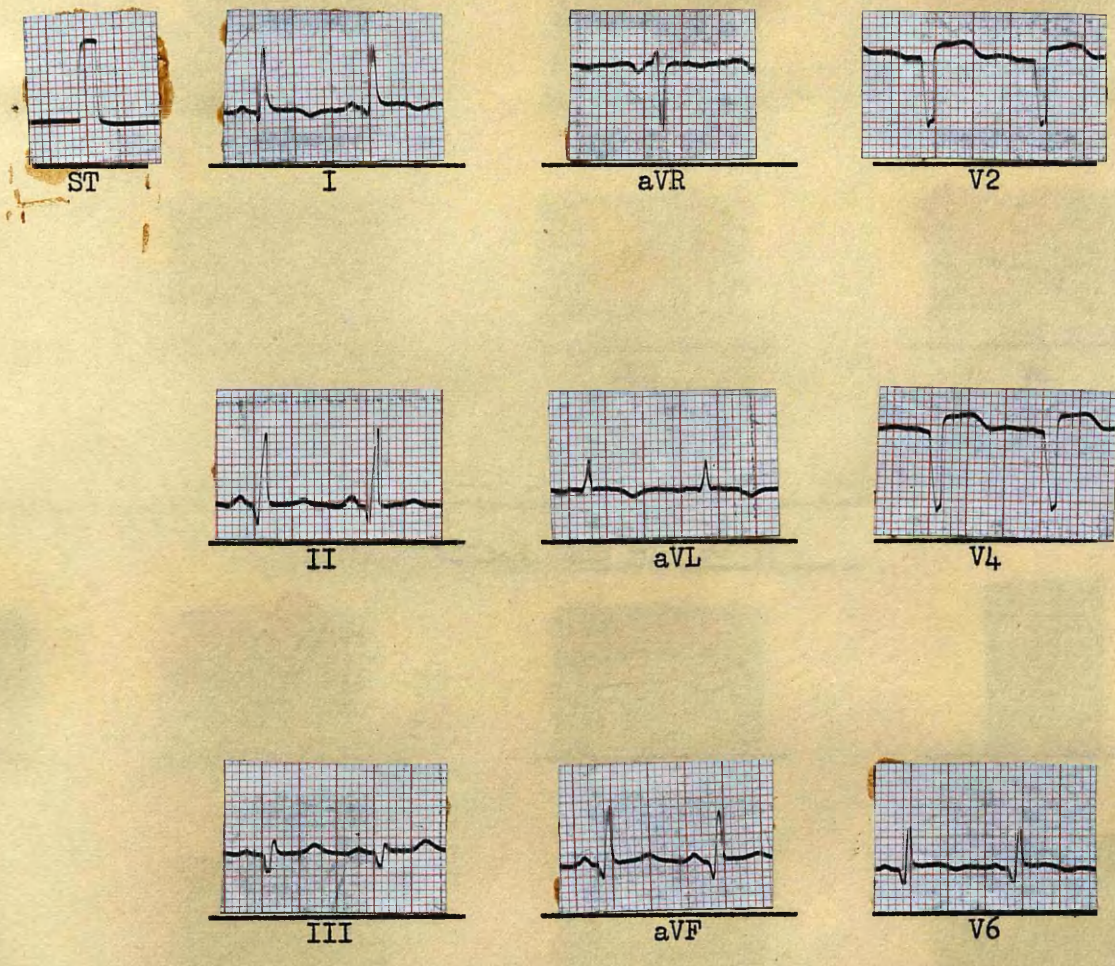
Treatment and Progress.

On admission, the patient was given morphine sulphate, gr.1/6., intramuscularly, and oxygen was administered because of the cyanosis. She settled quickly with this treatment and she was symptom-free on the day following admission.

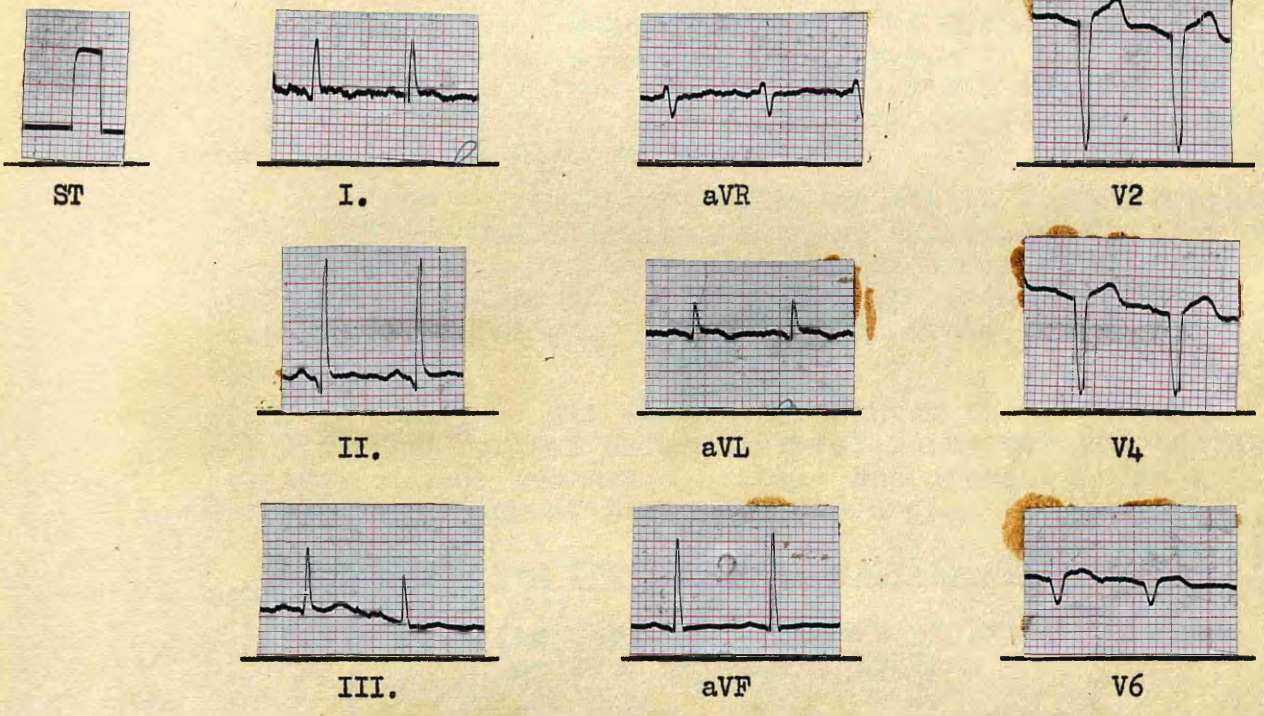
3.3.57: The patient suddenly became very breathless and remained so for seven hours. The attack subsided spontaneously. The patient denied having felt any chest pain.

4.3.57: B.P. 140/90 mm.Hg. Cardiac findings were as before. Chest: Numerous fine crepitations were heard at both lung bases /2

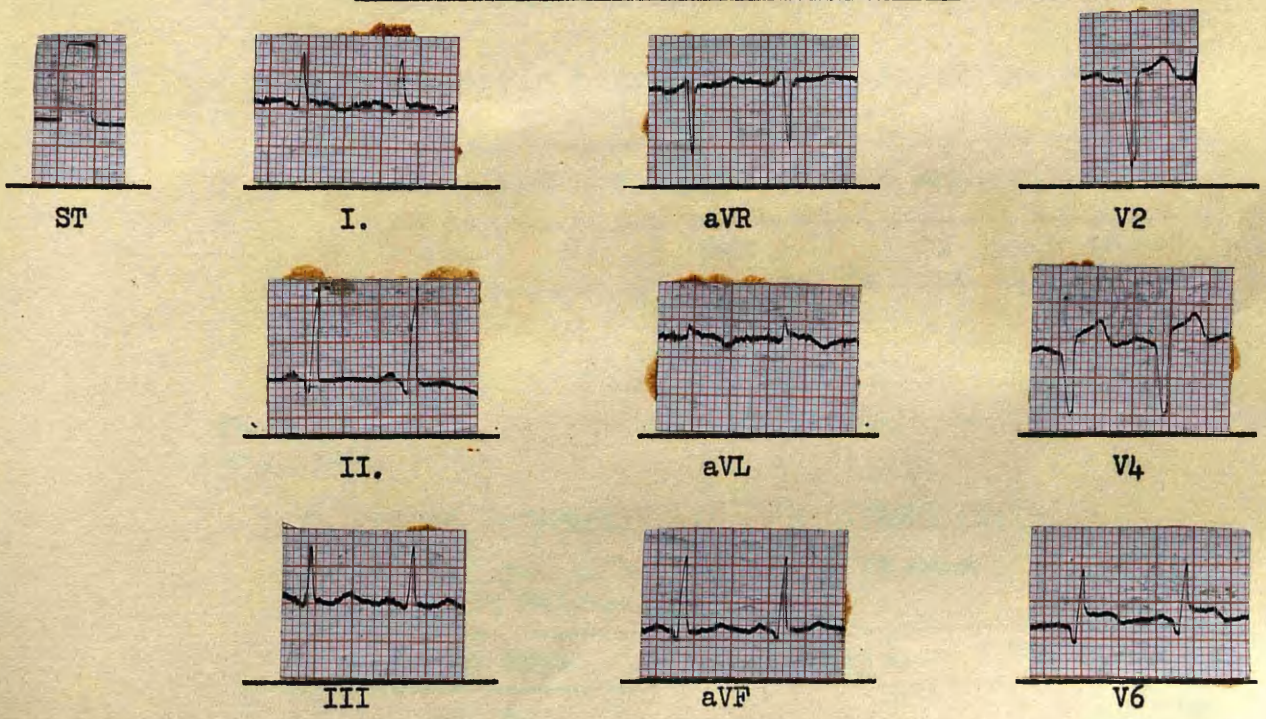
ELECTROCARDIOGRAM CASE NO. 19 (1)



ELECTROCARDIOGRAM CASE NO. 19 (2)



ELECTROCARDIOGRAM CASE NO. 19 (3)



30.3.57: The patient had remained symptom-free and there was no evidence remaining of congestive cardiac failure. She had been ambulant for a fortnight without symptoms. She was discharged to her home.

Electrocardiographic Findings.

I. 20.2.57: (3 days after onset of dyspnoea.) The electrocardiogram showed changes diagnostic of an acute, transmural, extensive antero septo lateral infarction. Changes suggestive of a possible old posterior myocardial infarction were also present.

II. 4.3.57: (24 hours after attack of sudden dyspnoea on 3.3.57.) The electrocardiogram confirmed the previous findings but, in addition, it showed changes possibly indicative of lateral extension of the infarcted area. An error in the siting of V.6 electrode could also account for the changes.

III. 27.3.57: The electrocardiogram showed changes suggestive of further antero-lateral ischaemia but again, the position factor obscures. There has probably been a lateral extension of the infarcted area.

Serial Serum Transaminase Activity (Units/ml/min.)

a) Time (in days) after Onset of Dyspnoea on 17th February, 1957.

3 days.	4 days.	5 days.	6 days.
17	12	9	7

b) Time (in hours) after Onset of Dyspnoea on 3rd March, 1957.

24 hrs.	48 hrs.	72 hrs.	96 hrs.	120 hrs.
51	60	40	20	15

Temperature Record.

The temperature was normal throughout the patient's stay in hospital.

Erythrocyte Sedimentation Rate (Westergren).

Time (in days) after Onset of Dyspnoea on 17th February, 1957.

3 days.	10 days.
3	6

/3

Erythrocyte Sedimentation Rate (Westergren). (ctd)

Time (in days) after Onset of Dyspnoea on the 3rd March, 1957.

3 days.
18

COMMENT:

Attacks of acute myocardial infarction were observed on 17.2.57 (19a) and on 3.2.57 (19b).

In the first attack, (19a)., the onset of symptoms of paroxysmal dyspnoea and congestive cardiac failure was suggestive of a poor risk acute myocardial infarction and the electrocardiograms were diagnostic of acute transmural myocardial infarction three days after the onset of the illness. The serum transaminase and erythrocyte sedimentation rate were normal, at this time, and there was no subsequent rise in either test related to this attack of myocardial infarction. No pyrexia or peripheral vascular failure were observed following the attack. It was concluded that the failure to find an elevated transaminase was due to the delay (72 hours) in obtaining serum following the myocardial infarction. It should be noted that tests on other sera performed on the same day gave high serum transaminase values.

In the second attack (19b)., there was again no chest pain but the sudden onset of severe and prolonged breathlessness was very suggestive of a fresh poor risk myocardial infarction. Serial electrocardiograms following this attack showed changes probably indicative of lateral extension of the previous transmural myocardial infarction. There was evidence of congestive cardiac failure and minimal peripheral vascular failure developed. Serum transaminase activity was at high levels 24 hours after the onset of dyspnoea. The erythrocyte sedimentation rate was elevated three days after the onset of the attack.

The recording of further chest leads would probably have clinched the diagnosis electrocardiographically but the assay was considered to have contributed early and valuable confirmatory evidence of myocardial infarction.

CASE NO. 20.

History of Present Illness.

A male, aged 54 years, a pattern-maker, was admitted to hospital on the 18th November, 1956, complaining of retrosternal pain of three and a half hours' duration.

For six months, the patient had had symptoms of angina pectoris on exertion, the pain disappearing after a few minutes' rest. Breathlessness on exertion had also been noted.

At 2.30 a.m. on the 18th November, 1956, he was awakened by a very severe crushing pain behind his sternum and he became very breathless. The pain radiated down his left arm and was referred into both shoulders and up both sides of his neck. He felt weak, cold and light-headed. The pain was present on admission to hospital at 6.15 a.m.

There was no relevant past history.

Clinical Findings on Admission.

The patient was obese, pale and the extremities were cold. He sweated profusely. There was no cyanosis or jugular vein congestion.

Cardiovascular System: B.P. 115/100 mm.Hg. The pulse was regular in rate (114 per minute), and rhythm. The apex beat was situated in the fifth interspace in the mid-clavicular line. The heart sounds were rapid and distant, and well marked protodiastolic triple rhythm was present.

Respiratory System: Rhonchi were heard on auscultation all over the lung fields.

No abnormality was detected on full clinical examination of other systems.

Treatment and Progress.

The chest pain responded to treatment with pethidine, 100 mgm., given by intramuscular injection. Treatment with anticoagulant drugs was started soon after admission and was continued until death.

19.11.56: There had been serious deterioration in the patient's condition. B.P. 70/40 mm.Hg. The pulse was impalpable; jugular venous congestion was present. The apex beat was now 1" outwith the mid-clavicular line. The heart sounds were very distant and protodiastolic triple rhythm was present. Pericardial friction was heard over the apical region.

Respiratory System: There were numerous medium crepitations heard on auscultation over both lung bases, especially over the left lung base.

Later in the day, the patient vomited several times, and he was pale and sweating. He was restless and mentally confused. On examination, the pulse and heart rate was found to be 40/minute.

20.11.56: The patient's condition was very grave. Mental confusion was severe and the patient was barely conscious. B.P. 70/0 mm.Hg. Pulse and heart rate was 32/minute. /2.

21.11.56: Encouraging improvement was noted. The patient's colour and peripheral circulation were much improved. B.P. 120/80 mm.Hg. The pulse was regular in rate (80/min.) and rhythm. Cardiac findings were unchanged.

25.11.56: There had been no recurrence of pain and satisfactory progress had been maintained. B.P. 120/70 mm.Hg. The pulse rate was 82/minute. The apex beat was again felt in the mid-clavicular line. There was a short systolic murmur at the mitral area.

29.11.56: Satisfactory progress had been maintained when his condition suddenly deteriorated. On waking, the patient complained of tingling and numbness of the ulnar aspect of his left hand and at 11.30 a.m., he became breathless, pale, and collapsed. The blood pressure could not be measured by auscultatory methods but, by palpation, the systolic blood pressure was 50 mm.Hg. The pulse was just palpable and its rate was 120/minute. The heart sounds were rapid, of poor quality and difficult to hear.

30.11.56: The patient's condition had been regarded as hopeless but he was given Omnopon, gr.1/3., by injection and Aminophyline, .25 mgm. intravenously. He rallied somewhat and the blood pressure had risen to 90/60 mm.Hg.

2.12.56: B.P. 100/70 mm.Hg. The patient complained of occasional aching praecordial pains of very short duration.

1.1.57: He had maintained good progress and had been sitting up in a chair. B.P. 100/70 mm.Hg.

3.1.57: Whilst having his evening meal, the patient suddenly fell forward, became cyanosed and, despite attempts at resuscitation, he died within 15 minutes. Permission for post-mortem examination was refused.

Electrocardiographic Findings.

I. 19.11.56: The first electrocardiogram was diagnostic of a recent, extensive, transmural antero septo lateral infarction with evidence of marked intraventricular conduction defect.

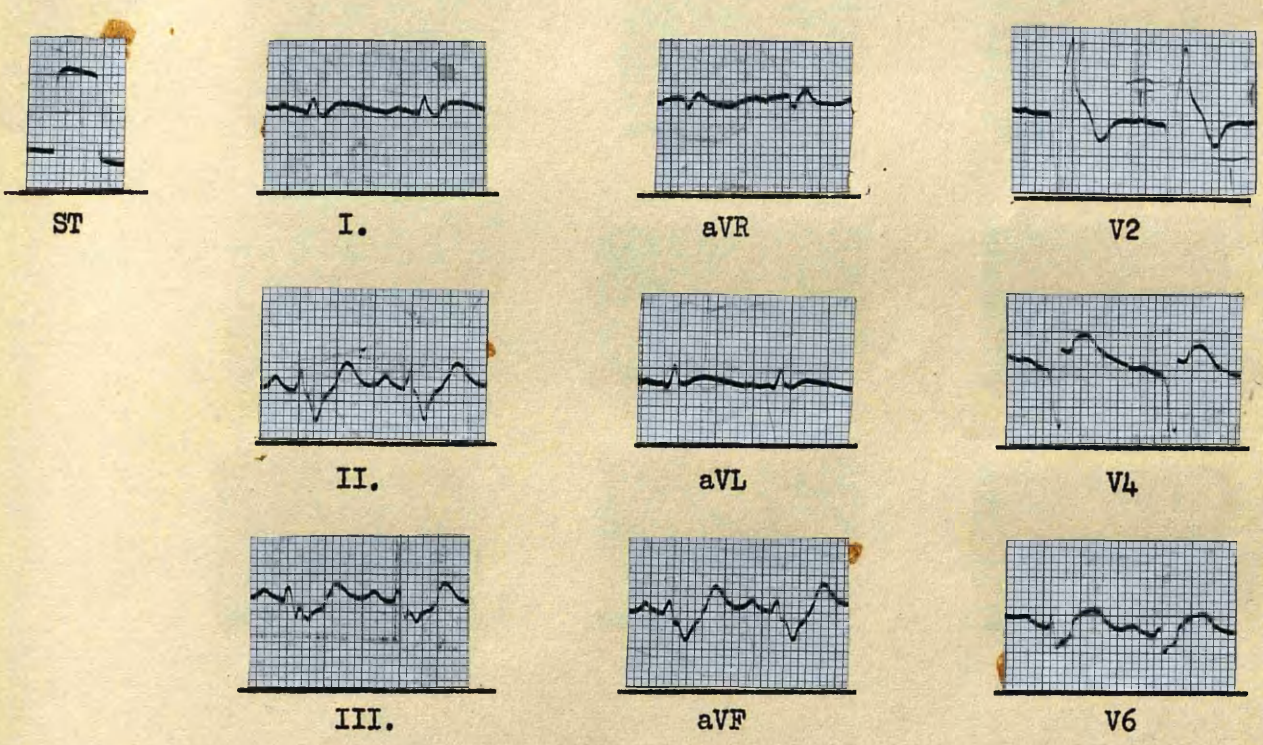
II. 20.11.56: The electrocardiogram showed changes diagnostic of complete heart block as well as those of recent antero septo lateral infarction.

III. 22.11.56: The electrocardiogram now showed no evidence of heart block, but showed sequential changes of antero septo lateral myocardial infarction, with severe intraventricular conduction defect.

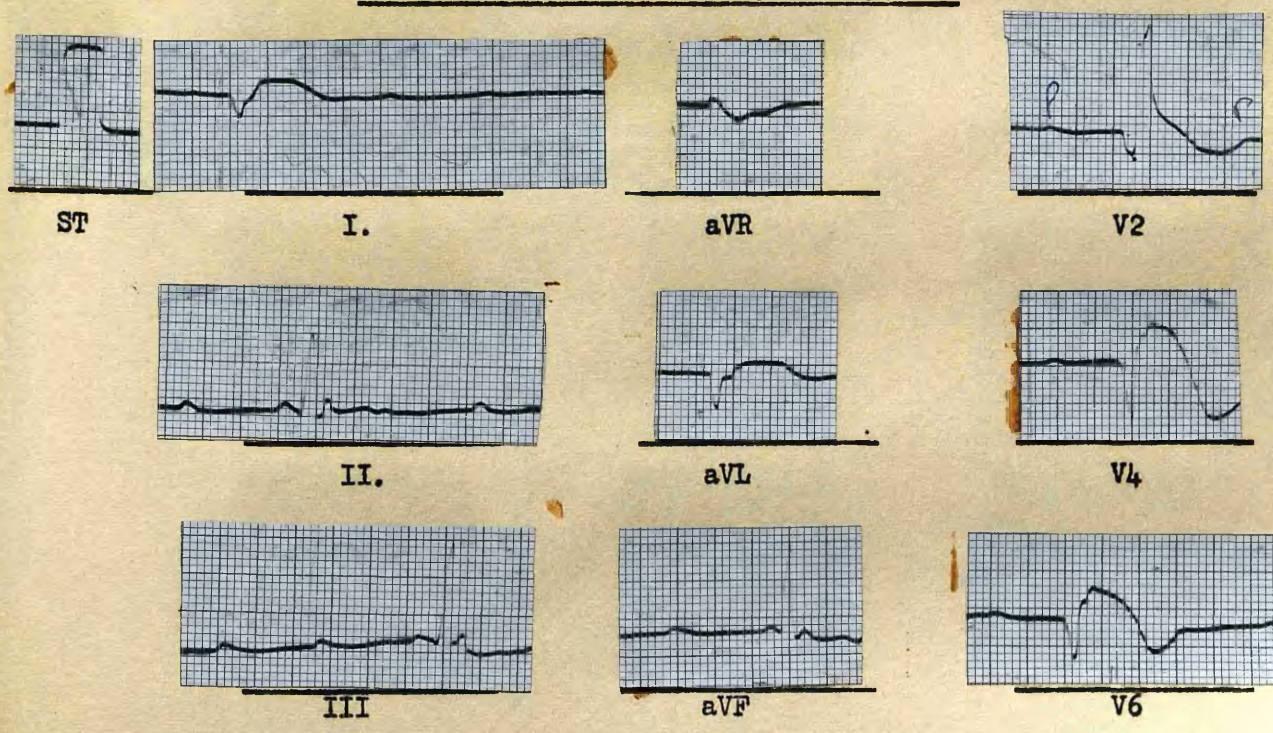
IV. 18.12.56: This electrocardiogram showed further post-infarction sequential changes and the intraventricular conduction defect was still present. There was no evidence of a second myocardial infarction.

It was unfortunate that no electrocardiogram was performed immediately following the episode of collapse and hypotension on the 29th November, 1956. /3

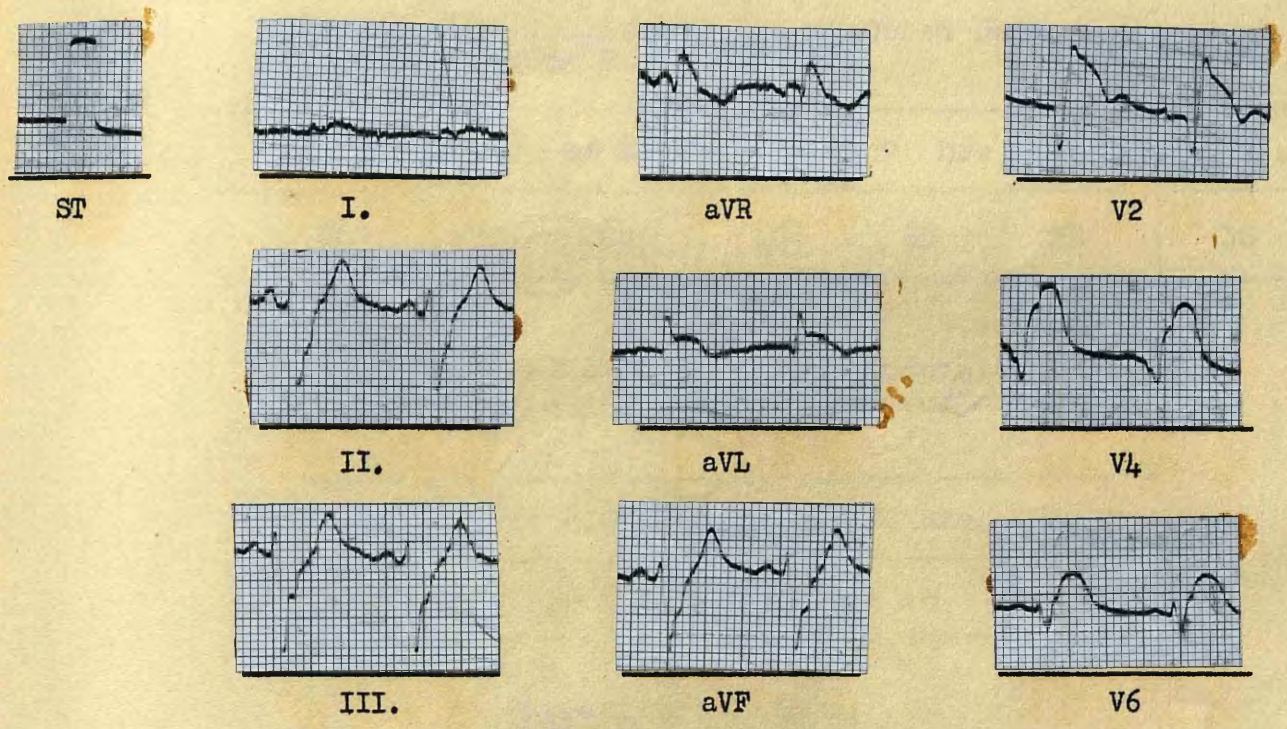
ELECTROCARDIOGRAM CASE NO. 20 (1)



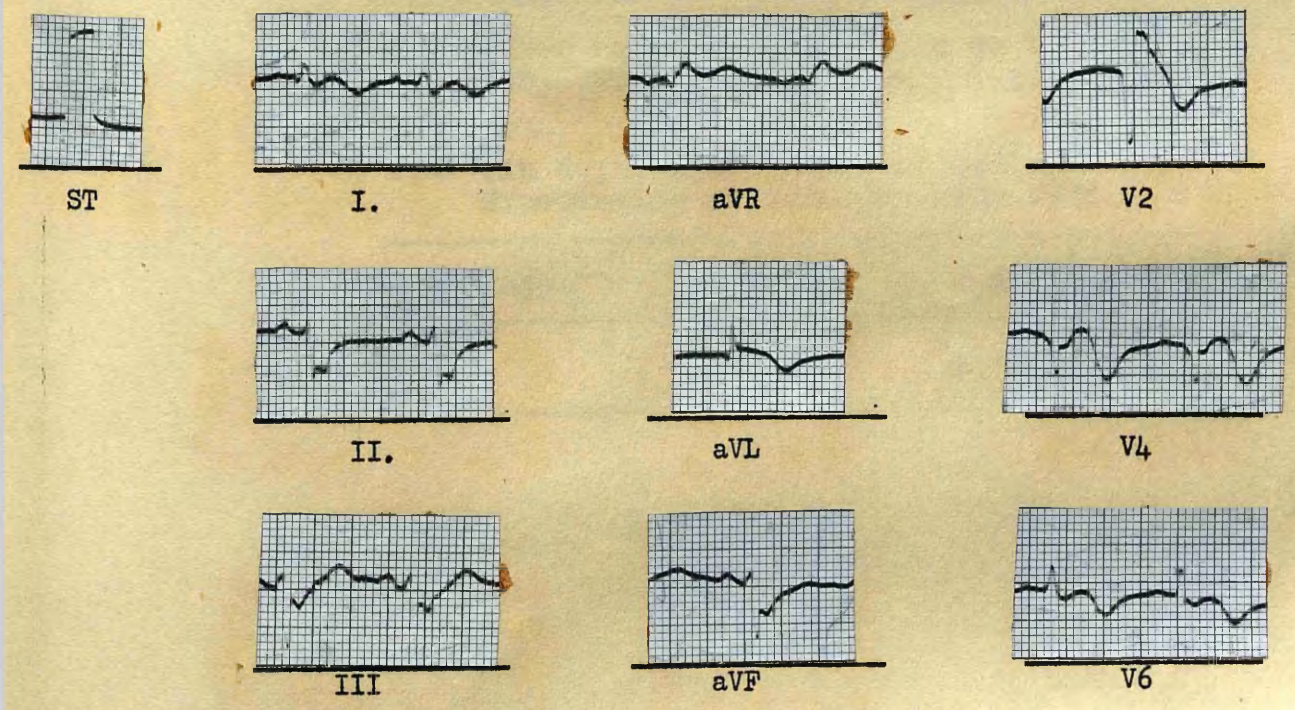
ELECTROCARDIOGRAM CASE NO. 20 (2)



ELECTROCARDIOGRAM CASE NO. 20 (3)



ELECTROCARDIOGRAM CASE NO. 20 (4)



Serial Serum Transaminase Activity (Units/ml/min.)

Time (in hours) After Onset of Chest Pain on 18th November, 1956.

7 hrs.	31 hrs.	54 hrs.	78 hrs.	102 hrs	126 hrs.	150 hrs.
50	130	250	140	80	70	35

Time (in hours) after Onset of Sudden Collapse and Hypotension on 29th November 1956.

2 hrs.	24 hrs.	48 hrs.	72 hrs.	96 hrs.
30	90	60	45	32

Temperature Record.

The temperature recorded on the 19th November, 1956, was 99.8°F. No further rise in temperature was recorded.

Erythrocyte Sedimentation Rate (Westergren).

Four days after onset of chest pain on the 18th November 1956, E.S.R. = 30 mm./ 1st.hour.

Time (in days) after Onset of Collapse and Hypotension on November 29th 1956.

7 days.	13 days.	29 days.
16	10	8

COMMENT:

The patient was considered to have sustained attacks of myocardial infarction on 18.11.56 (20a) and on 29.11.56 (20b).

In the first attack (20a)., the history and clinical findings were typical of acute myocardial infarction (poor risk). The electrocardiogram was diagnostic of transmural myocardial infarction. Pyrexia and a moderate - extremely marked degree of peripheral vascular failure were present, especially during the episode of heart block. Serum transaminase activity rose to high levels but the assay was not considered to have contributed to the diagnosis.

In the second attack (20b)., paraesthesiae in the left hand and dyspnoea at rest were the only complaints but their association with marked peripheral vascular failure of 24 - 48 hours' duration led to a confident clinical diagnosis of acute myocardial infarction. Unfortunately, electrocardiographic confirmation was not obtained. Serum transaminase activity rose to high levels and the assay was considered to have provided valuable confirmatory evidence of myocardial infarction. There was no pyrexia following this attack and, as the erythrocyte sedimentation rate had been elevated following attack (20b), the estimation of the erythrocyte sedimentation rate did not contribute to the diagnosis.

CASE NO.21.

History of Present Illness.

A female, aged 55 years, a housekeeper, was awakened by severe retrosternal pain at 5.30 a.m., on the 26th April, 1957, the pain being referred into her throat and down her right arm. The pain lasted for three hours but gradually subsided thereafter, having been accompanied by vomiting and sweating. The patient was admitted to hospital at 9 p.m., on the 26th April, 1957.

Past History.

The patient had been known to suffer from mitral stenosis of rheumatic origin since the age of 17 years, but led a fairly active life until 1955 when she began to complain of dyspnoea on exertion. At this time, auricular fibrillation was noted but, since the rate of fibrillation was slow, digitalis was not required for its control and, in 1956, she underwent the operation of simple mastectomy for spheroidal cell carcinoma of the right breast. This operation was followed by a course of radiotherapy which had resulted in post-irradiation fibrosis in the right lung. The blood pressure at this time was 180/90 mm.Hg.

Clinical Findings on Admission.

The patient was an overweight woman, whose extremities were cyanosed. There was no oedema or jugular venous congestion. Bilateral varicose veins were present. A right mastectomy scar was present with post-irradiation telangiectatic changes in the skin in the area surrounding the scar.

Cardiovascular System: B.P. 125/95 mm.Hg. The pulse was irregular in rate, rhythm and force. The pulse rate was 72/min. The apex beat was heard ½" outwith the mid-sternal line in the fifth interspace. The heart sounds were irregular, rate 80/min., and difficult to hear because of their softness. There was a long, rumbling diastolic murmur present at the mitral area.

Respiratory System: The percussion note was dull over the right middle zone of the right lung posteriorly. Bronchial breathing was present over this area.

Alimentary System: Liver dullness, by percussion, was noted 1" below the right costal margin in the mid-clavicular line.

No other clinical abnormality was found.

Treatment and Progress.

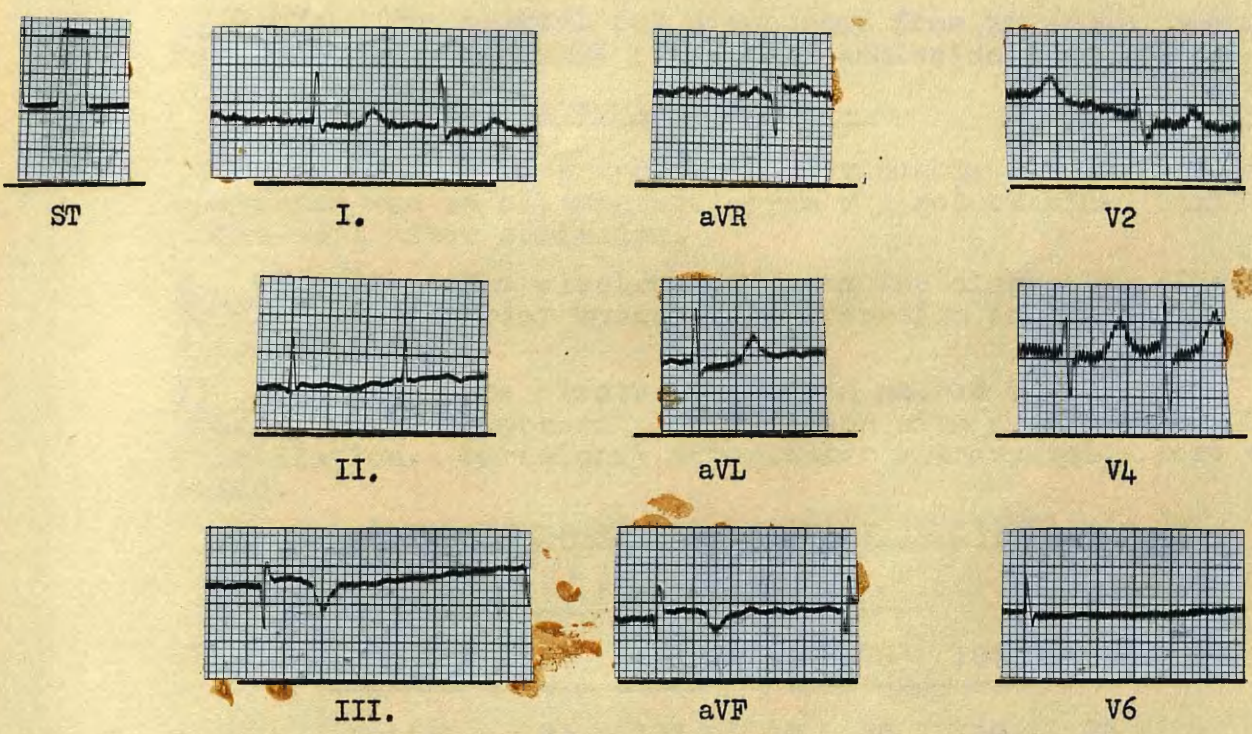
On admission, treatment with heparin and dindevan was started and continued for three weeks. Three hours following admission, the blood pressure had fallen to 90/70 mm.Hg.

27.4.57: B.P. 100/60 mm.Hg. There had been no recurrence of chest pain. Jugular venous congestion was now noted and the liver edge was palpable 1½" below the right costal margin.

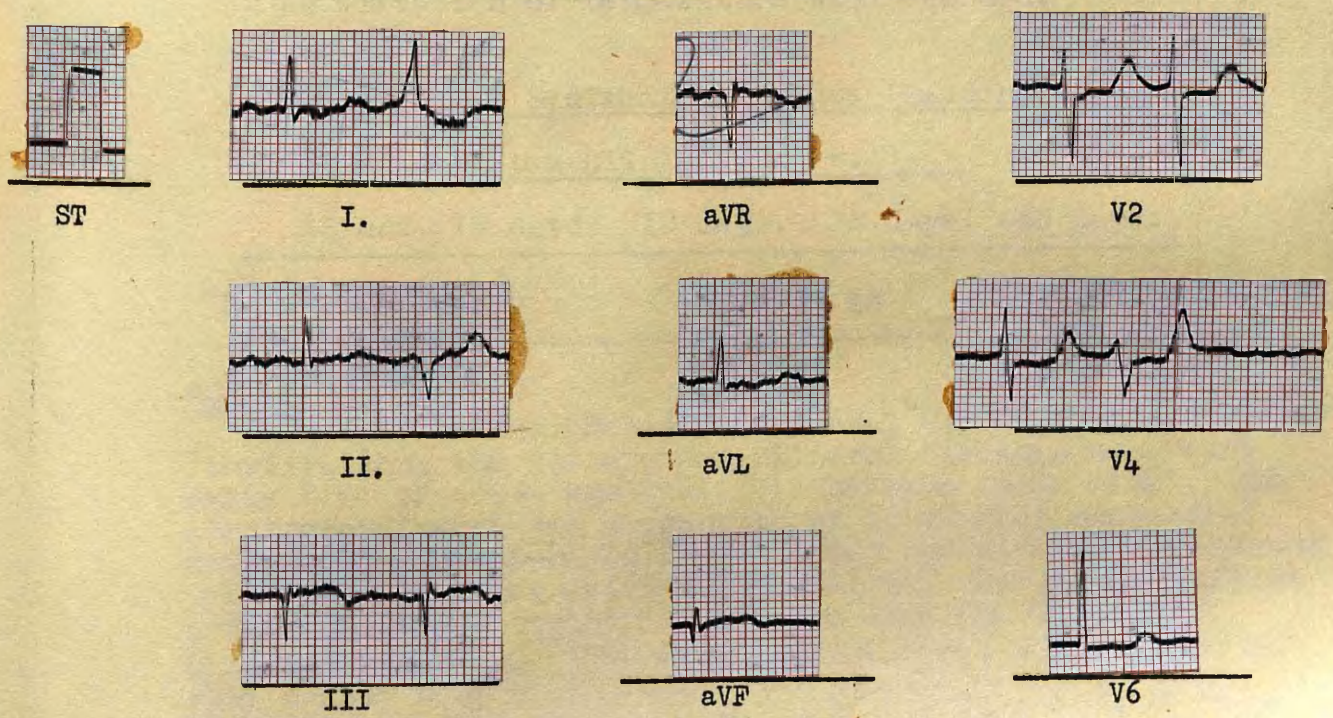
31.5.57: B.P. 120/80 mm.Hg. The patient was allowed out of bed.

/2

ELECTROCARDIOGRAM CASE NO. 21 (1)



ELECTROCARDIOGRAM CASE NO. 21 (2)



17.6.57: The patient was discharged from hospital, having been symptom-free since the day of admission.

Electrocardiographic Findings.

The electrocardiograph was unserviceable at the time of admission and an electrocardiogram was not examined until three days after admission.

I. 29.4.57: The electrocardiogram was diagnostic of acute transmural posterior myocardial infarction and auricular fibrillation.

II. 5.5.57: The electrocardiogram showed sequential changes of post-myocardial infarction with auricular fibrillation. Occasional ventricular extrasystoles were also noted.

Serial Serum Transaminase Activity)Units/ml/min.)

Time After Clinical Onset.

Hours.	15	27	54	78	102	126
Units.	85	135	90	50	30	25

Temperature Record.

No elevation of temperature was recorded.

Erythrocyte Sedimentation Rate (Westergren).

Time After Clinical Onset.

	15 hrs.	12 days	19 days.	33 days.	40 days.
mm/1st. hr.	14	22	22	18	8

COMMENT:

Despite the presence of mitral stenosis and auricular fibrillation, the history and clinical findings were very suggestive of acute myocardial infarction (poor risk). The electrocardiogram was diagnostic of transmural myocardial infarction. No pyrexia was observed but minimal to moderate peripheral vascular failure was present. Serum transaminase activity reached significant levels when the E.S.R. was slightly elevated. The electrocardiograph was not service: able at the time of the patient's admission and in these circumstances the transaminase assay was considered to have /3

/have contributed valuable confirmatory evidence of myocardial infarction.

CASE NO. 22.

History of Present Illness.

A male, aged 64 years, a labourer, was admitted to hospital on the 6th May, 1957, having collapsed in the street. Whilst walking to work, the patient felt light-headed and sat down to rest. With rest the sensation passed but, when he started to walk again, he felt the "world reeling about him" and he sank slowly to the ground. He felt no pain but began to retch continuously. He felt very weak and unable to stand.

Past History.

In 1936, the patient's right leg was amputated below the knee following an injury. In May, 1956, he was treated in hospital, the diagnosis being chronic bronchitis and sciatica. At this time, the blood pressure was 135/70 mm.Hg. Following treatment he was able to resume work. In January, 1957, he was forced to stop work because of a recurrence of left-sided sciatic pain. He was on his way to re-start his work when he developed the symptoms which led to his admission.

Clinical Findings on Admission.

The patient was a man of rather low intelligence and history-taking was difficult. He was moderately shocked. He wore an artificial limb.

Cardiovascular System: B.P. 140/95 mm.Hg. The pulse was regular in rate (64/minute) and rhythm. The apex beat was felt ½" outwith the mid-clavicular line in the fifth inter-space. The heart sounds were well heard, pure and of good quality.

Respiratory System: No abnormality was found on full clinical examination.

Central Nervous System: There was slight but definite weakness of the left face and limbs. The tendon reflexes on the left side were increased whilst the left plantar response was equivocal. Examination of the pupillary reflexes, cranial nerves, retinal and sensory nervous system revealed no abnormality.

The findings suggested the diagnosis of cerebral thrombosis with left hemiplegia. The shock present on admission and the sudden onset led to an electrocardiogram being performed.

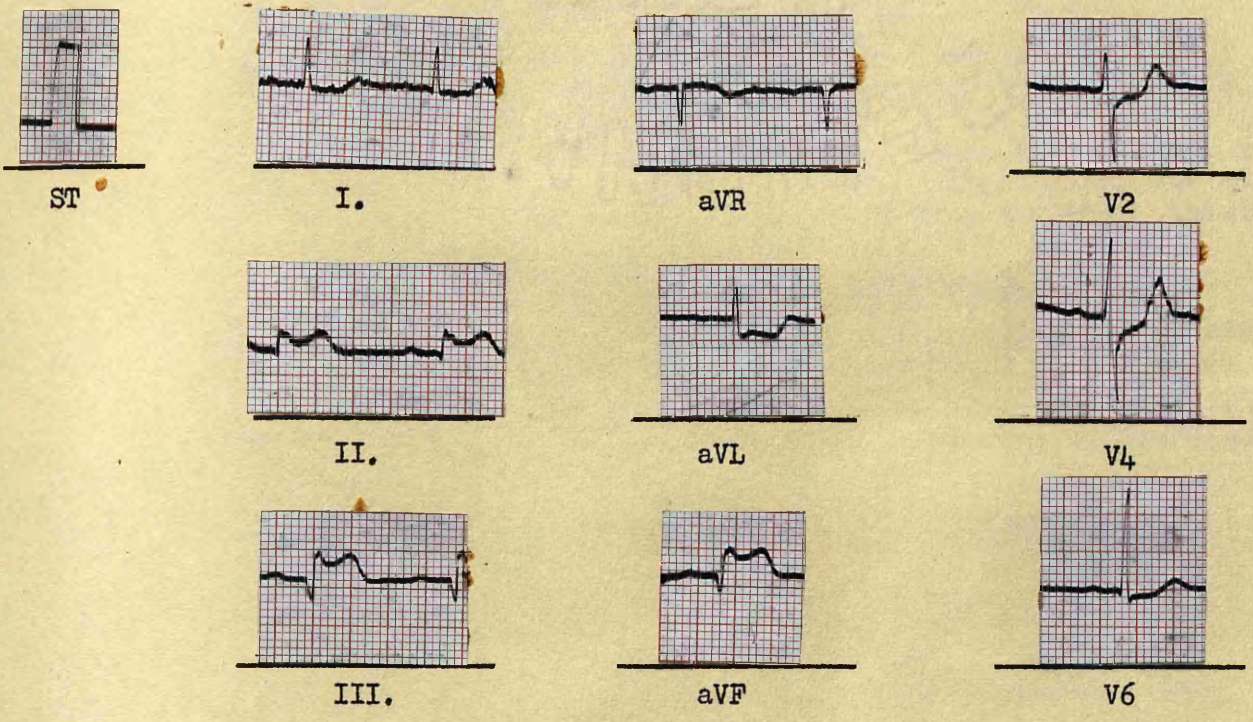
Treatment and Progress.

The signs of shock, pallor, skin coldness, sweating and retching passed off quickly (6 hours) following the administration of morphine gr.1/6 intramuscularly and rest in bed.

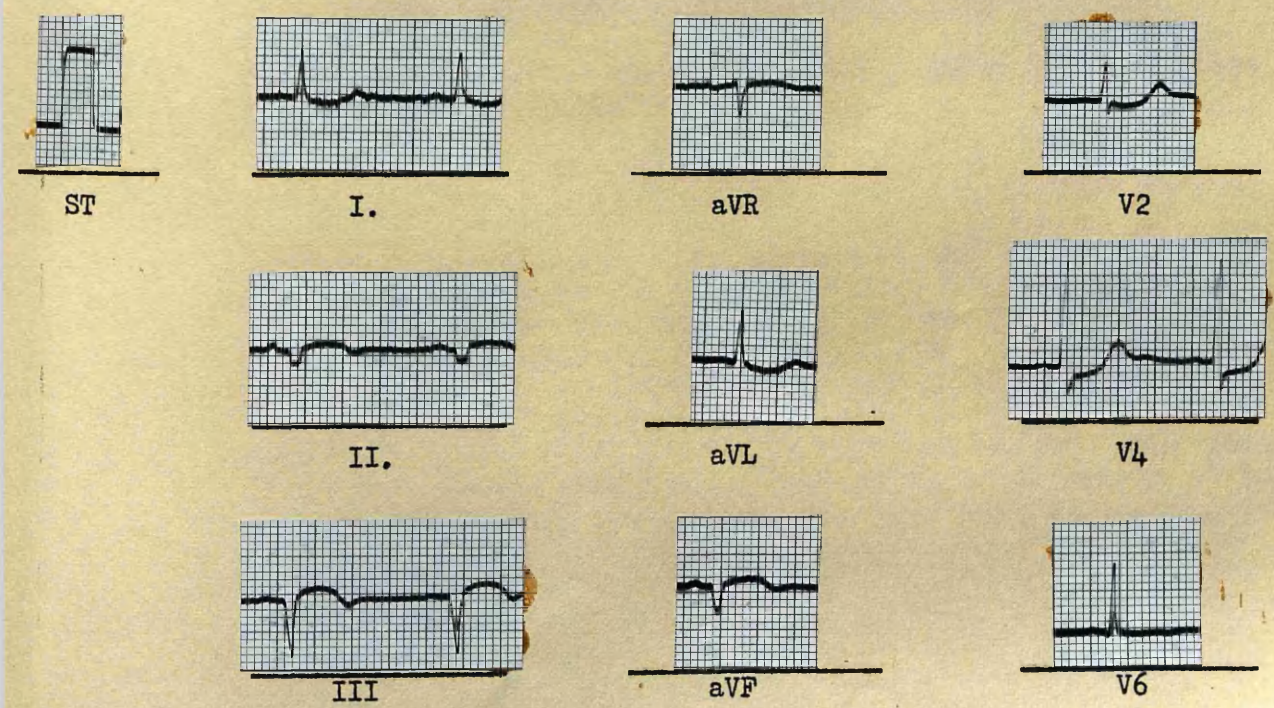
7.5.57: B.P. 110/70 mm.Hg. The patient was symptom-free but the hemiplegic weakness was very marked.

8.5.57: B.P. 120/75 mm.Hg. The patient complained of shortness of breath at rest and of pain across the lower abdomen. He was incontinent and the bladder was palpable 3" above the pubic bone. The incontinence was considered to be of overflow type, associated with hemiplegia. /2

ELECTROCARDIOGRAM CASE NO. 22 (1)



ELECTROCARDIOGRAM CASE NO. 22 (2)



14.5.57: B.P. 110/70 mm.Hg. The patient's general condition was improved. There had been some recovery in power of the left lower limb and in the left arm but the muscles of the left hand and wrist were powerless. There had been occasional incontinence of urine.

19.7.57: He was discharged to his own home. His convalescence had been prolonged because of his difficulty in learning to walk again with the aid of his artificial limb. He had succeeded but, unfortunately, there had been no return of power to his left hand and wrist. Throughout the period of observation the patient denied having suffered chest pain.

Electrocardiographic Findings.

I. 6.5.57: (3 hours after collapse in the street). The electrocardiogram showed changes diagnostic of an acute, extensive, transmural posterior myocardial infarction.

II. 17.5.57: The electrocardiogram showed sequential changes of an extensive, transmural posterior myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

6 hrs.	17 hrs.	41 hrs.	65 hrs.	89 hrs.	113 hrs.
37	198	208	150	72	35

Temperature Record.

The body temperature was normal throughout the period of observation.

Erythrocyte Sedimentation Rate (Westergren).

7 days	14th day.	21st day.	35th day	59th day.
92	42	22	4	6

COMMENT: The onset was atypical and the clinical findings diagnostic of thrombosis of the right middle cerebral artery with hemiplegia of the left limbs. The presence of minimal peripheral vascular failure raised the suspicion of acute myocardial infarction (poor risk), and the electrocardiograms were diagnostic of transmural myocardial infarction. No pyrexia was noted. The serum transaminase activity was elevated to high levels 17 hours after the onset of the illness. The electrocardiograms were diagnostic of myocardial infarction 3 hours after the onset of the illness, when serum transaminase activity was within normal limits. However, cerebral artery thrombosis may have contributed to the rise in serum transaminase activity and, in these circumstances, the assay was not considered to have contributed to the diagnosis.

CASE NO. 23.

History of Present Illness.

A male, aged 63 years, an engineer, was admitted to hospital on the 24th April, 1957, complaining of severe substernal retrosternal pain. For six months, the patient had felt praecordial tightness on exertion but he had not complained of pain until the 21st April, 1957, when he had a sharp retrosternal pain in the chest whilst walking uphill. This pain disappeared in a few minutes after resting. At 10.30 a.m., on the 24th April, 1957, whilst the patient was at work, he was seized with a severe retrosternal pain which did not disappear on resting; this pain radiated to the left wrist and it had been much alleviated before admission to hospital by an intramuscular injection of morphine sulphate, gr.1/2.

There was no relevant past or social history.

Clinical Findings on Admission.

The patient was obese, apprehensive and suffering from slight shock.

Cardiovascular System: B.P. 130/95 mm.Hg. The pulse was regular in rate (100/minute) and rhythm. The apex beat was felt in the mid-clavicular line in the fifth interspace. The heart sounds were difficult to hear and they were of poor quality.

Respiratory System: On auscultation many medium crepitations were heard over the lower lobe of the left lung, where the air entry was diminished.

No other abnormality was found on full clinical examination of other systems.

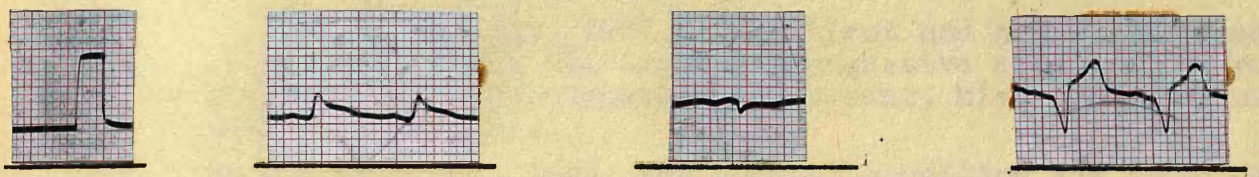
Treatment and Progress.

The chest pain waxed and waned for 24 hours after admission, but responded to repeated intramuscular doses of morphine sulphate, gr.$\frac{1}{4}$. Anticoagulant therapy was started shortly after admission and was continued for 28 days. The patient's condition rapidly deteriorated following admission. His B.P. fell to 95/80 mm.Hg. He became mildly confused, sweated profusely and cyanosis of lips, fingers and toes appeared.

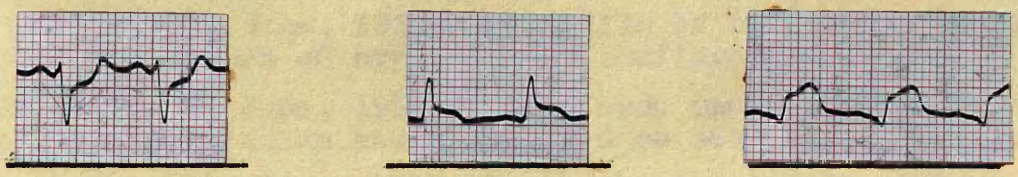
On the 25th April, 1957, his blood pressure was 90/70 mm.Hg., and tachycardia (120/minute) was present. The apex beat was no longer palpable but the heart dullness was outwith the mid-clavicular line in the fifth interspace. The heart sounds were of very poor quality. The findings on auscultation of the lungs were unchanged. Treatment with penicillin was started and continued for seven days.

On the 26th April 1957, his blood pressure was 100/80 mm.Hg. There were now signs of congestive cardiac failure. There was overfilling of the neck veins; the liver was enlarged 3"

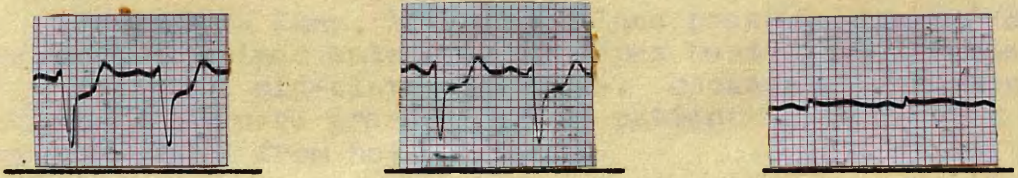
ELECTROCARDIOGRAM CASE NO. 23 (1)



ST I. aVR V2

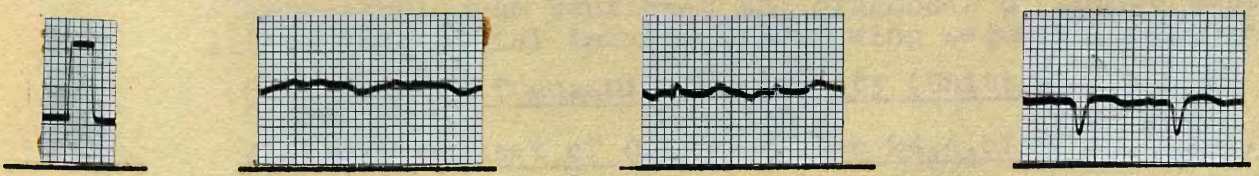


II. aVL V4

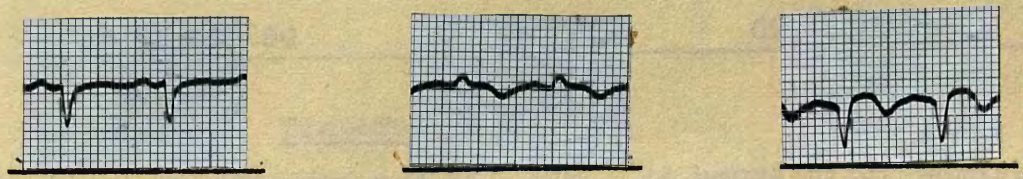


III. aVF V6

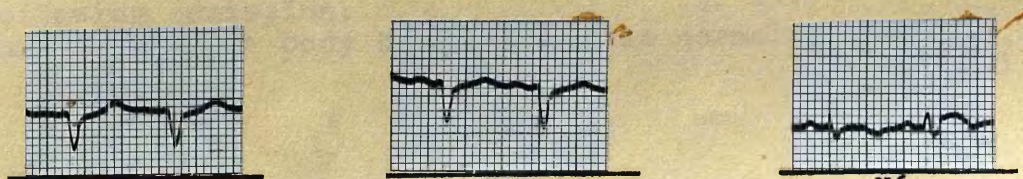
ELECTROCARDIOGRAM CASE NO. 23 (2)



ST I. aVR V2



II. aVL V4



III aVF V6

/ 3" below the right costal margin and there were numerous medium crepitations heard on auscultation over both lung bases, especially the right.

On the 2nd May, 1957, the patient had had no recurrence of chest pain and the signs of congestive cardiac failure had disappeared. Hypotension was present, his blood pressure being 90/75 mm.Hg.

On the 16th May, 1957, his general condition was good; his blood pressure was 95/80 mm.Hg. Tachycardia (110/minute) was present.

On the 3rd June, 1957, X-Ray film of his chest showed an enlarged heart of hypertensive configuration.

On the 7th June, 1957, he had made uneventful progress, although hypotension had been noted on several occasions.

By the 10th June, 1957, he had been ambulant without symptoms.

On the 15th June, 1957, his blood pressure was 105/80 mm.Hg. His heart remained enlarged, the apex beat being situated 1" outwith the mid-clavicular line. Occasional ventricular ectopic beats were present. The patient felt well and he was discharged from hospital.

Electrocardiographic Findings.

I. 24.4.57: (7 hours after onset of chest pain). The electrocardiogram showed changes diagnostic of a very extensive acute transmural antero septo lateral myocardial infarction.

II. 15.5.57: (21 days after onset of chest pain). The electrocardiogram confirmed the diagnosis of antero septo lateral myocardial infarction, showing sequential changes.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Chest Pain on 24.4.57 at 10.30 am.

4 hrs.	26 hrs.	50 hrs.	74 hrs.	6 days.	7 days.
33	200	153	80	69	35

Temperature Record.

The body temperature was 100.4°F., 24 hours after admission and temperatures of 99.6°F were observed for three days following admission.
Thereafter, the body temperature was normal.

/3

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Chest Pain on 24.4.57 at 10.30 a.m.

	4 hrs.	13 days.	19th day.	26th day.	33rd day.	42nd day.	48th day.
mm/ 1st.hr.	3	54	61	50	40	25	10

COMMENT:

The history and clinical findings were typical of acute myocardial infarction, and electrocardiogram was diagnostic of transmural myocardial infarction. The patient was considered a "poor risk" case because of intractable praecordial pain. Pyrexia and minimal-moderate peripheral vascular failure were present. Serum transaminase activity reached high levels. Both the erythrocyte sedimentation rate and transaminase activity were normal four hours after the onset of the illness. The assay was not considered to have contributed to the diagnosis.

CASE NO. 24.

A widow, aged 69 years, was admitted to the Victoria Infirmary, Glasgow, on 13.12.56., complaining of retrosternal pain and breathlessness.

For 10 years the patient had been breathless on exertion but she had had no other symptoms. On 12.12.56, at 7 p.m., the patient developed severe retrosternal pain of gripping nature which was referred into both upper arms. The pain lasted for three hours and was accompanied by vomiting which persisted after the pain had eased. She was admitted to hospital on 13.12.56.

There was no relevant past or family history.

Clinical Findings on Admission.

The patient was an elderly woman, who was slightly cyanosed. Slight jugular venous congestion was present.

Cardiovascular System: B.P. 150/100 mm.Hg. The pulse was regular in rate (98/min.) and rhythm. The apex beat was not palpable but the heart was enlarged, percussion indicating that the left heart border lay 1" outwith the mid-clavicular line. The heart sounds were faint but pure.

Respiratory System: A few fine crepitations were heard on auscultation over the bases of both lungs.

Treatment and Progress.

Anticoagulant therapy was started shortly after admission and continued for 28 days. The patient's recovery was uninterrupted. B.P. fell on 14.12.56 to 130/70 mm.Hg but, before discharge from hospital on 24.1.57, the B.P. was 160/90 mm.Hg.

Electrocardiographic Findings.

(Duplicate records are not available for inclusion in this study).

I. 19.12.56: (7 days after onset of pain on 13.12.56). The electrocardiogram showed the changes of left bundle branch blodk but the low voltage QRS complexes and the inversion of T wave in a.V.F. was suggestive of septal myocardial infarction in a horizontal heart; whether the infarction was recent or old was impossible to say.

II. 17.1.57: The electrocardiogram showed no significant sequential change.

Serial Serum Transaminase Activity (Units/ml/min.)

Hours.	25	49
Units.	220	117.

Temperature Record.

The temperature was 100°F 48 hours after admission, but was normal thereafter.

Erythrocyte Sedimentation Rate (Westergren).

Estimations were not performed.

Comment;

The history and clinical findings were very suggestive of acute poor risk myocardial infarction. The electrocardiogram, taken 7 days after the onset of the chest pain, showed the pattern of left bundle branch block and changes suggestive of septal myocardial infarction, although the age of the infarction could not be determined. Pyrexia and minimal peripheral vascular failure developed.

Serum transaminase activity was at high levels 25 hours after the onset of the illness.

The assay was considered to have been of great value in confirming the occurrence of acute myocardial infarction.

CASE NO. 25.

History of Present Illness.

A male, aged 57 years, an office worker, was admitted to hospital on the 20th March, 1957, having developed severe retrosternal pain whilst at rest at 6 p.m.

In 1950, when running for a 'bus, he had been seized with severe retrosternal pain which radiated down both arms, but which disappeared in an hour with rest. After this attack he had been subject to angina pectoris on exertion and when excited. The pains had been relieved by rest and by the use of trinitrin but they became more frequent and easily induced in December, 1956.

On January 19th., 1957, he had an attack of severe retrosternal pain whilst resting in bed. The pain lasted for three quarters of an hour despite the use of trinitrin, and it was associated with breathlessness at rest. He stayed in bed for four days and then resumed work. On February 8th., 1957, severe constricting retrosternal pain again came on at rest. This was associated with severe dyspnoea and lasted for four days despite the administration of morphine sulphate gr.$\frac{1}{4}$. Following this attack, the patient remained in bed for six weeks. He had been allowed up for short periods, but whilst in bed at 6 p.m., on March 20th 1957, he again had an attack of severe constricting substernal pain which was referred down the inner aspects of both arms. At 6.45 p.m., his family doctor gave him an intramuscular injection of morphine sulphate gr.$\frac{1}{4}$., and atropine sulphate, gr.1/100 and by 7.30 p.m., the pain had cleared.

There was no other relevant past or social history.

Clinical Findings on Admission.

The patient was a middle-aged man, of good colour. He was not shocked on admission.

Cardiovascular System: B.P. 135/85 mm.Hg. The pulse was regular in rate (100/minute) and rhythm. The apex beat was not defined and the heart sounds were distant, but pure.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Anticoagulant therapy was started soon after admission and was continued until May 22nd. 1957.

21.3.57: B.P. 130/80 mm.Hg. The patient was slightly dyspnoeic at rest and he was sweating. The heart sounds were difficult to hear. Examination of the chest revealed, on auscultation, numerous medium crepitations at both lung bases.

22.3.57: B.P. 130/80 mm.Hg. There had been no recurrence of pain but at 6 a.m. on March 24th, 1957, the patient complained /2

of low retrosternal pain which was referred across the chest and to the epigastrium. The pain was gripping in character and lasted for two hours. There was no change in clinical findings previously recorded.

26.3.57: B.P. 140/75 mm.Hg.

28.3.57: B.P. 110/70 mm.Hg.

29.3.57: The patient complained of gripping pain in left praecordium at 7.15 p.m., which lasted for 35 minutes. At 11.p.m., the pain recurred, accompanied by feeling of numbness and tingling in both arms and, on this occasion, the pain lasted for 30 minutes.

3.4.57: B.P. 140/80 mm.Hg. There had been no recurrence of pain but at 8.30 p.m., the patient had another attack of gripping retrosternal pain accompanied by tingling in both arms, which was not relieved by trinitrin. Repeated doses of intramuscular morphine sulphate, gr.$\frac{1}{4}$., failed to control the pain completely and it did not clear until 5 a.m. on April, 4th, 1957. Clinical findings were unchanged.

5.4.57: B.P. 120/70 mm.Hg. There had been no recurrence of pain but signs of congestive cardiac failure had appeared. There was overfilling of the neck veins; the liver was felt 1" below the right costal margin and sacral oedema was present. The left border of the heart was placed outwith the mid-clavicular line by percussion method; the heart sounds were difficult to hear and of very poor quality.

6.4.57: Two attacks of angina pectoris were relieved by trinitrin gr.1/ 150.

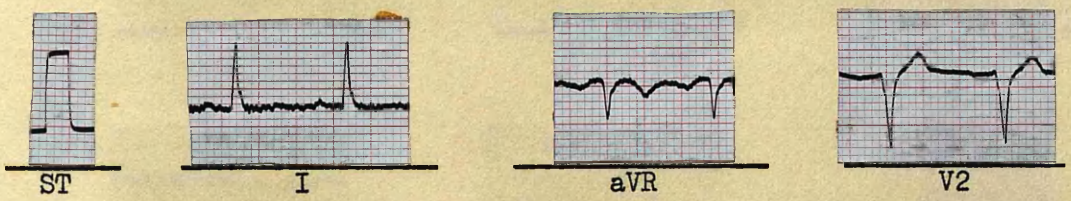
8.4.57: The patient had two further attacks of angina pectoris; the first required morphine sulphate, gr.$\frac{1}{4}$ intramuscularly for its relief, whilst the second attack responded to trinitrin therapy. Sacral oedema and hepatomegaly had cleared without special therapy but overfilling of the neck veins was present.

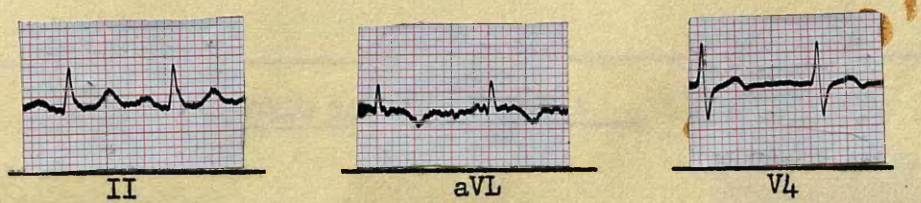
On 10.4.57 & 11.4.57, severe attacks of angina required morphine for their relief. Dyspnoea was associated with the attacks but no serious degree of shock accompanied them. B.P. was well maintained, being 120/80 mm.Hg, but signs of congestive cardiac failure again appeared and mersalyl therapy was started.

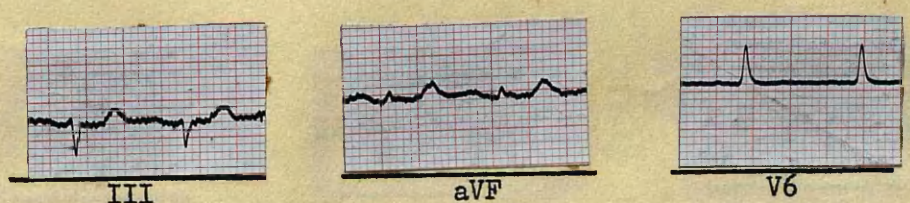
25.4.57: The congestive cardiac failure had responded to mersalyl therapy and the patient had had no recurrence of pain for thirteen days when he suffered another attack of retrosternal pain at 7 p.m., which was referred down his right arm. This was somewhat eased by morphine, gr.$\frac{1}{4}$

26.4.57: B.P. 130/55 mm.Hg. At 7 a.m., the patient awake, still complaining of severe gripping central chest pain and of gnawing pain in his left arm. The pain was eased by the intramuscular injection of morphine sulphate, gr.$\frac{1}{4}$ but persisted in mild form for 24 hours in both chest and left arm.

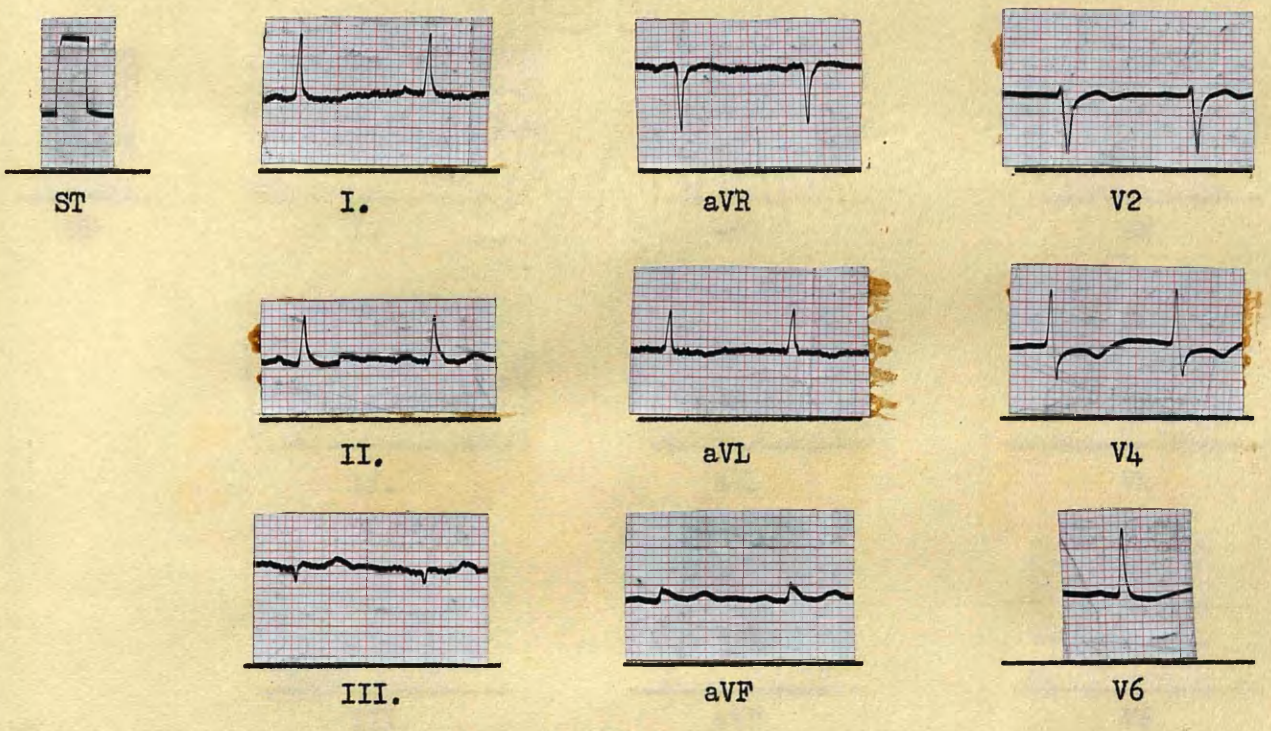
ELECTROCARDIOGRAM CASE NO. 25 (1)



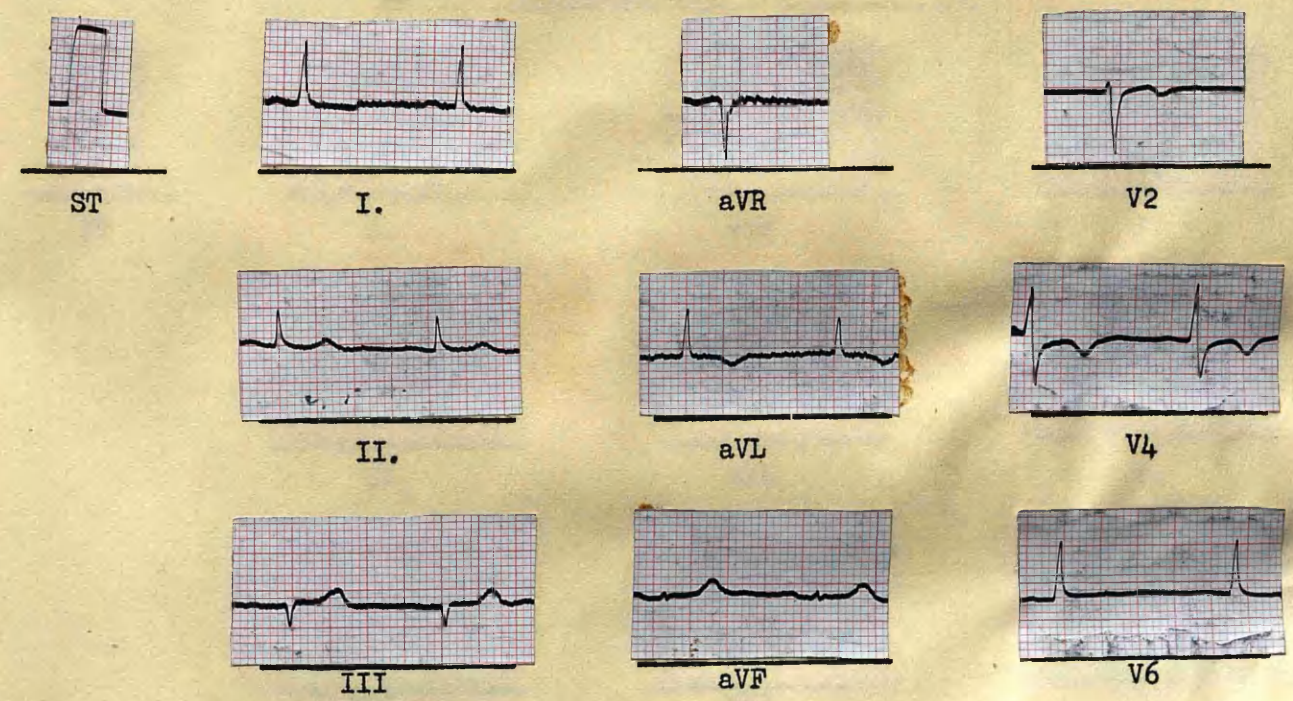




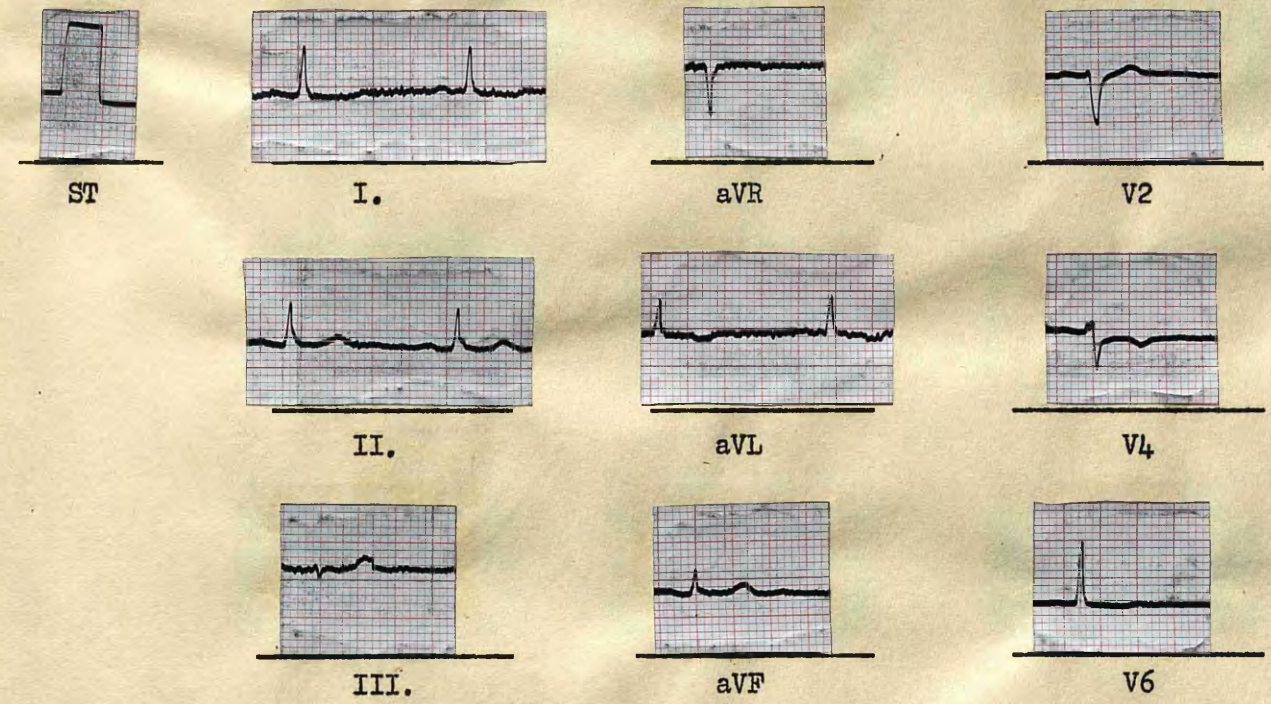
ELECTROCARDIOGRAM CASE NO. 25 (2)



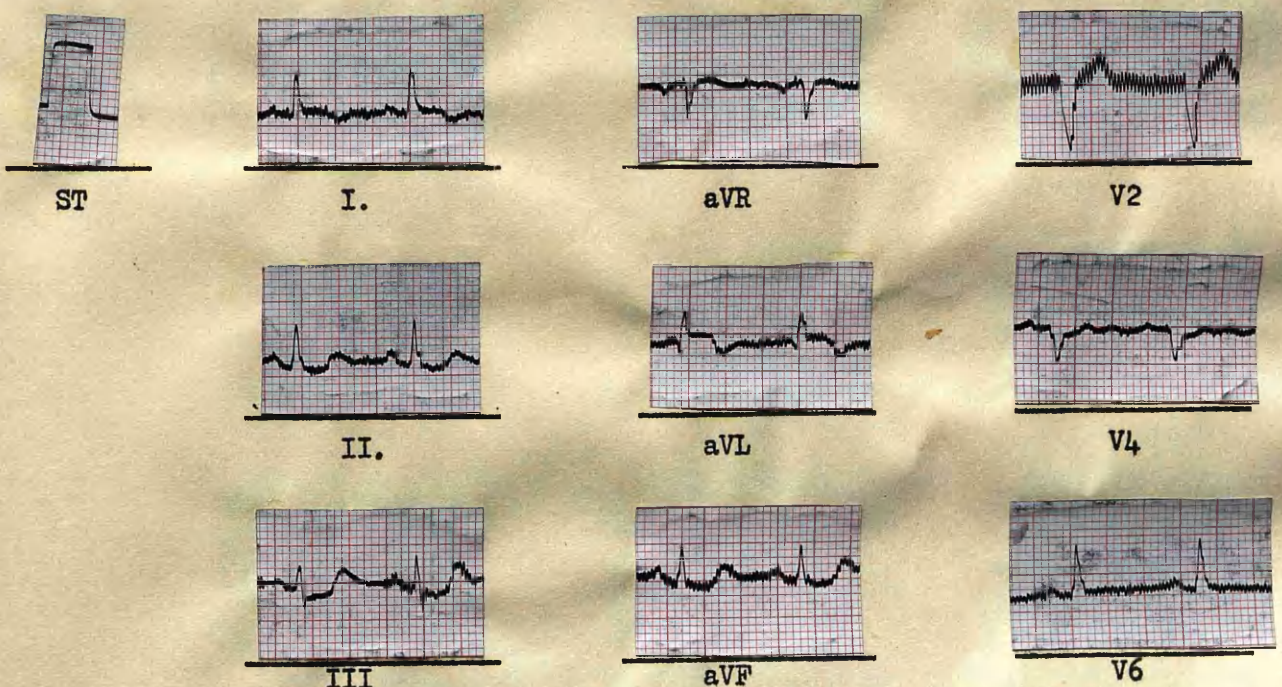
ELECTROCARDIOGRAM CASE NO. 25 (3)



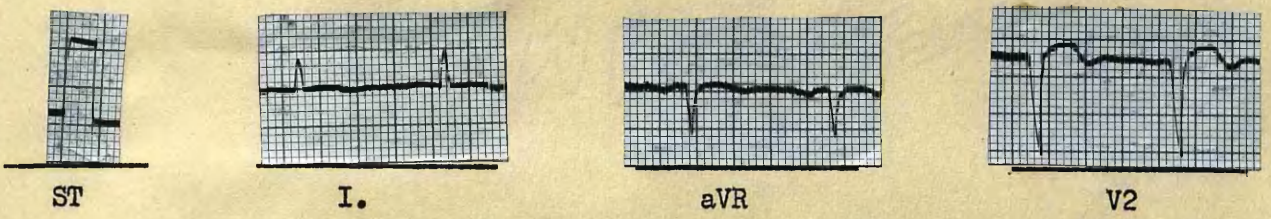
ELECTROCARDIOGRAM CASE NO. 25 (4)



ELECTROCARDIOGRAM CASE NO. 25 (5)



ELECTROCARDIOGRAM CASE NO. 25 (6)

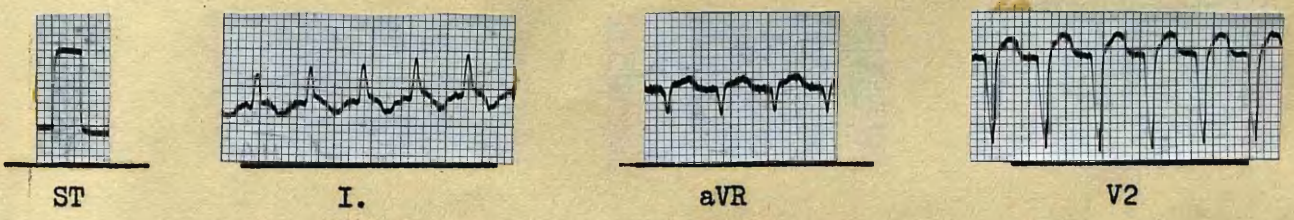


ST I. aVR V2

II. aVL V4

III. aVF V6

ELECTROCARDIOGRAM CASE NO. 27 (7)

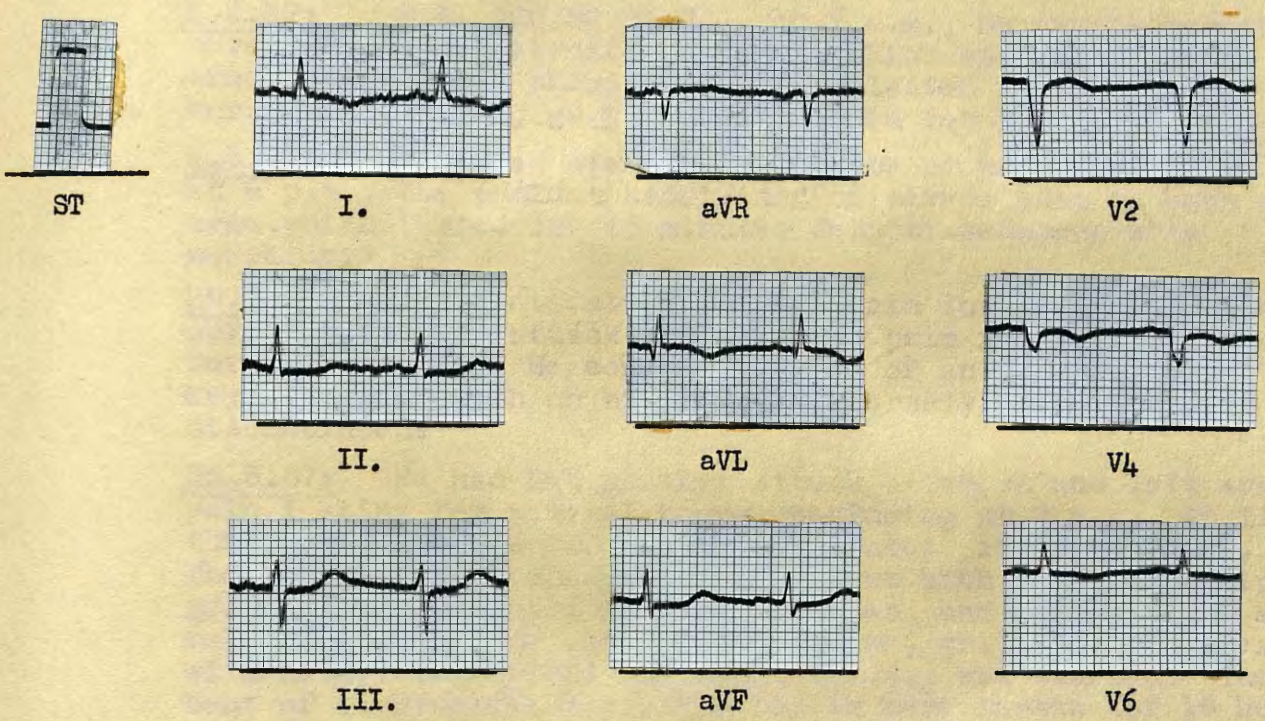


ST I. aVR V2

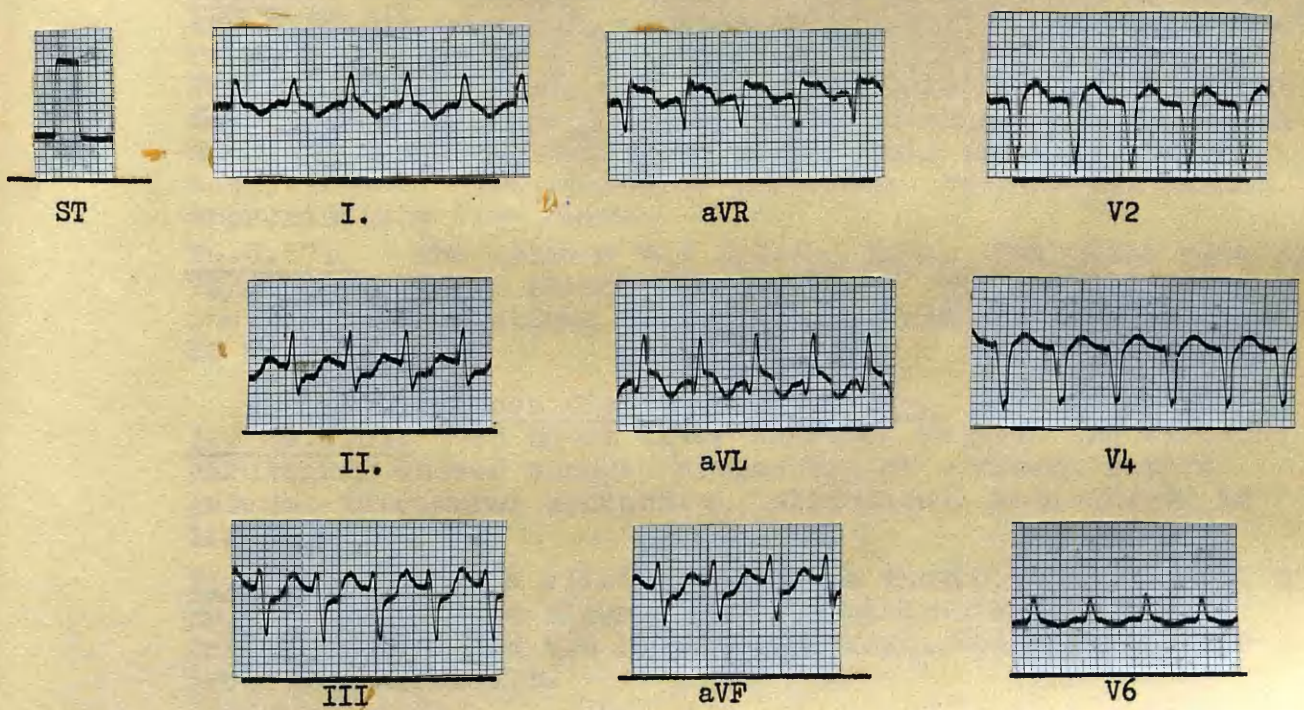
II. aVL V4

III aVF V6

ELECTROCARDIOGRAM CASE NO. 25 (8)



ELECTROCARDIOGRAM CASE NO. 25 (9)



30.4.57: B.P. 120/80 mm.Hg. The patient had another attack of angina pectoris which responded to trinitrin.

1.5.57: B.P. 120/80 mm.Hg. At 7 a.m., he complained of severe gripping retrosternal pain, which spread down both arms and into the throat, and which lasted for one hour. Morphine sulphate, gr.$\frac{1}{2}$., was required for its relief.

8.5.57: There had been no recurrence of pain for a week when, at 9 p.m., the patient complained of severe pain in both upper arms, which lasted for 15 minutes despite sedation with morphine.

25.5.57: The patient had had no pain for 17 days when he suffered another attack of "numbing" pain in both arms lasting for 30 minutes. He complained also of an irritating erythematosis rash on his body and mersalyl therapy was discontinued.

30.5.57: He had had another attack of chest and left arm pain lasting for several hours, beginning at 2 a.m. At 11 a.m., the pulse rate was 160 beats per minute; it was regular. The tachycardia responded to treatment with quinidine sulphate, grs.30., given orally in divided doses, and he was given a maintenance dose of quinidine sulphate, gr. 3 t.i.d. Treatment with methyl thiouracil 200 mgm., t.i.d., was started. The bout of tachycardia was estimated to have lasted for 16 hours.

By 10.6.57., the patient had been symptom-free and was allowed to sit in a chair and, by 17.6.57., he had had short walks in the ward and was symptom-free. X-Ray of his chest showed the size and shape of the heart to be within normal limits.

22.6.57: The patient complained of sudden onset of palpitation and dyspnoea at 3 a.m. When examined at 9 a.m., the pulse rate was 160 beats per minute and the rhythm was regular. The tachycardia again responded to quinidine treatment. It was felt that the prospect of his early discharge from hospital had excited the patient and precipitated the attack of tachycardia. The attack of paroxysmal tachycardia lasted approximately five hours.

24.6.57: The patient was allowed home. The pulse rate was 70/minute and the rhythm was regular. The patient was instructed to continue a maintenance dose of methyl thiouracil 50 mgm. daily.

Electrocardiographic Findings.

I. 20.3.57: (3 hours after onset of pain). The electrocardiogram showed changes diagnostic of a recent antero lateral intramural myocardial infarction. Note Q wave in lead a V L.

II. 26.3.57: The electrocardiogram showed changes which were suggestive but not diagnostic of septal extension of the infarction. Lead V.6 had been defaced, which made interpretation difficult.

/4

III. 5.4.57: The electrocardiogram showed changes consistent with the diagnosis of an acute antero septal intramural infarction. On review of the tracings, it was considered that this infarction had occurred before electrocardiogram "II" was taken.

IV. 15.4.57: The electrocardiogram showed partial reversion of the septal ST-T changes to the iso-electric line.

V. 26.4.57: The electrocardiogram showed changes diagnostic of an acute transmural antero septal myocardial infarction of fair extent.

VI. 1.5.57: The electrocardiogram showed sequential changes confirming the presence of the acute antero septal myocardial infarction noted in electrocardiogram "V".

VII. 30.5.57: The electrocardiogram showed supraventricular tachycardia, the heart rate being 210 - 220 / minute. Widespread ST-T deviations, accentuated from previous tracing, were present.

VIII. 5.6.57: The electrocardiogram showed reversion to normal rhythm. This tracing resembled that of "VI".

IX. 22.6.57: The electrocardiogram again showed supraventricular tachycardia (heart rate 200/min.) The widespread ST-T deviations previously noted in electrocardiogram "VII" had recurred.

Serial Serum Transaminase Activity(Units/ml/min.)

Time After Onset of Chest Pain on 20.3.57 at 6 pm.

Hours.	2	15	39	63
Units.	25	55	19	35

Time After Onset of Chest Pain on 24.3.57 at 6 a.m.

Hours.	12	36	60	84
Units.	55	80	43	30

Time After Onset of Chest Pain on 3.4.57 at 8.30 pm.

Hours.	13	27	51
Units.	16	19	20

Time After Onset of Chest Pain on 10.4.57 at 1 p.m.

Hours.	8	20	44	68
Units.	31	42	31	24

/5

Serial Serum Transaminase Activity (ctd.)

Time After Onset of Chest Pain on 25.4.57 at 7 p.m.

Hours.	12	36	84	108	132
Units.	100	116	80	49	30

Time After Onset of Chest Pain on 1.5.57 at 7 a.m.

Hours.	2	26	50	98
Units.	30	35	25	23

Time After Onset of Chest Pain and Tachycardia on 30.5.57 @ 2 am.

Hours.	7	31	54	78
Units.	42	80	35	25

Time After Onset of Tachycardia on 22.6.57 at 3 a.m.

Hours.	6	30	54
Units.	28	48	25

Temperature Record.

The temperature was 99.6°F 24 hours after chest pain on 20.3.57. Temperature was normal until 26.4.57 when a level of 100.2°F was recorded.

Thereafter, the temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren).

Time After Clinical Onset of Chest Pain on 20.3.57 at 6 p.m.

Days.	5	11
mm/1st.hour.	4	6

/6

Erythrocyte Sedimentation Rate (Westergren) (ctd).

Time After Onset of Chest Pain on 24.3.57 at 6 a.m.

Days.	7	14
mm/lst hr.	6	2

Time After Onset of Chest Pain on 3.4.57 at 8.30 pm.

Days.	5	12
mm/lst.hr	2	3

Time After Onset of Chest Pain on 10.4.57 at 1 p.m.

Days.	5	16
mm/lst hr.	3	7

Time After Onset of Chest Pain on 25.4.57 at 7 p.m.

Days.	1	5	11	17	24
mm/lst. hour.	7	30	10	6	3

Time After Onset of Chest Pain and Tachycardia on 30.5.57 @ 2 a.m

Days.	11
mm/lst.hr.	2

COMMENT:

The patient was considered to have suffered acute myocardial infarctions on 20.3.57 (25a) and on 24.3.57 (25b) and on 25.4.57 (25c).

In the first attack, (25a), the history and clinical findings were very suggestive of a poor risk myocardial infarction and the electrocardiogram was diagnostic of intramural myocardial infarction. Pyrexia was present but there was no evidence of peripheral vascular failure. Serum transaminase activity reached high levels 15 hours after the onset, while the E.S.R. was within normal limits five days after the onset of the illness. The transaminase assay was not considered to have contributed to the diagnosis.

In the second attack of myocardial infarction (25b) the history and clinical findings were suggestive of a poor risk myocardial infarction. Serial electrocardiograms confirmed the presence of a second intramural myocardial infarction. There was no pyrexia or evidence of peripheral vascular failure and the E.S.R. remained within normal limits. Serum transaminase activity, however, quickly rose to high levels 12 hours after the onset and the assay was considered to have provided early and valuable evidence of myocardial infarction, the first electrocardiogram, taken 2 days after the onset of the illness, not being diagnostic of acute myocardial infarction though suggestive of it.

In the third attack of myocardial infarction (25c), the history and clinical findings were typical of poor risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction. Pyrexia and minimal peripheral vascular failure were present. The E.S.R. was normal 24 hours after the onset of the illness. The serum transaminase activity rose to high levels 12 hours after the onset of the illness, but the assay was not considered to have contributed much to the diagnosis.

Attacks of angina pectoris at rest were also observed on 3.4.57 (25d) on 10.4.57 (25e) and on 1.5.57 (25f).

In the first attack, of angina pectoris (25d)., severe and typical anginal pain, which required morphine sulphate for its relief and which recurred over a period of 8½ hours, did not cause any deviation from normal in serum transaminase activity. The electrocardiogram following this attack showed the sequential changes of a previous and recent intramural myocardial infarction without evidence of fresh infarction. There was no pyrexia or sequential rise in the E.S.R. or evidence of peripheral vascular failure but signs of congestive cardiac failure appeared.

In the second attack of angina pectoris (25e) severe and repeated attacks of typical angina pectoris at rest, which were associated with dyspnoea at rest and which required morphine sulphate for their relief, were found to be associated with a rise in serum transaminase activity to borderline levels

/8

/levels 20 hours after the onset of the attacks. The electrocardiogram, five days following the attacks, showed no evidence of fresh myocardial infarction, but showed restoration of previous ST-T changes to the isoelectric line. There was no pyrexia or evidence of peripheral vascular failure although, following the onset of the attacks, signs of congestive cardiac failure reappeared.

In the third attack of angina pectoris at rest (25f)., severe and typical anginal pain lasted for one hour and required morphine sulphate for its relief. There was no pyrexia or evidence of peripheral vascular failure and serum transaminase activity remained normal following this attack. The electrocardiogram showed no evidence of a fresh myocardial infarction, but showed the sequential changes of previous and recent transmural myocardial infarctions.

Attacks of supraventricular tachycardia were studied on 30.5.57 (25g) and on 22.6.57 (25h).

In the first attack of supraventricular tachycardia (25g) the paroxysmal arrhythmia, which lasted for 16 hours, was accompanied by severe anginal pain lasting for several hours. The electrocardiogram confirmed the presence of supraventricular tachycardia and showed widespread ST-T deviations but no evidence of fresh myocardial infarction. There was no pyrexia or evidence of peripheral vascular failure and the E.S.R., 11 days following the onset of the arrhythmia, was normal. Serum transaminase activity, however, rose to high levels seven hours following the onset of the attack.

In the second attack of supraventricular tachycardia, (25h)., anginal pain was not a feature. The patient became dyspnoeic during the attack and complained of palpitations. The paroxysmal arrhythmia lasted for five hours and its presence was confirmed by electrocardiogram. There was no electrocardiographic evidence of fresh myocardial infarction. There was no pyrexia or evidence of peripheral vascular failure following this attack. The serum transaminase activity, however, rose to borderline levels 30 hours following the onset of the arrhythmia.

CASE NO. 26.

History of Present Illness.

A male, aged 55 years, a foreman plater, was admitted to hospital on the 8th April, 1957, complaining of retrosternal pain on exertion. On the morning of the 26th March, 1957, the patient was aware of a tightness felt across his chest and in the afternoon, when walking, he developed a severe retrosternal pain of constricting character which lasted fifteen minutes after resting. The feeling of praecordial oppression had been continuously present since this attack, the severe central chest pain having recurred on several occasions. On March 30th., 1957, he had had two attacks of angina pectoris during exertion; the first attack had come on whilst he was walking and had settled quickly in about one minute when he rested; the second attack occurred after climbing up and down a 60-ft. ladder and lasted for fifteen minutes. On April 1st., 1957, the retrosternal pain came on whilst the patient was walking. It was very severe and lasted for one hour. On the same evening he suffered a similar attack of pain when at rest in bed, which lasted for ten minutes. On the 8th April, 1957, the patient complained of an attack of anginal pain at 8 a.m., which lasted for ten minutes and which had occurred at rest, and he was admitted to hospital.

Clinical Findings on Admission.

The patient was a middle-aged man of rubicund appearance. There was no evidence of shock.

Cardiovascular System: B.P. 190/110 mm.Hg. The pulse was regular in rate (64/minute) and rhythm. The apex beat was palpable ½" within the mid-clavicular line and the heart sounds were pure and of good quality. No abnormality was found on full clinical examination of other systems.

Treatment and Progress.

The patient did not require narcotic or sedative drugs on admission.

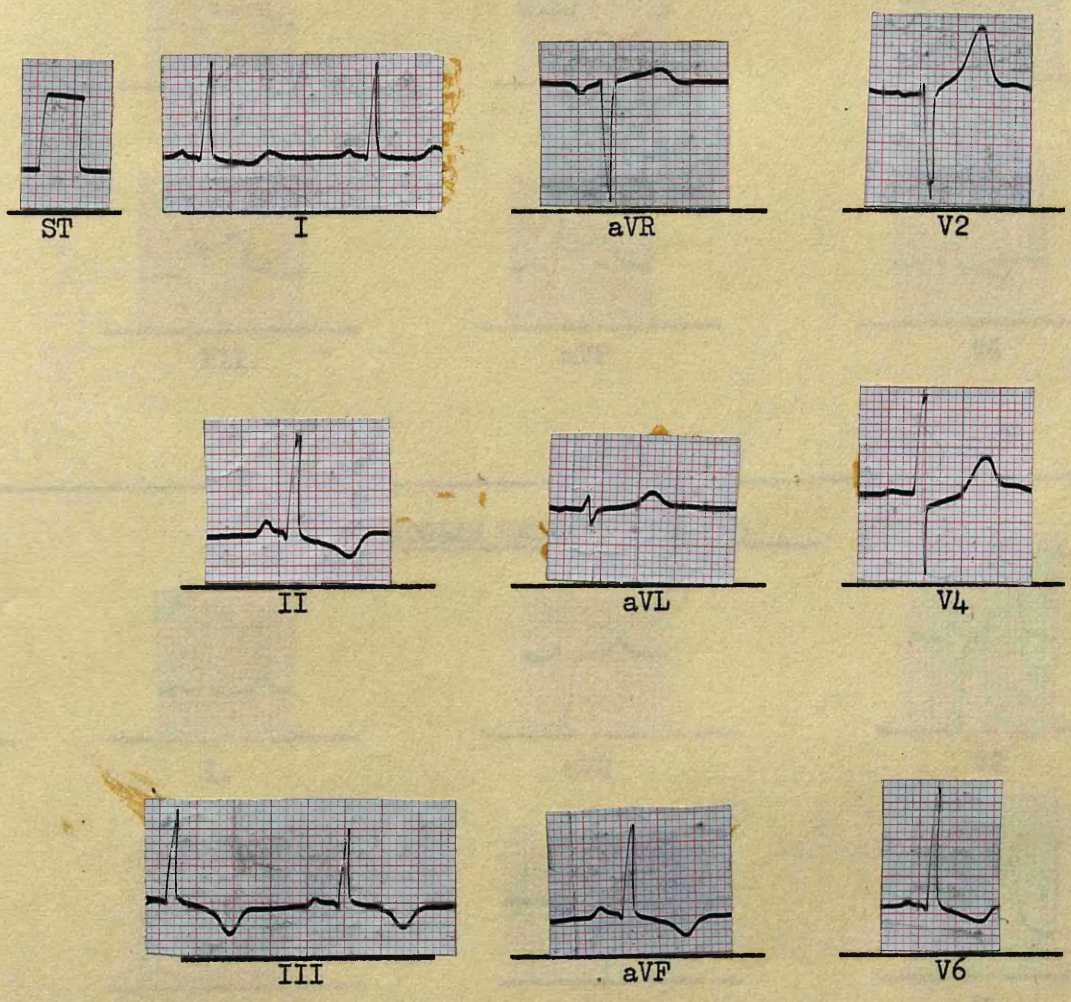
9.4.57: B.P. 160/100 mm.Hg. There had been no recurrence of pain and the patient's general condition was good.

13.4.57: B.P. 165/95 mm.Hg. He had had no symptoms and was well.

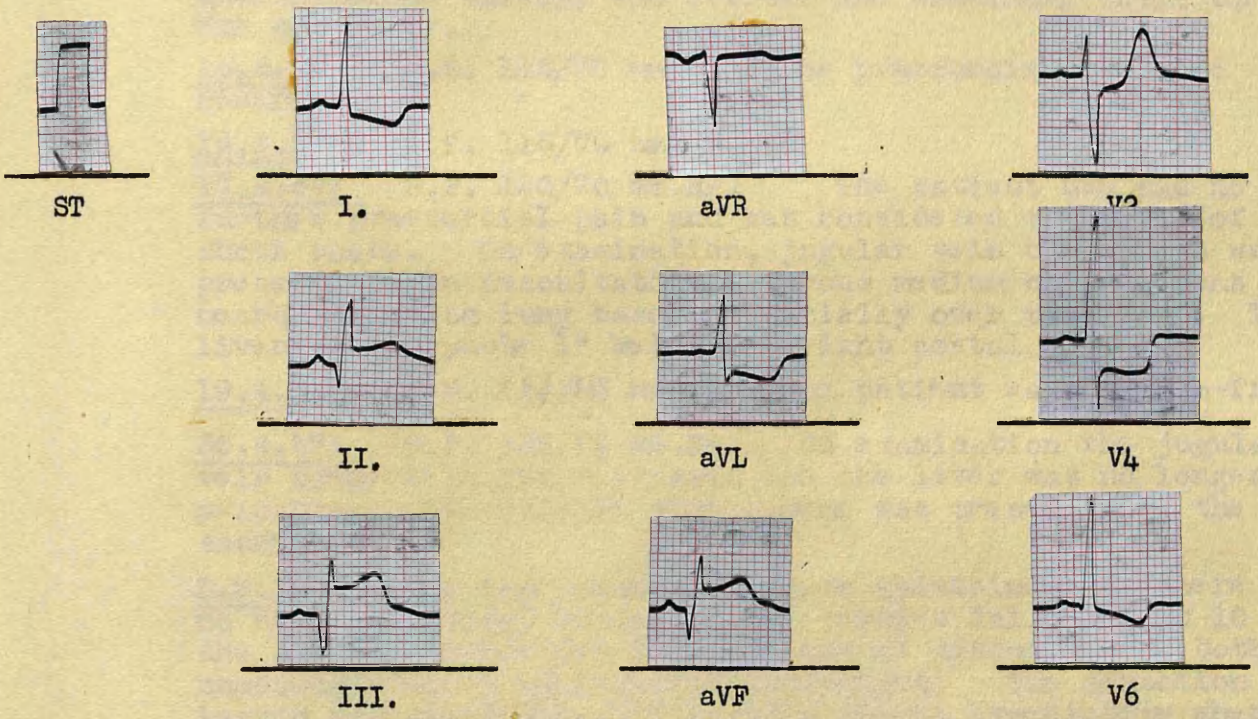
14.4.57: At 2.45 a.m., he awoke complaining of severe crushing retrosternal pain which was referred into his left shoulder. On examination, he was pale; he was sweating profusely and was in obvious distress. His B.P. was 130/80 mm.Hg. The pulse was rapid (120/minute) but regular in rhythm. The heart sounds were rapid and pure but of poor quality. The patient was given several intramuscular injections of Omnopon gr.1/3., and eventually the pain was

/2

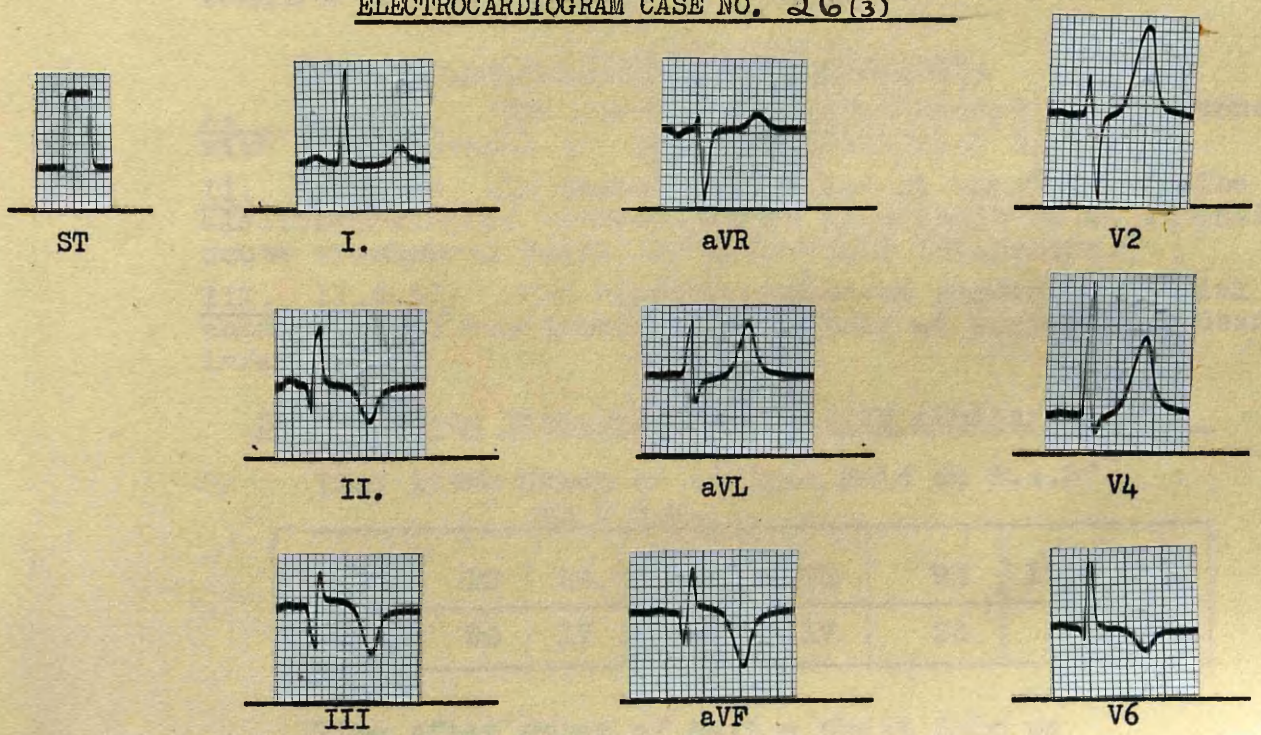
ELECTROCARDIOGRAM CASE NO. 26 (1)



ELECTROCARDIOGRAM CASE NO. 26(2)



ELECTROCARDIOGRAM CASE NO. 26(3)



/was much alleviated. He was aware, however, of discomfort in the praecordium and in both upper arms for 24 hours. Anticoagulant therapy was started and continued until the 7th May, 1957.

15.4.57: B.P. 115/70 mm.Hg. The praecordial pain had cleared.

16.4.57: B.P. 115/70 mm.Hg.

17.4.57: B.P. 120/70 mm.Hg. The patient had had no further praecordial pain and was considered to be out of the shock phase. On examination, jugular vein congestion was present. On auscultation numerous medium crepitations were heard over both lung bases, especially over the right. The liver was palpable 1" below the right costal margin.

19.4.57: B.P. 140/80 mm.Hg. The patient was symptom-free.

30.4.57: B.P. 130/75 mm.Hg. On examination the jugular vein congestion had regressed and the liver was no longer palpable. Very slight skin oedema was present over the sacrum.

2.5.57: The improvement had been maintained and there were no remaining signs of congestive cardiac failure. At 10 a.m., the patient complained of a feeling of discomfort in both arms, unaccompanied by praecordial discomfort. The sensation lasted for 10 minutes but cleared almost immediately when trinitrin gr. 1/200 was taken sublingually.

30.5.57: B.P. 140/75 mm.Hg. The patient had been ambulant without symptoms. He was considered to be fit to complete his convalescence at home.

Electrocardiographic Findings.

I. 8.4.57: The electrocardiogram showed changes consistent with the diagnosis of posterior myocardial ischaemia.

II. 15.4.57: (18 hours after onset of chest pain). The electrocardiogram showed changes diagnostic of an extensive, acute transmural posterior myocardial infarction.

III. 17.5.57: The electrocardiogram showed sequential changes which confirmed the diagnosis of posterior myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Anginal Pain on 8.4.57 at 8 a.m.

Hours.	12	24	48	72	96	120
Units.	20	17	16	17	23	27

Time After Onset of Severe Chest Pain on 14.4.57 at 2.45 a.m.

/ctd.....3

/ctd.
Serial Serum Transaminase Activity.

Time After Onset of Severe Chest Pain on 14.4.57 at 2.45 a.m.

Hours.	8	30	54	78	102	126	168
Units.	Haem.	193	139	94	66	37	30

Temperature Record.

The body temperature was 100.2°F., 24 hours after severe chest pain on 14.4.57 and a low-grade pyrexia 98° - 99.4°F., was recorded for three days.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Severe Chest Pain on 14.4.57.

	30 hrs.	14 days	22 days	28 days	35 days	42 days.
mm/1st hr.	19	45	32	42	34	26

Results of Bromsulphalein Tests:-

On 12.4.57 (4 days after onset of anginal pain) - No retention of dye.

On 16.4.57 (30 hours after onset of acute myocardial infarction) - 24% retention of dye.

On 21.4.57 (7 days after onset of acute myocardial infarction) - 13% retention of dye.

COMMENT:

On admission, myocardial infarction was suspected because of severe and recurrent attacks of angina pectoris but the electrocardiogram showed only evidence of myocardial ischaemia. The blood pressure was well maintained and there was no evidence of peripheral vascular failure or pyrexia. The serum transaminase activity remained normal following the attack of angina pectoris at rest which the patient suffered before admission to hospital. The patient was considered to have suffered a myocardial infarction on 14.4.57. The history and clinical findings were typical of poor risk myocardial infarction 18 hours after the onset of the illness. Pyrexia and a minimal to moderate degree of shock were present. The E.S.R. was abnormally high 30 hours following the onset of the illness and the serum transaminase rose to high diagnostic levels 30 hours after the onset of the illness. The assay was not considered to have contributed to the diagnosis.

Following the attack of myocardial infarction the patient developed signs of congestive cardiac failure.

This case illustrates well normal serum transaminase levels following an attack of myocardial ischaemia and grossly elevated levels following acute myocardial infarction.

CASE NO. 27.

History of Present Illness.

A male, aged 48 years, a machine-shop foreman, was admitted to hospital on the 28th March, 1957, complaining of interscapular pain. He had been awakened at 2 a.m., on the 28th March, 1957, by a severe gripping pain felt in the interscapular region, which radiated down the lateral aspect of the left upper arm and into the retrosternal region of the chest. The pain was agonising and made him sweat profusely. He was admitted to hospital at 11 a.m. on the 28th March, 1957.

History of Past Illnesses.

In November, 1956, the patient had experienced a similar pain on exertion which, although not of severe degree, had lasted for fifteen minutes. Since then, he had noted occasional gripping pain in the upper arms and across the chest when walking which, if he continued to walk, faded away.

Clinical Findings on Admission.

The patient was pale, restless, apprehensive and sweating. He complained of gripping interscapular pain.

Cardiovascular System: B.P. 100/80 mm.Hg. The pulse was regular in rate (140/minute) and rhythm. The apex beat could not be felt. The heart sounds were rapid, pure, but faint.

Respiratory System: On auscultation, occasional rhonchi were heard over both lung bases. No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

On admission, Omnopon gr.1/3, intramuscularly, was given with alleviation of pain. Anticoagulant therapy was started and continued until the 7th May, 1957.

On the 29th March, 1957, B.P. was 80/50 mm.Hg. The patient was shocked, heart sounds were faint and jugular venous congestion was noted. On the 2nd April, 1957, B.P. was 95/70 mm.Hg. The shock phase had passed but tachycardia and hypotension were still present.

On the 5th April, 1957, B.P. was 80/60 mm.Hg. The patient had no complaints. Congestion of the jugular veins was no longer present.

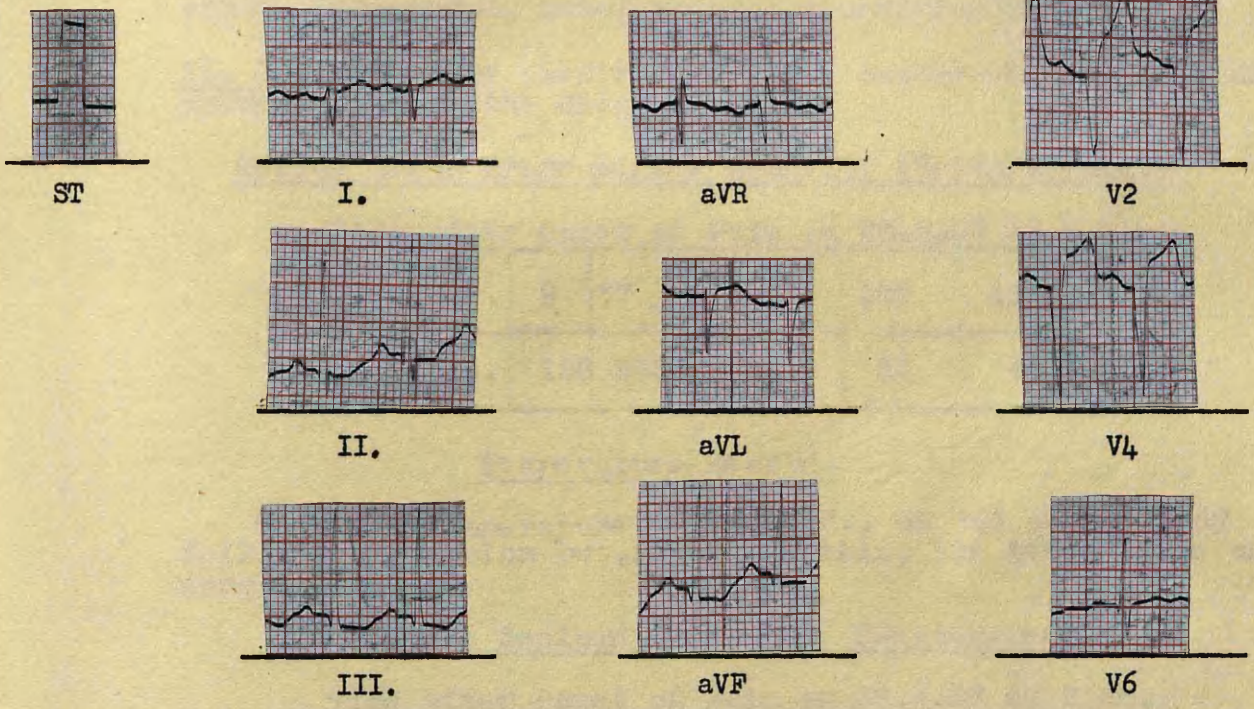
On the 6th May, 1957, B.P. was 100/70 mm.Hg., and the patient was allowed to sit in a chair for the first time. Convalescence was slow and hypotension marked for five weeks following the episode of infarction.

On the 27th May, 1957, B.P. was 100/60 mm.Hg. The patient had been ambulant and he was allowed to go home to complete his convalescence.

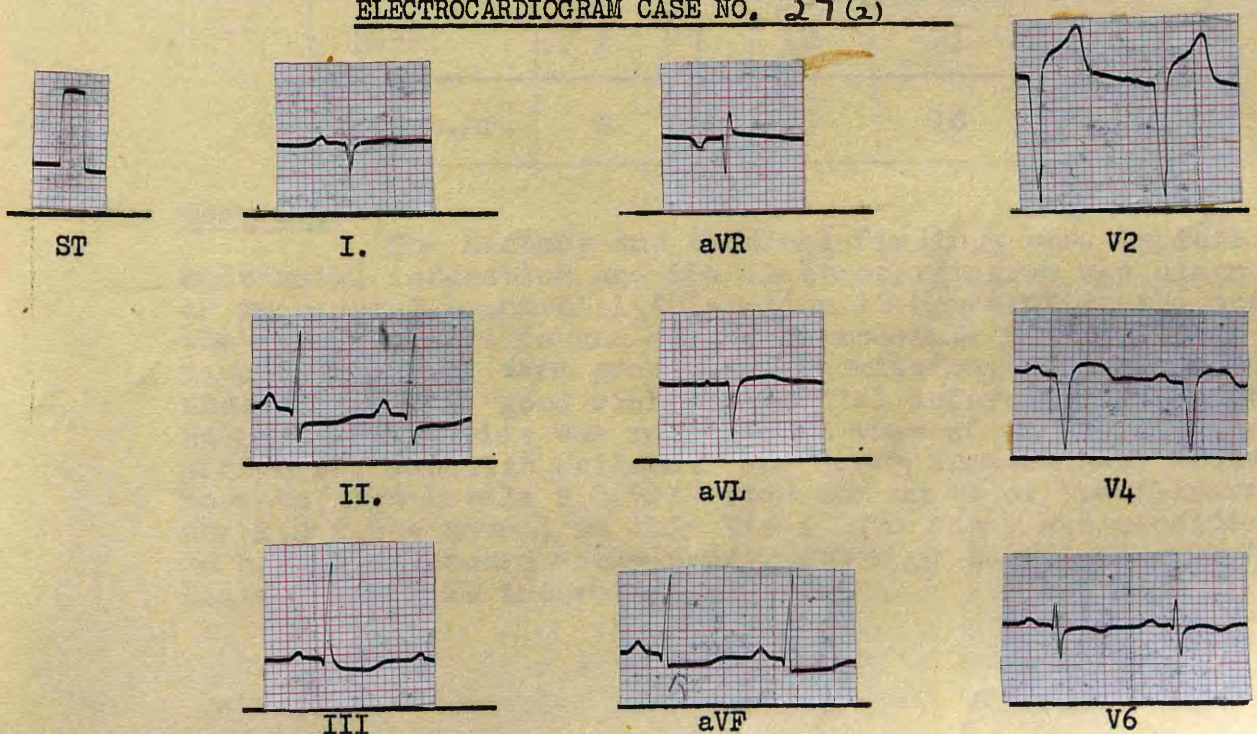
Electrocardiographic Findings.

I. 28.3.57: (12 hours after onset of chest pain.) The electrocardiogram showed changes diagnostic of an extensive, /2

ELECTROCARDIOGRAM CASE NO. 27 (1)



ELECTROCARDIOGRAM CASE NO. 27 (2)



acute, transmural, antero-septal myocardial infarction.

II. 3.4.57: The electrocardiogram showed sequential changes which confirmed the diagnosis.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Pain on 28.3.57 at 2 a.m.

Hours.	9	37	59	84	107	134
Units.	128	235	146	113	57	40

Temperature Record.

The body temperature was 99.4°F., on 2nd and 3rd day following admission but, following this, the temperature was normal.

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Pain on 28.3.57 at 2 am.

Hours.	9				
mm/1st.hr.	4				
Days.	2	7	14	21	33
mm/1st.hr.	9	16	5	10	4

Comment;

The history and clinical findings were typical of myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction 12 hours after the onset of the illness. Pyrexia and minimal - moderate peripheral vascular failure were present. On admission, the patient was thought to be a "good risk" myocardial infarction, but within 24 hours, this view was modified in view of increasing marked peripheral vascular failure. The serum transaminase activity rose to high levels 9 hours after the onset of the illness and the E.S.R. was normal at this time. The assay was considered to have contributed early confirmation of the diagnosis of acute myocardial infarction.

CASE NO. 28.

History of Present Illness.

A male, aged 78 years, a retired physician, was admitted to hospital on the 17th April, 1957, having had two attacks of chest pain since the 13th April, 1957. On the 13th April, 1957, the patient complained of sudden gripping retrosternal pain which caused him to faint. He recovered consciousness in about a minute but the pain lasted for ten minutes. He rested in bed following this attack but, on the 14th instant, he again complained of retrosternal pain, constrictive in character, which lasted for five minutes. He had had no further pain but was admitted for hospital care and anticoagulant therapy.

History of Past Illnesses.

The patient had suffered an attack of anginal pain on severe exertion 32 years before and he had lived carefully since that time. For ten years he had been subject to chronic bronchitis, worse in the winters, and he had a cough productive of grey-white sputum.

Clinical Findings on Admission.

The patient was an elderly man who was dyspnoeic at rest. Examination of Cardiovascular System: revealed B.P. 120/70 mm.Hg. The pulse was regular in rate (82/minute) and rhythm. The heart was enlarged; the left heart border, as determined by percussion, was 1" outwith the mid-clavicular line. There was a soft systolic murmur present at the mitral area, but the sounds were faint.

Respiratory System: The percussion note over both lung bases was diminished and, on auscultation, numerous medium crepitations and rhonchi were heard over both lung fields.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

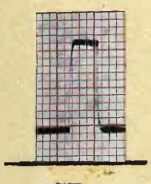
On admission, anticoagulant therapy was started and continued until the 23rd June, 1957, and the patient was given a course of intramuscular distaquaine penicillin, (600,000 I.U. daily), for the week following admission, because of chronic bronchial infection. He had no further attacks of pain but convalescence was prolonged because of recrudescences of chronic bronchitis. On the 22nd May, 1957, he was allowed to sit up in a chair and, eventually, was ambulant without symptoms. He was allowed home to complete his convalescence on the 1st.August, 1957.

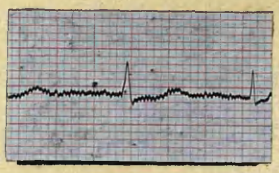
Electrocardiographic Findings.

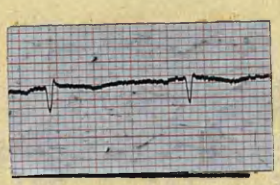
I. 14.4.57: (3 days before admission to hospital, and the day following severe chest pain on 13.4.57.) The electrocardiogram showed changes diagnostic of an acute transmural posterior myocardial infarction.

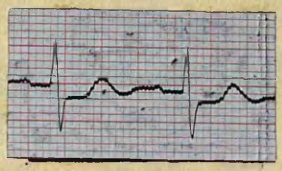
II. 3.7.57: /2

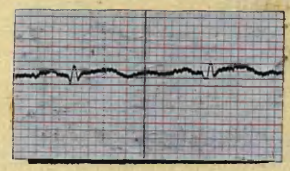
ELECTROCARDIOGRAM CASE NO. 28 (1)

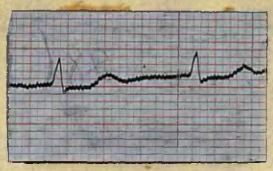

ST

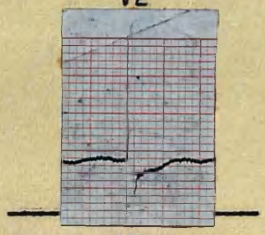

I.

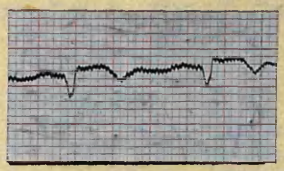

aVR

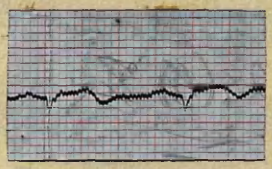

V2

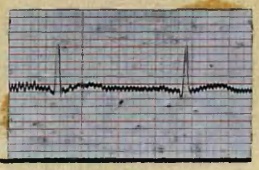

II.


aVL


V4

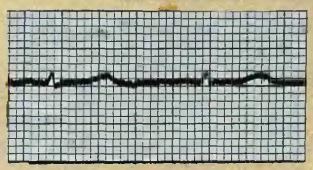

III.

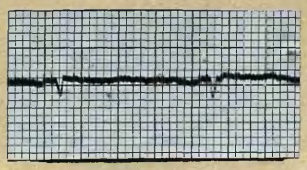

aVF

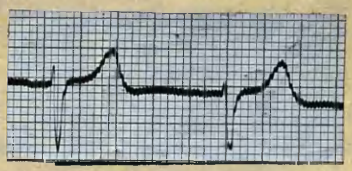

V6

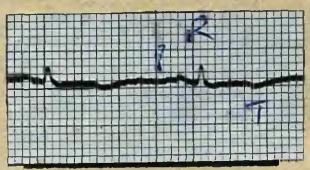
ELECTROCARDIOGRAM CASE NO. 28 (2)

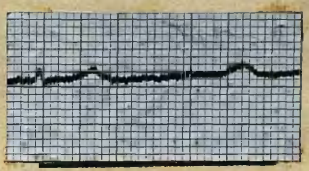

ST

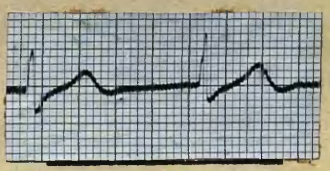

I.

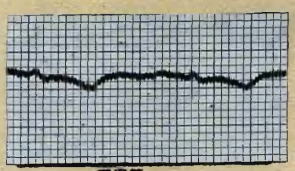

aVR

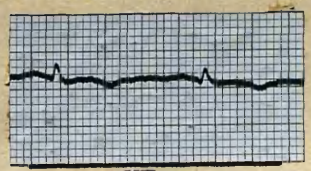

V2

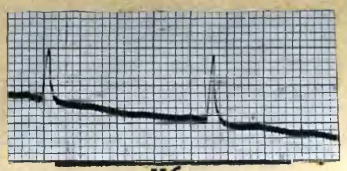

II.


aVL


V4


III


aVF


V6

II. 3.7.57: The electrocardiogram showed sequential changes which confirmed the diagnosis.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain on 13.4.57.

Hours.	120	144	168
Units.	57	45	36

Temperature Record.

The temperature was 99° - 100°F., for four days following admission but this pyrexia was considered to be due to a chest infection.

Erythrocyte Sedimentation Rate (Westergren.)

Time After Onset of Chest Pain on 13.4.57.						
Days.	5	12	17	26	33	40
mm/1st. hour.	60	32	40	25	26	40

COMMENT: The history and clinical findings were typical of acute myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction on the day of onset of the illness. The myocardial infarction was considered to be of "poor risk" type, because of the co-existence of acute or chronic bronchitis and emphysema and cardiomegaly. Pyrexia, ascribed to the presence of acute bronchitis, was noted but there was no evidence of peripheral vascular failure. Serum transaminase activity was found to be at low diagnostic levels, 5 days after the onset of illness, but the assay was not considered to have contributed to the diagnosis.

CASE NO. 29.

History of Present Illness.

A male, aged 55 years, a tobacconist, was admitted to hospital on the 4th May, 1957, having had a crushing pain in his chest at 10.30 p.m. On the 30th April, 1957, the patient had complained of a severe retrosternal pain, crushing in nature, which had radiated into the right upper arm. The pain came on when he was resting and lasted for three hours. He had never before experienced chest pain. He was confined to bed and, on the 4th May, 1957, at 10.30 p.m., he sat up in bed and experienced a similar attack of pain in the retrosternal region, which was referred into the right upper arm. This pain was not so severe as the first and lasted for thirty minutes. He was admitted to hospital at 11.30 p.m., on the 4th May, 1957.

There was no relevant past or social history.

Clinical Findings on Admission.

The patient was a well-built man, of good colour. He had no pain and was not shocked on admission.

Cardiovascular System: B.P. 100/70 mm.Hg. The pulse was regular in rate (88/minute) and rhythm. The apex beat could not be felt and the heart sounds were pure but distant. No abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Anticoagulant therapy was started after examination of the electrocardiogram and was continued for 28 days. The patient had no pain or dyspnoea following admission to hospital and he made uninterrupted progress. He was discharged from hospital on the 22nd June, 1957. At this time, his blood pressure was 140/80 mm.Hg., and no abnormality was present on clinical examination of the cardiovascular system.

Electrocardiographic Findings.

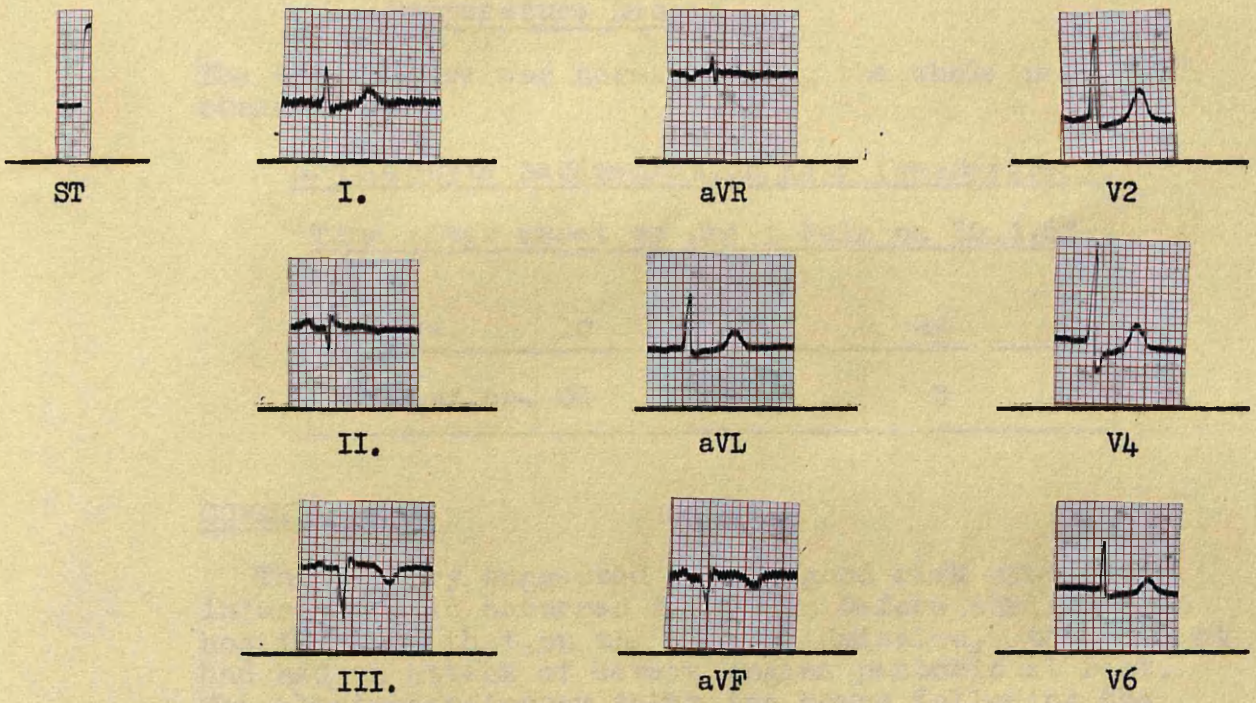
I. 5.5.57: (2 hours after onset of chest pain on 4.5.57). The electrocardiogram showed changes diagnostic of a fairly extensive acute transmural post-myocardial infarction.

II. 9.5.57: The electrocardiogram showed sequential changes which confirmed the previous diagnosis. There was no evidence of a fresh myocardial infarction.

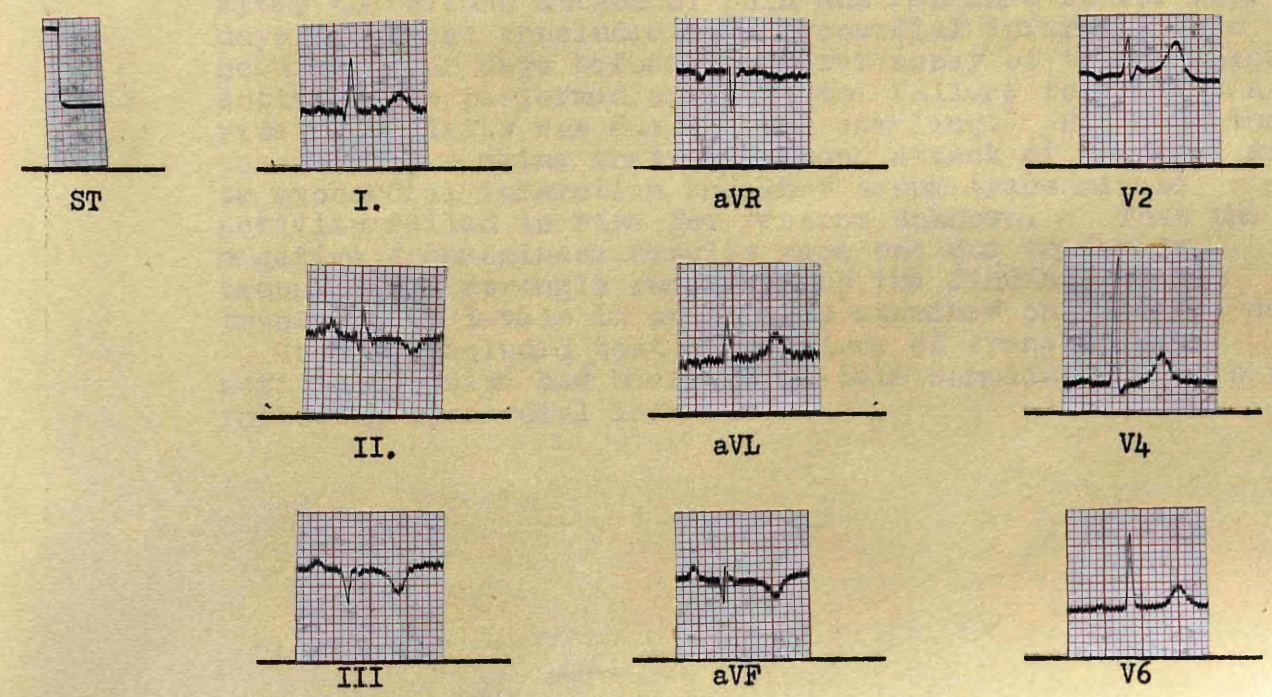
Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain on 4.5.57 at 10.30 p.m.					
Hours.	2	14	38	62	86
Units.	Haem.	34	23	20	22

ELECTROCARDIOGRAM CASE NO. 29 (1)



ELECTROCARDIOGRAM CASE NO. 29 (2)



Temperature Record.

The temperature was normal during the whole period of observation.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Chest Pain on 30.4.57.

Days.	10	17	24	
mm/1st.hr.	31	10	3	

COMMENT:

The history suggested that a good risk myocardial infarction had occurred four days before admission to hospital and that, on the day of admission, the patient had had an attack of severe angina pectoris at rest. The electrocardiogram, taken two hours following the second attack of pain and four days after the first, was diagnostic of transmural myocardial infarction. There was no pyrexia or evidence of peripheral vascular failure following admission to hospital.

Serum transaminase activity was normal two hours after the second attack of pain and remained so for four days. It was concluded that myocardial infarction had occurred four days before the first assay of transaminase activity was performed and that the failure to observe a rise in activity was due to poor sampling. However, the possibility remains that the second attack of pain was due to myocardial infarction and that serum transaminase activity failed to rise for reasons unknown. That the negative transaminase results were not due to faulty technique is strongly suggested by the finding of high transaminase levels in other sera examined on the same day.

It was concluded that the failure of transaminase activity to rise had been due to late sampling of the serum following myocardial infarction.

CASE NO. 30.

History of Present Illness.

A female, aged 74 years, a housewife, was admitted to hospital on the 15th February, 1957, complaining of retrosternal pain which had been present since the 6th instant. In 1948, the patient had collapsed whilst working, complaining of severe pain in the left side of her chest which was referred down her left arm. Following rest in bed she had complained, since that time, of pain in the left axilla and a feeling of tightness in the chest on climbing stairs. This sensation disappeared within a few minutes of her resting; she had no complaint of breathlessness. Since the 6th February, 1957, she had been conscious of a constant aching pain below the lower end of the sternum and a feeling of heaviness in both breasts; pain was also present in the inner aspects of both upper arms. The symptoms did not get worse after their onset but they were aggravated by slight exertion and she was subject occasionally to attacks of dyspnoea at night. For the same period she complained of continuous frontal headache and of a feeling of discomfort in both hypochondria, unrelated to meals. Her appetite was good and there were no other symptoms referable to the alimentary tract.

There was no relevant past or social history.

Clinical Findings on Admission.

The patient was a healthy looking, elderly woman. There was no evidence of shock or congestive cardiac failure and the pain was not severe.

Cardiovascular System: B.P. 110/55 mm.Hg. The pulse rate (82/minute) was irregular owing to the presence of occasional ventricular ectopic beats. The apex beat was not palpable or visible but, by percussion, the left border was determined as lying just outside the mid-clavicular line. The heart sounds were soft, but pure, and pericardial friction was not heard.

No abnormality was found on full clinical examination of other systems.

Treatment and Progress.

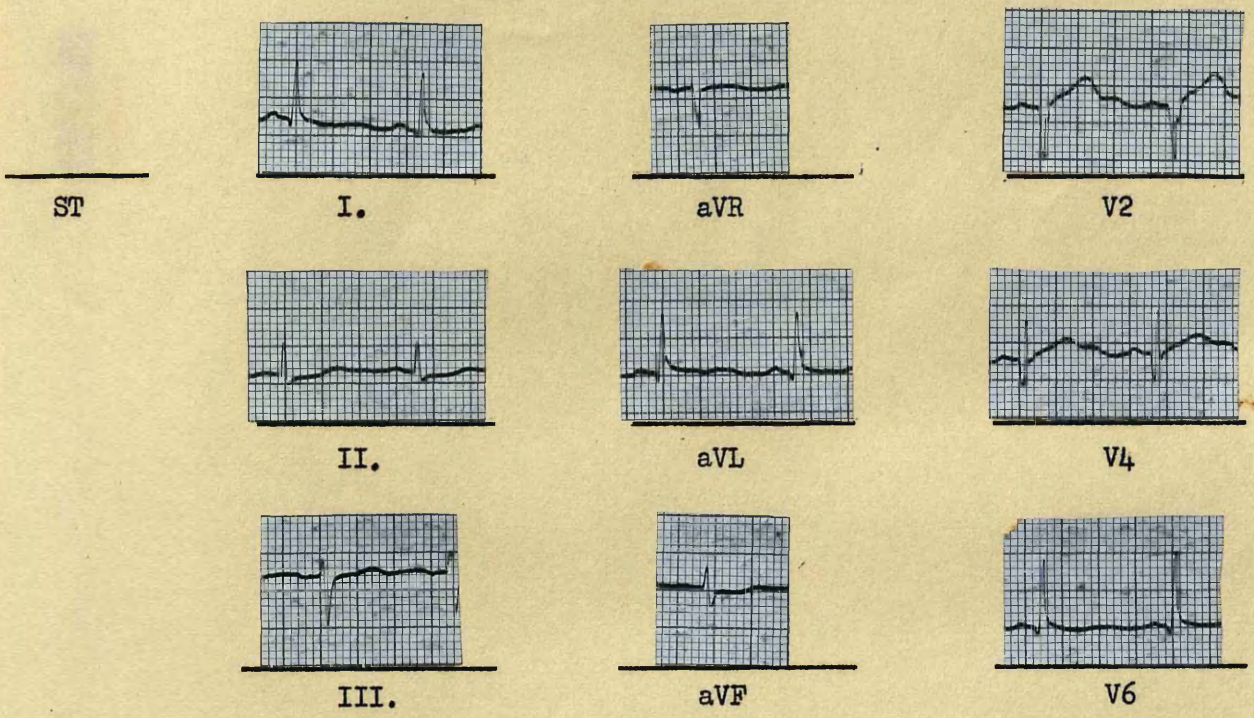
The slight pain of which the patient complained settled completely with rest in bed and she was symptom-free.

23.2.57: B.P. 110/60 mm.Hg. She suffered an attack of lower substernal pain whilst at rest. This pain lasted for thirty minutes but was quickly relieved by the administration of trinitrin, gr.1/150 sublingually.

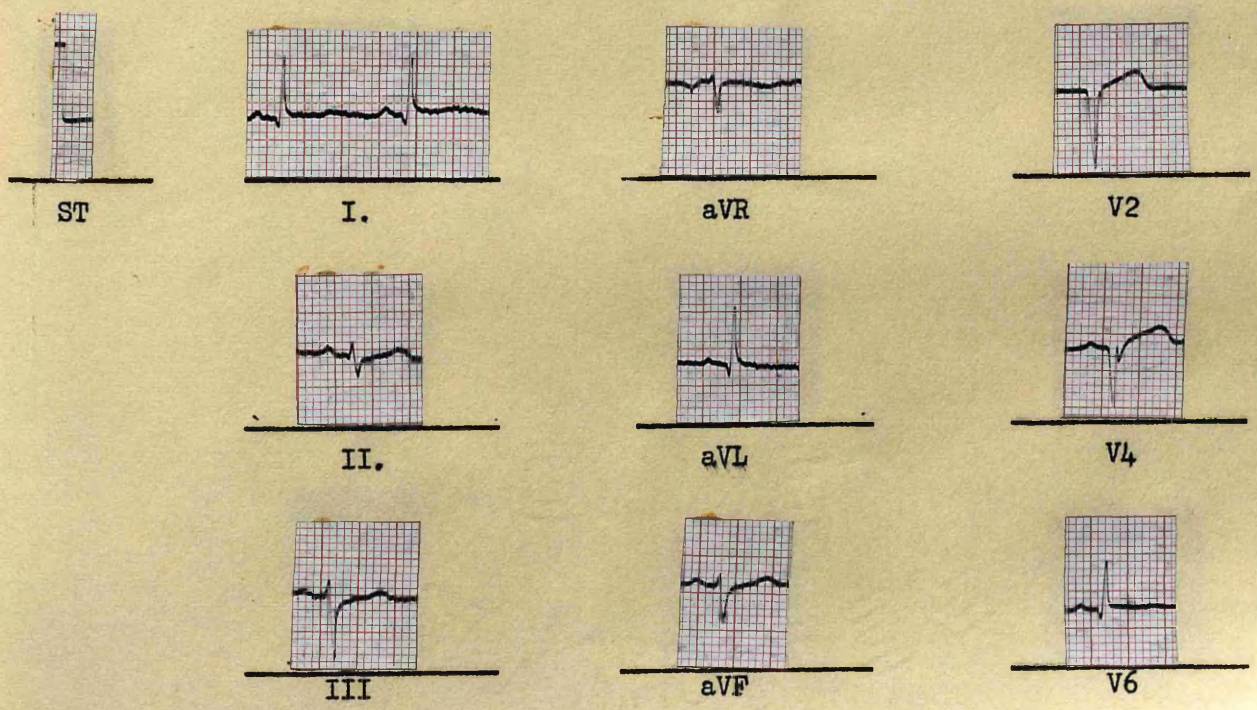
4.3.57: B.P. 140/75 mm.Hg. The patient had no further attacks of chest pain.

27.3.57: /2

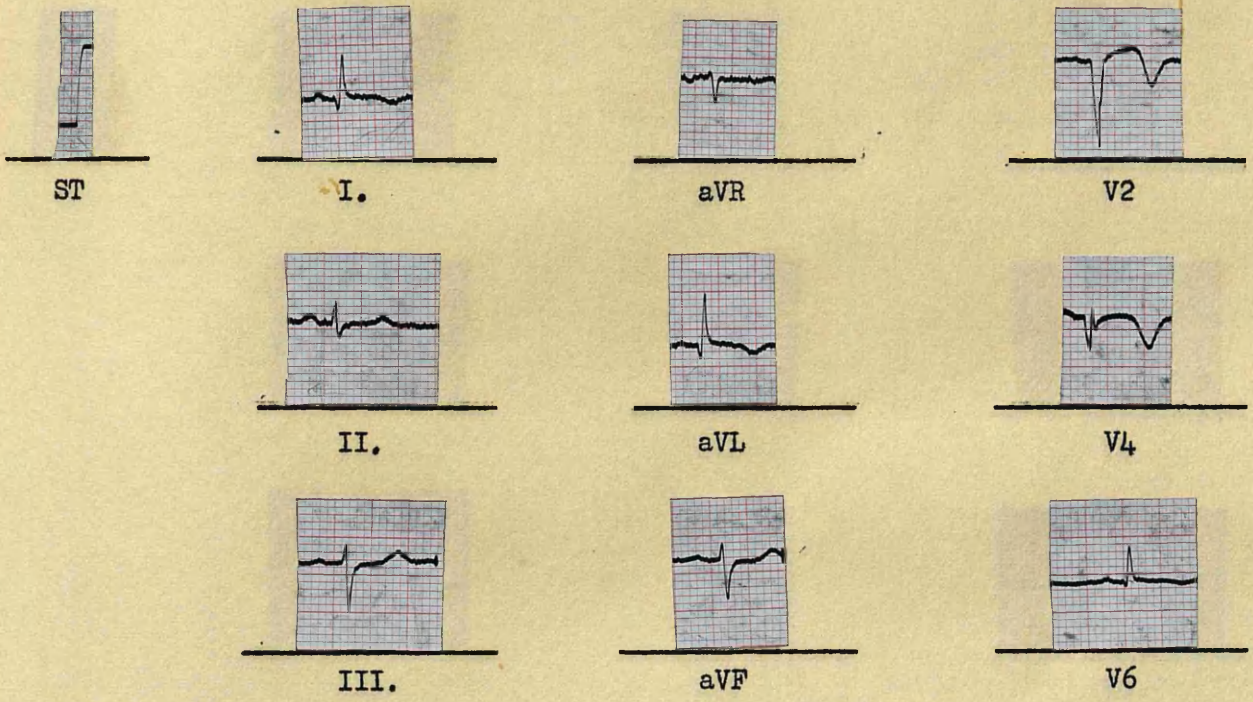
ELECTROCARDIOGRAM CASE NO. 30 (1)



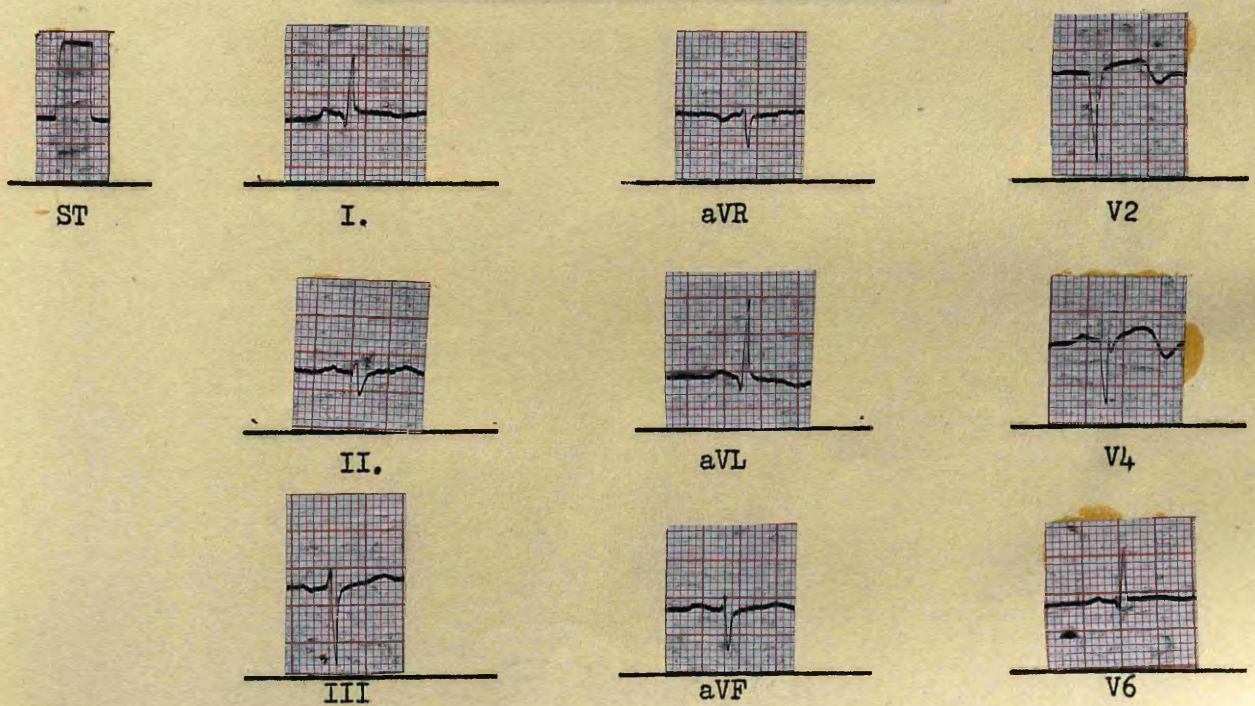
ELECTROCARDIOGRAM CASE NO. 30 (2)



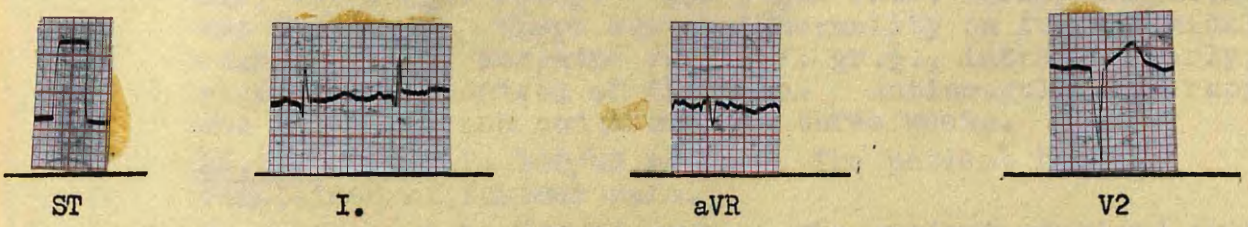
ELECTROCARDIOGRAM CASE NO. 30 (3)



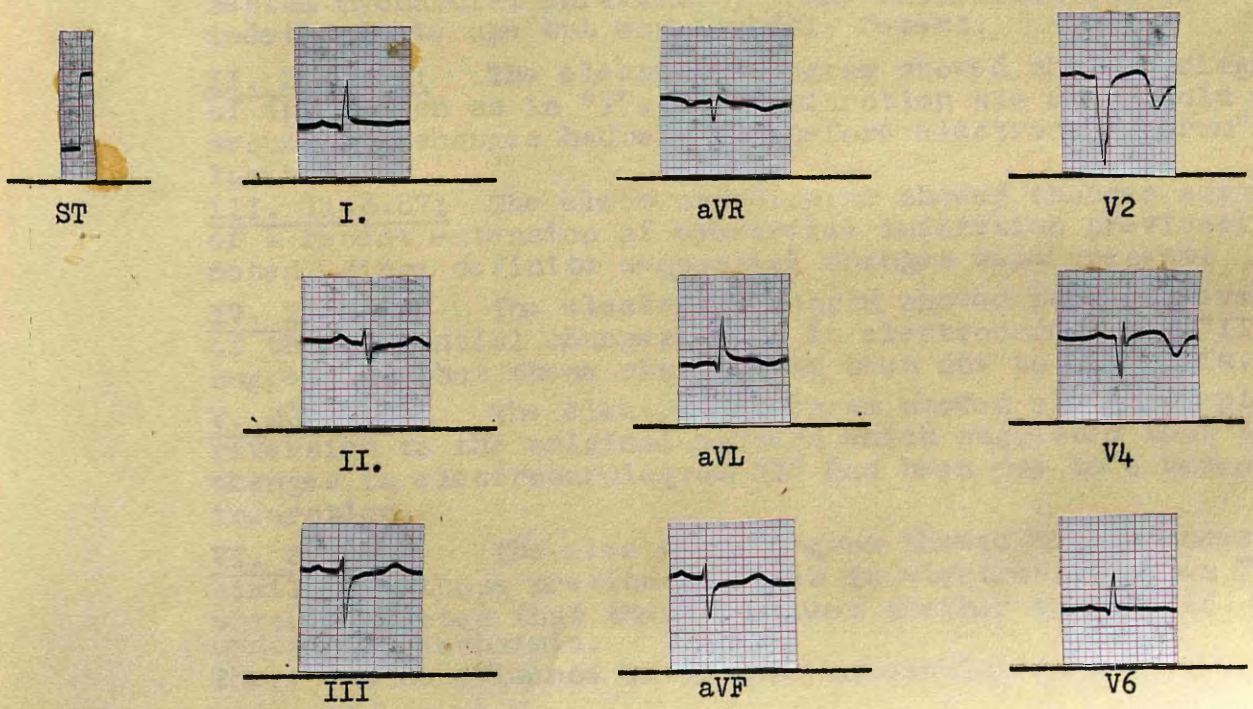
ELECTROCARDIOGRAM CASE NO. 30 (4)



ELECTROCARDIOGRAM CASE NO. 30 (5)



ELECTROCARDIOGRAM CASE NO. 30 (6)



27.3.57: She suffered an attack of sudden severe pain across the chest, referred into both upper arms, at 11.15 pm. B.P. was 120/70 mm.Hg. The pulse rate, during the attack, was 90/minute. There was no abnormality on full clinical examination. Morphine sulphate, gr.$\frac{1}{4}$., intramuscularly, was required for control of the pain. Anticoagulant therapy was commenced and continued for three weeks.

28.3.57: B.P. 100/65 mm.Hg. The patient had not complained of further pain.

29.3.57: B.P. 120/55 mm.Hg. The patient remained symptom-free.

2.4.57: B.P. 130/86 mm.Hg. The patient remained well.

23.4.57: B.P. 130/75 mm.Hg. The patient had been ambulant for eleven days without dyspnoea or pain.

26.4.57: X -Ray film of chest showed that the heart was centrally placed, slightly enlarged transversely and of hypertensive configuration. Atheromatous calcification of the wall of the aortic arch was present. A large oesophageal hiatus hernia was present.

27.4.57: The patient was keen to leave hospital and she was discharged on 27.4.57., which was disappointing since further investigation was obviously desirable in view of the finding of large hiatus hernia.

Electrocardiographic Findings.

I. 15.2.57: (9 days after onset of chest pain on 6.2.57). The electrocardiogram showed changes diagnostic of an antero septal myocardial infarction. The infarction was of indeterminate age but was probably recent.

II. 24.2.57: The electrocardiogram showed changes diagnostic of infarction as in "I". The infarction was either old or sequential changes hadoccurred before electrocardiogram"I"was taken.

III. 11.3.57: The electrocardiogram showed changes suggestive of a recent extension of myocardial infarction previously noted, since definite sequential changes were present.

IV. 27.3.57: The electrocardiogram showed partial reversion of the sequential changes noted in electrocardiogram "III" suggesting that these changes had been due to ischaemia.

V. 29.3.57: The electrocardiogram showed almost complete reversion to the original pattern which suggested that the changes in electrocardiogram "I" had been due to a recent infarction.

VI. 3.4.57: The electrocardiogram showed ST-T changes similar to those previously noted in electrocardiogram "III" which suggested that there had been another episode of myocardial ischaemia.

There was no evidence of a fresh myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain on 6.2.57.

Days.	9	10	11	12
Units.	29	33	30	19

Time After Onset of Chest Pain on 23.2.57.

Hours.	24	48
Units.	20	20

Time After Onset of Sudden Chest Pain on 27.3.57 at 11.15 p.m.

Hours.	¼	9½	33	48
Units.	16	35	19	23

Temperature Record.

The temperature was 99.6°F., on 17.2.57, but this was the only rise in temperature recorded.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Chest Pain on 6.2.57.

Days.	9	21	28
mm/1st.hour	14	17	8

Time After Onset of Sudden Chest Pain on 27.3.57 at 11.15 p.m.

Days.	7	14	21
mm/1st.hour.	48	13	9

COMMENT.

Serum transaminase activity was normal on repeated examination following two attacks of angina pectoris at rest.

The first attack of chest pain on 23.2.57 (30a) lasted for 30 minutes. The second attack on 27.3.57 (30b) was severe, requiring morphia for its relief but its exact duration was not recorded.

Interpretations of serial electrocardiograms were difficult. It was certain that a recent myocardial infarction had occurred but that no fresh infarction had occurred following the attacks of chest pain under discussion, the electrocardiogram showing the changes of myocardial ischaemia only.

Myocardial ischaemia, in this case, was probably related to the presence of a large hiatus hernia. The patient was re-admitted to hospital in September, 1957, and it was demonstrated that changes in the position and size of the hiatus hernia were related to attacks of angina pectoris at rest and to electrocardiographic changes of myocardial ischaemia. It was observed that, when the hernia was large and situated behind the heart, attacks of angina pectoris at rest and electrocardiographic changes of myocardial ischaemia occurred. When the hernia reduced in size, the electrocardiographic changes were no longer apparent and no attacks of angina pectoris occurred.

CASE NO. 31.

History of Present Illness.

A male, aged 58 years, a gardener, was admitted to hospital on the 17th March, 1957, complaining of severe retrosternal pain of five hours' duration. On the 16th March, 1957, at 11 p.m., he became aware of a sensation of tightness across the praecordium. This sensation became more marked and eventually was replaced by severe gripping retrosternal pain which did not radiate. It was very severe, causing him to sweat profusely and lasted for five hours. His family doctor delayed his admission to hospital because he considered him too shocked to tnansport him to hospital. His B.P. at this time was 90/40 mm.Hg.

There was no relevant past or social history.

Clinical Findings on Admission.

The patient was pale, apprehensive and sweating, and he was in a state of shock.

Cardiovascular System: B.P. 100/60 mm.Hg. The pulse was regular in rate (80/minute) and rhythm. The heart was not enlarged, the apex beat being palpable ½" within the mid-clavicular line in the fifth intercostal space. The heart sounds were pure and well heard. Proto diastolic gallop rhythm was present.

Treatment and Progress.

Praecordial pain, although less severe, was present on admission and responded to an intramuscular injection of Omnopon gr.1/3. Anticoagulant therapy was started on admission and continued until the 2nd May, 1957.

18.3.57: B.P. 90/50 mm.Hg. The patient was exhausted and pale, but restless. His condition had deteriorated. Jugular venous congestion was present. The liver edge was palpable 1" below the right costal margin and medium crepitations were heard over both lung bases on auscultation. Hypotension was now present.

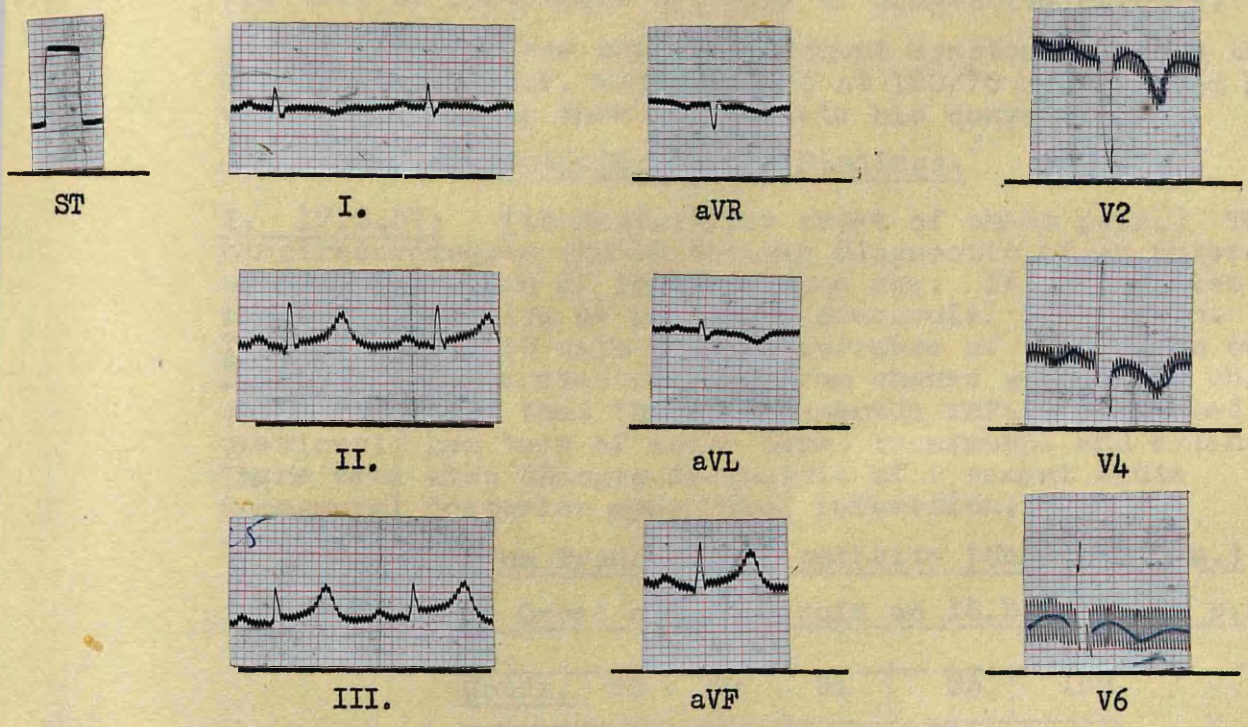
20.3.57: B.P. 95/60 mm.Hg. The patient's condition had improved. He was mentally clear and his skin colour had also improved.

22.3.57: B.P. 80/60 mm.Hg. The patient had seemed to be making reasonable progress and signs of congestion had cleared when, at 8.10 p.m., he was suddenly seized with retrosternal pain of gripping character whilst using a bedpan. The pain, which did not radiate, lasted for half an hour. On examination, he was shocked and again pale, sweating and apprehensive. Morphine sulphate, gr.1/4 was administered intramuscularly with good effect.

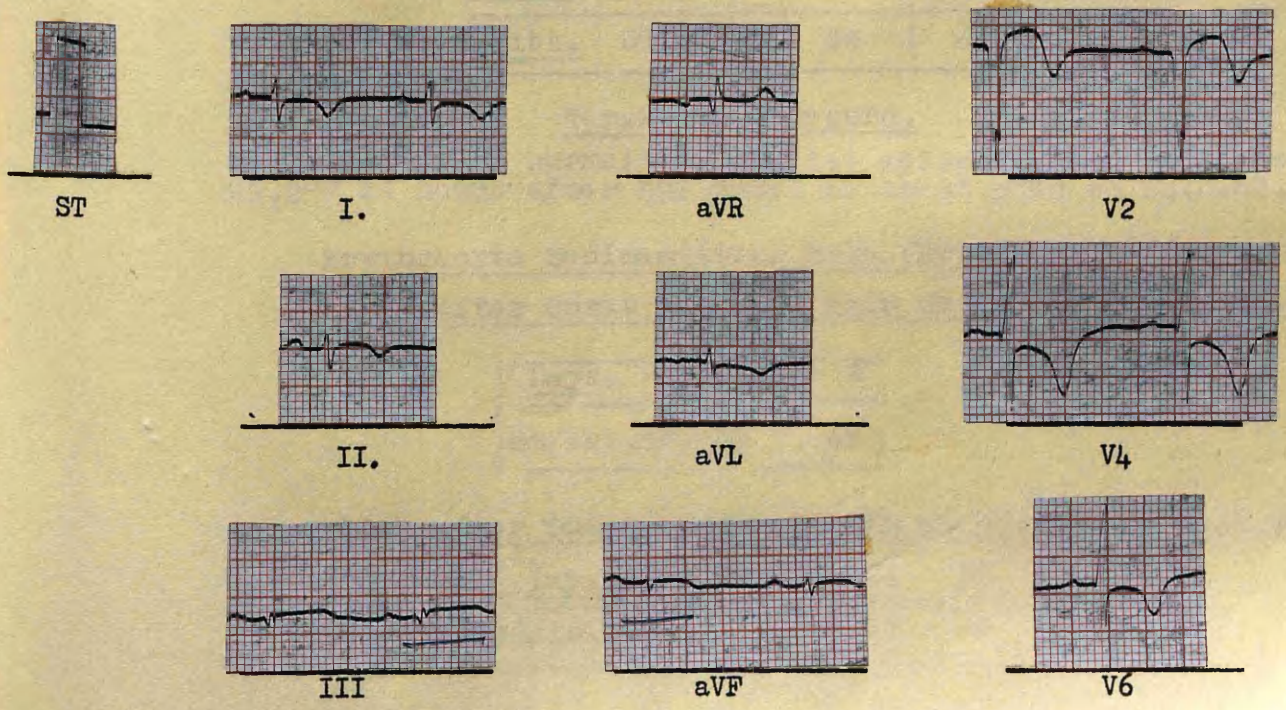
24.3.57: B.P. 80/60 mm.Hg. He had had no further praecordial pain when, at 2.30 p.m., he had another attack of retrosternal pain which lasted for half an hour. On this occasion, the pain began at rest and, following it, the patient was pale and sweated profusely.

/2

ELECTROCARDIOGRAM CASE NO. 31 (1)



ELECTROCARDIOGRAM CASE NO. 31 (2)



22.4.57: B.P. 115/65 mm.Hg. The patient had made good progress uninterrupted by further attacks of pain and there had been no recurrence of shock or congestive changes.

28.4.57: He was ambulant without symptoms and, on the 9th May, 1957, B.P. was recorded at 120/70 mm.Hg., and he was allowed to go home to complete his convalescence.

Electrocardiographic Findings.

I. 17.3.57: (15 hours after onset of chest pain.) The electrocardiogram showed changes diagnostic of an antero-septal infarction of indeterminate age. It showed also ST-T changes suggestive of posterior myocardial infarction.
II. 28.3.57: (6 days after recurrence of chest pain on 22.3.57.) The electrocardiogram showed sequential changes which indicated that the antero-septal infarction noted previously had been of acute type, transmural and extensive. There were also changes diagnostic of a recent acute transmural posterior myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest pain on 16.3.57 at 11 p.m.

Hours.	15	38	61	83	109
Units.	85	84	60	28	19

Time After Onset of Chest Pain on 22.3.57 at 8.10 pm.

Hours.	½	14	38	86	111
Units.	37	107	54	49	30

Temperature Record.

Temperature was normal after first episode of pain. It was 99.2°F 24 hours after the onset of chest pain on 22.3.57.

Erythrocyte Sedimentation Rate (Westergren.)

Time After Onset of Chest Pain on 16.3.57 at 11 pm.

Days.	2	4
mm/1st.hr.	40	47

Time After Onset of Chest Pain on 22.3.57 at 8.10 pm.

Days.	5	12	19	26	33	40
mm/1st.hr.	96	48	32	13	3	5

COMMENT:

Attacks of myocardial infarction occurred on 16.3.57 (31a) and on 22.3.57 (31b). In the first attack of myocardial infarction (31a)., the history and clinical findings were typical of a poor risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction of indeterminate age. There was no pyrexia but minimal - moderate peripheral vascular failure was present and signs of congestive cardiac failure appeared following the attack. Serum transaminase activity rose to high levels 15 hours after the onset of pain and the assay was not considered to have contributed early evidence of the occurrence of acute myocardial infarction.

In the second attack of acute myocardial infarction (31b)., the history and clinical findings were very suggestive of myocardial infarction and the electrocardiogram 6 days after the onset of the attack was diagnostic of a fresh myocardial infarction. Pyrexia was present following this attack but peripheral vascular failure was of a minimal degree. Serum transaminase activity rose to high levels 14 hours after the onset of the illness. The assay was considered to have contributed early and valuable evidence of acute myocardial infarction, especially in view of the delay in obtaining electrocardiographic evidence of myocardial infarction. It was also considered to have clarified the time of onset of the myocardial infarction, since the serum transaminase reached high levels before the onset of the severe attack of angina pectoris at rest on 24.3.57 (31c)., which did not differ in any clinical respect from that associated with acute myocardial infarction.(31b). Further, this attack of angina pectoris at rest did not cause a further rise in serum transaminase activity, which suggests that it was not accompanied by myocardial necrosis.

CASE NO. 32.

History of Present Illness.

A male, aged 46 years, a welder, was admitted to hospital on the 11th April, 1957, complaining of intermittent chest pain of ten days' duration. On the 30th March, 1957, he experienced a mild attack of gripping retrosternal pain at rest which did not radiate, lasted for about half an hour and then gradually cleared. Following this, he had had eight attacks of anginal pain of gradually increasing severity. On the 10th April, 1957, he complained of very severe crushing retrosternal pain which radiated into the jaw and down the inner aspect of the left upper arm. This pain lasted for fourteen hours.

History of Past Illnesses.

The patient had been treated at home for a myocardial infarction in 1954. Since this illness he had been subject to occasional attacks of dyspnoea whilst in bed at night and slept with four pillows.

Clinical Findings on Admission.

The patient was a healthy, well-built man. He was not shocked.

Cardiovascular System: B.P. 135/95 mm.Hg. The pulse was regular in rate (84/minute) and rhythm. The apex beat was palpable ½" within the mid-clavicular line in the fifth interspace. The heart sounds were pure and well heard. No abnormality was found on full examination of other systems.

Treatment and Progress.

In view of the past history of myocardial infarction and recent praecordial pain, treatment with anticoagulants was started on admission and continued for 28 days. There was no recurrence of anginal pain, no fall in blood pressure and the patient had an uneventful convalescence. He was discharged from hospital on the 25th May, 1957.

Electrocardiographic Findings.

I. 1912.54. The electrocardiogram showed changes diagnostic of an acute, extensive, transmural antero septal infarction.

II. 11.4.57: (24 hours following onset of chest pain on 10.4.57).

III.21.4.57:

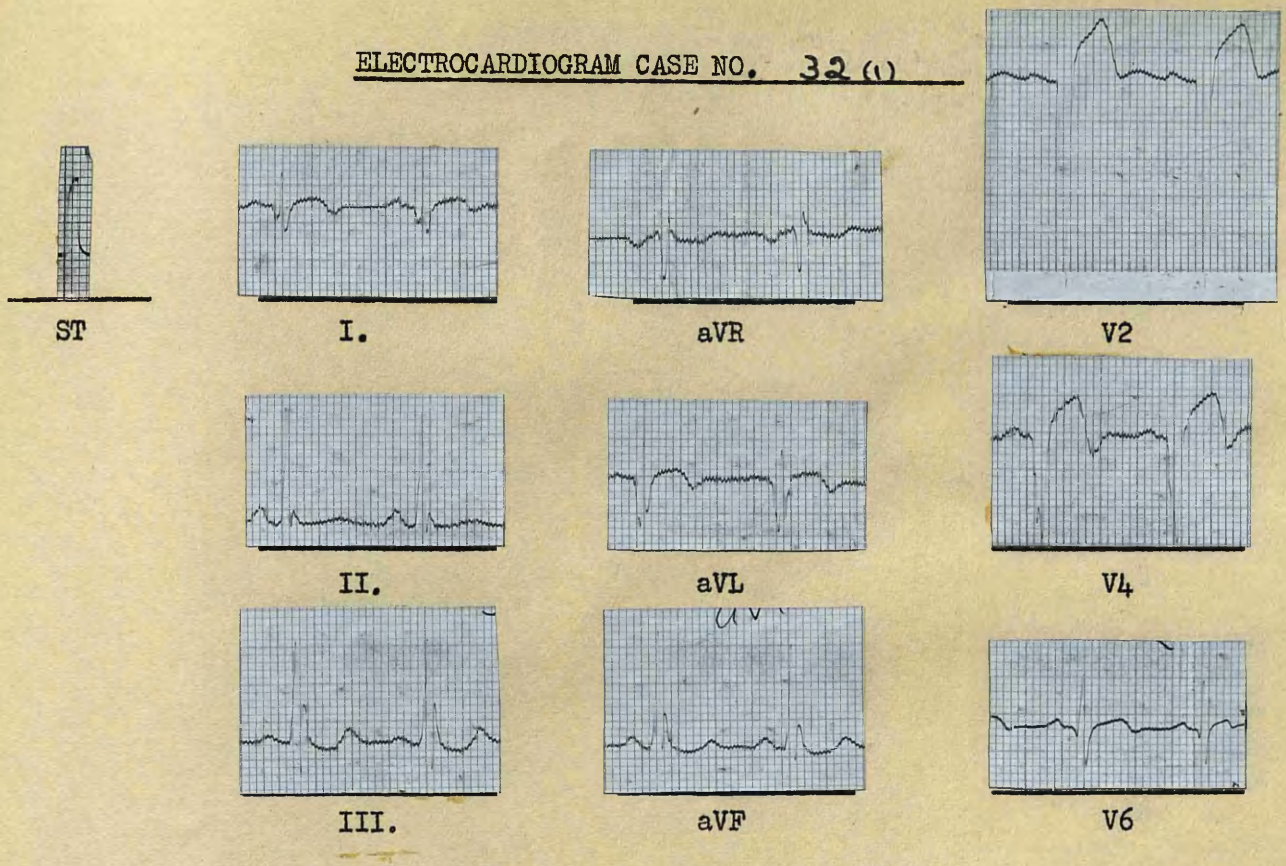
IV. 14.5.57: These serial electrocardiograms showed changes diagnostic of an old transmural antero septal myocardial infarction, and indicative of myocardial ischaemia of antero lateral distribution.. There was no evidence of a recent myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min).

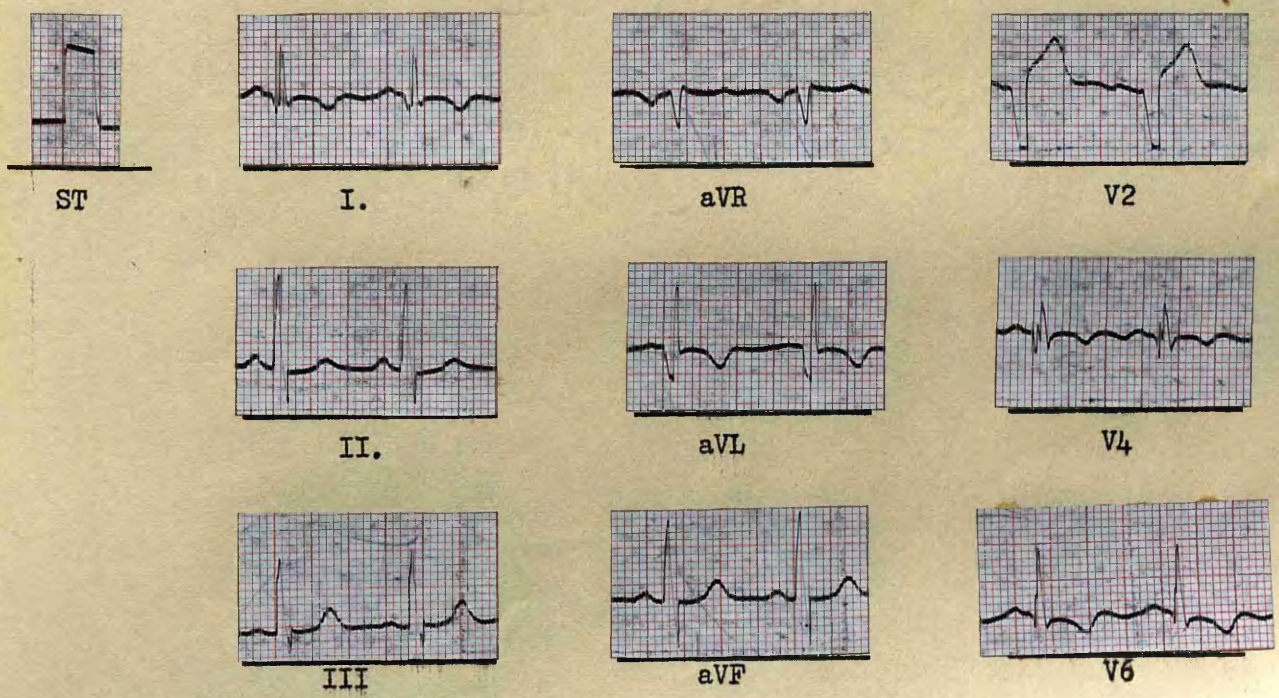
Time After Onset of Chest Pain on 10.4.57.

Hours.	12	30	54
Units.	26	31	24

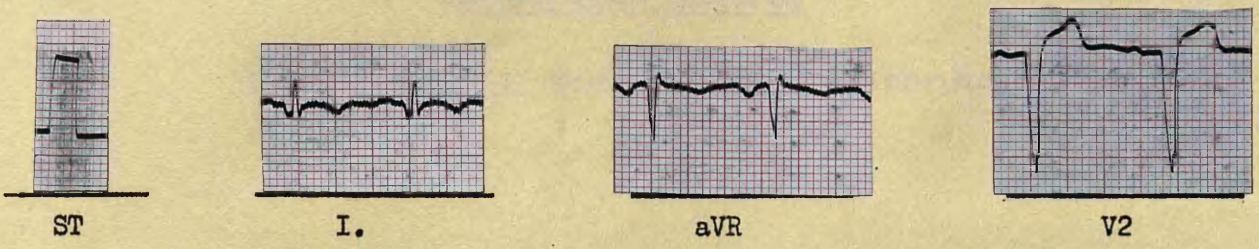
ELECTROCARDIOGRAM CASE NO. 32 (1)



ELECTROCARDIOGRAM CASE NO. 32 (2)



ELECTROCARDIOGRAM CASE NO. 32 (3)

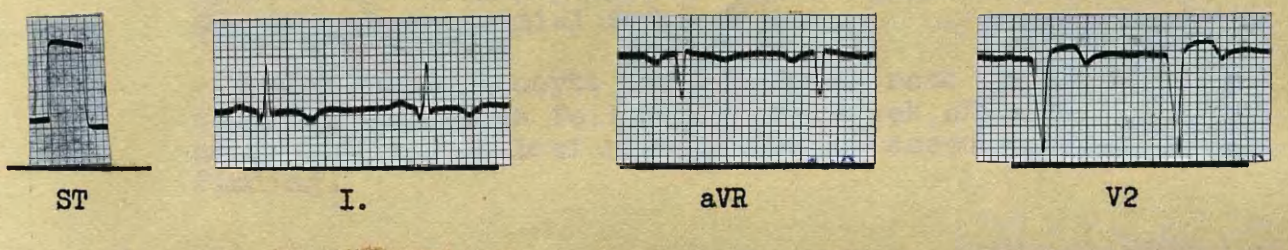


ST I. aVR V2

II. aVL V4

III. aVF V6

ELECTROCARDIOGRAM CASE NO. 32 (4)



ST I. aVR V2

II. aVL V4

III aVF V6

Temperature Record.

No elevation of temperature was recorded.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Chest Pain on 10.4.57.

	12 hrs.	14 days.	19 days.	28 days.	35 days.
mm/1st.hr 12	24	43	38	18	

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of angina pectoris at rest lasting fourteen hours.

Serial electrocardiograms were indicative of antero-lateral myocardial ischaemia and diagnostic of an old transmural myocardial infarction.

The erythrocyte sedimentation rate was elevated to abnormal levels following the attack of chest pain and no extra-cardiac lesion was found to account for this finding.

CASE NO. 33.

History of Present Illness.

A male, aged 56 years, a fitter, was admitted to hospital on the 6th May, 1957, complaining of severe retrosternal pain of 1¾ hours' duration. At 8.45 a.m., when walking briskly the patient developed a severe crushing pain in the retrosternal region of his chest, which radiated into his right arm. It forced the patient to stop walking and with rest it cleared away in about five minutes. When the pain had disappeared, he began to walk home but had gone only a few yards when a similar pain recurred. On this occasion the pain was so severe that he fell to the ground and lost consciousness momentarily. The pain lasted for 1¾ hours and was relieved in half an hour by the intramuscular injection of morphine sulphate gr.1/4 and atropine sulphate gr.1/100 at 10 a.m. He was admitted to hospital at 2.30 p.m., on the 6th May, 1957.

Past History.

For four months the patient had had short lasting attacks of angina pectoris on exertion but there had been no chest pain on exertion or at rest for a week before his admission to hospital. In 1947, he had been treated for generalised psoriasis at the Southern General Hospital, Glasgow.

Clinical Findings on Admission.

The patient was a well built, middle-aged man. He was not shocked and there was no evidence of congestive cardiac failure. Patches of psoriasis were present on his limbs and trunk.

Cardiovascular System: B.P. 125/90 mm.Hg. The pulse was regular in rate (64/minute) and rhythm. The apex beat was not palpable. By percussion method the heart was not grossly enlarged. The heart sounds were pure but faintly heard.

Full clinical examination of other systems revealed no abnormality.

Treatment and Progress.

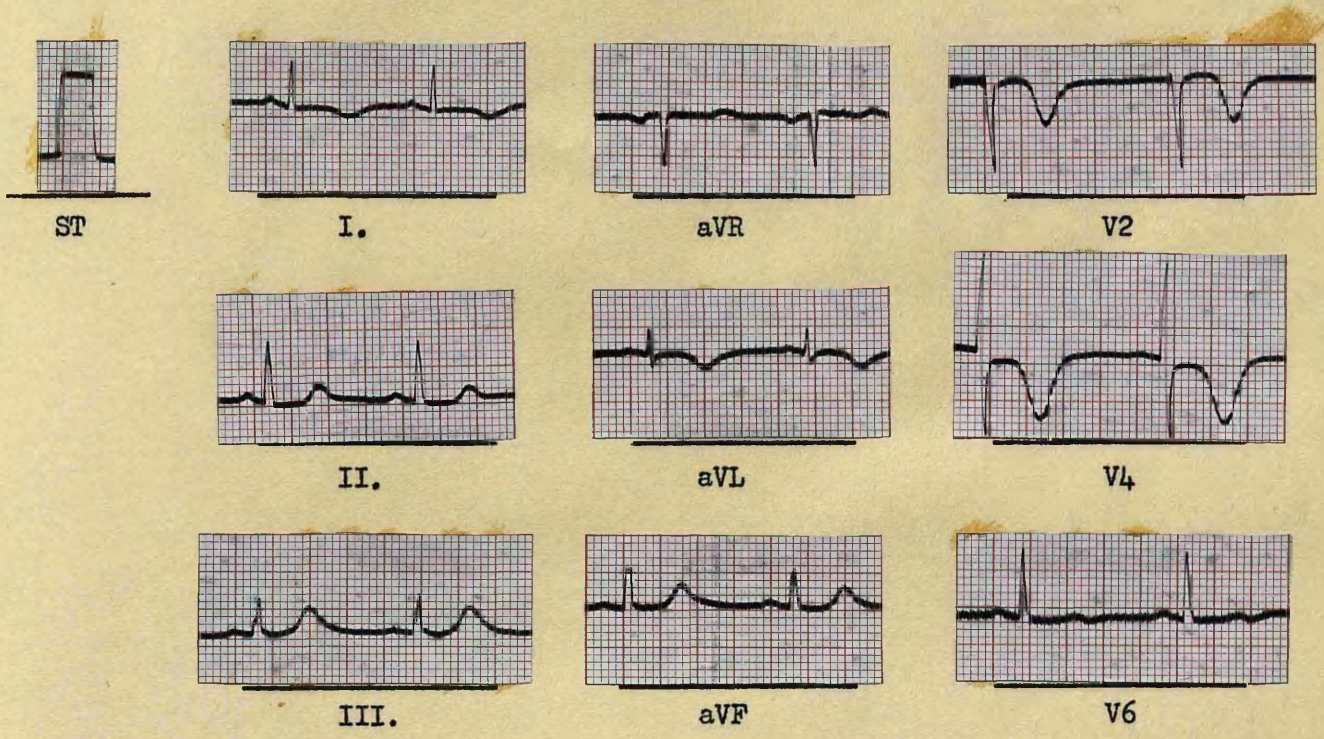
He had no pain on admission. In view of the history of angina pectoris and equivocal electrocardiographic findings, anticoagulant therapy was started and continued for 21 days. The patient remained symptom-free. No significant fall in blood pressure was recorded e.g., 120/70 mm.Hg., and 120/65 mm.Hg., during the period of observation in hospital.

On the 5th June, 1957, the lesions of psoriasis on his hand were active. There was exudate and inflammation. These were controlled by skin applications and he was allowed home to complete his convalescence on June 17th 1957.

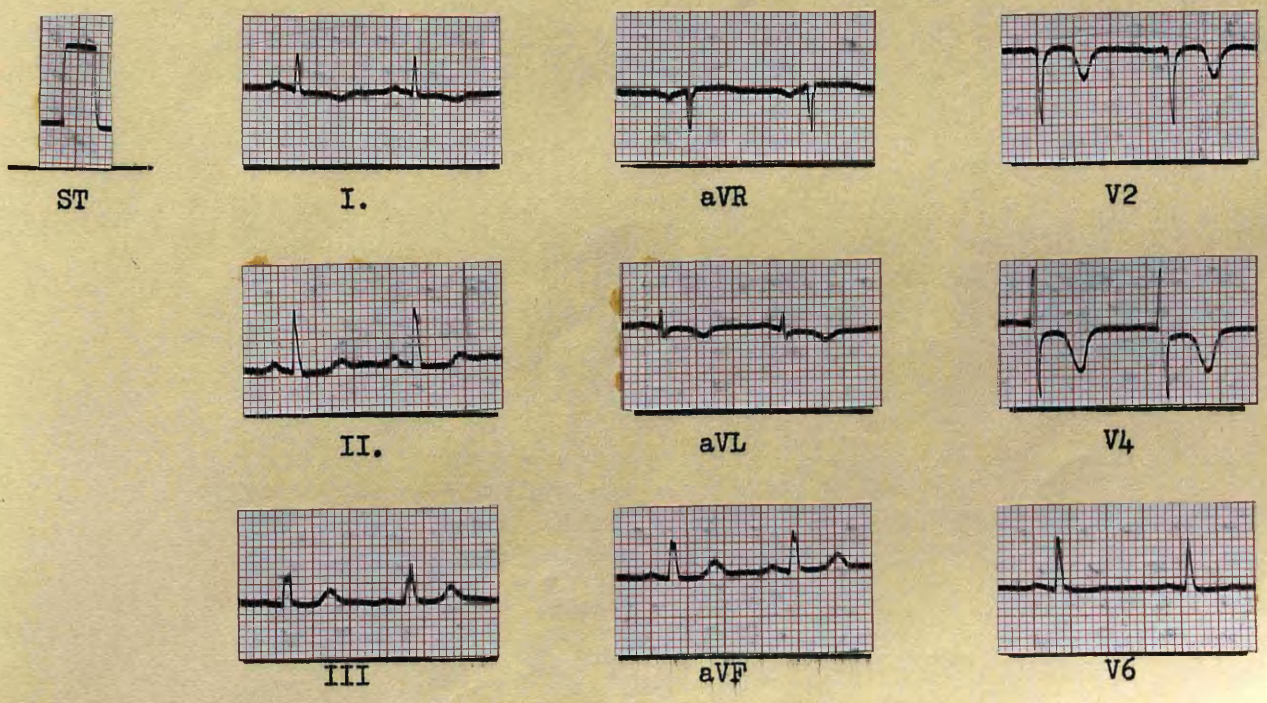
Electrocardiographic Findings.

I. 6.5.57: (11 hours after onset of chest pain at 8.45 a.m. on the 6th May, 1957). The electrocardiogram showed changes diagnostic of an extensive transmural antero-septal myocardial infarction of indeterminate age.

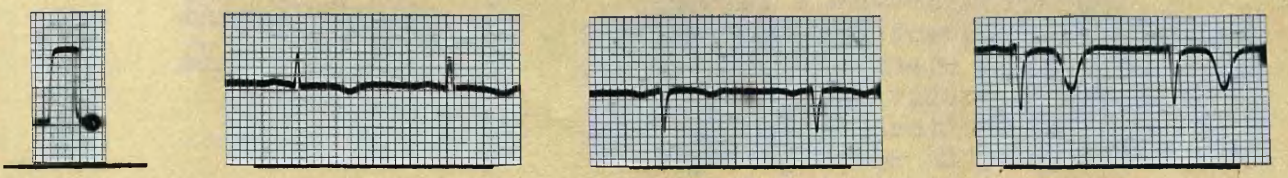
ELECTROCARDIOGRAM CASE NO. 33 (1)



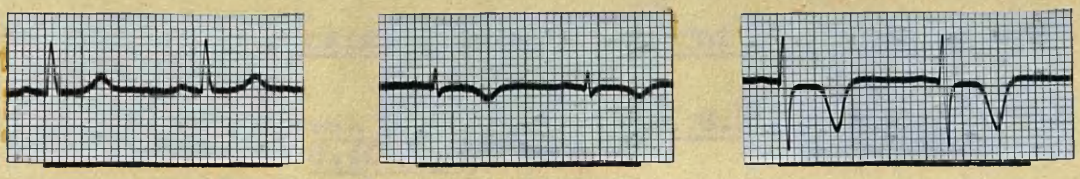
ELECTROCARDIOGRAM CASE NO. 33 (2)



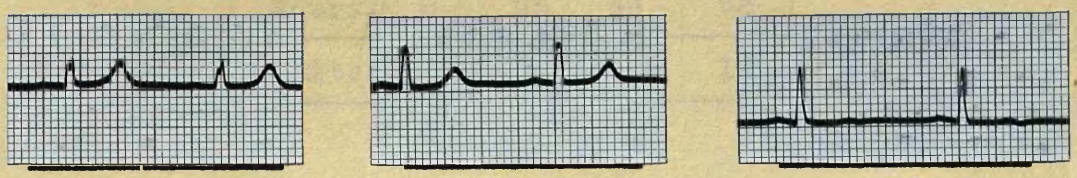
ELECTROCARDIOGRAM CASE NO. 33 (3)



ST I. aVR V2

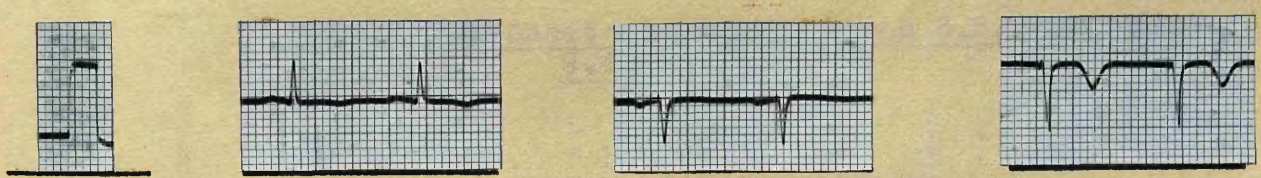


II. aVL V4

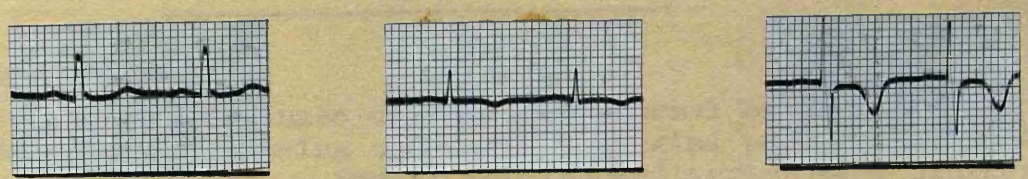


III. aVF V6

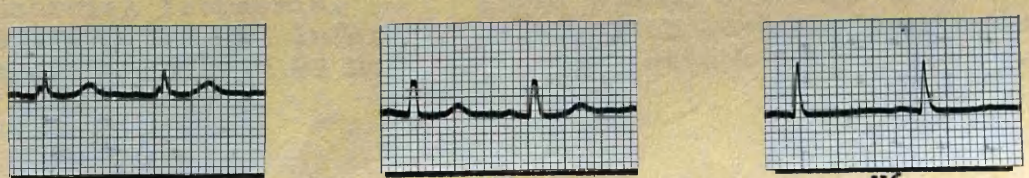
ELECTROCARDIOGRAM CASE NO. 33 (4)



ST I. aVR V2



II. aVL V4



III aVF V6

II. 13.5.57:)
III. 18.5.57:) Serial electrocardiograms confirmed the aforementioned diagnosis but there was no electrocardiographic evidence of recent myocardial infarction, the changes being compatible with antero-septal myocardial ischaemia.
IV. 5.6.57: (

Serial Serum Transaminase Activity (Units/ml/min).

Time After Onset of Chest pain on 6.5.57 at 8.45 a.m.

Hours.	8	25	49	73
Units.	27	23	30	18

Temperature Record.

No elevation of temperature was recorded.

Erythrocyte Sedimentation Rate (Westergren.)

Time After Onset of Chest Pain on 6.5.57 at 8.45 a.m.

Days.	1	7	14
mm/1st.hr.	17	4	6

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of angina pectoris at rest lasting 1¾ hours. Serial electrocardiograms were diagnostic of an old transmural myocardial infarction and antero-septal myocardial ischaemia. There was no evidence of a recent myocardial infarction. The erythrocyte sedimentation rate was elevated 24 hours after the attack of chest pain.

CASE NO.34.

History of Present Illness.

A male, aged 63 years, a music teacher, was admitted to hospital on 23.5.57 having had an attack of sudden severe retrosternal pain at 8 p.m. At 8 p.m., on the day of admission, the patient, while sitting by the fire, suddenly developed very severe crushing retrosternal pain which radiated down the inner aspect of the left arm. He felt intense nausea, complained of feeling cold and began to sweat freely. The pain remained severe despite an intramuscular injection of morphine sulphate, gr 1/4 given by his family doctor, and he was admitted to hospital on 23.5.57 at 9.30 p.m.

Past History.

A fortnight before admission, the patient had complained of a feeling of tightness in his chest in the retrosternal region. This sensation had been noted only on one occasion during the night and had lasted for quarter of an hour. For four years, the patient had had symptoms of intermittent claudication in the left leg.

Clinical Findings on Admission.

The patient was very distressed and obviously severely shocked. He was confused and rolled about the bed in agony. Because of this, examination was made very difficult. He sweated freely, the extremities were cold and dyspnoea was present.

Cardiovascular System: B.P. 110/60 mm.Hg. The pulse was regular in rate (98/min.) and rhythm. The heart was enlarged, the left border was estimated by percussion to be 1½" outwith the mid-clavicular line. The heart sounds were very difficult to hear but they were pure.

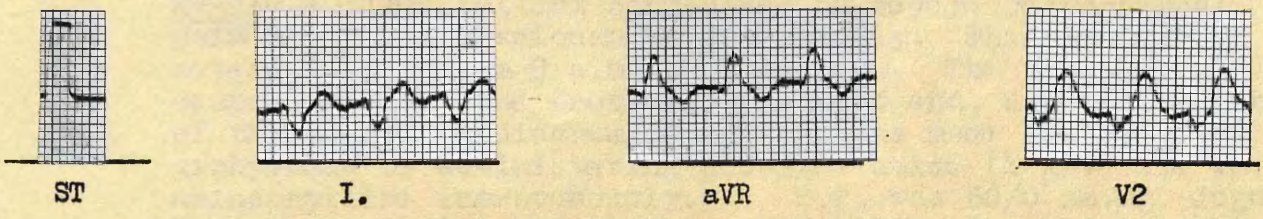
Respiratory System: Examination of the respiratory system was limited but there were numerous rhonchi anteriorly. No other abnormality was found on cursory examination of other systems.

Treatment and Progress.

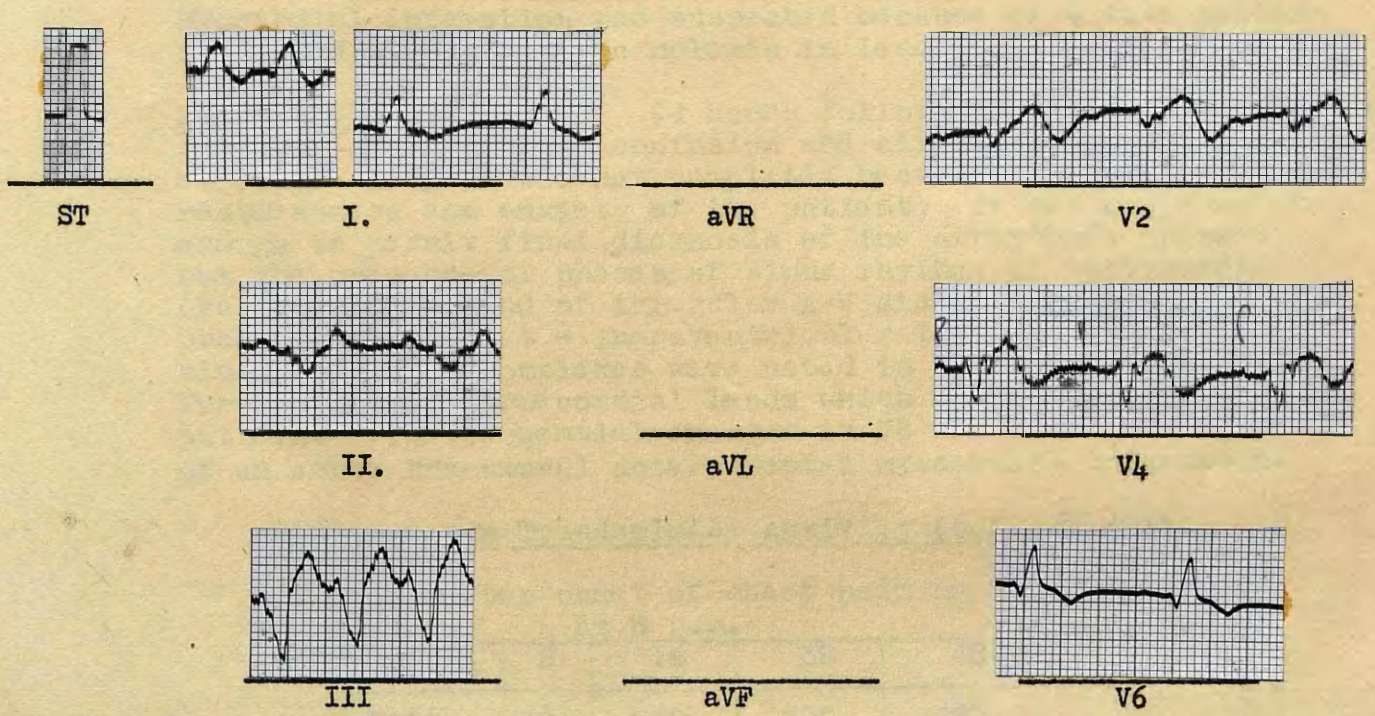
Pethidine (100 mgm.) was administered intravenously and this resulted in control of pain. Anticoagulant therapy was started on admission and was continued until the patient's death.

24.5.57: B.P. 80/50 mm.Hg. There had been no recurrence of pain. The patient was less apprehensive but jugular vein congestion was present and the patient was dyspnoeic on the slightest exertion. Marked tachycardia was noted (140/min.) which lasted for two hours. /2

ELECTROCARDIOGRAM CASE NO. 34 (1)



ELECTROCARDIOGRAM CASE NO. 34 (2)



25.5.57: The patient complained of severe retrosternal pain and lost consciousness momentarily. This recurred several times from 8 a.m. until 10 a.m. The patient was desperately ill and profoundly shocked and, after examination of the electrocardiogram, an attempt was made to end the arrhythmia by administering procaine amide (1 gm.) and .5 gm. aminophylline intravenously. B.P. was 50/0 mm.Hg. Jugular venous congestion was marked; the liver edge was palpable 2" below the right costal margin and there was a trace of sacral oedema.

The arrhythmia cleared after two hours, whether spontaneously or due to the administration of procaine amide, was not clear.

At 3 p.m., the patient again complained of severe retrosternal pain and he became very restless and confused. Tachycardia (160/min.) was noted but this settled without special treatment, to be replaced by an irregular bradycardia. This, in turn, gave way to a regular pulse rate of 80/min. Profound hypotension persisted, B.P. 50/0 mm.Hg., and the patient's condition progressively deteriorated until he died at 3.10 a.m. on 26.5.57. Permission for a post mortem examination was refused.

Electrocardiographic Findings.

I. 24.5.57: (10 a.m.) (14 hours after onset of pain.) The electrocardiogram showed changes suggestive of an intraventricular conduction defect and sinus tachycardia (rate 140/min.) Myocardial infarction was suspected because of Q wave pattern in V6 and abnormal QRS complexes in leads I, II, III.

2: 25.5.57 - 3 p.m. (4 hours following onset of tachycardia associated with mental confusion and circulatory collapse. The electrocardiogram was not completed because of the great restlessness and anxiety of the patient; it was not complete enough to permit final diagnosis of the arrhythmia present but the presence of phases of sinus rhythm, of tachycardia (rate 140/min.) and of irregular A-V dissociation (in V2 & V4) probably meant that a supraventricular tachycardia was present since broad QRS complexes were noted in all these phases and, furthermore, in praecordial leads which were of similar pattern. The sequential changes in V2 and V4 were diagnostic of an acute transmural antero-septal myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after onset of chest pain on 23.5.57 at 8 p.m.

Hours.	3	16	38	48
Units.	30	240	200	493.

/3

Temperature Record.

Temperatures of 99.4°F and 100°F were recorded 24 and 48 hours after admission respectively.

Erythrocyte Sedimentation Rate (Westergren).

No estimations were performed.

COMMENT: The history and clinical findings were typical of poor risk myocardial infarction but serial electrocardiograms were required before the electrocardiographic patterns were diagnostic of transmural myocardial infarction, myocardial infarction being suspected in the first electrocardiogram examined 14 hours after the onset of the illness. Pyrexia and marked to extremely marked peripheral vascular failure were present. Serum transaminase activity rose to high levels 16 hours after the onset of the illness. The assay was considered to have contributed early and useful confirmation of the presence of myocardial infarction. Very high levels of serum transaminase activity attained 48 hours after the onset of the illness and the arrhythmia present may have contributed to these, although further myocardial infarction was not excluded.

CASE NO. 35.

History of Present Illness.

A male, aged 59 years, an engineer, was admitted to hospital on the 24th May, 1957, having collapsed in the street at 9 p.m. At 5 a.m., on the 24th May the patient was wakened by a constricting retrosternal pain which was moderately severe for about an hour. He went to work, however, and he was conscious of discomfort in the praecordial region and in the left upper arm throughout the working day. He observed that the discomfort was less when he had the opportunity to rest. When cycling home in the evening he stopped to talk to a friend when, without warning, he lost consciousness for a few seconds. On recovering consciousness he found that he had vomited and that he had severe constricting pain in the retrosternal region of the chest which radiated down the inner aspect of his left arm. He had vomited several times before admission to hospital and coffee-ground material had been noted on the last occasion.

Past History.

Since 1954, the patient had had symptoms of mild angina pectoris on exertion which passed off quickly with rest. For 20 years the patient had been subject to bouts of dyspepsia. The last attack had been in 1956. In 1955 the clinical diagnosis ofa duodenal ulcer had been confirmed by barium meal examination.

Clinical Findings on Admission.

The patient was a middle-aged, overweight man. He was shocked, restless and apprehensive. His extremities were cold and cyanosed. He was dyspnoeic on the slightest exertion.

Cardiovascular System: B.P. 120/80 mm.Hg.(approx.) The pulse was irregularly irregular with a rate of approximately 140/minute. The apex beat was not felt. The heart sounds were faint, rapid and irregular in force and rhythm.

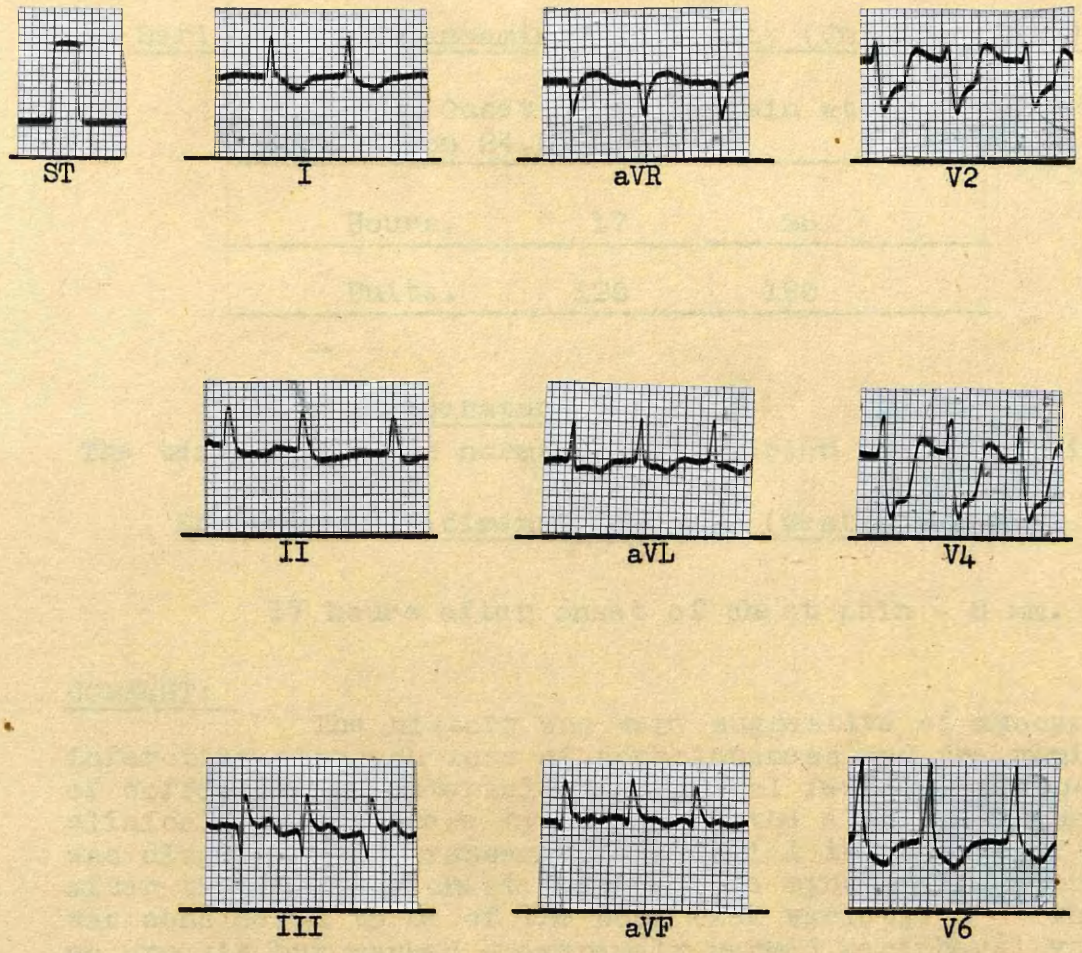
Respiratory System: The percussion note was slightly diminished over both lung bases. On auscultation, numerous sibilant rhonchi were heard throughout the lung fields and many fine crepitations at both lung bases. No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Pethidine (100mgm.) was administered intramuscularly on admission. Anticoagulant therapy was not given because of the history of duodenal ulcer and possible recent haematemesis. The patient's condition progressively deteriorated after admission and at 11 p.m., the B.P. was 90/70 mm.Hg., and he was very dyspnoeic. Digoxin, .5 mg (intravenous) was administered at 11.30 p.m., on the 24th May, 1957 and at 6.30 a.m., on the following day without benefit.

At 9 a.m. on the 25th May, 1957, the patient was severely shocked. He complained of retrosternal pain, crushing in character /2

ELECTROCARDIOGRAM CASE NO. 35



/ and he vomited once. The pulse was noted to be regular in rate (100/minute) and the B.P. was 80/60 mm.Hg. The prognosis was considered to be poor and the patient died suddenly at 3 p.m. Permission for a post mortem examination was refused.

Electrocardiographic Findings.

I. 24.5.57: (17 hours after onset of chest pain at 5 a.m. on 24.5.57). The electrocardiogram showed changes diagnostic of an acute transmural posterior myocardial infarction associated with very deep depression of S-T segment over the chest leads which may be due to posterior myocardial infarction or acute anterior coronary insufficiency. Auricular fibrillation was present (rate 130-140/min.)

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain at 5 a.m. on 24.5.57.

Hours.	17	26
Units.	120	190

Temperature Record.

The temperature was normal during period of observation.

Erythrocyte Sedimentation Rate (Westergren).

17 hours after onset of chest pain - 8 mm.

COMMENT:

The history was very suggestive of myocardial infarction although loss of consciousness and the vomiting of coffee ground material were unusual features. The clinical findings were typical, and the electrocardiogram was diagnostic of transmural myocardial infarction 17 hours after the onset of chest pain. The myocardial infarction was considered to be of the poor risk variety. There was no pyrexia but marked - extremely marked peripheral vascular failure developed. The serum transaminase activity rose to high levels 17 hours after the onset, the E.S.R. being normal at this time. Auricular fibrillation (rate 130-140/min.) was present but it is impossible to say whether it contributed to the rise in serum transaminase activity. The assay was not considered to have contributed to the diagnosis.

CASE NO. 36.

History of Present Illness.

A male, aged 52 years, a house painter, was admitted to hospital on the 29th May, 1957, complaining of pain in both arms and in the retrosternal region, of 15 hours' duration.

On the 3rd November, 1956, while sitting in a cinema, the patient suddenly felt cold, broke into a sweat and became violently sick. He was transported home and remained in this condition for some hours. He was seen by his family doctor who advised him to rest in bed. On November 17th. 1956, during the night, he suddenly became acutely dyspnoeic and shocked but recovered from this attack with treatment from his doctor. On neither of these occasions did the patient complain of pain in the chest and only on close questioning did it appear that he felt a feeling of tightness in the praecordium for a few days after the second incident. He was kept in bed until January, 1957, his family doctor having made the clinical diagnosis of severe myocardial ischaemia. Following a period of convalescence lasting two months, the patient returned to work. Since January, 1957, however, he had had attacks of gripping pain in the left upper arm precipitated by exertion and relieved by rest and by the use of sublingual trinitrin.

On the 27th May, 1957, when he awakened, he felt breathless at rest but he remained in bed and the breathlessness wore away. On the 29th May, 1957, at 9 a.m., whilst at rest, he suddenly developed a severe constricting pain in both upper arms, the pain being felt more acutely in the left arm; a less severe pain, of similar character, was felt in the retrosternal region. These pains had persisted until his admission to hospital at 11 p.m., on the 29th May, 1957.

There was no other relevant past or social history.

Clinical Findings on Admission.

The patient was a man of middle age. He had good colour. He was not shocked but was dyspnoeic on the slightest exertion. There was slight neck vein congestion but there was no skin oedema.

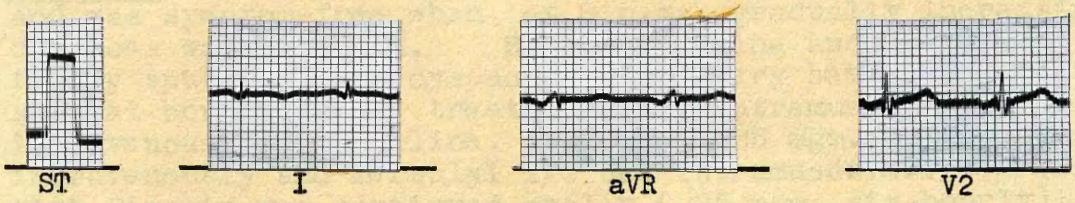
Cardiovascular System: B.P. 115/85 mm.Hg. The pulse was regular in rate (96/minute) and rhythm. The apex beat was not palpable but the left heart border, as determined by percussion, was 1" outwith the mid-clavicular line. The heart sounds were pure, but distant.

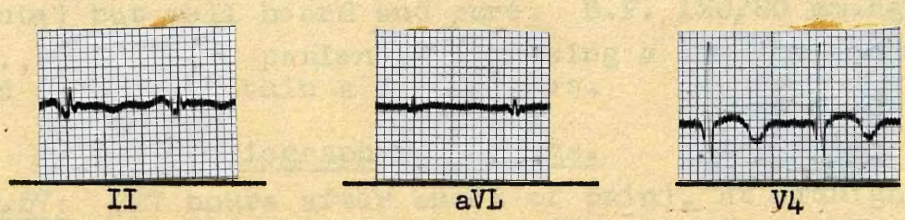
Respiratory System: There was a diminished percussion note over the lower half of the left lung posteriorly. On auscultation, numerous bubbling râles were heard throughout the lung fields, but especially at the lung bases.

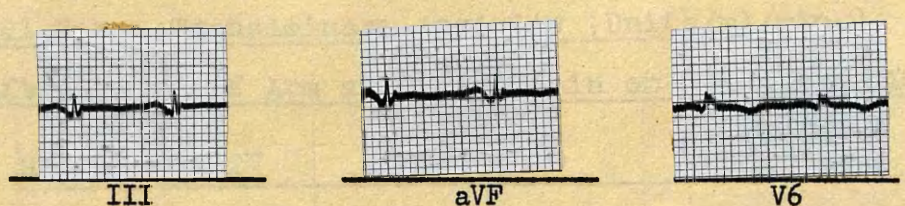
Alimentary System: The liver edge was palpable 1" below the right costal margin. No other abnormality was found on full clinical examination.

/2

ELECTROCARDIOGRAM CASE NO. 36 (1)







Treatment and Progress.

On admission, anticoagulant therapy was started and continued until the death of the patient.

30.5.57: 9 a.m. B.P. 95/70 mm.Hg. The patient's condition was unchanged; at 2 p.m., on the same day, the B.P. was again 95/70 mm.Hg. He suddenly developed acute dyspnoea without accompanying chest or arm pain. Oxygen, intravenous aminophylline and intramuscular morphine were effective in controlling the symptoms which cleared away in about one hour.

31.5.57: B.P. 95/70 mm.Hg. The patient felt well and was not dyspnoeic. Tachycardia was noted (120/minute). Jugular vein congestion and hepatomegaly were still present.

4.6.57: The patient had had no further attacks of dyspnoea and was symptom-free when, at 8 p.m., gradually increasing dyspnoea was observed. He was sweating and coughed up pink, frothy sputum. The dyspnoea became very severe and lasted for several hours despite treatment with intramuscular morphine and intravenous aminophylline. Digoxin .25 mgm. was administered intravenously and mersalyl 1/2 cc. intramuscularly. Treatment with Digoxin was continued orally (.25 mgm. six-hourly).

5.6.57: He was less acutely dyspnoeic. On examination of the chest, scattered rhonchi were heard on auscultation. The left border of the heart, as determined by percussion, was now 2" outwith the mid-clavicular line. The heart sounds were rapid (108/minute) but well heard and pure. B.P. 120/80 mm.Hg.

At 7 p.m., whilst the patient was smoking a cigarette, he collapsed and died within a few minutes.

Electrocardiographic Findings.

I. 30.5.57: (27 hours after onset of pain), at midnight.

The electrocardiogram showed changes diagnostic of an acute septo lateral myocardial infarction. The Q waves in V.2 and V.4 were pathological but no QS configuration was present. The infarction was considered to be probably of transmural type.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Arm and Chest Pain on 29.5.57 at 9 am.

Hours.	27	36	60	84
Units.	120	80	60	35.

Time After Onset of Left Ventricular Failure on 4.6.57 at 8 pm.

Hours.	11
Units.	75.

/3

Temperature Record.

Irregular pyrexia 99.6°F to 99.8°F was present from day of admission until death.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Arm and Chest Pain on 29.5.57 at 9 a.m.

	27 hours.	5 days.
mm/1st.hr.	27	63

Post Mortem Findings.

Post mortem examination showed gross enlargement of the heart due to dilatation of the left ventricle. The other chambers and valves of the heart showed no abnormality. The circumflex branch of the left coronary vessel was occluded at a point approximately 2 inches from its commencement. The thrombus in this area was old and probably of one week's duration. The related area of muscle supplied by this vessel showed evidence of old infarction and there was a distinct dilatation of the ventricular wall just below the mitral valve. The anterior branch of the left coronary artery was not thrombosed, but there was only a tiny lumen remaining in the vessel over its first 1½ inches. The related area of myocardium showed recent infarction probably of 24 hours' duration. The posterior vessel was also severely affected by atheromatous degeneration, but still patent. A small accessory artery with separate ostium was present.

The main viscera showed chronic venous congestion and moderate enlargement.

No other abnormality was found on examination of the organs of the body.

The left lung was densely adherent and some old fibrosed tubercle was present in the right upper lobe.

Death was considered to be due to old and new myocardial infarction.

Results of Histological Examination. /4

Results of Histological Examination.

Heart: In the sections examined, areas of old and recent infarction were present.

Liver: Moderate chronic venous congestion was present.

COMMENT:

Attacks of acute myocardial infarction were observed on 29.5.57 (36a) and on 4.6.57 (36b).

In the first attack (36a)., the history and clinical findings were typical of poor risk myocardial infarction and the electrocardiogram was diagnostic of acute myocardial infarction, probably transmural in type, 27 hours after the onset of the illness. Pyrexia, minimal peripheral vascular failure and frank congestive cardiac failure were present. Serum transaminase activity reached high levels 27 hours after the onset and the erythrocyte sedimentation rate was raised at this time. The assay was not considered to have contributed to the diagnosis.

In the second attack (36b)., the clinical findings were those of left ventricular failure of severe degree and the diagnosis of a second poor risk acute myocardial infarction was considered very likely. Pyrexia and a minimal degree of peripheral vascular failure developed. When the serum transaminase activity was found to have risen again,11 hours after the onset, to high levels, the diagnosis was considered to be certain and electrocardiograms were not performed. The assay was considered to have provided valuable confirmation of the occurrence of a fresh myocardial infarction.

At post mortem examination, the presence of myocardial infarctions was confirmed.

CASE NO. 37.

History of Present Illness.

A female, aged 62 years, a housewife, was admitted to hospital on the 10th June, 1957, complaining of sudden dyspnoea which began while she was restingat 1 p.m. The sudden severe breathlessness was associated with a sense of constriction felt across the praecordium and with palpitation. The attack of dyspnoea lasted for fifteen minutes. The patient had had several similar, but milder attacks of dyspnoea for three weeks prior to admission to hospital but they were increasing in frequency and she had had a severe attack on the 7th and 9th June, 1957. She denied having any chest pain.

Past History.

In July, 1956, the patient first noted symptoms consistent with the diagnosis of paroxysmal cardiac dyspnoea and in August, 1956, she was treated in Edinburgh Royal Infirmary for three weeks. Since then she had been dyspnoeic on moderate exertion. She had also suffered from diabetes mellitus since 1947 and required 44 units P.Z.I. daily for its control.

Clinical Findings on Admission.

The patient was an overweight, elderly woman, who was neither distressed nor shocked. The lips were slightly cyanosed.

Cardiovascular System: B.P. 165/95 mm.Hg; the pulse was regular in rate (100/minute) and rhythm. The apex beat was not felt but the heart was enlarged, the left border being 1½" outwith the mid-clavicular line as determined by percussion.

Respiratory System: On auscultation, numerous fine and medium crepitations were heard throughout the lung fields, but especially at the lung bases.

Alimentary System: On palpation, the liver edge was felt 1" below the right costal margin.

The urine contained 2% glucose and a trace of acetone.

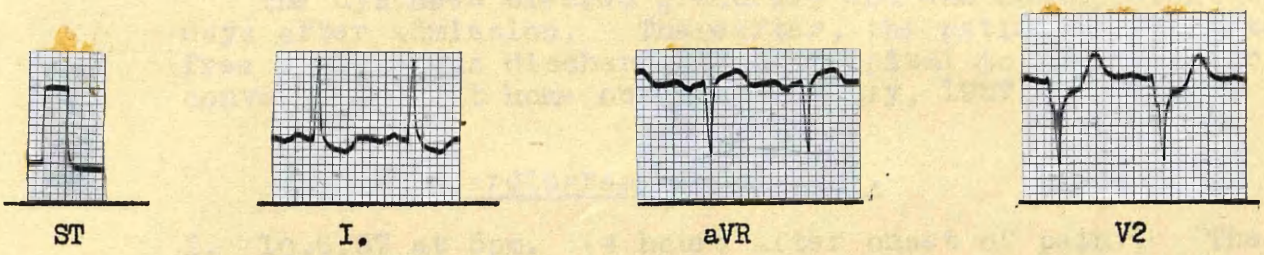
No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

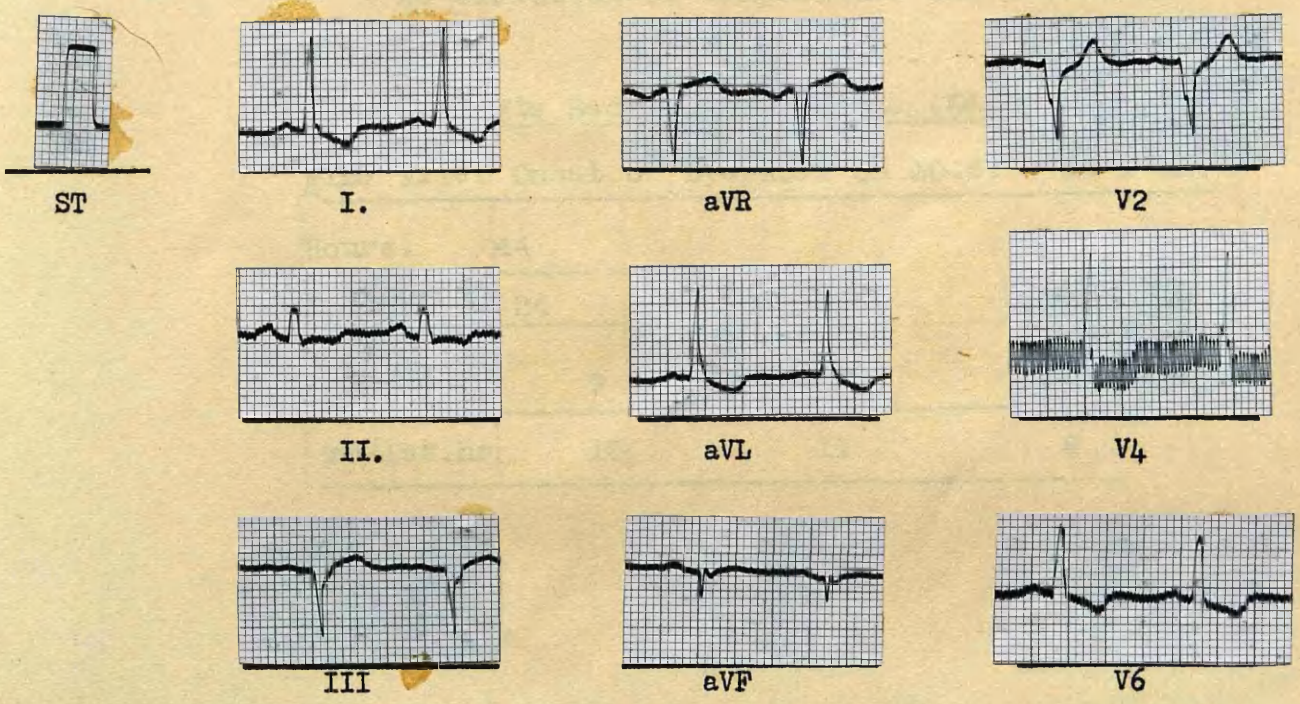
A test dose (0.5 cc.) of mersalyl was given intramuscularly shortly after admission and regular therapy with this drug (2 cc. twice weekly) was instituted and continued for five weeks. Treatment with soluble insulin was also started, care being taken to avoid hypoglycaemic reactions and, eventually, the diabetic state was stable on a low salt diet (caloric value 800) and a daily dose of I.Z.S. (lente) insulin, 44 units.

/2

ELECTROCARDIOGRAM CASE NO. 37 (1)



ELECTROCARDIOGRAM CASE NO. 37 (2)



The dyspnoea cleared gradually and was not apparent three days after admission. Thereafter, the patient was symptom-free and she was discharged from hospital to complete her convalescence at home on the 20th July, 1957.

Electrocardiographic Findings.

I. 10.6.57 at 5pm. (4 hours after onset of pain). The electrocardiogram showed changes diagnostic of an acute transmural posterior myocardial infarction.

II. 16.6.57: The electrocardiogram showed sequential changes which confirmed the diagnosis of posterior myocardial infarction. A probable left ventricular strain pattern was also noted.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Dyspnoea on 10.6.57 at 1 pm.

Hours.	22	44
Units.	98	65

Temperature Record.

No elevation of temperature was recorded.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Dyspnoea on 10.6.57 at 1 pm.

Hours.	44		
mm/1sthr.	24		
Days.	9	16	23
mm/1st.hr	16	11	8

COMMENT: /3

COMMENT:

The absence of pain in this case was unusual but the development of sudden severe dyspnoea at rest raised the suspicion of acute myocardial infarction. There was no pyrexia or evidence of peripheral vascular failure but signs of congestive cardiac failure were present. The electrocardiogram was diagnostic of transmural myocardial infarction and the infarction was regarded as of poor risk type. Serum transaminase activity reached high levels 22 hours after the onset, but the assay was not considered to have contributed much to the diagnosis.

CASE NO. 38.

History of Present Illness.

A male, aged 56 years, a gateman, was admitted to hospital on May 31st 1957 at 12.30 a.m., complaining of severe retrosternal pain of 5 hours' duration. He had returned from work on the evening of May 30th and complained of feeling very unwell; at 7.30 p.m., he developed a severe sharp retrosternal pain which radiated down the inner aspect of the right arm and he became very breathless. On admission, the pain had become less severe. He had had short attacks of similar pain for 12 months, occurring both at rest and on exertion. These attacks had been thought by the patient to be due to flatulence.

Past History.

In 1951, the patient had developed symptoms of intermittent claudication in the right leg. His symptoms grew gradually worse and in 1953 the right leg was amputated because of dry gangrene. During this time the blood pressure had been repeatedly measured and the diastolic pressure was always between 105/110 mm.Hg.

Clinical Findings on Admission.

The patient was cold and shocked on admission. He was restless, apprehensive and confused. Jugular vein congestion was present.

Cardiovascular System: B.P. 110/80 mm.Hg. The pulse was regular in rate (120/min.) and rhythm. The apex beat was not felt but the heart was enlarged, the left border, as determined by percussion, being 1½" outwith the mid-clavicular line. The heart sounds were rapid and very distant.

Respiratory Sytem: On auscultation, scattered rhonchi and a few fine crepitations were heard over both lung bases.

Alimentary System: The liver edge was felt 1" below the costal margin and was tender on palpation. No other abnormality was discovered on full clinical examination of other systems.

Treatment and Progress.

Morphine 1/4 gr. intramuscularly relieved the retrosternal pain and anticoagulant therapy was started. Unfortunately, the patient's condition progressively deteriorated and severe shock was present. Hypotension /2

Hypotension was marked, the B.P. being 80/40 mm.Hg., and the patient died suddenly at 4.10 a.m. on Junelst 1957.

Permission for a post-mortem examination was refused.

Electrocardiographic Findings.

The patient died before electrocardiographic tracings were performed.

Serial Transaminase Activity (Units/ml/min.)

Time After Onset of Retrosternal Pain on 30.5.57 at 7.30 p.m.

Hours.	5	14
Units.	30.	73.

Temperature Record.

The temperature was 99.8°F on May 31st 1957.

Erythrocyte Sedimentation Rate (Westergren.)

No estimations were performed.

COMMENT:

The history and clinical findings were typical of a poor risk myocardial infarction. Pyrexia and marked peripheral vascular failure developed. The patient died before electrocardiograms were performed. Serum transaminase activity reached high levels 14 hours after the onset of the illness.

The assay, in the absence of electrocardiographic evidence, was considered to have provided early and valuable confirmation of the occurrence of acute myocardial infarction.

CASE NO. 39.

History of Present Illness.

A male, aged 55 years, a clerk, was admitted to hospital on 23.5.57., complaining of retrosternal pain of six hours' duration. On 2.5.57., the patient first felt gripping retrosternal pain on fast walking. The pain had compelled him to rest. The pain cleared on resting, but it became more easily induced until, on 16.5.57., he was advised to rest in bed. He was symptom-free until the evening of 22.5.57., when he developed, whilst in bed, severe gripping retrosternal pain lasting for ½-hour. On 23.5.57., six hours before admission he again developed severe gripping retrosternal pain which, on this occasion, radiated into the neck, jaw and down the left arm. Shortly after the onset of this attack, he was dyspnoeic on slight exertion. The pain was still present on admission.

Past History.

The patient had had haematemesis from a duodenal ulcer on two occasions, the last occasion being in 1956. He had had no dyspeptic symptoms since 1956.

Clinical Findings on Admission.

The patient was a healthy looking man who, although he complained of continuing severe pain, was not unduly distressed.

Cardiovascular System: B.P. 110/80 mm.Hg. The pulse was regular in rate (90/min.) and rhythm. The apex beat was felt 4" from the mid-sternal line in the fifth interspace. The heart sounds were pure and well heard.

Treatment and Progress.

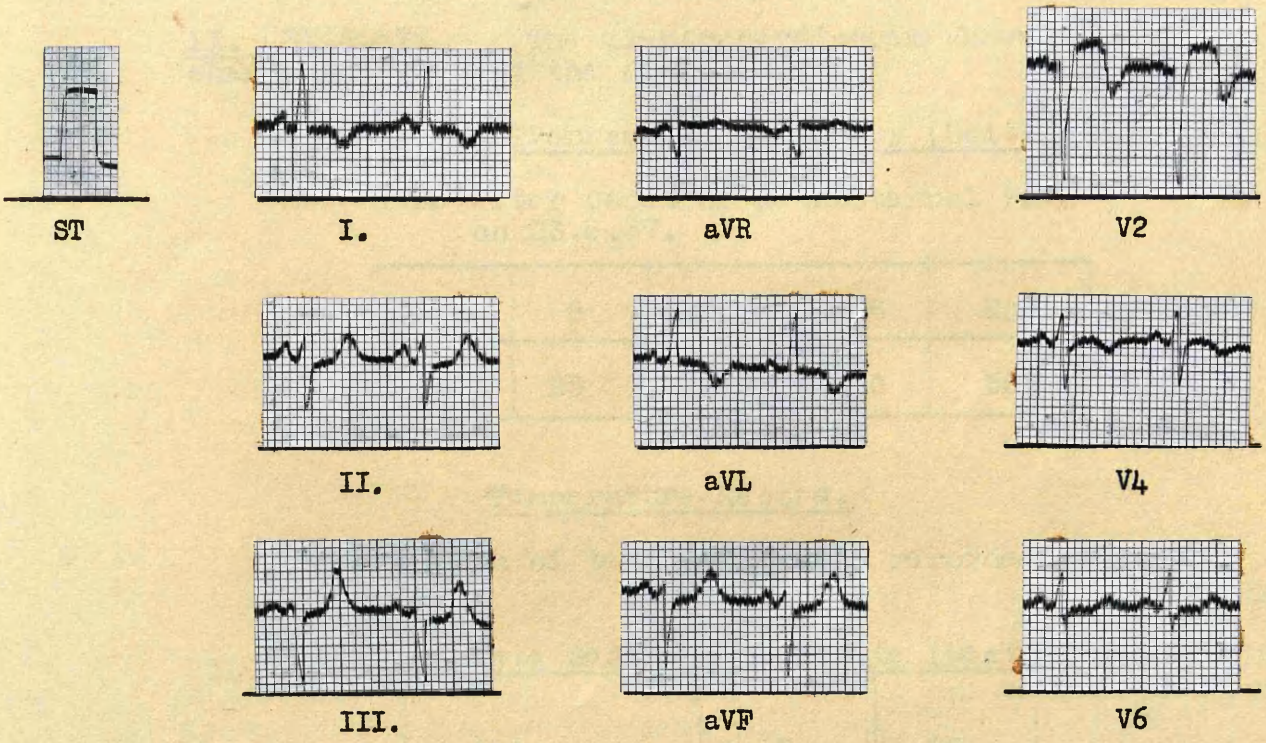
The retrosternal pain quickly responded to the intramuscular injection of morphine sulphate, gr 1/4. Despite the history of duodenal ulcer, anticoagulant therapy was started and was continued, without evidence of bleeding, until 31.6.57. The patient made an uninterrupted recovery and he was discharged home to complete his convalescence on 6.7.57. Before discharge, B.P. was 130/80 mm.Hg.

Electrocardiographic Findings.

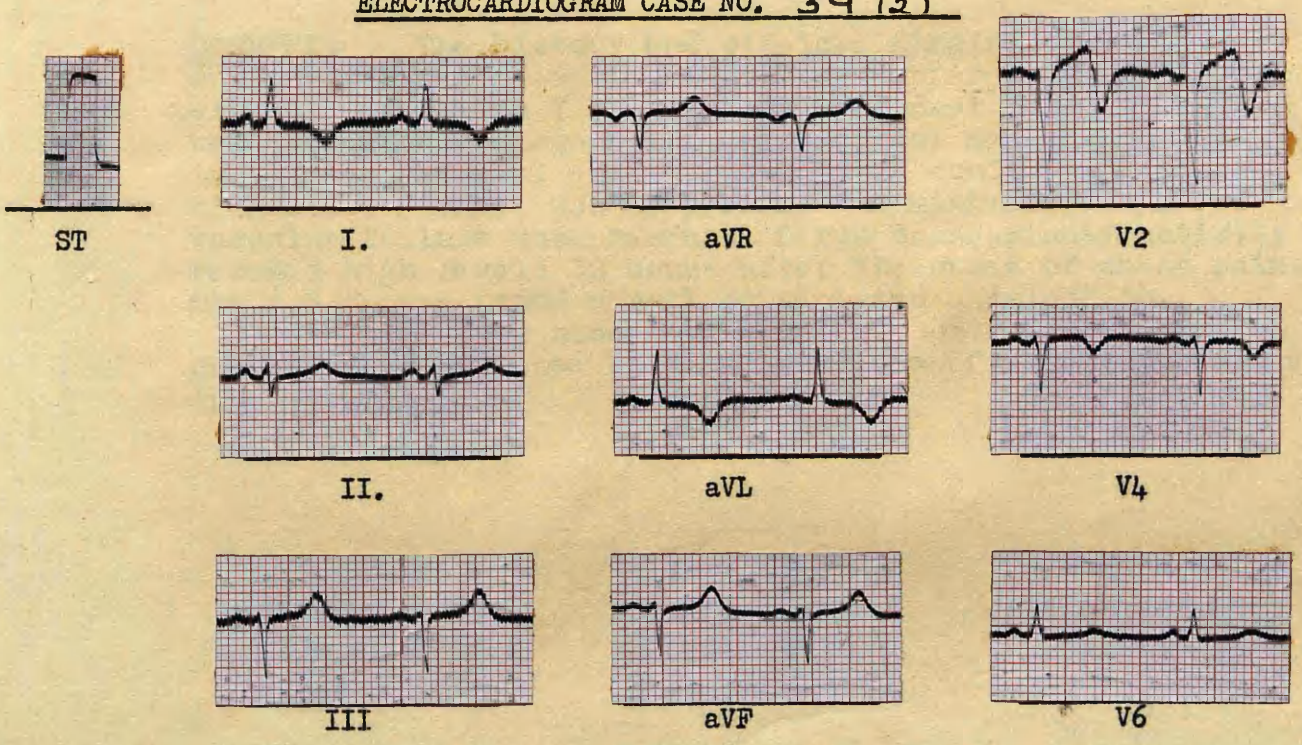
I. 23.5.57: (10.30 p.m) (7 hours after onset of chest pain). The electrocardiogram showed changes diagnostic of an acute intramural anterior myocardial infarction. A small r wave was present in V2.

/2

ELECTROCARDIOGRAM CASE NO. 39 (1)



ELECTROCARDIOGRAM CASE NO. 39 (2)



II. 31.5.57: The electrocardiogram showed sequential changes confirming the diagnosis.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Retrosternal Pain on 23.5.57.

Hours.	6	32	56	80
Units.	25	58	50	30

Temperature Record.

No elevation of temperature was recorded.

Erythrocyte Sedimentation Rate (Westergren).

Days.	7	28
mm/1st.hr.	8	5

COMMENT: The history and clinical findings were very suggestive of a good risk myocardial infarction and the electrocardiograms 7 hours after the onset of the illness were considered diagnostic of intramural myocardial infarction. Serial electrocardiograms confirmed the diagnosis. There was no pyrexia but minimal peripheral vascular failure was present. Serum transaminase activity reached high levels 32 hours after the onset of chest pain. The E.S.R. was found normal on repeated examination.

The assay was considered to have contributed early confirmatory evidence of the occurrence of acute myocardial infarction.

CASE NO. 40.

History of Present Illness.

A male, aged 43 years, a storeman, was admitted to a surgical ward on 7.6.57., complaining of sudden onset of lower sternal and epigastric pain of one hour's duration. The patient was seized with severe gripping pain in the epigastrium and under the lower end of the sternum when running for a bus. The pain radiated to both scapular regions and down both arms. For three months, he had had mild symptoms of angina pectoris on sternuous exertion. He had been admitted to hospital as a case of suspected perforation of a duodenal ulcer.

There was no relevant past history.

Clinical Findings on Admission.

The patient was an obese man, who was not distressed.

Cardiovascular System: B.P. 115/75 mm.Hg. The pulse was regular in rate (94/min.) and rhythm. The apex beat was not felt. The heart sounds were pure, but faintly heard.

Alimentary System: The abdomen was obese; there was no rigidity of the abdominal muscles although there was marked tenderness on palpation in the epigastrium.

Respiratory System: On auscultation, scattered rhonchi were heard over both lung fields.

Treatment and Progress.

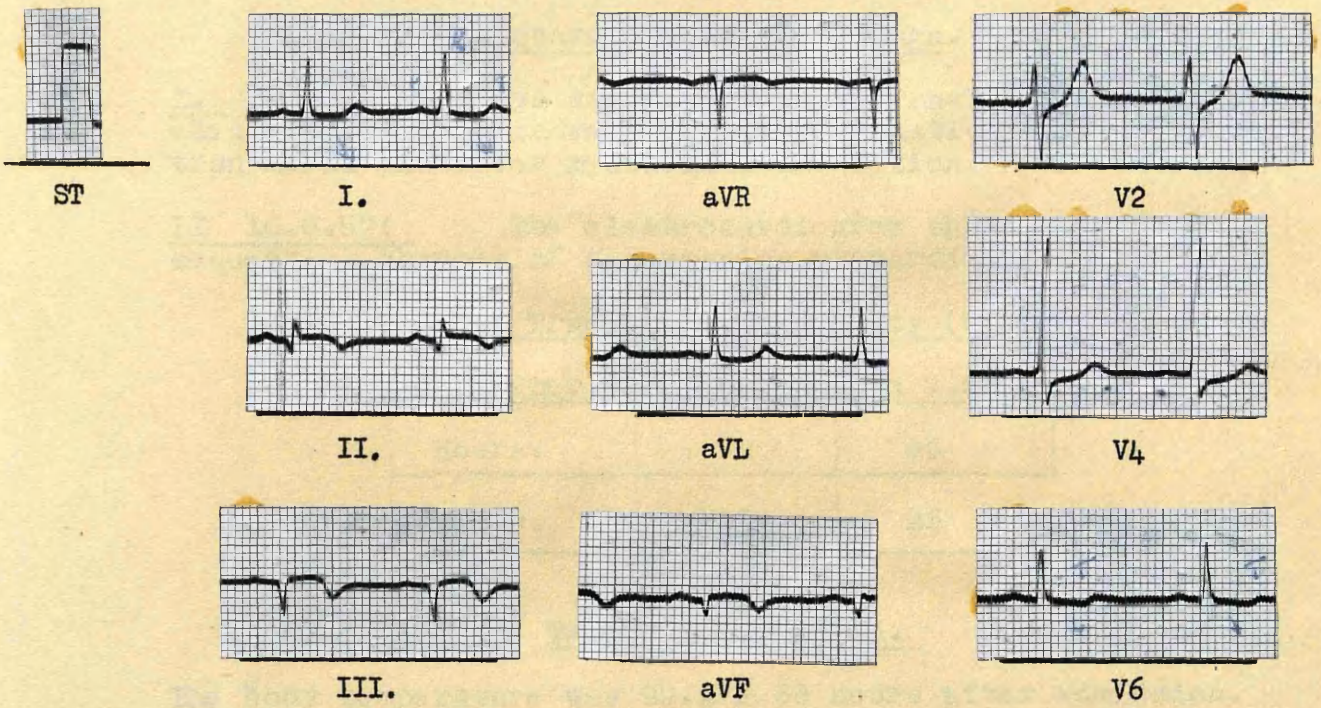
8.6.57: The patient still complained of epigastric pain which radiated down both arms and was also referred into both scapular regions.

9.6.57: He was free from pain, although slight tenderness on deep palpation was present in the epigastrium.

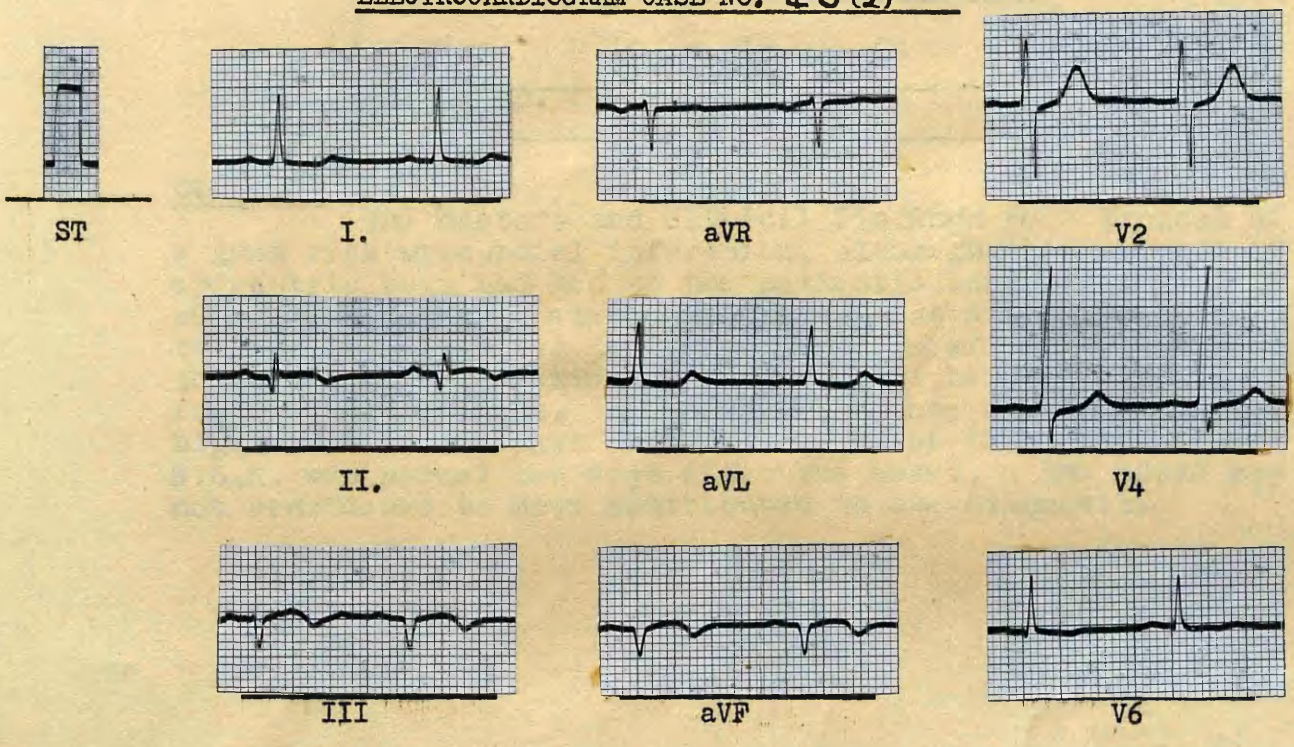
10.6.57: B.P. 110/75 mm.Hg. The patient had had no recurrence of pain and there was no abdominal tenderness. The diagnosis of perforated duodenal ulcer had not been confirmed and an electrocardiogram was obtained and serum transaminase estimated.

12.6.57: B.P. 100/75 mm.Hg. The diagnosis of posterior myocardial infarction having been made, the patient was transferred to a medical ward. No special therapy was indicated and he made an uninterrupted recovery. He was considered fit for discharge home to complete his convalescence on 20.7.57.

ELECTROCARDIOGRAM CASE NO. 40 (1)



ELECTROCARDIOGRAM CASE NO. 40 (2)



Electrocardiographic Findings.

I. 10.6.57: (3 days after onset of sternal pain.) The electrocardiogram showed changes diagnostic of an acute transmural posterior myocardial infarction.

II 16.6.57: The electrocardiogram showed minor sequential changes of a posterior myocardial infarction.

SerialSerum Transaminase Activity (Units/ml/min.)

Time after Onset of Pain on 7.6.57.

Hours.	72	85
Units.	65	25

Temperature Record.

The body temperature was 99.2°F 36 hours after admission. The record was normal apart from this.

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Pain on 7.6.57.

Days.	10	18	24	31
mm/1st.hr.	4	12	12	8

COMMENT:

The history and clinical findings were typical of a good risk myocardial infarction, although the presence of epigastric pain had led to the patient's admission to a surgical unit. The electrocardiogram was diagnostic of transmural myocardial infarction, 3 days after the onset of the illness. Pyrexia and minimal peripheral vascular failure were present. Serum transaminase activity was at high levels three days after the onset of the illness. The E.S.R. was normal ten days after the onset. The assay was not considered to have contributed to the diagnosis.

CASE NO. 41.

History of Present Illness.

A male, aged 51 years, a minister of religion, was admitted to hospital on 7.6.57., at 7 p.m., complaining of pain in the arm and chest of 2½ hours' duration. At 4.30 p.m., on the day of admission, the patient suddenly felt a very severe pain, gnawing in character, in the left scapular region which was referred into the retrosternal region and down the inner aspect of the left arm to the elbow. The pain remained severe despite an intramuscular injection of morphine gr. ½ and atropine sulphate, gr.1/150 at 5 p.m., and was still present on admission at 7 p.m.

Past History.

The patient had been subject to attacks of winter bronchitis for five years. He had been dyspnoeic on moderate exertion for three years having gained much weight in that time. In November 1956., while walking, he was seized by a severe pain in the left scapular region, which forced him to stop walking. This pain lasted for five minutes. In the month before admission, the patient had complained of epigastric pain 1½ hours after meals.

Clinical Findings on Admission.

The patient was an obese man, who was not shocked but he complained of praecordial pain.

Cardiovascular System: B.P. 150/80 mm.Hg. The pulse was regular in rate (76/min.) and rhythm. The apex beat was not felt; the heart sounds were pure and well heard.

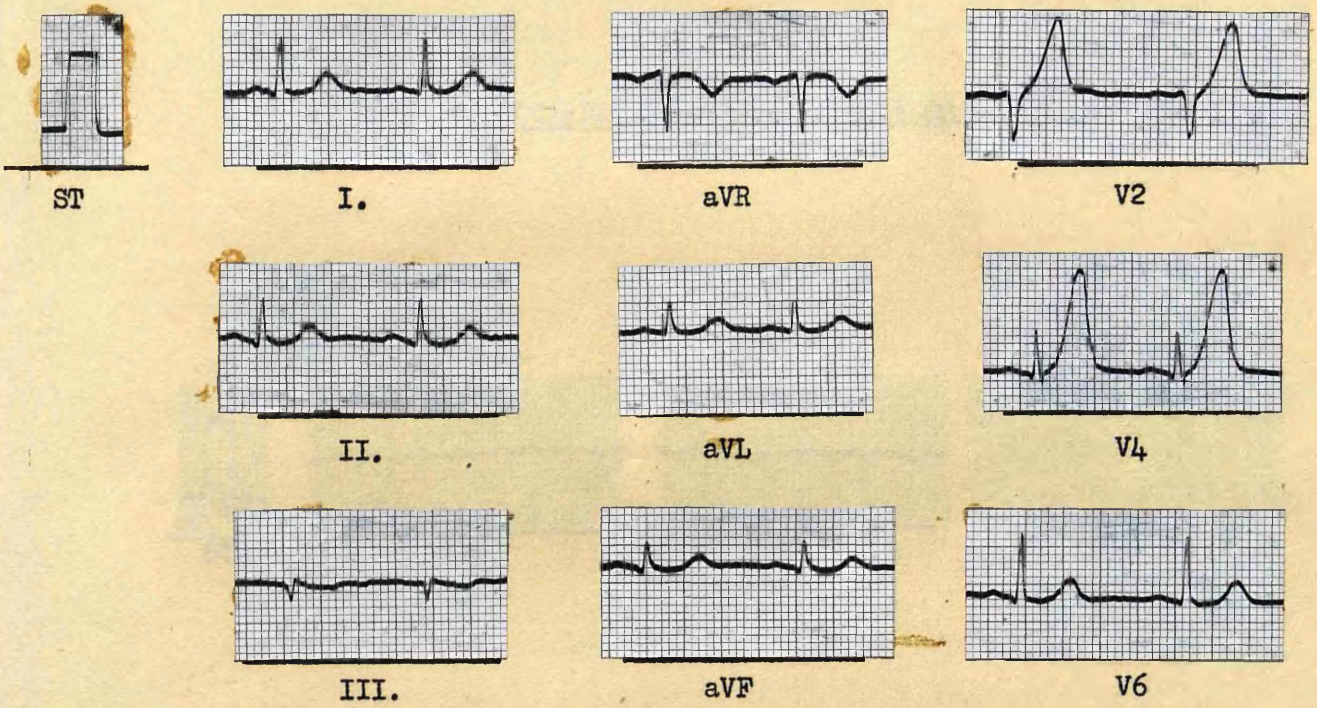
Respiratory System: On auscultation, numerous fine crepitations were heard over the left lung anteriorly. No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

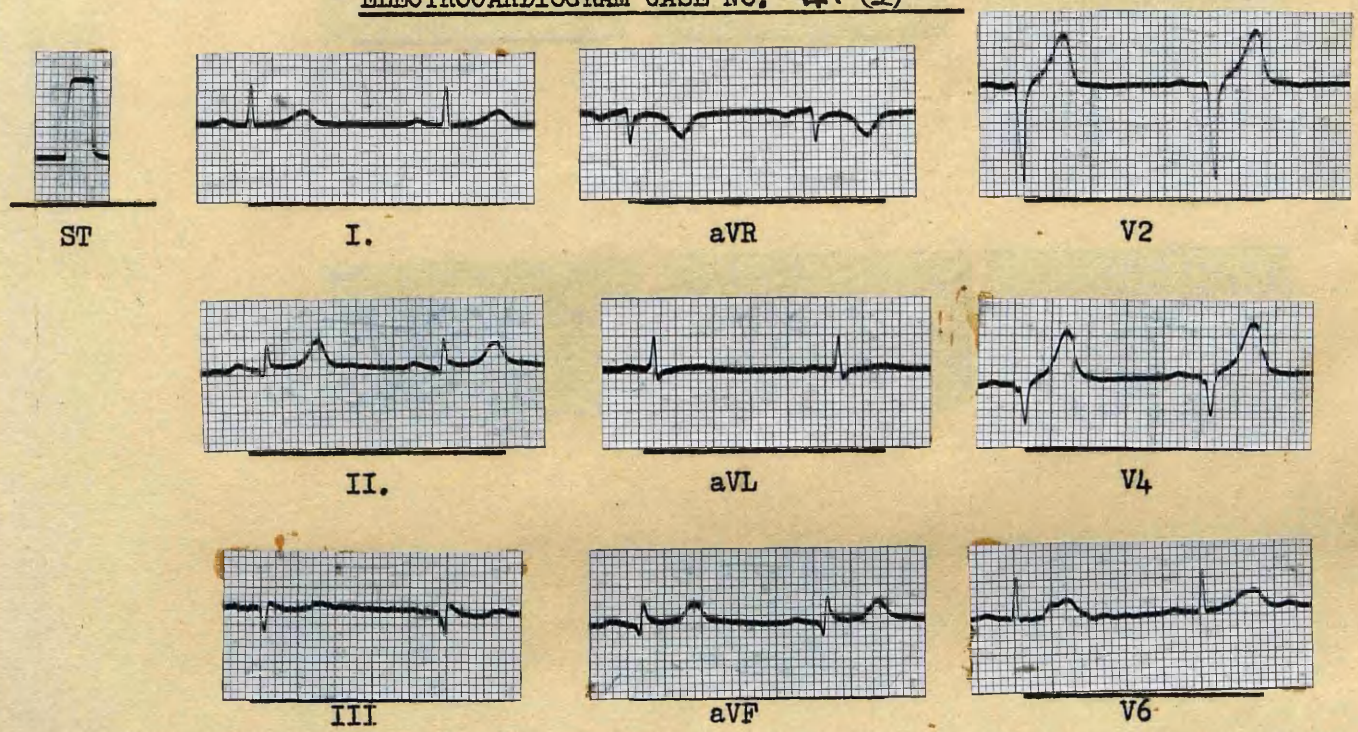
Pain was controlled by the administration of morphine sulphate, gr.¼ intramuscularly, and there was no recurrence of chest pain during the period of observation. Because of the history of dyspepsia anticoagulant therapy was not given on admission, but the patient developed phlebothrombosis in the deep veins of the left calf on 17.6.57 and anticoagulant therapy was then started and continued for three weeks. B.P. was 120/80 mm.Hg. on 8.6.57 and remained at this level until the patient's discharge from hospital on 21.7.57.

/2

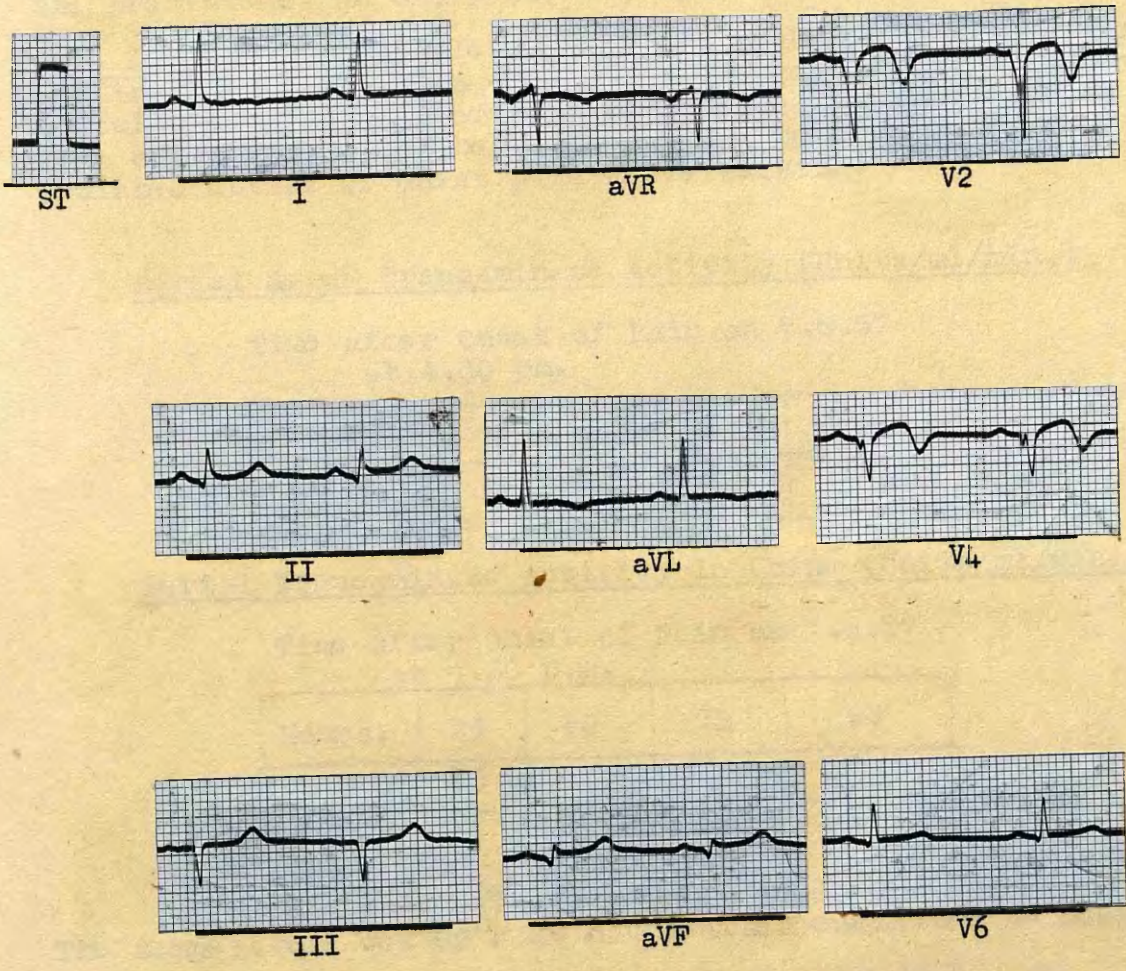
ELECTROCARDIOGRAM CASE NO. 41 (1)



ELECTROCARDIOGRAM CASE NO. 41 (2)



ELECTROCARDIOGRAM CASE NO. 41 (3)



Electrocardiographic Findings.

I. 7.6.57: ($3\frac{1}{2}$ hours after onset of pain.) The electrocardiogram showed changes very suggestive but not diagnostic of acute posterior myocardial infarction, although there was probably a pathological Q wave in aV.F and a QS wave in V2 with steep symmetrical T waves in V2.

II. 8.6.57: ($21\frac{1}{2}$ hours after onset of pain.) The electrocardiogram now showed a QS pattern in V4 which was diagnostic of an acute antero-septal myocardial infarction. The presence of a pathological Q wave in a.V.F. was confirmed suggesting the presence of an old posterior myocardial infarction.

III. 16.6.57: The electrocardiogram showed changes which confirmed the diagnosis of a recent acute transmural antero-septal and old posterior myocardial infarction, which may have occurred in November 1956., when the patient had an isolated attack of chest pain while walking.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Pain on 7.6.57 at 4.30 pm.

Hours.	4	17	47	68
Units.	30	77	40	25

Serial Transaminase Activity in Urine (Units/ml/min.)

Time after Onset of Pain on 7.6.57 at 4.30 p.m.

Hours.	24	48	72	96
Units.	10	16	12	9

Temperature Record.

The temperature was 99°F 24 hours after admission to hospital.

Erythrocyte Sedimentation Rate (Westergren)

Time after Onset of Pain on 7.6.57 at 4.30 pm.

4 hours.	10 days.	17 days.
mm/1st.hr. 8	26	8

COMMENT:

The history was suggestive of myocardial infarction. The initial electrocardiogram was very suggestive but not diagnostic of transmural myocardial infarction 3½ hours after the onset of the illness, although serial electrocardiograms were diagnostic of myocardial infarction. The infarction was thought to be of good risk type but it became clear later that the patient had had a previous myocardial infarction and, consequently, should have been regarded as a poor risk case. Pyrexia was present but there was no evidence of peripheral vascular failure. Serum transaminase activity reached high levels 17 hours after the onset and before the second electrocardiogram was examined, while the E.S.R. was normal four hours after the onset of the illness. The assay was considered to have provided early and valuable diagnostic aid. The importance of examining the serum 6 - 24 hours following an acute myocardial infarction is well illustrated since the specimen examined in this period was the only one found to exhibit abnormal transaminase activity.

CASE NO. 42.

History of Present Illness.

A male, aged 54 years, a stores clerk, was admitted to hospital on 15.5.57, complaining of retrosternal pain of 3½ hours' duration. 3½ hours before admission, the patient developed severe constricting retrosternal pain, which radiated down the left arm. He felt nauseated, began to sweat and became breathless. He had had a similar, but less severe, attack of pain on 12.5.57, which was followed by dyspnoea of moderate exertion.

Past History.

In October 1956., the patient had had severe pain in the neck which was referred down both arms. These symptoms were ascribed to prolapse of a cervical disc.

Clinical Findings on Admission.

The patient was a well built man who was mildly shocked and who complained of gripping, retrosternal pain.

Cardiovascular System: B.P. 140/90 mm.Hg. The pulse was regular in rate (82/min.) and rhythm. The apex beat was not felt. The heart sounds were pure, but distant.

Respiratory System: On auscultation, a few crepitations were heard over both lung fields posteriorly.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Pain was controlled by the intramuscular administration of pethidine, 100 mgm. Anticoagulant therapy was started soon after admission and was continued for four weeks.

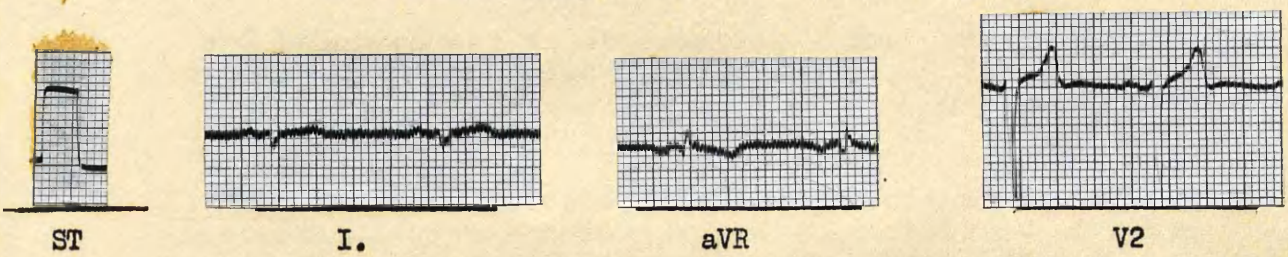
16.5.57: Pericardial friction was heard to the left of the sternum in the fourth interspace. B.P. 130/80 mm.Hg.

20.5.57: The patient complained of severe retrosternal pain, gripping in character, which lasted for one hour and which required pethidine for its relief.

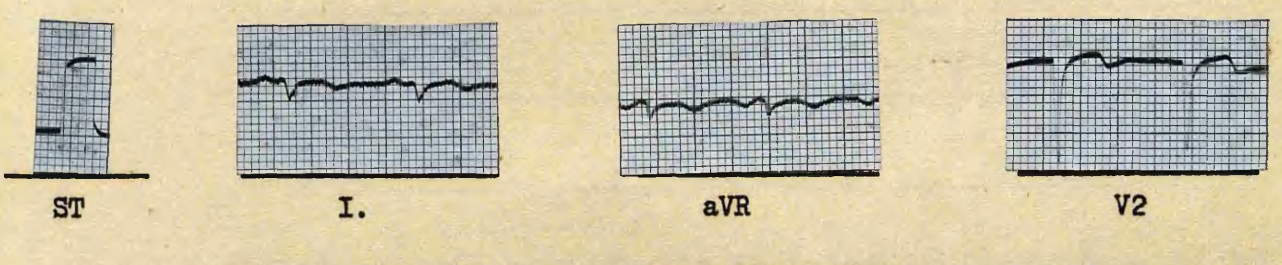
A second myocardial infarction was suspected and further transaminase estimations were performed.

There was no further fall in blood pressure /2

ELECTROCARDIOGRAM CASE NO. 42 (1)



ELECTROCARDIOGRAM CASE NO. 42 (a)



/ and progress was uninterrupted. The patient was discharged from hospital on 22.6.57.

Electrocardiographic Findings.

I. 15.5.57: (4 hours after onset of chest pain.) The electrocardiogram showed changes diagnostic of an acute transmural antero-septal myocardial infarction.

II. 30.5.57: The electrocardiogram confirmed the diagnosis of antero-septal myocardial infarction with sequential changes indicating lateral extension of the infarction. The infarction was considered to be extensive.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after onset of Retrosternal Pain on 15.5.57 at 9.45 p.m.

a)

Hours.	5	15	39	62	86
Units.	Haem.	135	180	84	38

Time after onset of Pain on 20.5.57.

b)

Hours.	24	48
Units.	82	36

Serial Transaminase Activity in Urine (Units/ml/min.)

Time after onset of Retrosternal Pain on 15.5.57.

Hours.	24	48	72	96
Units.	16	12	10	16

Temperature Record.

No elevation of temperature was recorded.

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Retrosternal Pain on 15.5.57 at 9.45 pm.

Hours.	15	8 days	15 days	21 days.
mm/1st. hr.	32	54	14	9

COMMENT:

Attacks of myocardial infarction were observed on 15.5.57 (42a)and on 20.5.57 (42b). In the first attack (42a)., the history and clinical findings were typical of good risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction 4 hours after the onset of the illness. There was no pyrexia and a minimal degree of peripheral vascular failure was present. Serum transaminase activity rose to high levels, 15 hours after the onset of the illness and the E.S.R. was elevated at this time. The assay was not considered to have contributed to the diagnosis.

In the second attack (42b)., an attack of severe angina pectoris at rest raised the suspicion of a fresh myocardial infarction, although there was no pyrexia or evidence of peripheral vascular failure. Serum transaminase activity reached high levels 24 hours after the onset of pain. An electrocardiogram, performed several days later, was diagnostic of extension of the previous myocardial infarction. This infarction was regarded as a poor risk one. The assay was considered to have provided early and valuable aid in the diagnosis of extension of the myocardial infarction.

CASE NO. 43.

History of Present Illness.

A female, aged 43 years, a housewife, was admitted to hospital on 15.5.57., complaining of repeated attacks of retrosternal pain. On 14.5.57., at 8 a.m., while sitting in a chair after polishing the grate the patient felt a severe crushing pain behind the sternum which was referred down both arms, especially the left. This attack of pain lasted for 30 minutes.

On 15.5.57., a similar pain recurred on three occasions. One attack started at 8 a.m., which lasted for 45 minutes, another at 9 a.m., lasting for 10 minutes and yet another at 10 a.m. The latter lasted for one hour.

Past History.

The patient had never previously had chest pain but she had noticed progressive exertional dyspnoea for one year.

Clinical Findings on Admission.

The patient was overweight but was neither shocked nor in pain.

Cardiovascular System: B.P. 110/60 mm.Hg. The pulse was regular in rate (64/min.) and rhythm. The apex beat was palpable $\frac{1}{2}$" within the mid-slavicular line in the fifth interspace. The heart sounds were pure and of good quality. No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Anticoagulant therapy was begun shortly after admission and was continued for 28 days.

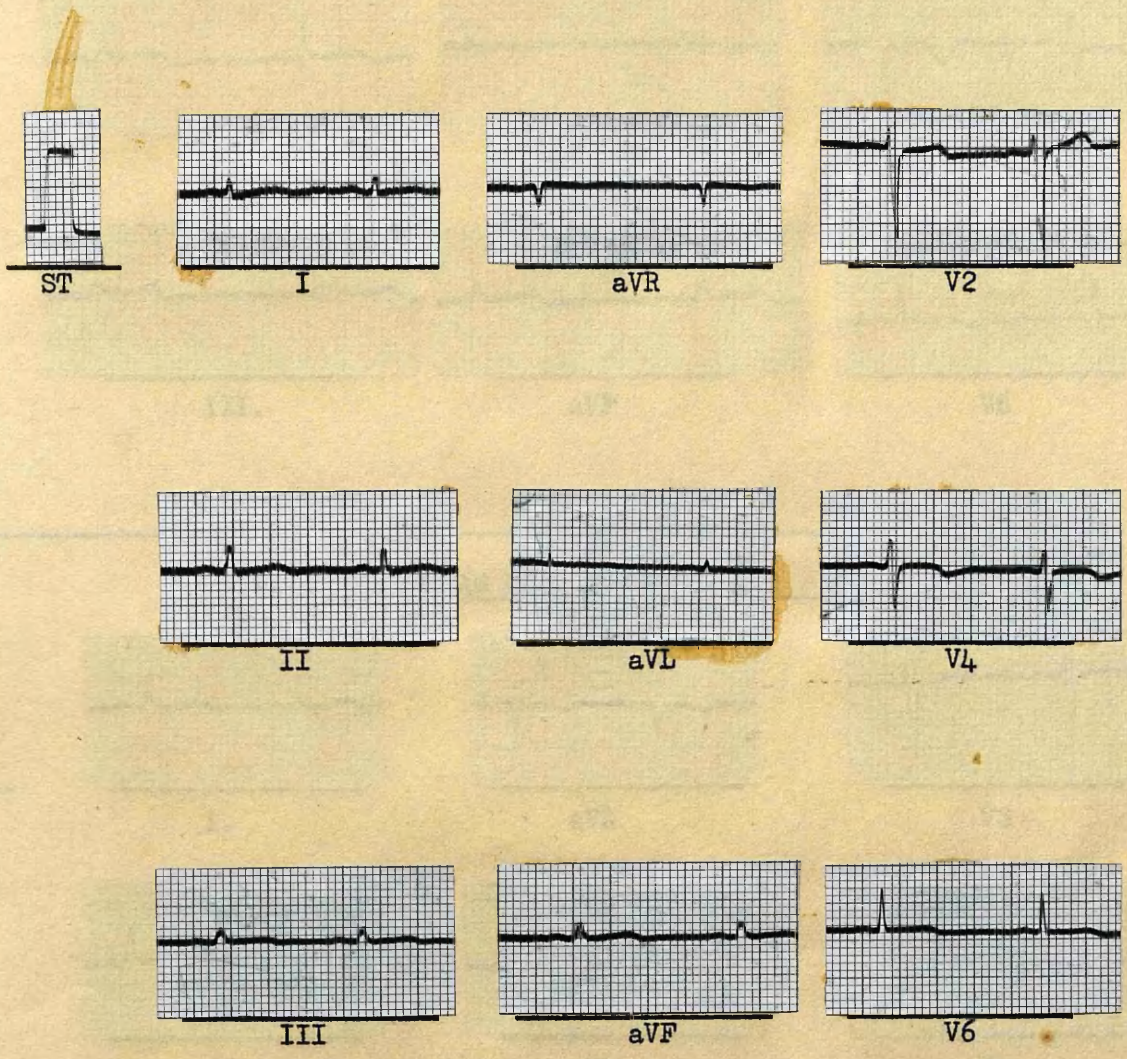
16.5.57: B.P. 80/50 mm.Hg. There had been no recurrence of pain and the patient's general condition was excellent.

17.5.57: B.P. 90/55 mm.Hg. There had been no recurrence of pain. The patient had no further symptoms referrable to the cardiovascular system and was discharged from hospital on 29.6.57: The blood pressure was 100/60 mm.Hg.

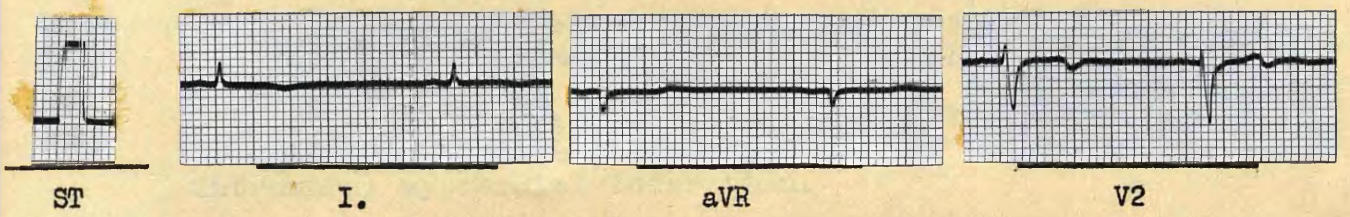
Electrocardiographic Findings.

I. 15.5.57: (26 hours following chest pain on 14.5.57 at 8 a.m.) The electrocardiogram showed changes diagnostic of an acute intramural septo-lateral myocardial infarction.

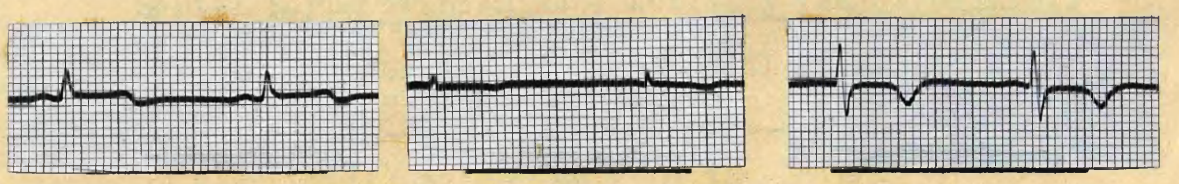
ELECTROCARDIOGRAM CASE NO. 43 (1)



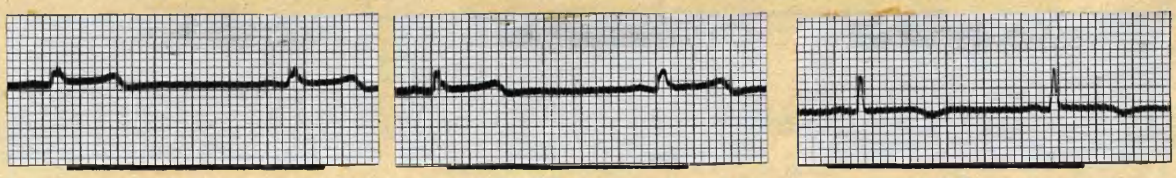
ELECTROCARDIOGRAM CASE NO. 43 (2)



ST I. aVR V2

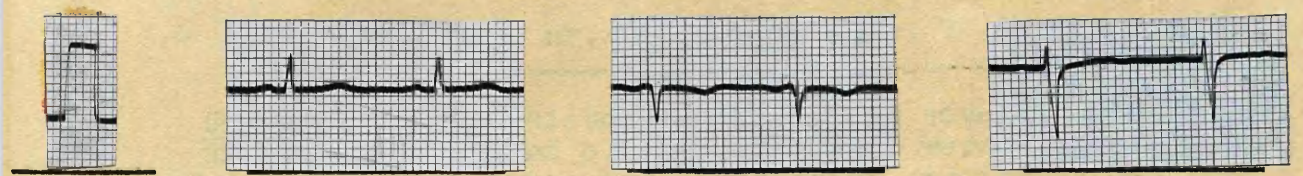


II. aVL V4

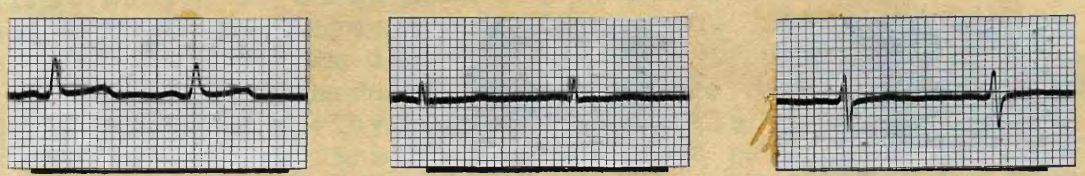


III. aVF V6

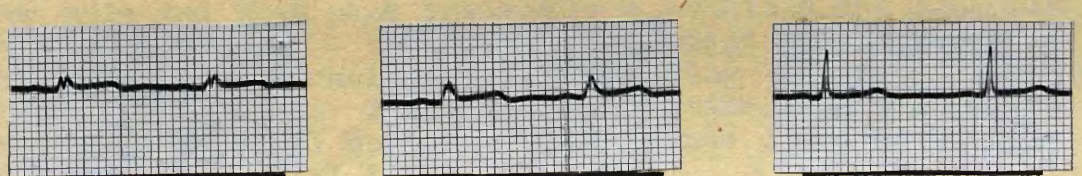
ELECTROCARDIOGRAM CASE NO. 43 (3)



ST I. aVR V2



II. aVL V4



III aVF V6

II. 17.5.57: The electrocardiogram showed further T wave inversion in V4 and V6 confirming the diagnosis.

III. 16.6.57: The electrocardiogram showed restitution of the T waves which provided additional evidence of an intramural myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Retrosternal Pain on 14.5.57 at 8 a.m.

Hours.	32	49	73
Units.	56	21	11

Temperature Record.

No elevation in temperature was recorded.

Erythrocyte Sedimentation Rate (Westergren.)

Time after Onset of Chest pain on 15.5.57 at 8 a.m.

32 hours.	21 days.
mm/1st. hr. 4	mm/1st.hr. 7

COMMENT: The history of recurrent severe attacks of angina pectoris and clinical findings were very suggestive of a good risk myocardial infarction and the first electrocardiogram taken 26 hours following the onset of the first attack of chest pain was considered diagnostic of acute intramural myocardial infarction. Serial electrocardiograms confirmed this diagnosis. No pyrexia or evidence of peripheral vascular failure developed. Serum transaminase activity was at high levels 32 hours after the onset of the first attack of chest pain, but this was the only abnormal level found on repeated examination and it was considered that late sampling of the serum accounted for this and that peak transaminase activity had probably been reached before the patient's admission to hospital. The E.S.R. was normal 32 hours following the onset of the first chest pain. The assay was considered to have contributed useful confirmatory evidence of the occurrence of acute myocardial infarction.

CASE NO. 44.

History of Present Illness.

A male, aged 48 years, a labourer, was admitted to hospital on 24.5.57., complaining of retrosternal pain of 6 hours' duration.

At 1 a.m. on 24.5.57., the patient, when sitting, was seized with a severe, gripping pain in the left upper arm which spread across his chest to the right shoulder. The pain continued until after he received an intramuscular injection of morphine sulphate, gr.1/4. at 8 a.m. on 24.5.57.

Past History.

The patient had previously had two moderately severe pains in the left arm on exertion which lasted for fifteen minutes. The first of these pains occurred in 1951., while the second occurredin April, 1957. The patient had lesions of the skin of the trunk due to mycosis fungoides.

Clinical Findings on Admission.

The patient was a well built man who had no pain.

Cardiovascular System: B.P. 100/60 mm.Hg. The pulse was regular in rate (80/min.) and rhythm. The heart was not enlarged, the apex beat being palpable 1" within the mid-clavicular line in the fifth interspace. The heart sounds were pure, but distant.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Anticoagulant therapy was started shortly after admission to hospital and was continued for three weeks. Hypotension persisted for three weeks, but before discharge from hospital on 6.7.57., the B.P. was 120/80 mm.Hg.

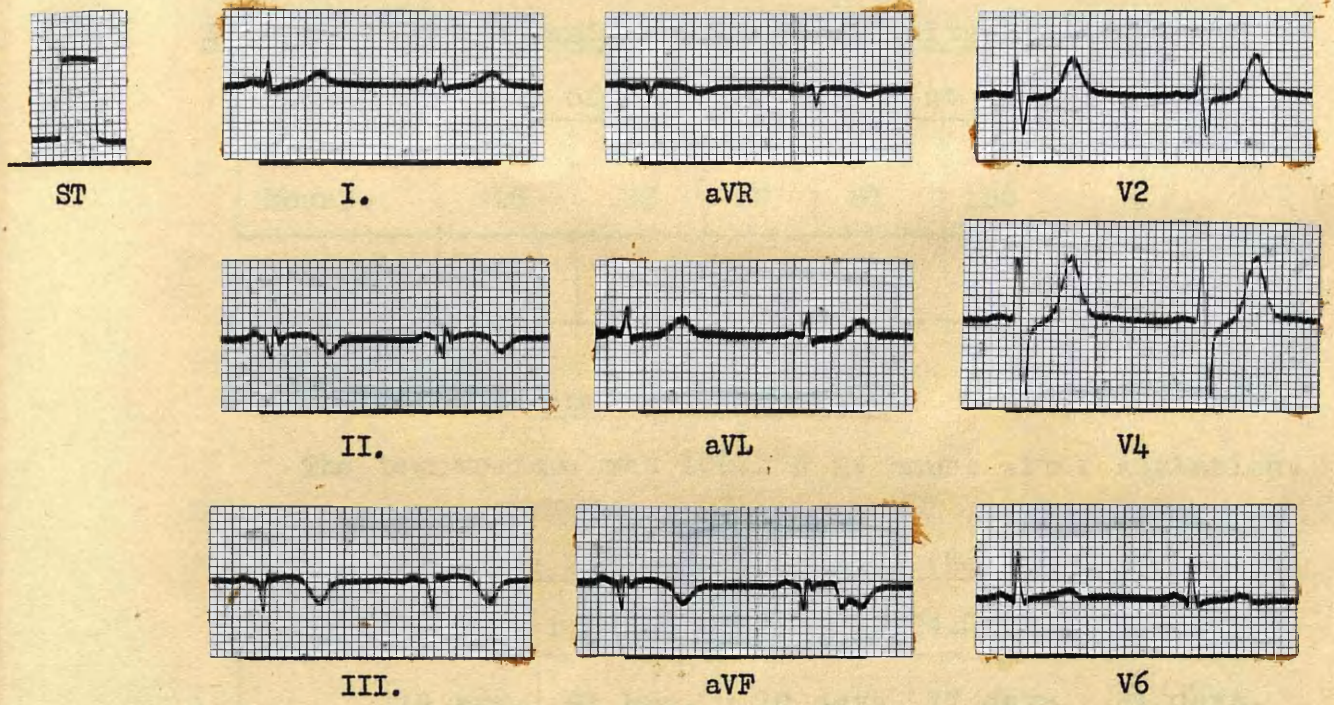
Electrocardiographic Findings.

I. 24.5.57: (16 hours after onset of pain on 24.5.57.). The electrocardiogram showed changes diagnostic of an acute transmural posterior myocardial infarction.

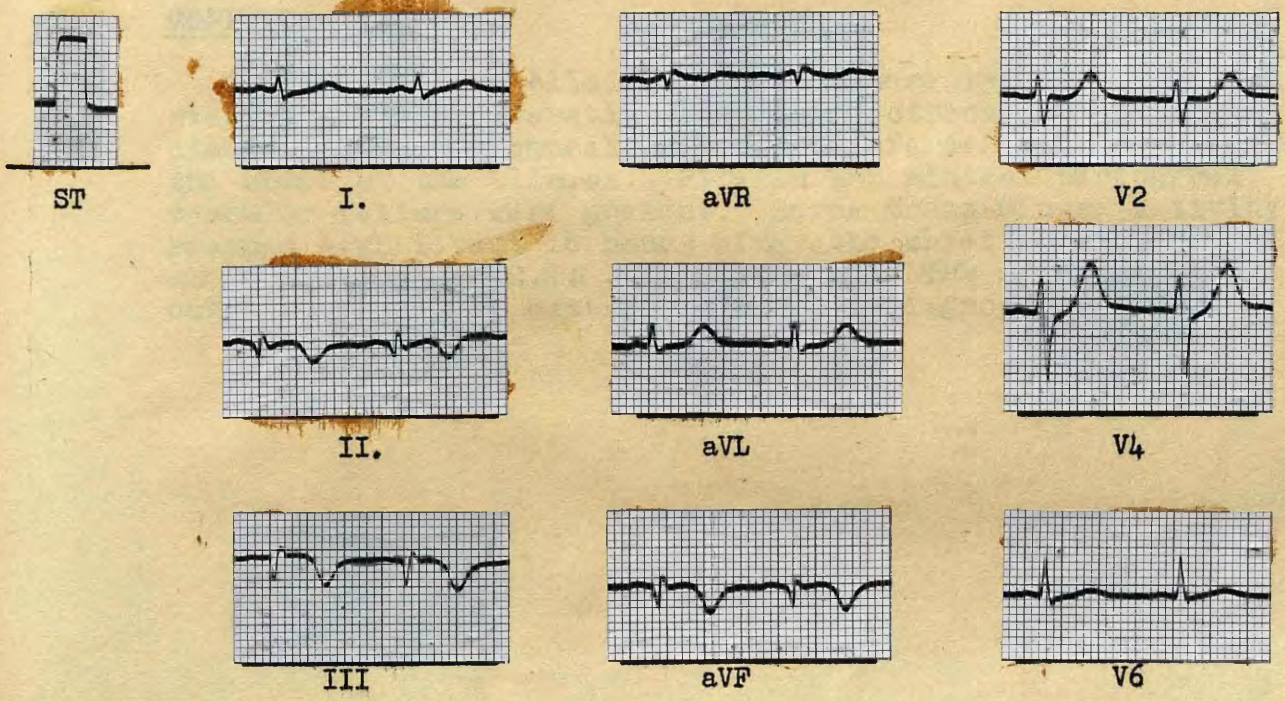
II. 8.6.57: The electrocardiogram showed little change and was still diagnostic of posterior myocardial infarction.

/2

ELECTROCARDIOGRAM CASE NO. 44 (1)



ELECTROCARDIOGRAM CASE NO. 44 (2)



Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Pain on 24.5.57 at 1 a.m.

Hours.	16	33	57	81	105
Units.	90	173	62	50	25

Temperature Record.

The temperature was 100.2°F 24 hours after admission.

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Pain on 24.5.57 at 1 a.m.

	16 hrs.	81 hrs.	10 days	17 days.	31 days.
mm/1st. hr.	7	60	45	9	7

COMMENT:

The history and clinical findings were typical of a good risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction 16 hours after the onset of the illness. Pyrexia and minimal peripheral vascular failure were present. Serum transaminase activity reached high levels 16 hours after the onset of the pain, at which time the E.S.R. was normal. The assay was not considered to have contributed to the diagnosis.

CASE NO. 45.

History of Present Illness.

A male, aged 63 years, a retired civil servant, was admitted to hospital on 25.5.57., complaining of retrosternal pain of six hours' duration. 6 hours before admission, the patient developed severe retrosternal pain of constricting character while resting. He became breathless shortly after the onset of pain and felt nauseated. The pain lasted for about 45 minutes and then cleared, but returned one hour later, when it was referred down the left arm; the pain continued until the patient's admission to hospital.

Past History.

The patient had developed mild symptoms of angina pectoris on exertion one year previously and retired from his work because of this.

Clinical Findings on Admission.

The patient was a thin, anxious man, who complained of continuing retrosternal pain. He was mildly shocked.

Cardiovascular System: B.P. 115/70 mm.Hg. The pulse was regular in rate and rhythm. The heart was not enlarged, the left border of the heart, as determined by percussion, being within the mid-clavicular line. The heart sounds were distant but apical prodiastolic gallop rhythm was present. No murmurs were heard.

Respiratory System: On auscultation, scattered rhonchi were heard throughout the lung fields. Numerous fine crepitations were present over the base of the left lung posteriorly. No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

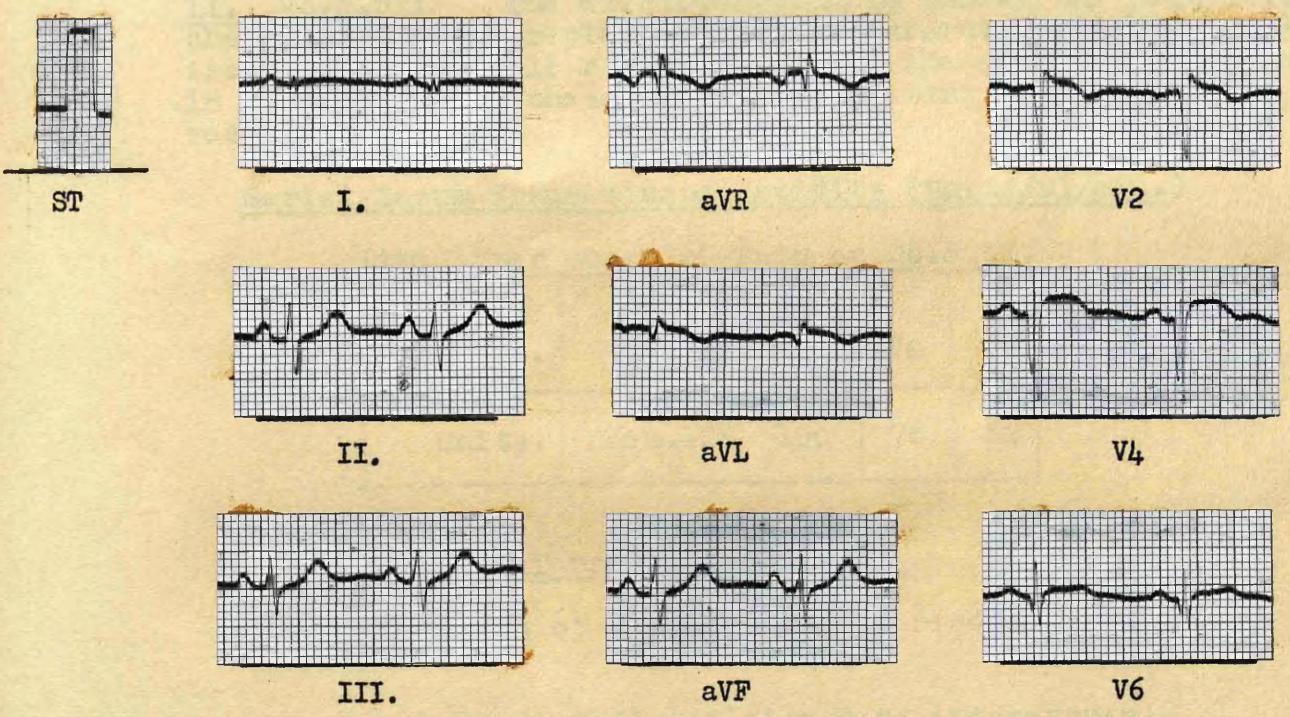
Pain was quickly controlled by the intramuscular injection of morphine sulphate, gr.1/4. Anticoagulant therapy was started soon after admission and was continued for 28 days. The patient was symptom-free on the day following his admission and remained so throughout the period of observation. Before his discharge from hospital on 16.7.57., the B.P. was 140/80 mm.Hg.

Electrocardiographic Findings.

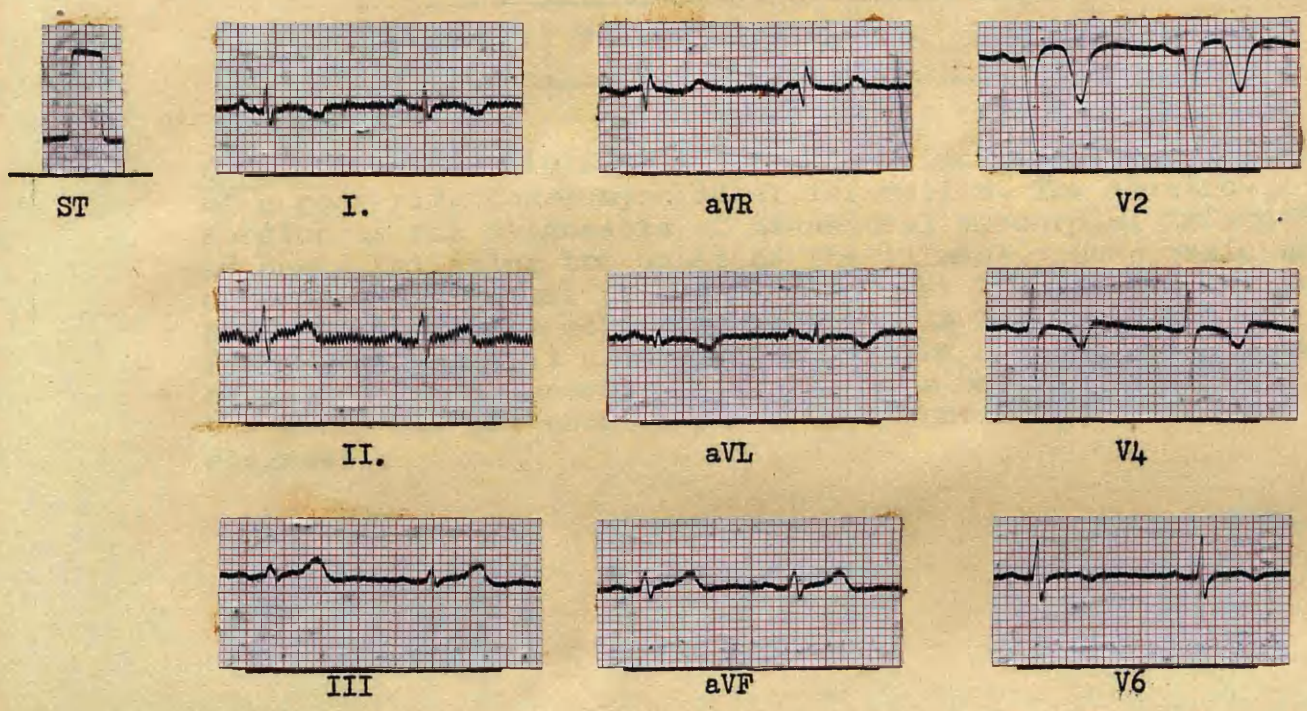
I. 26.5.57:(19 hours after onset of chest pain.) The electrocardiogram showed changes diagnostic of an acute transmural antero-septal myocardial infarction.

/2

ELECTROCARDIOGRAM CASE NO. 45 (1)



ELECTROCARDIOGRAM CASE NO. 45 (2)



II. 23.6.57: The electrocardiogram showed the sequential changes of antero-septal myocardial infarction with lateral ischaemia. A small r wave in V2 and the absence of a Q wave in V4 were noted, these changes suggesting some degree of recovery.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after onset of Pain on 25.5.57.					
Hours.	6	19	46	70	93
Units.	Haem.	126	100	76	32

Temperature Record.

No elevation of temperature was recorded.

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Pain on 25.5.57.					
Days.	5	11	18	26	33
mm/1st.hr.	24	37	42	30	13

COMMENT:- The history and clinical findings were indicative of a poor risk acute myocardial infarction. The electrocardiogram was diagnostic of transmural myocardial infarction, 19 hours following the onset of the illness. No pyrexia was observed but minimal peripheral vascular failure was present. Serum transaminase activity reached high levels 19 hours following the onset of the illness. The E.S.R. was examined 5 days after the onset and was found to be elevated. The assay was not considered to have contributed to the diagnosis.

CASE NO.46.

History of Present Illness.

A male, aged 51 years, a railway clerk, was admitted to hospital on 9.6.57., having had a severe pain in his chest which lasted for half an hour. The patient had been washing dishes when he suddenly felt breathless and was forced to sit down. A few minutes later, he developed a severe constricting pain in the lower sternal region which did not radiate. The pain lasted for half an hour, and it was so severe that he felt nauseated.

Past History.

On 20.5.57., the patient had had a similar retrosternal pain whilst walking which compelled him to stop and which was accompanied by dyspnoea. This attack lasted for 30 minutes but the patient had had no further symptoms until the day of admission.

In 1948., a subtotal thyroidectomy had been performed on the patient because of thyrotoxicosis.

Clinical Findings on Admission.

The patient was a rather excitable man, who had a mild degree of exophthalmos. There was no evidence of shock on admission.

Cardiovascular System: B.P. 140/100 mm.Hg. The pulse was regular in rate (80/min.) and rhythm. The apex beat was palpable $\frac{1}{2}$" within the mid-clavicular line in the fifth inter-space. The heart sounds were clearly heard. There was a soft V.S. murmur at the mitral area.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Anticoagulant therapy was started shortly after admission to hospital and was continued for 21 days.

10.6.57: B.P. 110/70 mm.Hg. The patient was symptom-free.

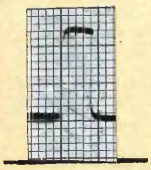
He made an uninterrupted recovery and on his discharge from hospital on 17.7.57., B.P. was 120/70 mm.Hg.

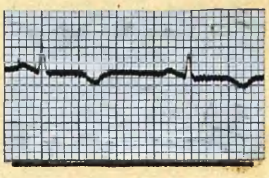
Electrocardiographic Findings.

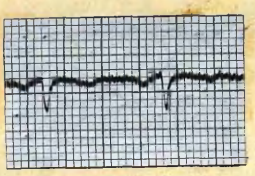
I. 9.6.57: (5 hours after onset of chest pain on 9.6.57). The

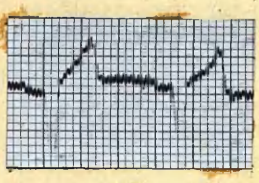
/2

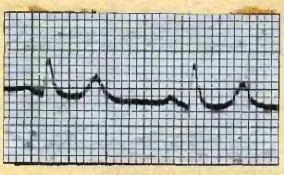
ELECTROCARDIOGRAM CASE NO. 46 (1)

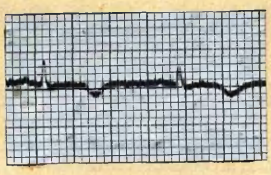

ST

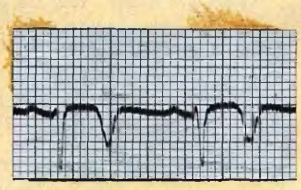

I.

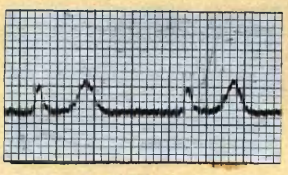

aVR

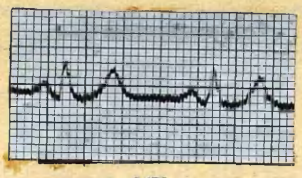

V2

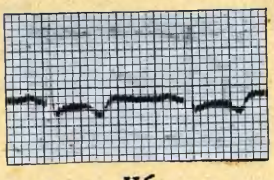

II.


aVL


V4

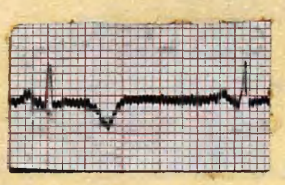

III.

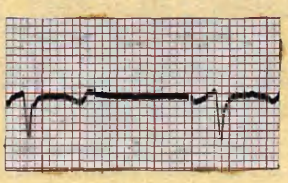

aVF

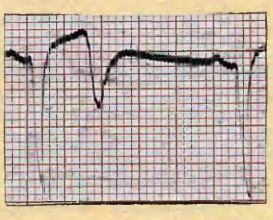

V6

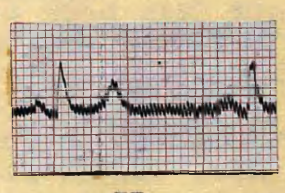
ELECTROCARDIOGRAM CASE NO. 46 (2)

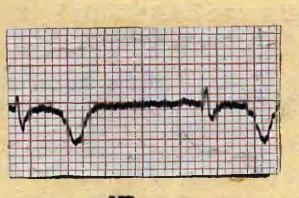

ST

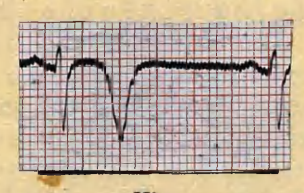

I.

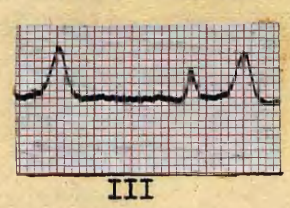

aVR

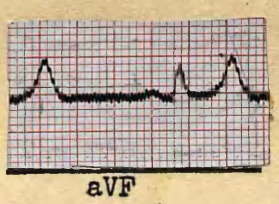

V2

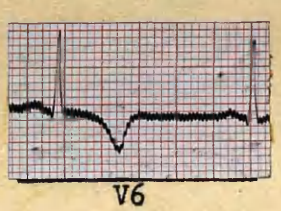

II.


aVL


V4


III


aVF


V6

electrocardiogram was diagnostic of an acute antero-septo-lateral myocardial infarction. A pathological Q wave was present in V2 and V4. The infarction was probably transmural in type.

II. 23.6.57: The electrocardiogram showed sequential changes diagnostic of acute antero-septal myocardial infarction. The presence of Qs pattern in V2 confirmed transmural type of infarction. The infarction was also considered to be extensive.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Pain on 9.6.57.					
Hours.	5	22	44	71	98
Units.	27	66	105	58	34

Temperature Record.

The temperature was normal throughout the period of observation.

Erythrocyte Sedimentation Rate (Westergren).

Time after onset of Pain on 9.6.57.					
	5 hrs.	4 days	11 days	18 days.	25 days.
mm/1st. hour.	16	9	10	3	5

COMMENT: The history and clinical findings were indicative of a good risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction 5 hours after the onset of the illness. There was no pyrexia but a minimal degree of peripheral vascular failure developed. Serum transaminase activity reached high levels 22 hours after the onset of the illness. The E.S.R. was abnormally high 5 hours after the onset while serum transaminase levels were normal. The assay was not considered to have contributed to the diagnosis.

CASE NO. 47.

History of Present Illness.

A male, aged 56 years, a company director, was admitted to hospital on 17.7.57., complaining of severe upper abdominal pain. At 1.40 a.m. on 16.7.57., the patient had been wakened by an aching pain in the throat which spread down and across the chest and settled in the epigastrium. The pain was severe and constricting in character but it was helped by an injection of pethidine, 100 mgm. at 2.30 a.m. and had cleared completely by 12.30 pm. At 7 p.m. on 16.7.57., the pain recurred. Its character and distribution were as before, but it did not respond to analgesic drugs and he was admitted to hospital on 17.7.57.

Past History.

In 1925., a nephrectomy had been performed on the patient because of suspected tuberculosis of the right kidney. He had been well until the onset of the present illness.

Clinical Findings on Admission.

The patient was a middle-aged man of florid complexion. He complained of upper epigastric pain. Jugular venous congestion was present but he was not shocked.

Cardiovascular System: B.P. 115/85 mm.Hg. The pulse was regular in rate (76/min.) and rhythm. The apex beat was not palpable but the heart was not enlarged grossly, the left border, as determined by percussion, being ¼" within the mid-clavicular line. The heart sounds were pure and of good quality. No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

The pain was controlled by the injection, intramuscularly, of morphine sulphate, gr 1/4. Anticoagulant therapy was started shortly after admission to hospital and continued for 28 days.

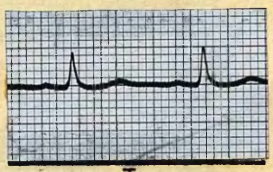
18.7.57: B.P. 110/80 mm.Hg. The patient was symptom-free.

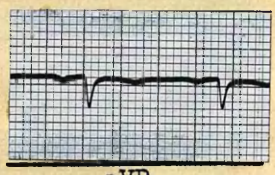
22.7.57: The patient complained of sudden pain over the left lower ribs, in the left hypochondrium and left renal area. The pain was described as like toothache and was continuous. It had started at 1 a.m., and lasted for one hour, but was succeeded by a period of anuria lasting for 12 hours. Catheterisation of the bladder produced 2 ounces of blood-stained urine.

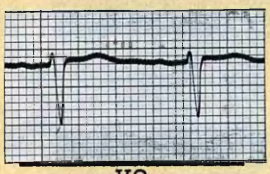
/2

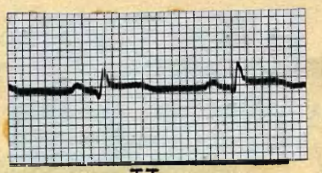
ELECTROCARDIOGRAM CASE NO. 47 (1)

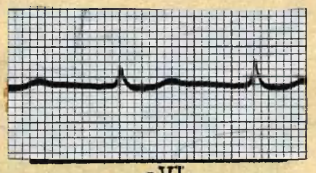

ST

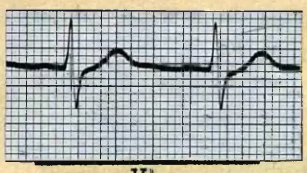

I

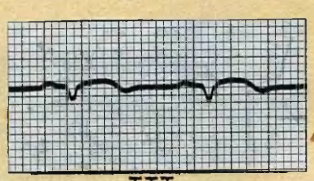

aVR

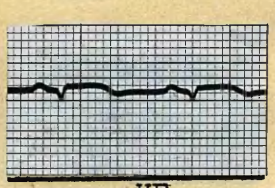

V2

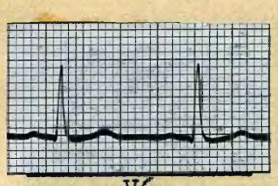

II


aVL

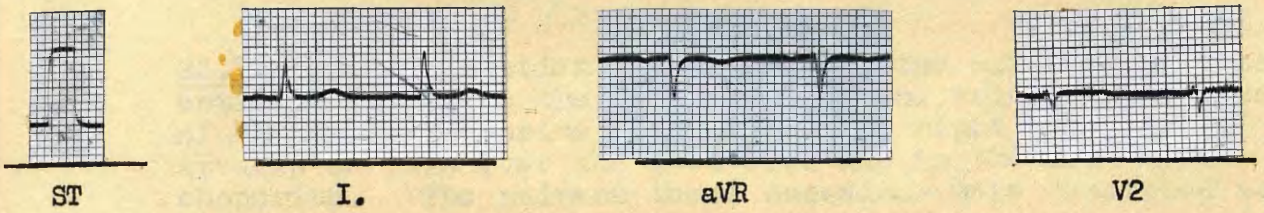

V4


III

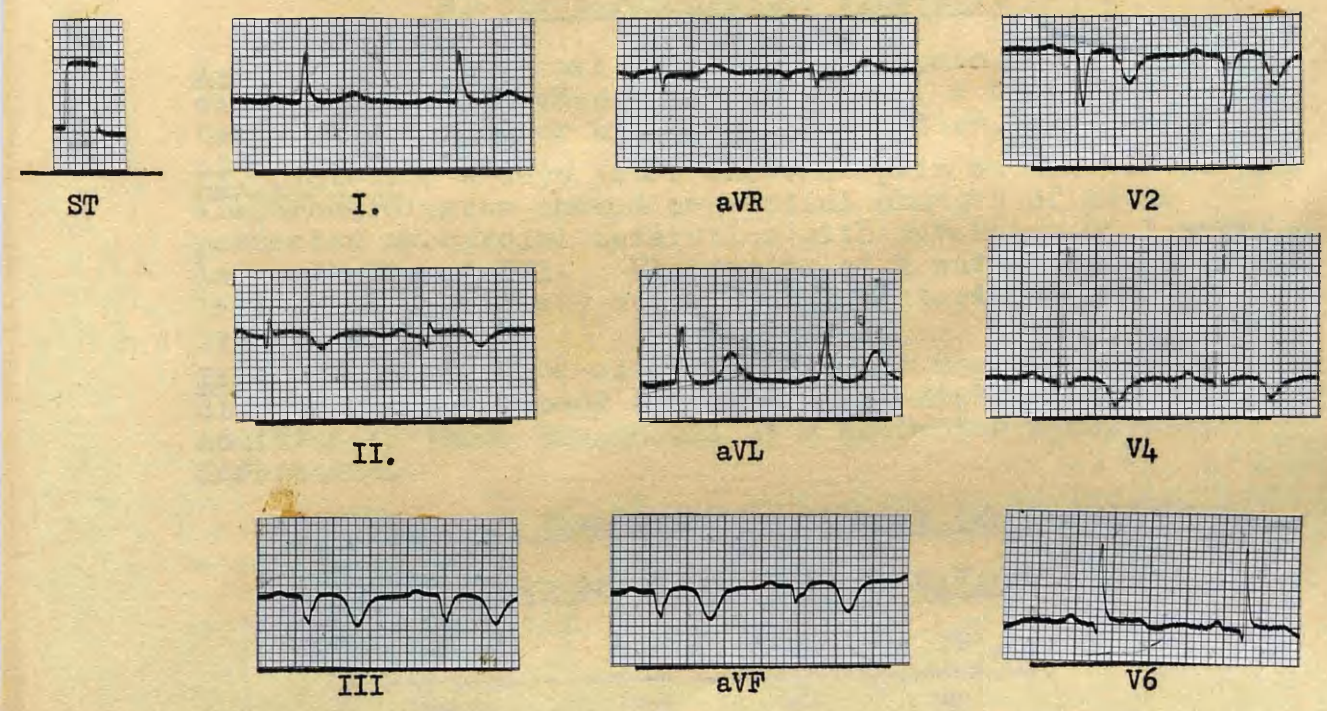

aVF


V6

ELECTROCARDIOGRAM CASE NO. 47 (2)



ELECTROCARDIOGRAM CASE NO. 47 (3)



23.7.57: The patient was passing urine normally (80 ozs.) until 7 p.m. In the next 24 hours, he voided only 3 ozs. of blood-stained urine and, during the night, had two attacks of pain over the left ribs and in the left hypochondrium. The pains on these occasions were described as colicky.

24.7.57: B.P. 120/90 mm.Hg. At 7.30 p.m., the patient again voided urine normally. The urine contained R.B.C. on microscopic examination.

25.7.57: B.P. 90/60 mm.Hg. Mild attack of left hypochondrial pain of gripping character occurred.

The patient was considered to have sustained a renal embolism with infarction in his single kidney. A fresh infarction of the myocardium was also considered probable in view of the fall in blood pressure. There was no radiological evidence of urinary calculi or bacteriological evidence of renal infection. Following these episodes of pain accompanied by anuria the patient made an uninterrupted recovery and, before his discharge from hospital on 1.9.57, the B.P. was 115/80 mm.Hg.

17.10.57: B.P. 170/115 mm.Hg. When seen as an outpatient, he was feeling well.

Electrocardiographic Findings.

I. 17.7.57: (37 hours after onset of pain.) The electrocardiogram showed changes diagnostic of a recent acute transmural posterior myocardial infarction.

II. 1.8.57: (9 days after onset of pain on 22.7.57). The electrocardiogram showed sequential changes of acute posterior myocardial infarction with inversion of T waves in leads II and III. Flattening of T waves in the chest leads was noted, very suggestive of anterior myocardial ischaemia.

III. 19.8.57: The electrocardiogram now showed changes diagnostic of a recent anterior myocardial infarction in addition to those diagnostic of a posterior myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Pain on 16.7.57.			
Hours.	33	55	79
Units.	110	63	22

/3

Time after Onset of Pain on 22.7.57.

Hours.	24	48
Units.	75	46

Temperature Record.

The temperature was elevated, 99.6°F on the day of admission and a temperature of 99°F was recorded on 24.7.57 and 25.7.57. The record was otherwise normal.

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Pain on 16.7.57.

Hours.	33
mm/1st. Hour.	4

Time after Onset of Pain on 22.7.57.

11 hours.	7 days.	14 days.
mm/1st.hr. 40	11	4

COMMENT:

Attacks of myocardial infarction were observed on 16.7.57 (47a) and on 22.7.57 (47b).

In the first attack (47a)., the history and clinical findings were typical of a good risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction 37 hours after the onset of the illness. Pyrexia was present but there was no evidence of peripheral vascular failure. Serum transaminase activity rose to high levels 33 hours after the onset of the illness, at which time the E.S.R. was normal. The assay was considered to have contributed little to the diagnosis of acute myocardial infarction.

In the second attack (47b)., the site of pain was atypical and the presence of haematuria and anuria led to a diagnosis of embolism of the patient's remaining kidney with consequent anuria. The development of pyrexia, minimal

/minimal peripheral vascular failure and recurrent pain suggested that a second myocardial infarction of poor risk type had occurred but the electrocardiogram recorded 7 days after the onset showed only changes very suggestive of anterior myocardial ischaemia without evidence of fresh infarction, although sequential changes of the previous myocardial infarction were noted. The electrocardiogram showed changes diagnostic of transmural myocardial infarction 21 days after the onset of atypical pain. There had been no recurrence of symptoms in the period between these two electrocardiograms and it was concluded that the sequential changes of infarction had been unusually slow in their development.

Serum transaminase activity reached high levels 24 hours after the onset of this atypical pain. Renal infarction had occurred and might have contributed to the rise in transaminase activity but, on review of the case, it was considered that the assay had contributed early and valuable confirmatory evidence of myocardial infarction in a difficult case.

CASE NO. 48.

History of Present Illness.

A female, aged 73 years, a housewife, was admitted to hospital on 2.4.57., complaining of retrosternal pain. For seven years she had had mild symptoms of angina pectoris and dyspnoea on exertion which, six months before her admission, had become progressively more severe until, in February 1957, she was advised to rest in bed. Since then, she had been subject to short attacks of gripping retrosternal pain whilst at rest. On the evening of 1.4.57., the patient developed a severe constricting retrosternal pain which lasted for one hour; six hours later, the pain recurred and lasted for five hours. The pain felt like a load pressing on her chest and was referred down the left arm, and she became breathless. She was admitted to hospital 16 hours after the onset of severe pain.

Clinical Findings on Admission.

The patient was an old lady, who was orthopnoeic. Cyanosis of the lips was present but she had no pain.

Cardiovascular System: B.P. 140/90 mm.Hg. The pulse was regular in rate (90/min.) and rhythm. The apex beat was situated in the sixth interspace 3" from the mid-sternal line. The heart sounds were well heard. There was a high pitched V.S. murmur at the mitral area.

Respiratory System: On auscultation, numerous medium crepitations were heard over both lung bases posteriorly. No other abnormality was found on full clinical examination.

Treatment and Progress.

Anticoagulant therapy was started shortly after admission.

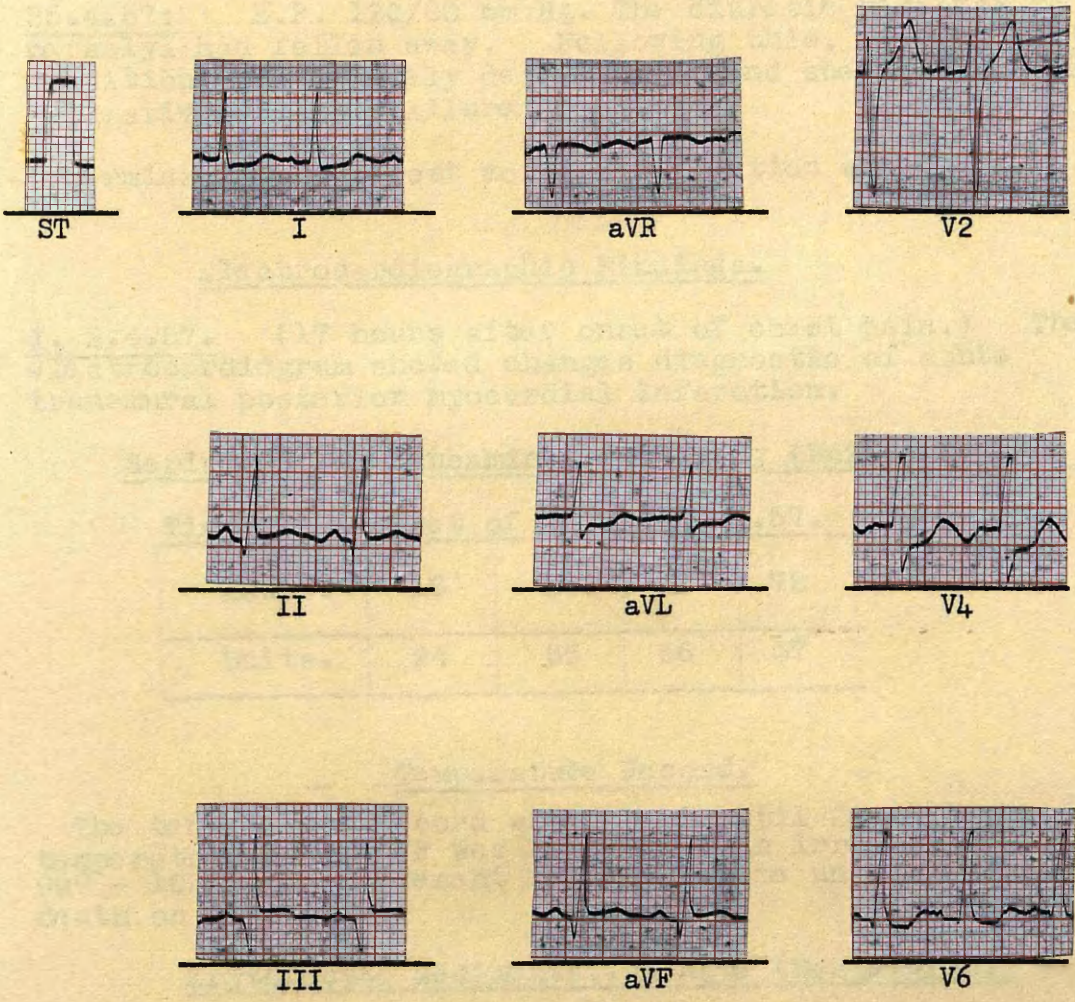
3.4.57: B.P. 120/70 mm.Hg. The patient was dyspnoeic on the slightest exertion. Treatment with mersalyl was started and an encouraging diuresis was noted.

10.4.57: When some improvement in the dyspnoea had been noted, the patient developed sudden vice-like retrosternal pain, which was referred down the inner aspect of the left arm. The pain was accompanied by intense dyspnoea and signs of pulmonary oedema. The pain lasted for 30 minutes but responded quickly to intramuscular injection of morphine sulphate, gr1/6.

11.4.57: B.P. 110/70 mm.Hg. The patient remained dyspnoeic and signs of pulmonary congestion were still present. Jugular

/2

ELECTROCARDIOGRAM CASE NO. 48



Jugular vein congestion, hepatomegaly and minimal sacral oedema were observed.

24.4.57: B.P. 120/80 mm.Hg. The patient's condition had deteriorated. The heart was enlarged, the apex beat being felt 4½" from the mid-sternal line in the sixth interspace. The signs of congestive cardiac failure were more marked. The patient had two further attacks of severe anginal pain lasting 20 and 30 minutes respectively during the day.

25.4.57: B.P. 120/80 mm.Hg. The diuretic response to mersalyl had fallen away. Following this, the patient's condition progressively deteriorated and she died in gross congestive cardiac failure on 1.5.57.

Permission for a post mortem examination was refused.

Electrocardiographic Findings.

I. 2.4.57. (17 hours after onset of chest pain.) The electrocardiogram showed changes diagnostic of acute transmural posterior myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Pain on 1.4.57.

Hours.	16	26	48	72
Units.	24	55	56	37

Temperature Record.

The temperature record was normal until 24.4.57 when a temperature of 99.6°F was recorded. An irregular pyrexia 99° - 103.2°F was present from this time until the patient's death on 1.5.57.

Erythrocyte Sedimentation Rate (Westergren.)

Time after Onset of Pain on 1.4.57.

Days.	1	7	14	23
mm/1st.hr.	65	46	24	60

COMMENT:

over...3.

COMMENT:

The history and clinical findings were typical of a good risk acute myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction 17 hours after the onset of the illness. There was no pyrexia but a minimal degree of peripheral vascular failure developed. Serum transaminase activity reached high levels 26 hours after the onset., but the E.S.R. was abnormally high.

The assay was not considered to have contributed to the diagnosis.

CASE NO. 49.

History of Present Illness.

A male aged 53 years, an engineer, was admitted to hospital on July 16th 1957, complaining of chest pain of 4 days' duration.

On July 12th, the patient developed severe crushing retrosternal pain which radiated to the left side of the chest. The pain lasted for one hour and was relieved by an injection of morphine sulphate. On July 13th and 14th., he had attacks of similar pain lasting twenty minutes and 30 minutes respectively.

At 2 a.m. on July 16th., the retrosternal pain returned and was very severe. The pain was accompanied by breathlessness. The pain lasted for 7 hours until the patient's admission to hospital.

Past History.

In December, 1955, the patient had had a cerebral thrombosis which caused a left hemiplegia. Since 1955 he had suffered from intermittent claudication. In July 1956 he had had an attack of severe chest pain which was demonstrated by electrocardiograph to be due to myocardial infarction. He had not worked for 18 months but had had no pain in his chest since June 1956.

Clinical Findings on Admission.

The patient was a well built man of good colour. He was not shocked.

Cardiovascular System: B.P. 150/105 mm.Hg. The pulse rate was 88 beats per minute; occasional ventricular ectopic beats were present. The heart was enlarged, the apex beat being 1" outwith the mid-clavicular line. The heart sounds were clearly heard and pure.

Central Nervous System: Signs of a left hemiparesis were present.

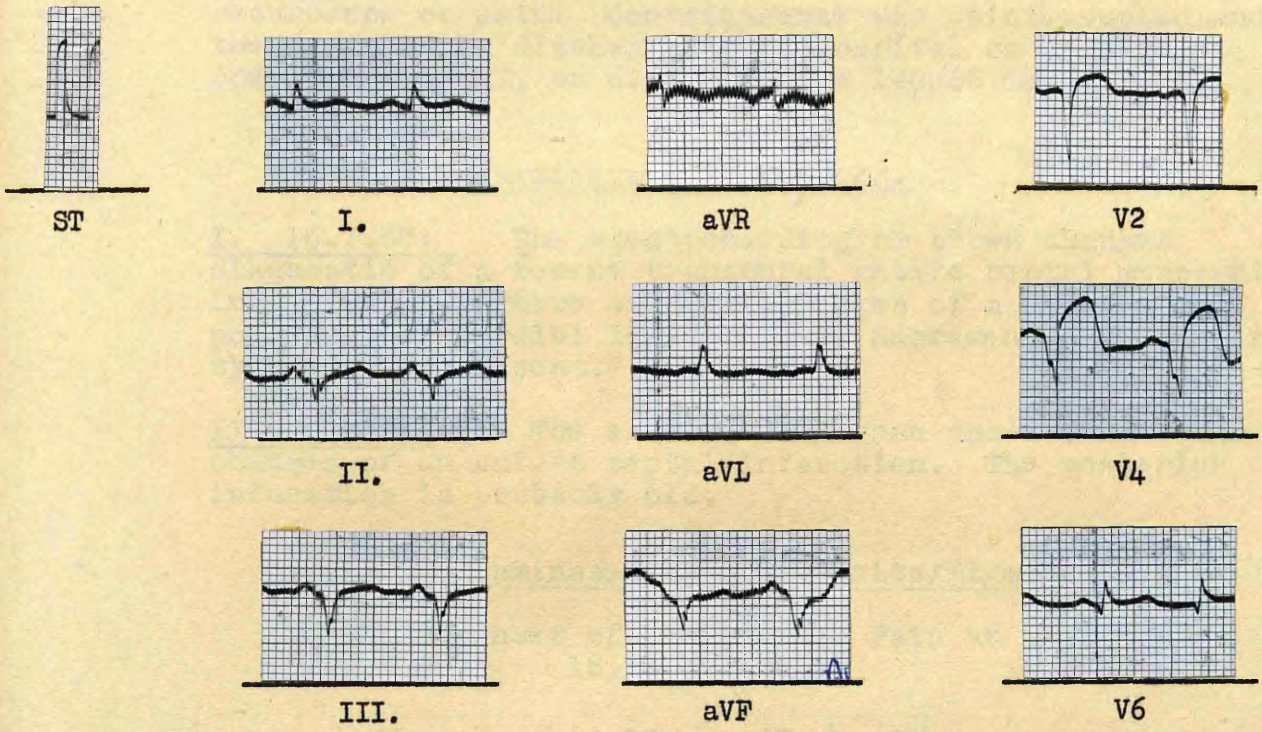
No other abnormality was fonnd on full clinical examination of other systems.

Treatment and Progress.

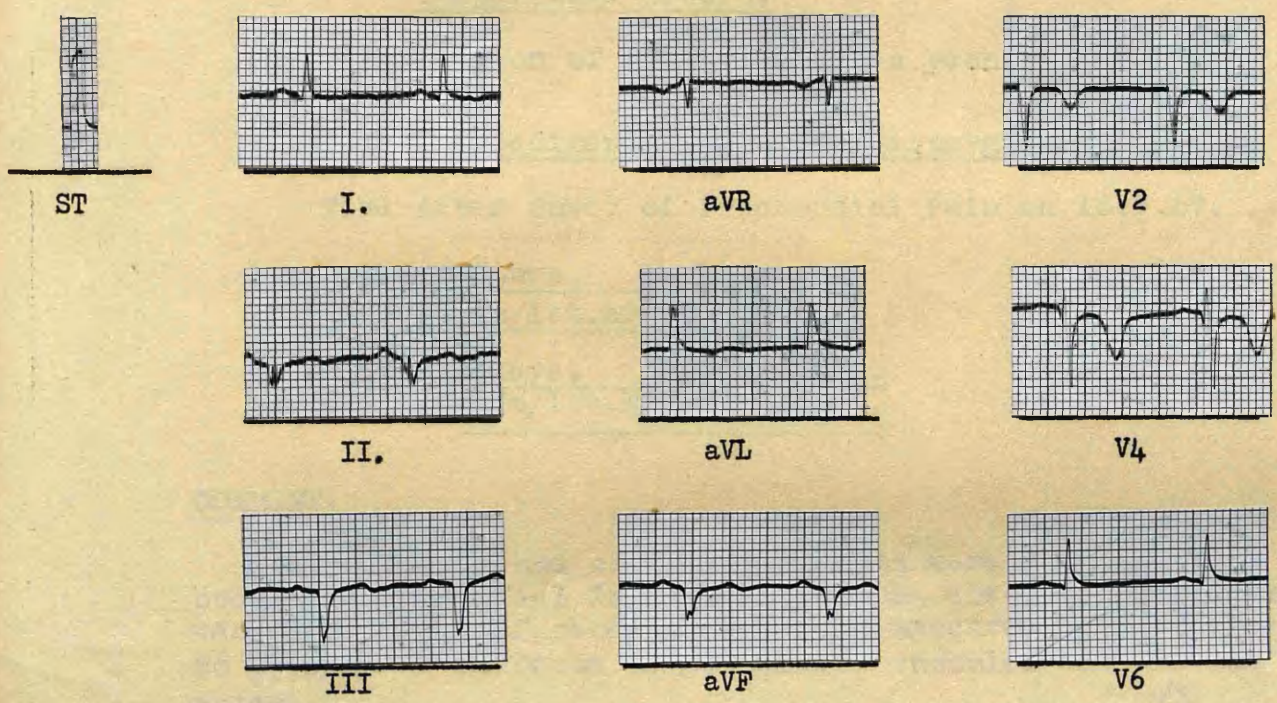
Pain was controlled by the intramuscular injection of Omnopon gr. 1/3. Anticoagulant therapy was started shortly after admission and was continued for 21 days.

/2

ELECTROCARDIOGRAM CASE NO. 49 (1)



ELECTROCARDIOGRAM CASE NO. 49 (2)



17.7.57: B.P. 140/90 mm.Hg. There had been no recurrence of pain. Convalescence was uninterrupted and the patient was discharged from hospital on September, 3rd 1957. B.P. on discharge was 140/85 mm.Hg.

Electrocardiographic Findings.

I. 16.7.57: The electrocardiogram shows changes diagnostic of a recent transmural antero septal myocardial infarction. There are also changes of a transmural posterior myocardial infarction. Supraventricular extra systoles are present.

II. 29.8.57: The electrocardiogram shows sequential changes of an antero septal infarction. The posterior infarction is probably old.

Serial Transaminase Activity (Units/ml/min.).

Time After Onset of Praecordial Pain at 2 a.m. on 16.7.57.

Hours.	13	27	51
Units.	45	30	25

Temperature Record.

No elevation of temperature was recorded.

Erythrocyte Sedimentation Rate (Westergren.)

Time After Onset of Praecordial Pain on 16.7.57.

Hours.	13.	
mm/1st.hr.	35	
Days.	7	14.
mm/1st.hr	46	35.

COMMENT:

The history and clinical findings were indicative of a poor risk myocardial infarction and the electrocardiograms were diagnostic of recent transmural myocardial infarction. No pyrexia or evidence of peripheral vascular failure was noted.

/3

The first attack of chest pain had occurred four days before the first transaminase assay and electrocardiogram were performed and this pain might have represented the onset of transmural myocardial infarction. However, the attack of chest pain on the day of admission was severe and more prolonged than previous pains.

The serum transaminase activity reached borderline levels, 13 hours after the onset of the second attack of anginal pain. The erythrocyte sedimentation rate was abnormally high at this time.

The interpretation of the findings is difficult. The myocardial infarction may have occurred four days before admission, in which case the borderline values of transaminase activity may represent a previously elevated activity falling to normal or a rise to borderline levels following severe post-infarction angina, since borderline transaminase activity has been observed in this study following severe angina pectoris. Alternatively, the attack of pain on the day of admission was symptomatic of acute transmural myocardial infarction and the transaminase activity of serum failed to reach high levels for reasons unknown. Faults in technique in the performance of the test are unlikely to have been factors since other sera, showing high transaminase activity, were examined on the same day.

It was concluded that the borderline values of transaminase activity were due either to late sampling following myocardial infarction or to severe myocardial ischaemia following myocardial infarction.

CASE NO. 50.

History of Present Illness.

A male, aged 60 years, a commercial traveller, was admitted to hospital on January 11th 1957., complaining of severe retrosternal pain of 8 hours' duration. In 1951, the patient had an attack of retrosternal pain at rest which passed off fairly quickly. Since then, he had reduced his tobacco consumption and had avoided over-eating. He had had no further pain and had never been unduly breathless on exertion.

At 7 a.m., on January 11th 1957, he was aware of retrosternal tightness but went to business as usual. At 3 p.m., he developed severe crushing retrosternal pain which was little affected by the intramuscular injection of morphine sulphate, gr.1/2. at 5 p.m. B.P. was 120/80 mm.Hg.

At 7 p.m., he was restless and complaining of severe constriction in the chest. He was shocked and slightly cyanosed. B.P. was 100/80 mm.Hg. He was admitted to hospital at 9 p.m., on January 11th 1957.

Past History.

The patient had had symptoms suggestive of ulcer dyspepsia for 20 years.

Clinical Findings on Admission.

The patient was a middle-aged man. He was anxious and slightly dyspnoeic. There was no cyanosis but the patient was restless and complained of a feeling of retrosternal tension.

Cardiovascular System: B.P. 120/80 mm.Hg. The pulse was regular in rate (100/min.) and rhythm. The apex beat was not felt but the heart was not enlarged; the left border of the heart, as determined by percussion, was within the mid-clavicular line. The heart sounds were distant but pure.

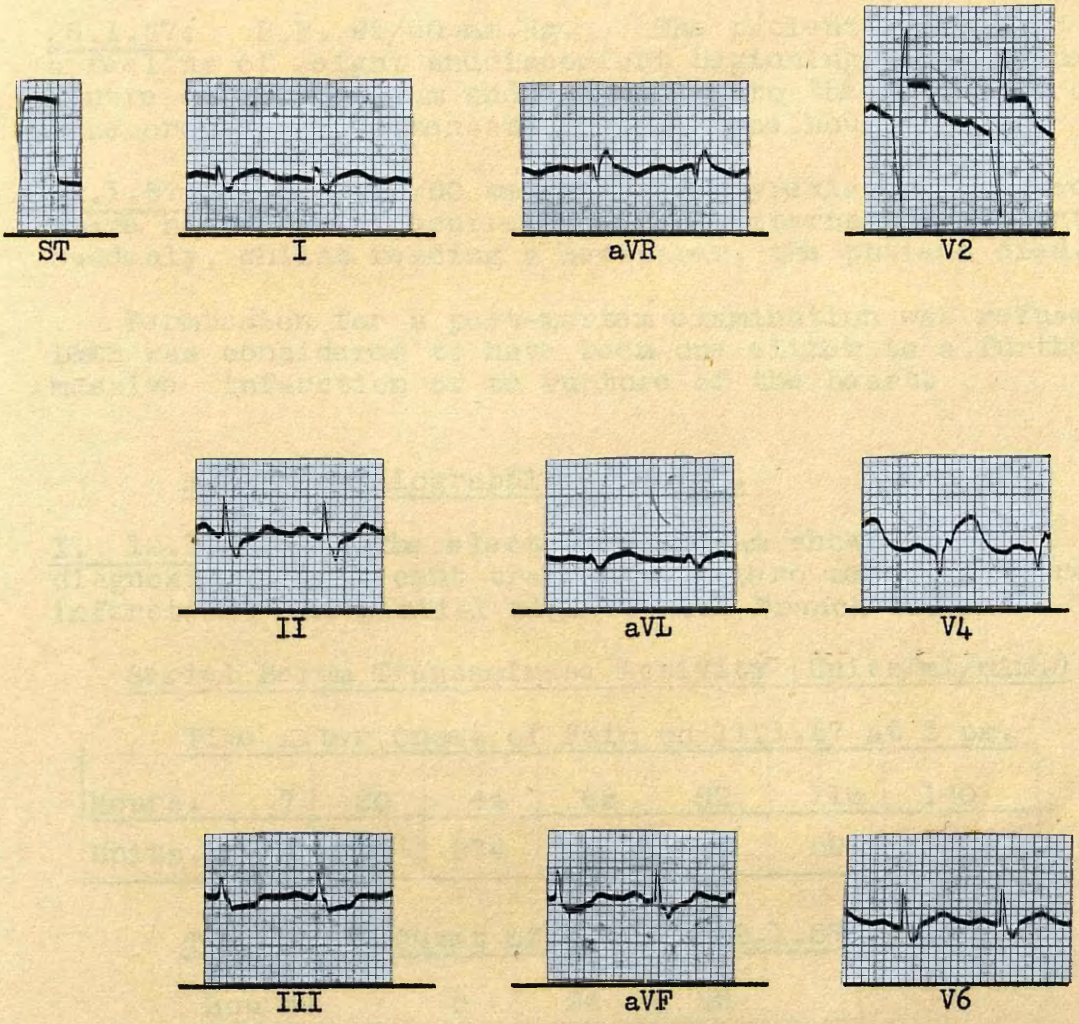
No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Pethidine, 100 mgm., given intravenously, controlled the patient's restlessness and retrosternal discomfort. Anticoagulant therapy was started shortly after admission but was discontinued on January 15th 1957 because the patient developed acute dyspepsia. He had acute pain in the epigastrium and occasional retching produced blood-streaked vomit.

12.1.57: B.P. 100/60 mm.Hg. At 1.30 p.m., the patient complained of tightness in the chest. He was very restless.

ELECTROCARDIOGRAM CASE NO. 50



19.1.57: B.P. 95/65 mm.Hg. Apart from occasional post-prandial epigastric discomfort, the patient was well but the heart sounds were of very poor quality.

22.1.57: B.P. 85/55 mm.Hg. Short attacks of dyspnoea at rest were noted.

24.1.57: B.P. 85/60 mm.Hg. Despite hypotension and pyrexia, the patient looked and felt well.

26.1.57: B.P. 95/60 mm.Hg. All investigations were negative.

28.1.57: B.P. 95/60 mm.Hg. The patient complained of a feeling of weight anddiscomfort beginning beneath the centre of the sternum and referred into the left side of the praecordium. The sensation lasted one hour.

31.1.57: B.P. 95/60 mm.Hg. The pyrexia had settled and there had been no recurrence of retrosternal discomfort when suddenly, whilst reading a newspaper, the patient died.

Permission for a post-mortem examination was refused. Death was considered to have been due either to a further massive infarction or to rupture of the heart.

Electrocardiographic Findings.

I. 12.1.57: The electrocardiogram showed changes diagnostic of a recent transmural antero septal myocardial infarction, and partial right bundle branch block.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Pain on 11.1.57 at 3 pm.

Hours.	7	20	44	68	92	116	140
Units.	40	183	274	118	73	59	34.

Time After Onset of Pain on 28.1.57.

Hours.	0	24	48
Units.	24	26	28

Temperature Record.

A temperature of 99.4°F was recorded 24 hours after onset of pain and body temperatures of 100°F were recorded each day for 5 days following admission. Low grade pyrexia 98°F - 100.2°F was noted from 21.1.57 until death on 31.1.57.

/3

Erythrocyte Sedimentation Rate (Westergren)

Time After Onset of Pain on 11.1.57 at 3 pm.

Hours.	20	
mm/1st.hr	4	
Days. 4		10
mm/1st.hr 45		30

COMMENT:

The history and clinical findings were indicative of a poor risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction 20 hours after the onset of the illness. Pyrexia and minimal - moderate peripheral vascular failure developed. Serum transaminase activity reached high levels 20 hours after the onset of the illness. The erythrocyte sedimentation rate, at that time, was normal although it was raised later. The assay was not considered to have contributed to the diagnosis.

An attack of angina pectoris was observed on 28.1.57 and no rise in serum transaminase activity was recorded following it. No electrocardiograms were performed subsequent to this attack. The patient died suddenly three days after this attack of pain.

CASE NO. 51.

History of Present Illness.

A female, aged 70 years, a housewife, was admitted to hospital on July 18th 1957., having complained of attacks of retrosternal pain on July 12th and 17th.

For five years the patient had complained of a feeling of tightness in the chest on hurrying. This sensation had always cleared within a minute or two of her resting. The symptom was not severe and she lead an active life until, on July 12th 1957, she suddenly developed a constricting pain retrosternally which was referred into the interscapular area and down the arms. The pain had come on whilst the patient was hurrying upstairs and did not disappear when she rested. It lasted for 18 hours and, following its onset, the patient was breathless at rest. She had rested in bed and had been symptom-free when, on July 17th., she developed an aching, gripping pain over the left praecordium which, though not so severe as the previous pain, lasted for 6 hours. On the day of admission, she was free of pain and feeling well.

Past History.

In October, 1956, a cholecystectomy had been performed on the patient for cholecystitis and cholelithiasis.

Clinical Findings on Admission.

The patient was an elderly woman. She looked well. There was no evidence of shock or congestive cardiac failure. B.P. was 130/70 mm.Hg. The pulse was regular in rate (96/min.) and rhythm. The heart was enlarged, the apex beat being felt ½" outwith the mid-clavicular line. The heart sounds were pure and of good quality.

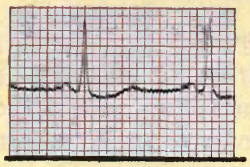
No other abnormality was found on full clinical examination.

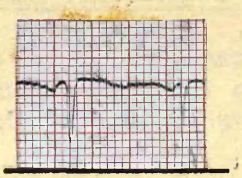
Treatment and Progress.

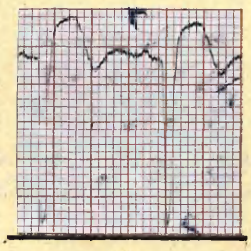
Anticoagulant therapy was started shortly after admission to hospital. The patient's convalescence was uninterrupted although the blood pressure fell to 100/50 mm.Hg. When she was allowed home to complete her convalescence on September 6th 1957, the blood pressure was 115/60 mm.Hg. /2

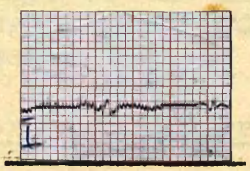
ELECTROCARDIOGRAM CASE NO. 51 (1)

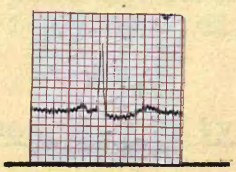

ST

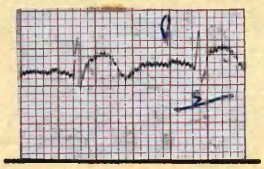

I.

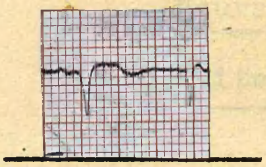

aVR

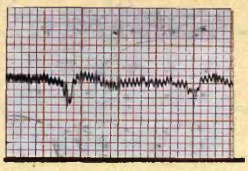

V2

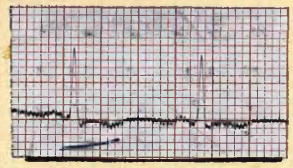

II.


aVL


V4

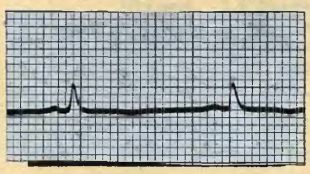

III.

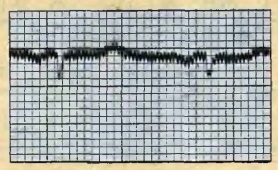

aVF

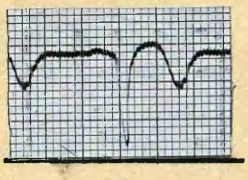

V6

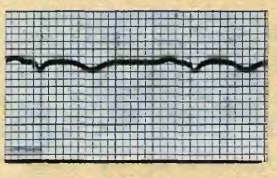
ELECTROCARDIOGRAM CASE NO. 51 (2)

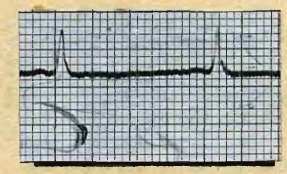

ST

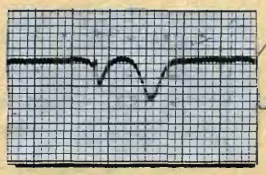

I.

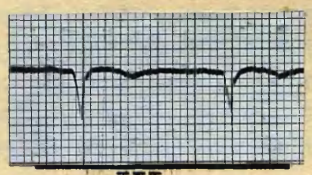

aVR

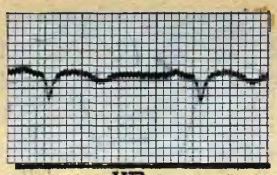

V2

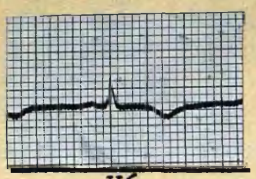

II.


aVL


V4


III


aVF


V6

Electrocardiographic Findings.

I. 18.7.57: The electrocardiogram showed changes consistent with the diagnosis of an old posterior transmural myocardial infarction and a recent transmural antero septal myocardial infarction.

II. 13.8.57: The electrocardiogram showed sequential changes of the antero septal myocardial infarction. The changes of an old posterior myocardial infarction were still present.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Pain on 17.7.57.

Hours.	24	48	72
Units.	15	21	19

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Pain on 17.7.57.

Days.	5	12	23	35	42.
mm/lst.hr.	57	40	25	18	19.

COMMENT:

The history and clinical findings, as well as the electrocardiographic findings, were diagnostic of a recent transmural myocardial infarction of poor risk type. There was no evidence of pyrexia or peripheral vascular failure. The serum transaminase activity was normal on repeated examination following admission and the erythrocyte sedimentation rate was at high levels five days after the patient's admission to hospital. It was considered that myocardial infarction had occurred six days before admission to hospital and that the attack of anginal pain which occurred on the day before admission had not been due to myocardial infarction. Consequently, the failure to detect /3

/ detect increased serum transaminase activity was ascribed to late sampling of the serum.

The alternative, though unlikely explanation is that the attack of pain on the day before admission was due to myocardial infarction and that, for reasons unknown, the serum transaminase activity failed to rise. That faulty technique in the performance of the test was not the explanation of the failure of transaminase activity to reach high levels is suggested by the finding of high activity in other sera tested on the same day.

CASE NO. 52

History of Present Illness.

A male, aged 55 years, a boiler fireman, was admitted to hospital on 21.5.57 complaining of breathlessness at rest. Until September, 1956, the patient had been well but, at that time, he began to complain of breathlessness on exertion and of retrosternal discomfort, which passed off quickly with rest.

On 7.5.57., he suddenly developed a pain in the left lower chest posteriorly which radiated round the chest to the praecordial region. The pain was pressing in type and unrelated to breathing or coughing; it lasted in a mild form for seven days. Following the onset of this pain, the patient became breathless at rest and developed a cough productive of frothy sputum. On several occasions since 14.5.57 he had wakened at night conscious of a feeling of tightness in the praecordium; he also sweated profusely.

He had had a severe attack of praecordial discomfort of this type lasting 30 minutes during the early hours of the morning of 21.5.57 when he was admitted to hospital.

Clinical Findings on Admission.

The patient sat comfortably in bed but the slightest exertion made him dyspnoeic.

Cardiovascular System: B.P. 155/85 mm.Hg. The pulse was regular in rate (110/min.) and rhythm. The apex beat was not felt but the heart was slightly enlarged, the left border of the heart as determined by percussion being $\frac{3}{4}$" outwith the mid-clavicular line. The heart sounds were pure and poorly heard. Pre-systolic gallop rhythm was present.

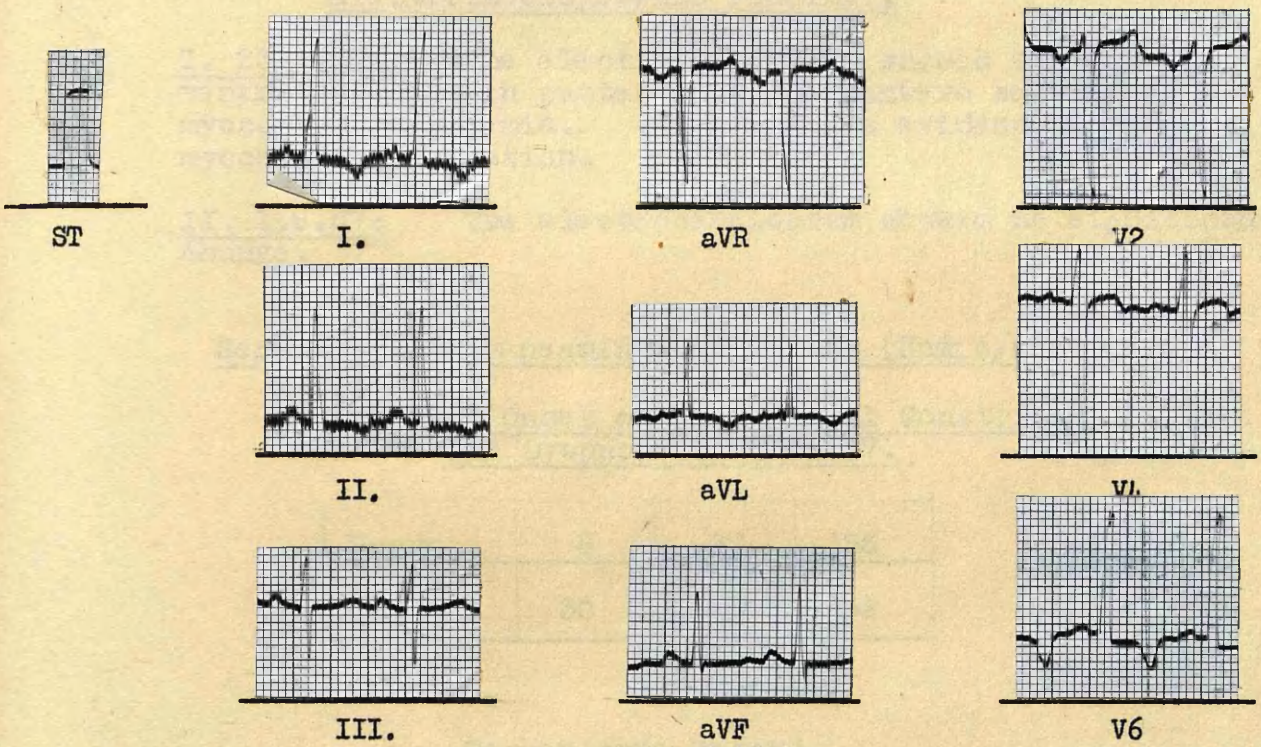
Respiratory System: On auscultation, numerous high pitched rhonchi were heard throughout the lung fields and medium crepitations were heard at the base of the left lung posteriorly.

No other abnormality was found on full clinical examination of other systems.

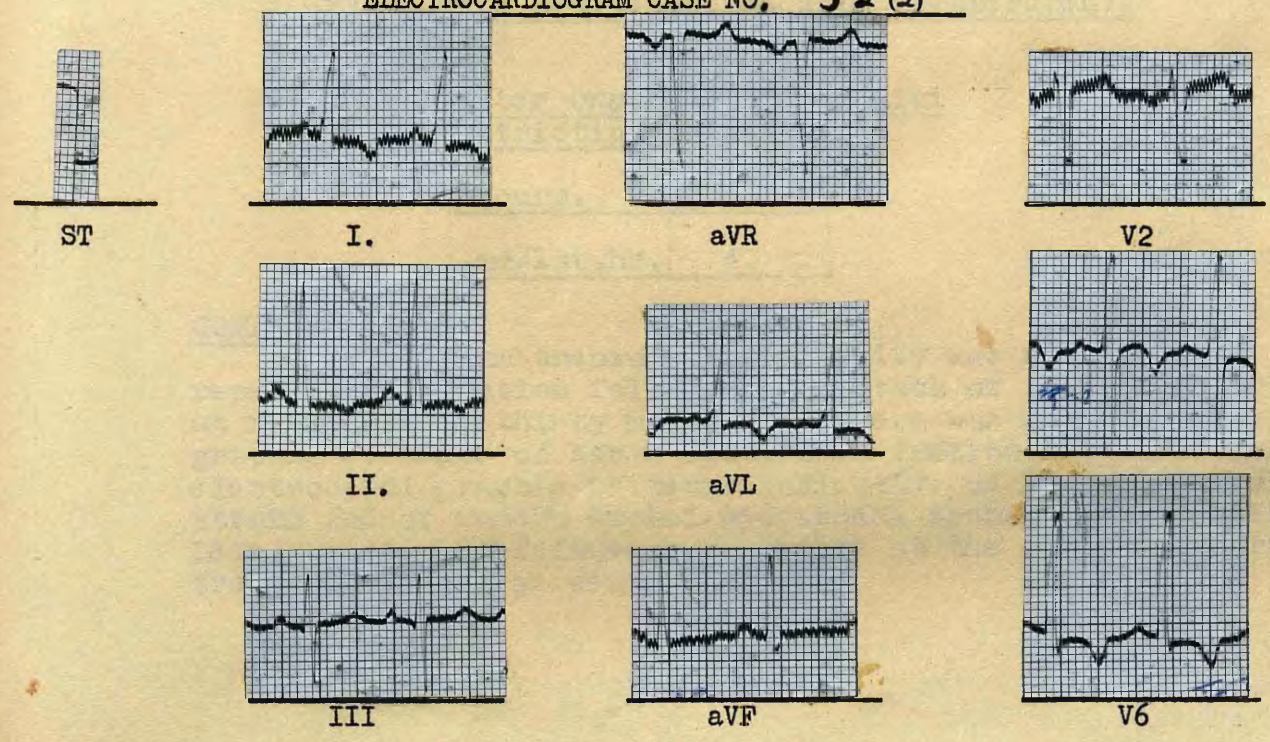
Treatment and Progress.

With a low salt diet and rest in bed, the patient gradually became symptom-free. The B.P. fell to levels of 130/70 mm.Hg. in the week following admission to hospital. Before he was discharged home on 29.6.57., B.P. was 140/80 mm.Hg.

ELECTROCARDIOGRAM CASE NO. 52 (1)



ELECTROCARDIOGRAM CASE NO. 52 (2)



Electrocardiographic Findings.

I. 23.5.57 The electrocardiogram showed a basic left ventricular strain pattern and also antero septal myocardial ischaemia. There was no evidence of a recent myocardial infarction.

II. 1.6.57: The electrocardiogram showed no significant change.

Serial Serum Transaminase Activity (Unit s/ml/min.)

Time After Onset of Praecordial Constriction and Dyspnoea on 21.5.57.

Hours.	8	32	56
Units.	30	25	32

Temperature Record.

The temperature was normal.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Praecordial Constriction on 21.5.57.

Hours.	32
mm/1st.hr.	4.

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of angina pectoris at rest lasting thirty minutes. There was no electrocardiographic evidence of acute myocardial infarction, although electrocardiographic patterns indicative of left ventricular strain and of antero septal myocardial ischaemia were present. Left ventricular failure was present at the time when serum transaminase assays were performed.

CASE NO. 53.

History of Present Illness.

A widow, aged 57 years, a ward orderly, was admitted to hospital on 12.5.57 having had an attack of retrosternal pain. At noon on 12.5.57., she developed a feeling of constriction below the sternum; she felt nauseated and vomited several times. The sensation of constriction gave way to a vice-like retrosternal pain, which was referred into the jaw. The attack lasted for 45 minutes.

Past History.

In 1953, the patient had had a similar attack of pain. After resting in bed for five weeks, she had been symptom-free until 12.5.57.

Clinical Findings on Admission.

The patient was a pale, tired woman. There was no complaint of pain and she was not shocked.

Cardiovascular System: B.P. 110/80 mm.Hg. The pulse was regular in rate (92 beats per minute) and rhythm. The apex beat could not be felt but the left border, as determined by percussion, was within the mid-clavicular line. The heart sounds were faintly heard but they were pure.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Anticoagulant therapy was started soon after admission to hospital and continued for 28 days. The patient's convalescence was uninterrupted and she was discharged from hospital on 9.7.57. B.P. at that time was 130/90 mm.Hg.

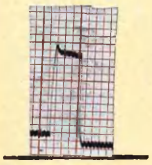
Electrocardiographic Findings.

I. 12.5.57: (6 hours after onset of pain). The electrocardiogram shows changes suggestive of acute coronary insufficiency.

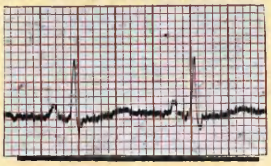
II. 19.5.57: The electrocardiogram showed restitution of the ST-T durations confirming that there had been acute coronary insufficiency. There was no evidence of myocardial infarction.

/2

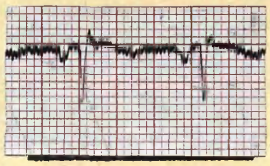
ELECTROCARDIOGRAM CASE NO. 53 (1)



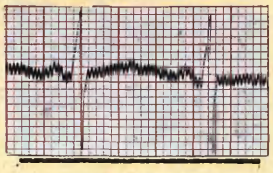
ST



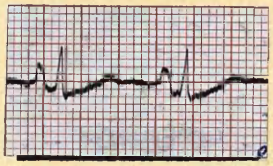
I.



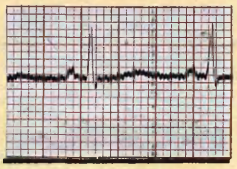
aVR



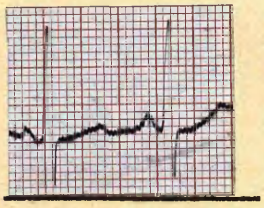
V2



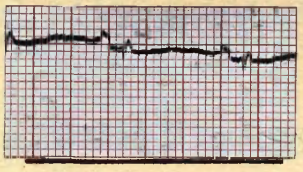
II.



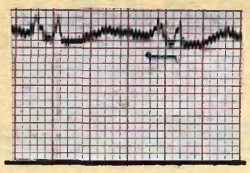
aVL



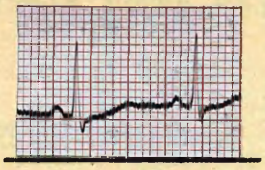
V4



III.



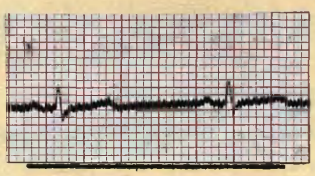
aVF



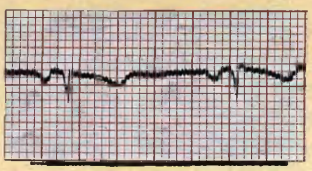
V6

ELECTROCARDIOGRAM CASE NO. 53 (2)

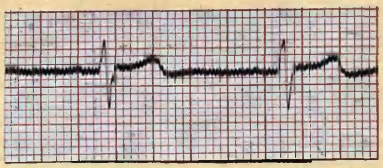
ST



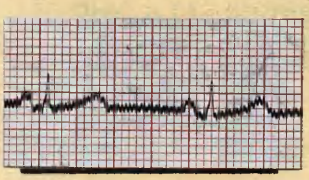
I.



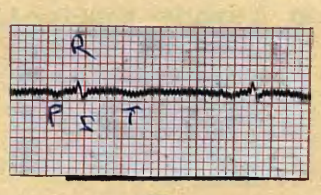
aVR



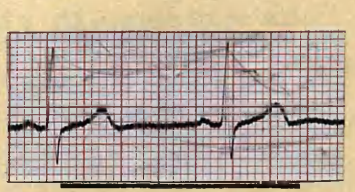
V2



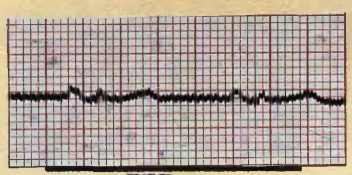
II.



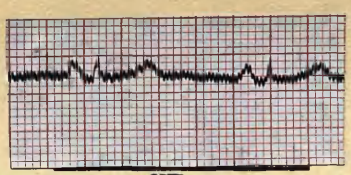
aVL



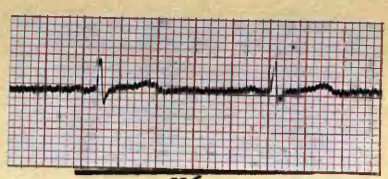
V4



III



aVF



V6

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain on 12.5.57 at noon.

Hours.	8	24	48
Units.	23	31	28

Temperature Record.

The temperature was elevated to 100.8°F 16 hours following admission. It fell to normal levels three days after admission and remained normal.

Erythrocyte Sedimentation Rate (Westergren).

Days.	2	8	15	22
mm/1st.hr.	13	2	10	9

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of angina pectoris at rest lasting 45 minutes. There was no electrocardiographic evidence of acute myocardial infarction.

The electrocardiograms showed changes diagnostic of acute coronary insufficiency.

CASE NO. 54.

A female, aged 45 years, a shop assistant, was admitted to hospital on 7.1.57, complaining of gripping retrosternal pain. The patient had been healthy and active until, three months before admission, after being involved in a bus accident and following her only son's departure to the Services, she developed gripping retrosternal pain on moderate exertion. The pain was relieved by rest and the use of trinitrin. Despite spells of bed rest and giving up work, this pain had become more severe and precipitated by less and less effort until, on 1.1.57., the pain came on while she was resting. Since then, the patient had many attacks of severe constricting retrosternal pain at rest which was often accompanied by parasthesiae in the right arm. The pain usually lasted about 15 -,30 minutes, was easily induced by excitement and especially liable to come on 15 minutes after a meal.

Social History.

The patient had separated from her husband 9 years previously.

Clinical Findings on Admission.

The patient was tired, tense and overweight. Examination of the cardiovascular system revealed a B.P. of 120/75 mm.Hg. The pulse was regular in rate (80 beats/min.) and rhythm. The heart was not enlarged, the apex beat being situated ½" within the mid clavicular line in the fifth interspace. The heart sounds were soft but pure.

Respiratory System: On auscultation, fine crepitations were heard over both lung bases posteriorly. No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

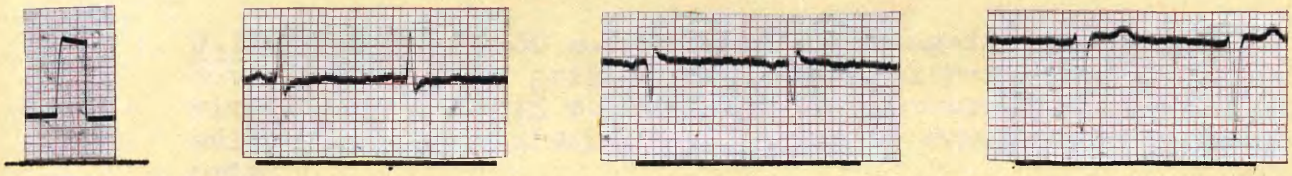
Anticoagulant therapy was started on the day following admission, 8.1.57., and was continued until the death of the patient.

7.1.57: The patient had two attacks of severe anginal pain accompanied by dyspnoea, sweating and intense anxiety, lasting half an hour. Trinitrin gr. 1/150th failed to relieve the pain which eventually responded to the administration of morphine sulphate gr. 1/4 intramuscularly.

8.1.57: B.P. 120/70 mm.Hg. At 8 p.m., the patient developed severe anginal pain which responded partially to the intramuscular injection of morphine sulphate.

9.1.57: /2

ELECTROCARDIOGRAM CASE NO. 54 (1)

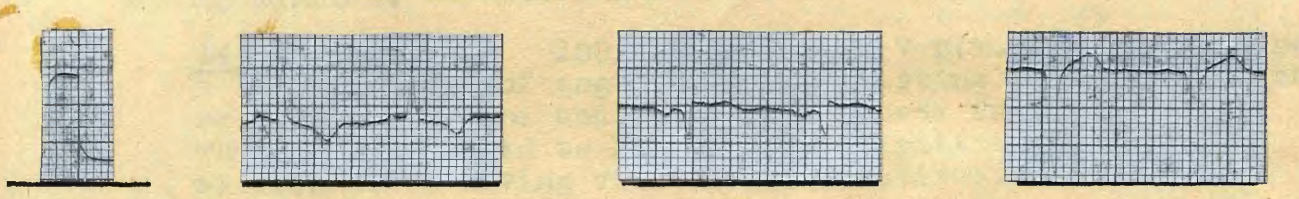


ST I. aVR V2

II. aVL V4

III. aVF V6

ELECTROCARDIOGRAM CASE NO. 54 (2)



ST I. aVR V2

II. aVL V4

III aVF V6

9.1.57: At 2.30 a.m., the patient again developed severe continuous gripping retrosternal pain associated with a burning pain suggestive of heartburn. Morphine sulphate, gr.1/4 given intramuscularly again relieved the pain.

At 5.30 a.m., the patient was nauseated and vomited 6 ozs. of green turbid fluid. She was very apprehensive and felt that death was near. Cyanosis of the lips and dyspnoea were present. Oxygen was administered by B.L.B. mask and pethidine 100 mgm. was given intravenously.

At 6 a.m., the patient was sleeping, cyanosis of the feet and hands was present. The patient was sweating profusely but her limbs were cold.

B.P. 95/75 mm.Hg. Tachycardia (120/beats/min.) was present. The heart sounds were rapid and of poor quality. Acute myocardial infarction was diagnosed but no assays of serum transaminase were performed.

10.1.57: B.P. 100/80 mm.Hg. The patient had improved and there had been no further attacks of anginal pain.

13.1.57: The patient continued to have mild attacks of anginal pain on the slightest exertion lasting five minutes and at 2 p.m., she developed severe anginal pain which required pethidine for its relief. The severe attack occurred when the patient was using a bedpan and lasted for 20 minutes.

14.1.57: B.P. 100/60 mm.Hg. At 7 p.m., the patient had a severe attack of angina pectoris lasting 30 minutes which required pethidine and morphine sulphate for its relief. This attack seemed to have been precipitated by the excitement of having visits from relatives.

15.1.57: B.P. 100/80 mm.Hg. The patient had another severe attackof angina pectoris, lasting 30 minutes.

17.1.57: The patient had had several mild attacks of pain but seemed to be making some progress when she died suddenly.

Permission for post mortem examination was refused.

Electrocardiographic Findings.

I. 13.12.56: (Before admission to hospital;)the electrocardiogram showed changes suggestive of lateral coronary insufficiency of chronic type.

II. 7.1.57: The electrocardiogram showed changes diagnostic of intramural myocardial infarction (lateral) and of antero-lateral coronary insufficiency of chronic type. The infarction was probably of some days' duration. /3

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Pain on 7.1.57.

HOURS.	24	48	72
UNITS.	30	19	20

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren.)

Estimations were not performed.

COMMENT: The history and clinical findings were very suggestive of a poor risk myocardial infarction but the time of onset could not be determined accurately because of the frequent and prolonged bouts of angina pectoris. The electrocardiograms were diagnostic of intramural myocardial infarction and the infarction was thought to be of some days' duration. This accorded well with the clinical view that the first attack of severe angina pectoris at rest, which occurred six days before the patient's admission to hospital, probably was due to acute myocardial infarction. There was no pyrexia or evidence of peripheral vascular failure for two days following admission. Serum transaminase activity was found to be normal on repeated examination following admission and this was considered to be due to late sampling following myocardial infarction.

CASE NO. 55.

History of Present Illness.

A male, aged 64 years, a plumber, was admitted to hospital on 18.6.57., complaining of retrosternal pain of three days' duration. For one year, the patient had been breathless on moderate exertion but he had never had pain in the chest. On 15.6.57., at 3 a.m., the patient awakened complaining of a dull, aching pain in the retrosternal region. The pain, which was not referred, was present throughout that day and then gradually wore away; he remained, however, aware of continual retrosternal discomfort until, on 18.6.57., the pain became more severe and shifted into the left praecordium and he was transferred to hospital

There was no relevant past history.

Clinical Findings on Admission.

The patient complained of a dull ache in the left breast. Jugular vein congestion was present but there was no other evidence of congestive cardiac failure.

Cardiovascular System: B.P. 115/75 mm.Hg. The pulse was regular in rate (104/min.) and rhythm. The apex beat was felt in the fifth left interspace ½" within the mid-clavicular line. The heart sounds were pure and fairly well heard. Well marked pericardial friction was heard just medial to the mitral area.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

The praecordial pain responded quickly to the intramuscular injection of pethidine, 100 mgm. Anticoagulant therapy was started shortly after admission and was continued for 21 days. The patient had no further chest pain and he made good progress. B.P. was 120/80 mm.Hg., before his discharge from hospital on 24.7.57.

Electrocardiographic Findings.

I. 18.6.57; The electrocardiogram showed changes diagnostic of a recent, transmural antero-septal acute myocardial infarction and of an old posterior myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

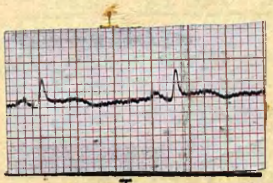
Time after onset of Pain on 15.6.57.

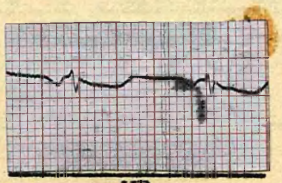
Hours.	80
Units.	90

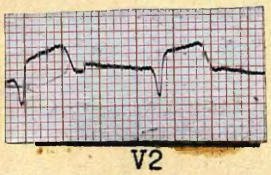
/2

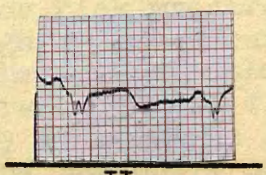
ELECTROCARDIOGRAM CASE NO. 55

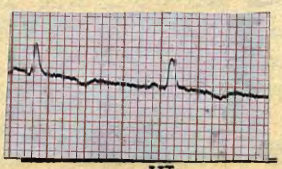

ST

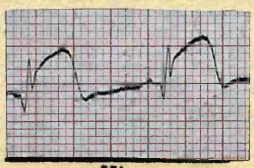

I

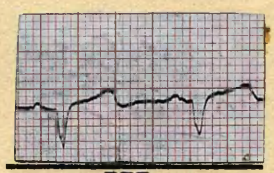

aVR

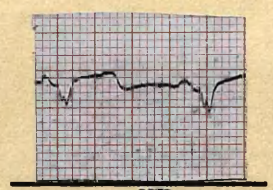

V2

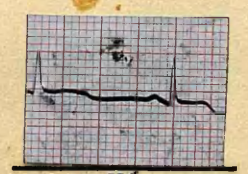

II


aVL


V4


III


aVF


V6

Temperature Record.

The body temperature for 48 hours after admission was 99°F - 100.8°F and thereafter normal.

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Pain on 15.6.57.

Hours.	80
mm/Ist. hour.	30

COMMENT:

The history and clinical findings were indicative of a poor risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction three days after the onset of the illness. Pyrexia and minimal peripheral vascular failure were present. Serum transaminase activity was at high levels when first examined 80 hours following the onset of the illness. The E.S.R. was raised. The assay was not considered to have contributed to the diagnosis.

CASE NO.56.

History of Present Illness.

A female, aged 77 years, a housewife, was admitted to hospital on 19.4.57., complaining of attacks of retro-sternal pain. On 14.4.57., the patient, whilst busy with her housework, was seized with a severe, crushing retrosternal pain which, in 15 minutes passed off with rest. The pain radiated down the right arm into the finger tips. As the pain cleared, she was conscious of a sense of oppression below the sternum. Three hours later the pain recurred while the patient was lying in bed and again the pain lasted for 15 minutes. She felt nauseated and vomited. On 15.4.57., and on the evening of 18.4.57., the patient had two further attacks of severe angina pectoris at rest, each attack lasting for 15 minutes.

Past History.

In 1942, a right nephrectomy was performed for renal calculus. Since then the patient had had no attacks of renal colic. In 1952 she had been told that she suffered from hypertension but she had never been unduly breathless and, until 14.4.57., she had not been subject to chest pain.

Clinical Findings on Admission.

The patient was an elderly, alert, obese woman of good colour. She was not shocked.

Cardiovascular System: B.P. 190/105 mm.Hg. The pulse was regular in rate (80/min.) and rhythm. The apex beat was not felt. The heart sounds were clearly heard and they were of good quality and pure.

Respiratory System: On auscultation, numerous fine crepitations were heard over the right lung base posteriorly.

No other abnormality was found on full clinical examination of other systems.

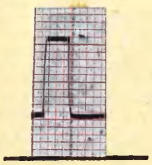
Treatment & Progress.

The patient remained symptom-free after admission to hospital and required no special treatment beyond rest in bed and a low salt reducing diet. B.P. fell to 130/70 mm.Hg on 22.4.57 but, before the patient's discharge from hospital on 18.5.57., it had risen to 145/85 mm.Hg.

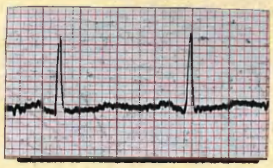
Electrocardiographic Findings.

/2

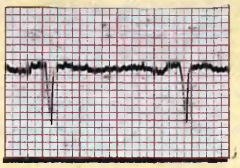
ELECTROCARDIOGRAM CASE NO. 56 (1)



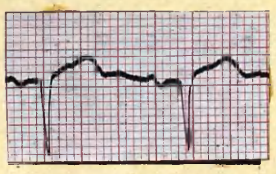
ST



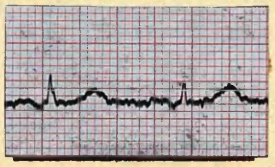
I.



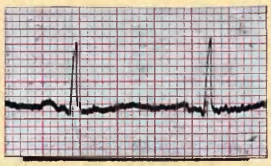
aVR



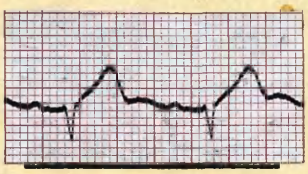
V2



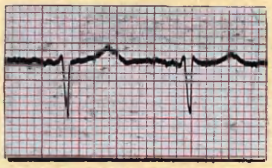
II.



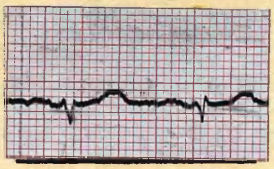
aVL



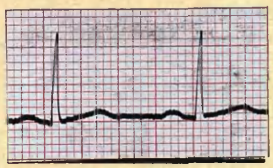
V4



III.

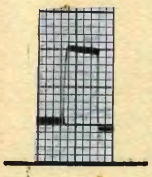


aVF

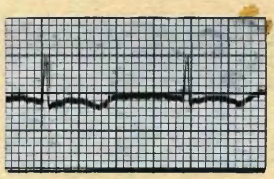


V6

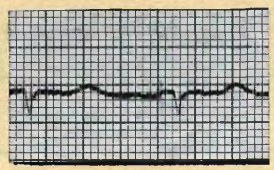
ELECTROCARDIOGRAM CASE NO. 56 (2)



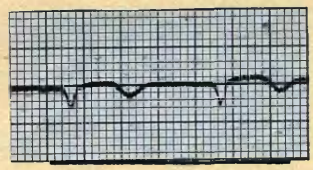
ST



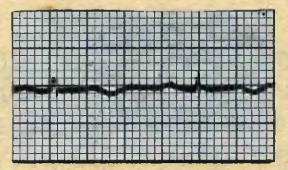
I.



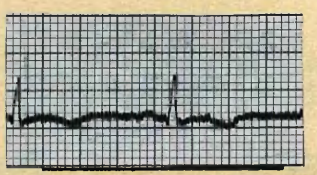
aVR



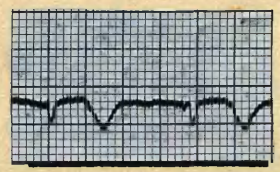
V2



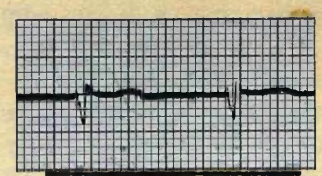
II.



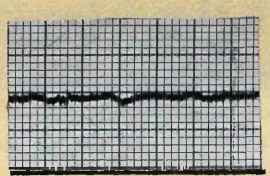
aVL



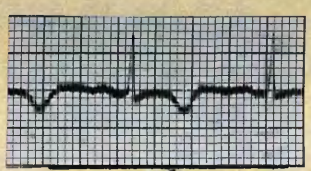
V4



III



aVF



V6

Electrocardiographic Findings. (ctd.)

I. 19.4.57: (5 p.m.) The electrocardiogram showed changes diagnostic of an transmural anterior myocardial infarction of indefinite age but which could be recent.

II. 29.4.57: The electrocardiogram confirmed the diagnosis of a recent widespread antero-septal lateral myocardial infarction.

Serial Serum Transaminase Activity (Unit s/ml/min.)

Time after Onset of Chest Pain on 18.4.57.

Hours.	24	48	72
Units.	35	30	32

Temperature Record.

The body temperature was normal throughout the period of observation.

Erythrocyte Sedimentation Rate (Westergren.)

Time After Onset of Chest Pain on 18.4.57.

Days.	4	16
MM/1st.Hr.	33	10

COMMENT: The history and clinical findings were indicative of acute good risk myocardial infarction and the electrocardiograms were diagnostic of recent transmural myocardial infarction. No pyrexia or peripheral vascular failure developed during the period of observation. Serum transaminase activity was normal on repeated examination. The E.S.R. reached abnormal levels four days after the patient's admissionto hospital.

The interpretation of these findings is difficult. There were four attacks of anginal pain before admission and it is thought that acute myocardial infarction probably occurred five days before the patient was admitted to hospital and that the transaminase activity of serum was normal because

/ normal because too long a time had elapsed before the assay was performed following infarction. The appearance of the electrocardiograms lent support to this view.

CASE NO. 57.

History of Present Illness.

A male, aged 52 years, a cobbler, was admitted to hospital on 19.7.57, complaining of retrosternal and left arm pain. The patient had been breathless on moderate exertion for one year. At 3 p.m., on 19.7.57., whilst painting, he developed a gripping pain in the left upper arm which disappeared on resting. At 6.30 p.m., he felt a sudden, severe, gripping retrosternal pain which lasted for 20 minutes despite resting. At 9 p.m., he felt nauseated and vomited on four occasions. These symptoms lasted for one hour and when he was admitted to hospital, he was symptom-free.

Clinical Findings on Admission.

The patient was a tall man; he felt well, but was anxious. There was no evidence of congestive cardiac failure or shock.

Cardiovascular System: B.P. 110/80 mm.Hg. The pulse was regular in rate (76/min.) and rhythm. The heart was not enlarged. The apex beat was just palpable 1" within the mid-clavicular line. The heart sounds were soft but pure. Splitting of the first mitral sound was present.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

The patient had no recurrence of pain and he made good progress, being discharged from hospital on 22.7.57. B.P. 120/70 mm.Hg.

Electrocardiographic Findings.

I. 20.7.57: (8½ hours after onset of pain.) The electrocardiogram showed changes in leads I and A.V.L. which might have been due to lateral infarction.

II. 23.7.57: The electrocardiogram showed no sequential change and, therefore, there is no evidence of infarction.

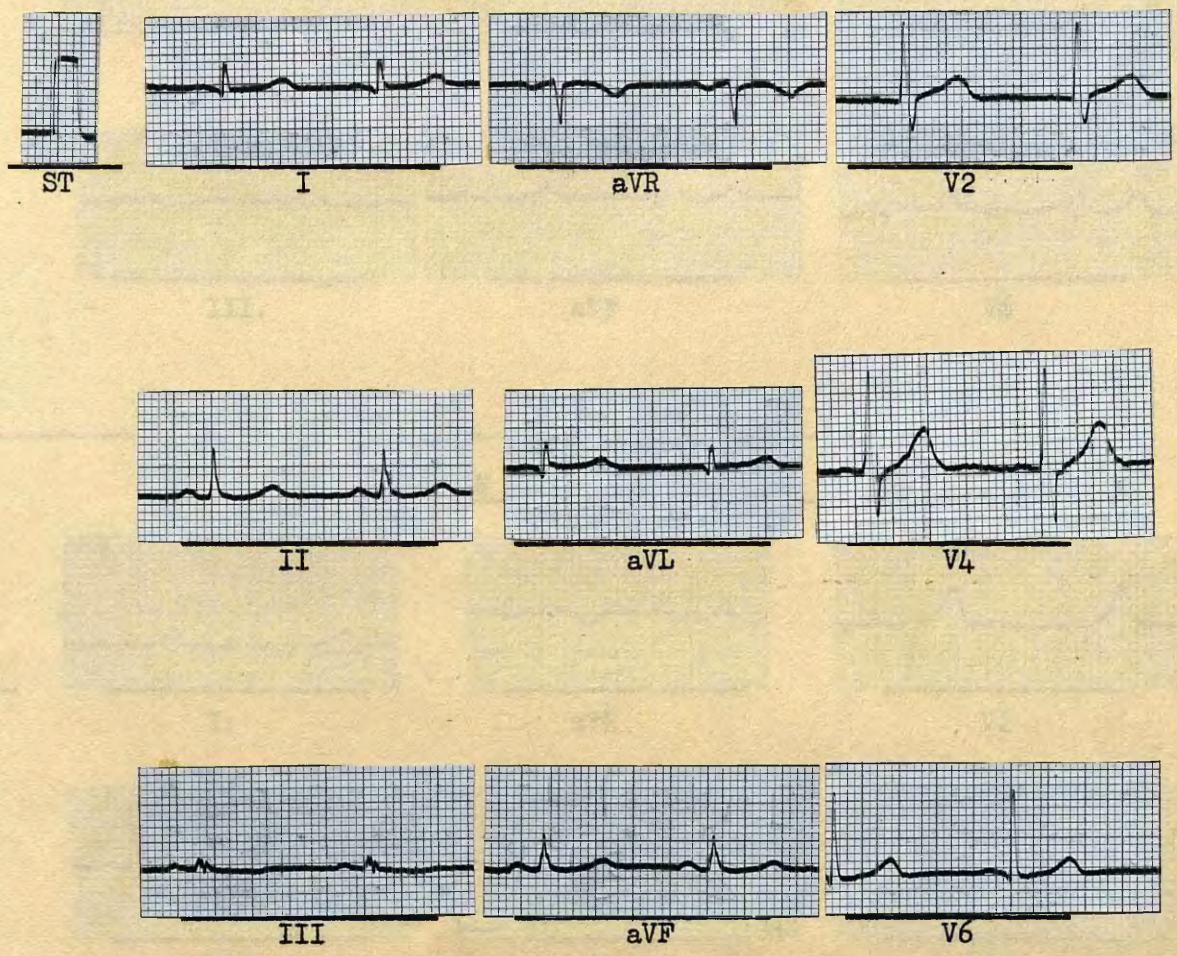
III. 30.7.57: The electrocardiogram showed no significant change.

Serial Serum Transaminase Activity (Units/ml/min.)

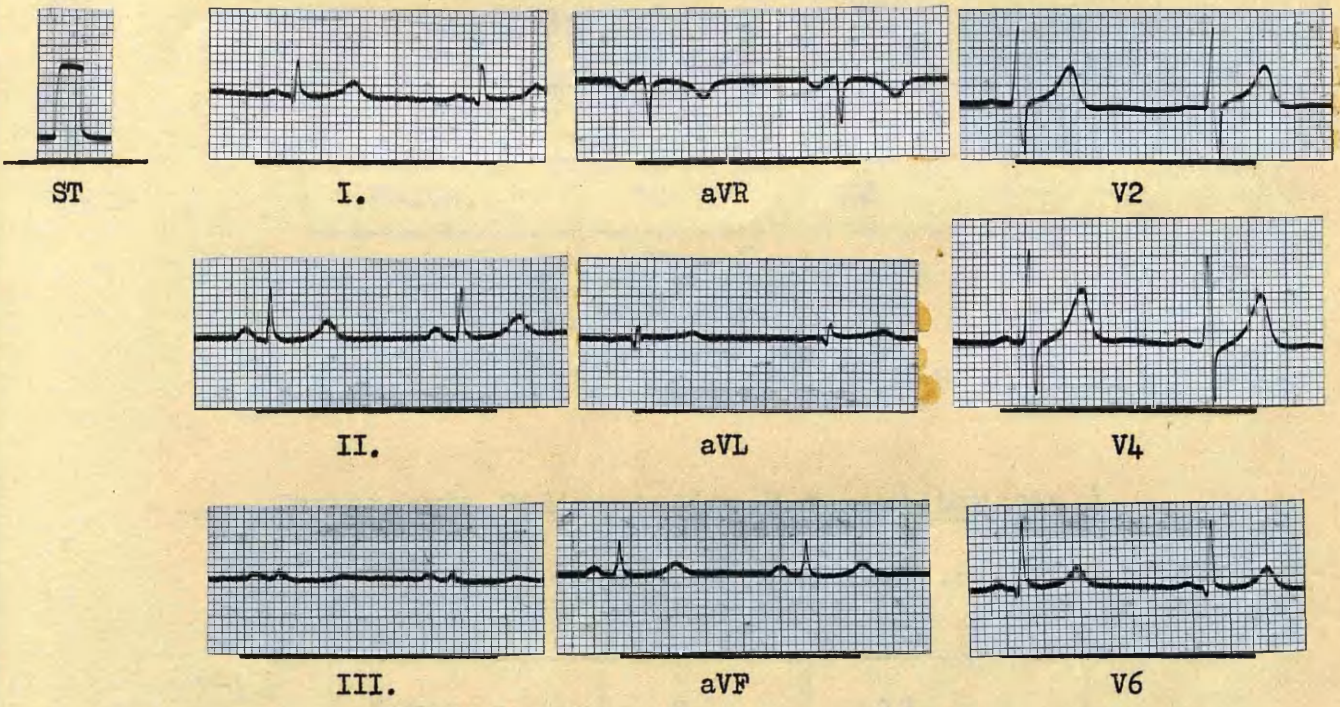
Time after onset of pain on 19.7.57.
at 3 pm.

/2 ctd.

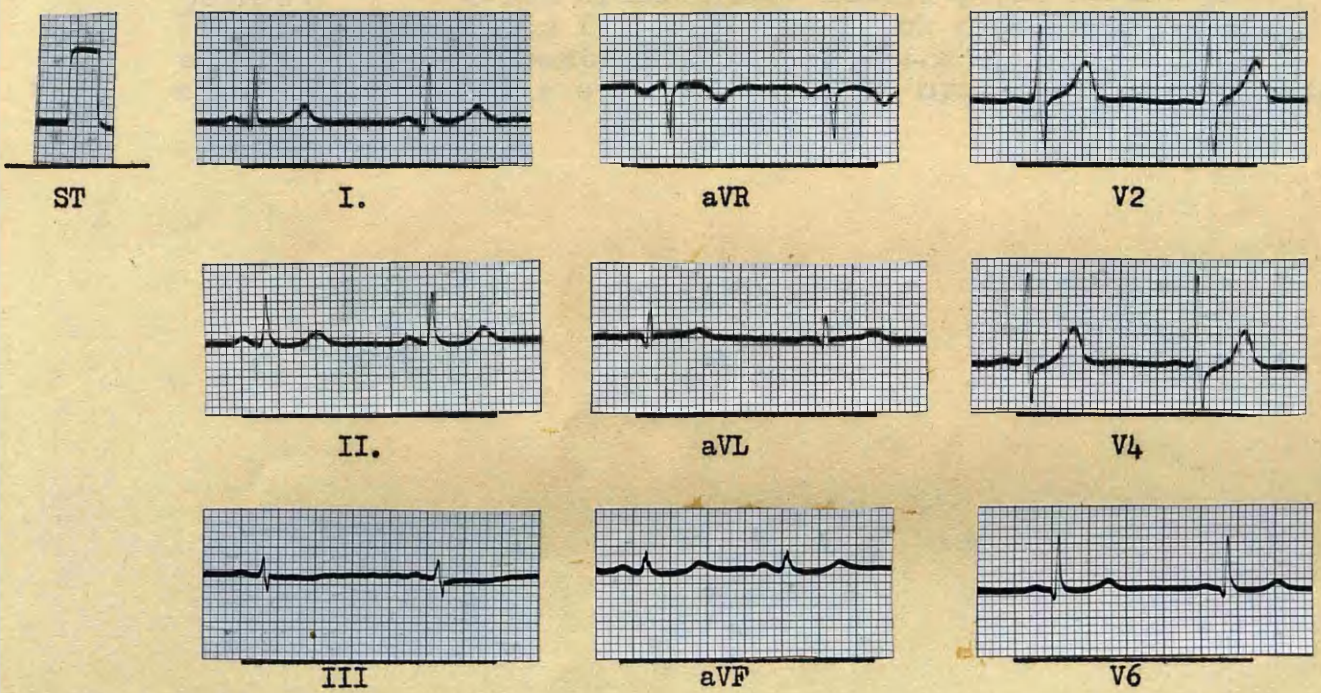
ELECTROCARDIOGRAM CASE NO. 57 (1)



ELECTROCARDIOGRAM CASE NO. 57(2)



ELECTROCARDIOGRAM CASE NO. 57(3)



Serial Serum Transaminase Activity (ctd.)

Time after Onset of Pain on 19.7.57 at 3 p.m.

Hours.	18	42
Units.	33	28

Temperature Record.

The temperature showed no elevation.

Erythrocyte Sedimentation Rate (Westergren.)

Time after Onset of Pain on 19.7.57 at 3 p.m.

Days.	3	17
mm/1st.hr.	10	2

COMMENT: Serum transaminase activity was normal on repeated examination following an attack of angina pectoris at rest lasting twenty minutes. There was no electrocardiographic evidence of acute myocardial infarction.

CASE NO. 58.

History of Present Illness.

A female, aged 62 years, a housewife, was admitted to hospital on 15.2.57 complaining of gripping substernal pain on effort of six weeks' duration. For six weeks, the patient had complained of gripping substernal pain on effort which was, on occasions, referred down the left arm to the elbow. The pain always subsided in about five minutes on resting, but on 8.2.57, while resting in bed, she had a more severe pain of the same type which awakened her. This lasted for fifteen minutes. She was advised to stay in bed but, on 9.2.57., she suffered another attack of similar pain, lasting 10 minutes. On 12.2.57., she had a severe attack of choking retrosternal pain at rest which lasted for 1½ hours. The pain radiated down the left arm and passed off slowly. On 14.2.57 at 5 p.m., she had another attack of anginal pain at rest which lasted for 20 minutes.

Past History.

Since 1952., the patient had become increasingly breathless on exertion and had tried to change house in order to avoid climbing stairs. She had never been breathless at rest. In 1939., she had a hysterectomy performed for bleeding uterine fibroids and had been subject to recurrent attacks of cystitis since then.

Clinical Findings on Admission.

The patient was an obese, florid woman. There was no evidence of congestive cardiac failure or shock. She had no pain on admission. A large ventral hernia was noted.

Cardiovascular System: B.P 205/100 mm.Hg. The pulse was regular in rate (68/min) and rhythm. The heart was enlarged, the apex beat being palpable in the 6th left intercostal space, 1" outwith the mid-clavicular line. The heart sounds were well heard and pure. The second aortic sound was accentuated.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

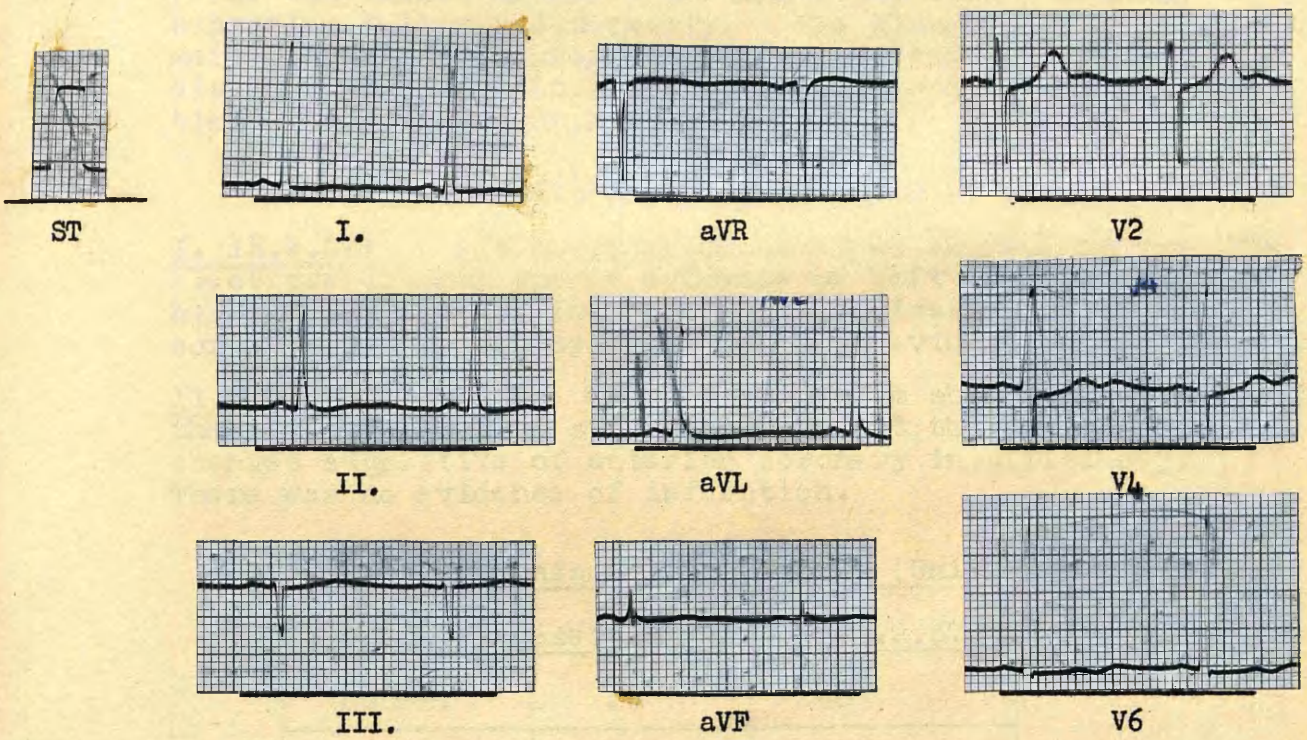
The patient was given a reduction diet.

16.2.57: She had an attack of fairly severe retrosternal pain lasting 10 minutes which came on at rest. B.P. was 170/95 mm.Hg.

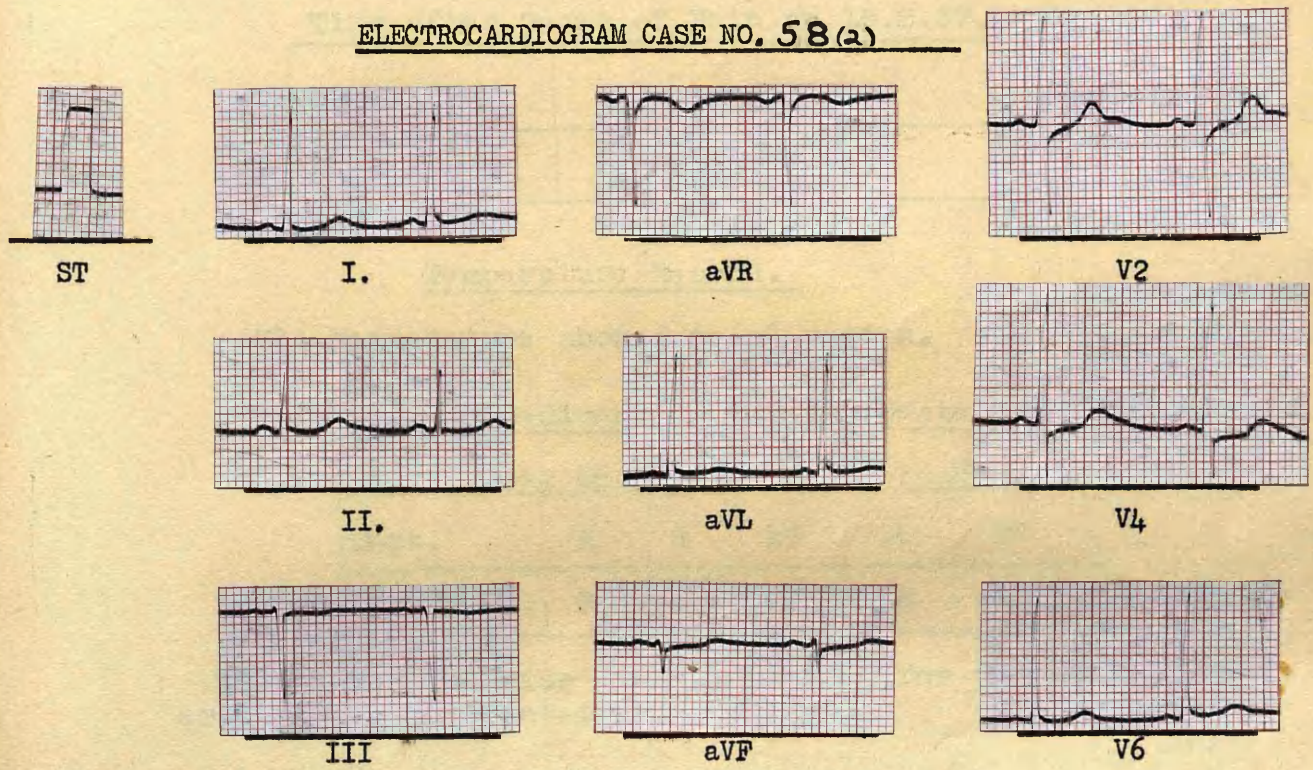
Following this, the patient had no recurrence of chest pain although, in the first week of her stay in hospital, she

/2

ELECTROCARDIOGRAM CASE NO. 58(1)



ELECTROCARDIOGRAM CASE NO. 58(2)



/ she complained of short lasting attacks of a choking sensation felt retrosternally. The blood pressure was well maintained and her progress was uninterrupted until her discharge from hospital on 19.3.57., blood pressure at that time being 170/100 mm.Hg.

Electrocardiographic Findings.

I. 15.2.57: (24 hours after onset of anginal pain.) The electrocardiogram showed evidence of left ventricular hypertrophy and strain and changes indicative of mild acute coronary insufficiency. There was no evidence of infarction.

II. 24.2.57: The electrocardiogram showed improvement in the left ventricular strain pattern but there were residual changes suggestive of anterior coronary insufficiency. There was no evidence of infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Pain on 14.2.57.

Hours.	24	48
Units.	20	16

Time after Onset of Pain on 16.2.57.

Hours.	2	24
Units.	16.	28

Temperature Record.

The temperature showed no elevation.

Erythrocyte Sedimentation Rate (Westergren.)

Time after Onset of Pain on 14.2.57.

Days.	2	6	13	20	27
mm/1st.hr.	2 0	15	22	18	15

No extra-cardiac cause was found for this elevation in erythrocyte sedimentation rate.

/3

COMMENT :

Serum transaminase activity was found to be normal following two attacks of angina pectoris at rest.

The first attack (58a) on 14.2.57 lasted for twenty minutes and the second attack (58b) on 16.2.57, for ten minutes.

There was no electrocardiographic evidence of acute myocardial infarction but the electrocardiograms showed changes indicative of acute coronary insufficiency following the first attack.

CASE NO. 59.

History of Present Illness.

A male, aged 80 years, a draughtsman, was admitted to hospital on 31.7.57 at 8.30 p.m., complaining of severe chest pain.

The patient had been breathless on moderate exertion for 10 years but, in June, 1957., he began to have non-radiating gripping retrosternal pain which came on with exertion, but passed off quickly with rest. For the same period, he had noticed increasing dyspnoea on exertion.

At 2 a.m., on 31.7.57., he was awakened by a severe central chest pain which lasted, despite the use of trinitrin, gr.1/150., for half an hour. At 9 a.m., he had a short recurrence of pain which was relieved by trinitrin. The pain recurred at 4 p.m., and was only beginning to ameliorate at 8.30 p.m., after a third intramuscular injection of morphine sulphate, gr. 1/4.

Past History.

The patient had enjoyed good health and he had been working until the onset of pain on 31.7.57.

Clinical Findings on Admission.

The patient was a well preserved elderly man who was obese. Neck vein congestion and minimal sacral skin oedema were present.

Cardiovascular System: B.P. 165/100 mm.Hg. The pulse was regular in rate (80/min.) and rhythm. The apex beat was pslpable in the 5th left intercostal space in the mid-clavicular line. The heart sounds were pure but rather soft.

No other abnormality was found on full clinical examination.

Treatment and Progress.

Anticoagulant therapy was started shortly after admission. The patient's condition progressively deteriorated. B.P. fell to hypotensive levels, 80/60 mm.Hg., the patient became restless and confused and there was evidence of peripheral circulatory failure. He died on 1.8.57 at 2.40 a.m. Permission for post mortem examination was not granted.

Electrocardiographic Findings.

I. 31.7.57: (19 hours following onset of chest pain on 31.7.57). The electrocardiogram showed changes diagnostic of acute transmural antero-septal myocardial infarction.

/2

Duplicate records are not available for inclusion in this study.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Chest Pain.	
Hours.	19
Units.	120

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren).

No estimations were performed.

COMMENT: The history and clinical findings were indicative of a poor risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction. There was no pyrexia but moderate peripheral vascular failure developed. Serum transaminase activity was at high levels 19 hours after the onset of pain, but the assay was not considered to have contributed to the diagnosis.

CASE NO. 6o.

History of Present Illness.

A female, aged 52 years, a housewife, was admitted to hospital on 1.3.57 complaining of retrosternal pain on slight exertion and at rest. In 1955., the patient gradually became breathless on moderate exertion and in October, 1956., she began to experience severe retrosternal pain on slight exertion which radiated into both upper arms and which cleared rapidly with rest. The pain was associated with increasing dyspnoea on exertion and, in December, 1956, she was confined to bed. While resting at home she had been subject to short attacks of angina pectoris at rest and attacks of paroxysmal cardiac dyspnoea.

Because of her failure to improve with domiciliary treatment, she was admitted to hospital on 1.3.57 following an attack of gripping retrosternal pain, which lasted for twenty minutes on 28.2.57.

Past History.

There was no past history of rheumatic fever, acute tonsillitis, chorea or nephritis.

Clinical Findings on Admission.

The patient was a pale, middle-aged woman, who preferred to sit up in bed. She was not dyspnoeic at rest. There was no evidence of congestive cardiac failure.

Cardiovascular System: B.P. 130/70 mm.Hg. The pulse was regular in rate (100/min.) and rhythm. The heart was enlarged, the apex beat being situated 5" from the mid-sternal line in the 6th left intercostal space. A systolic thrill was felt at the aortic area and was conducted into the carotid vessels. A harsh systolic murmur was present at all areas but was maximal at the aortic area. A short diastolic murmur was present at the aortic area.

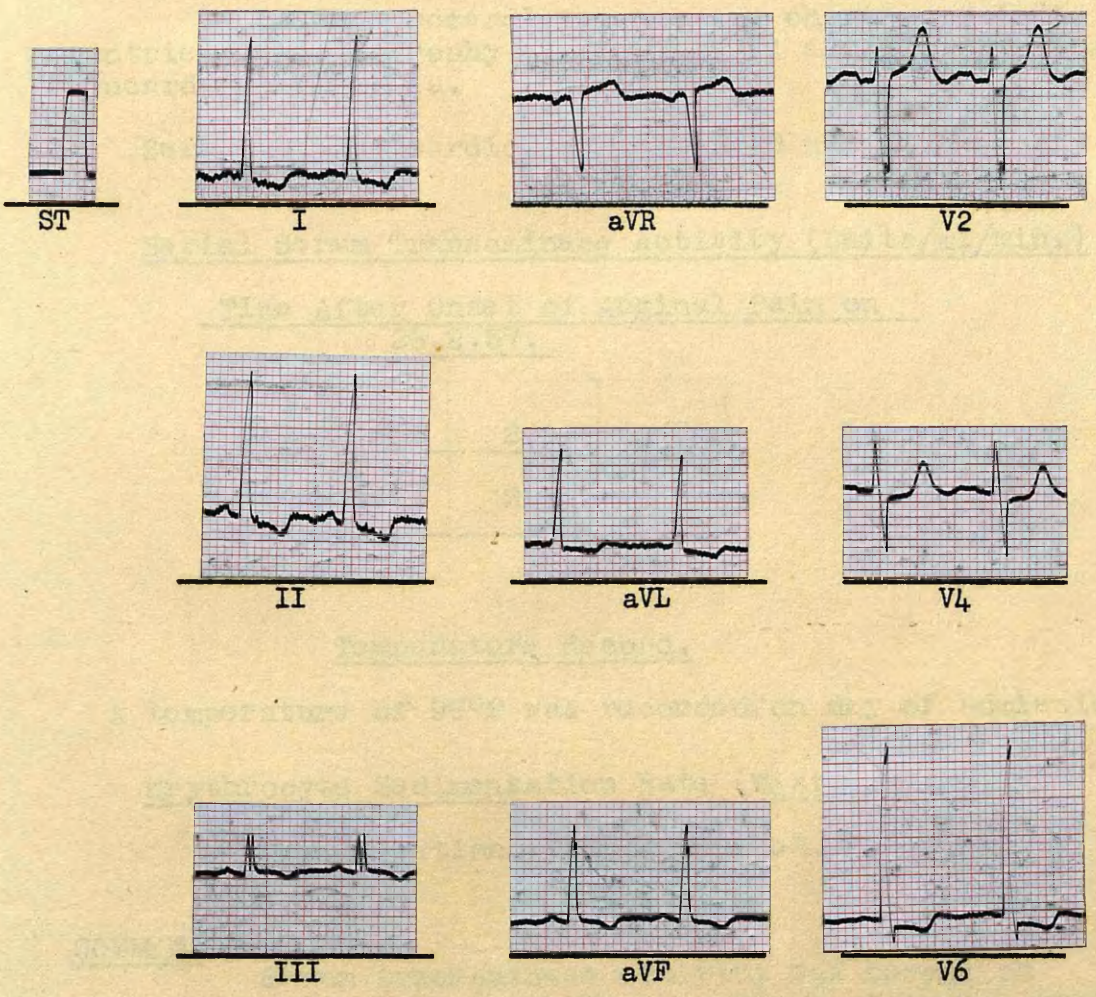
Examination of the blood revealed an iron deficiency anaemia. Hb. was 60%.

Treatment and Progress.

The patient, whilst at home, had been digitalised and digitalis leaf, gr. 1 b.d., was continued. She was also given a salt poor, 1500 calorie diet and trinitrin gr.1/150 as required for anginal pain. Full investigation failed to

/2

ELECTROCARDIOGRAM CASE NO. 60



/ to reveal a neoplastic or haemorrhagic lesion to account for the anaemia which responded to treatment with ferrous gluconate. The patient was discharged from hospital on 23.3.57., feeling well.

The final diagnosis was aortic stenosis and incompetence.

Electrocardiographic Findings.

I. 1.3.57: (6 p.m. - 24 hours after onset of anginal pain).

The electrocardiogram showed changes of left ventricular hypertrophy and strain and also of antero septal myocardial ischaemia.

Serial electrocardiograms revealed no change.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Anginal Pain on 28.2.57.

Hours.	24	48
Units.	24	19

Temperature Record.

A temperature of 99°F was recorded on day of admission.

Erythrocyte Sedimentation Rate (Westergren).

No estimations were performed.

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of angina pectoris at rest lasting for 20 minutes. There was no electrocardiographic evidence of acute myocardial infarction but electrocardiographic changes, indicative of left ventricular hypertrophy and strain and of antero septal myocardial ischaemia were present. Physical signs of aortic valve disease were present, stenosis of the valve being the predominant lesion.

CASE NO. 61.

History of Present Illness.

A male, aged 43 years, a museum attendant, was admitted to hospital on 13.12.56, having had attacks of retrosternal pain. At 4.30 a.m. on 11.12.56, the patient, having visited the lavatory, felt vertiginous after climbing a flight of stairs and, on reaching the bedroom, fell unconscious and was noted by his wife to be rolling his eyes and jerking his limbs. The attack lasted for about ten minutes. When he regained consciousness he was pale and sweating and for 1½ hours complained of a sensation of numbness and tightness in the throat, praecordial region and upper arms. He was confined to bed and he was admitted to hospital on 13.12.56.

Past History.

Since September, 1956, he had complained of tightness in the suprasternal notch, in the upper praecordium, and in the inner aspects of both upper arms and of breathlessness on exertion.

Clinical Findings on Admission.

The patient was a robust, overweight individual. He was anxious. There was no evidence of shock or congestive cardiac failure.

Cardiovascular System: B.P. 115/80 mm.Hg. The pulse was regular in rate (60/min.) and rhythm. The heart was not enlarged, the apex beat being situated 1" within the mid-clavicular line in the 5th left intercostal space. The heart sounds were pure and well heard.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

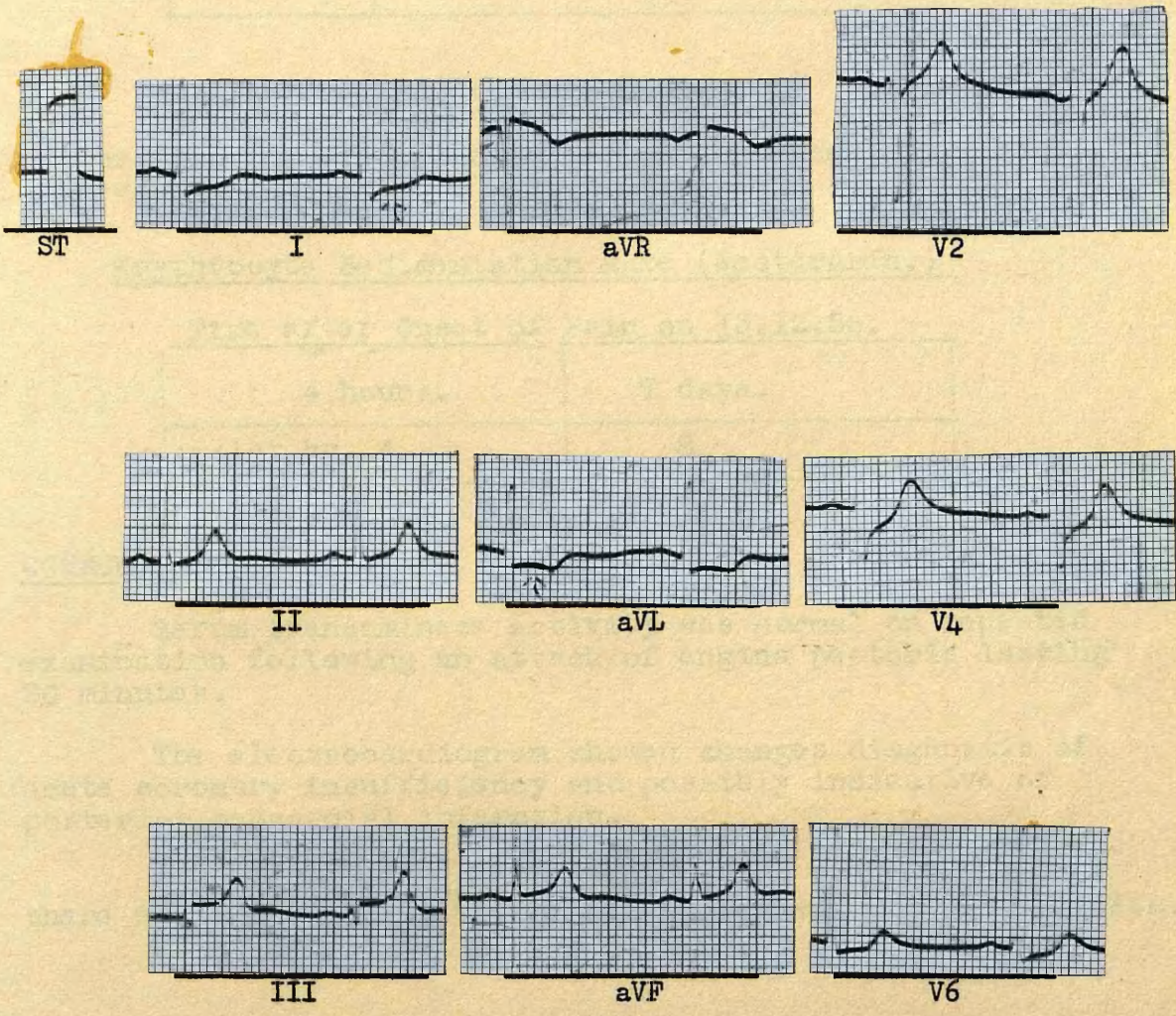
Four hours after admission, the patient complained of retrosternal pain referred into the right upper arm, which lasted for 20 minutes. The blood pressure did not fall and the pain responded to treatment with trinitrin, gr. 1/150.

14.12.56: Anticoagulant therapy was started and mycardol tab. ii t.i.d. p.c., was administered. The patient had no further symptoms and he was discharged from hospital on 24.12.56.

Electrocardiographic Findings.

I. 13.12.56: (During pain on 13.12.56). The electrocardiogram showed changes diagnostic of acute coronary insufficiency

ELECTROCARDIOGRAM CASE NO. 61



/ insufficiency but posterior myocardial infarction was still a possibility. Serial electrocardiograms were not performed.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Pain on 13.12.56.

Hours.	4	16	40
Units.	18	20	20

Temperature Record.

The temperature was normal throughout the period of observation.

Erythrocyte Sedimentation Rate (Westergren.)

Time after Onset of Pain on 13.12.56.

4 hours.	7 days.
mm/1st.hr. 4	8

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of angina pectoris lasting 20 minutes.

The electrocardiogram showed changes diagnostic of acute coronary insufficiency and possibly indicative of posterior myocardial infarction.

Serial electrocardiograms were not performed, but there was no clinical evidence of acute myocardial infarction.

CASE NO. 62.

History of Present Illness.

A male, aged 63 years, a sheet metal worker, was admitted to hospital on 24.2.57., complaining of retrosternal pain, induced by exertion, of eleven months' duration. In March, 1956, the patient first developed a gripping retrosternal pain when climbing a steel gangway. The pain spread across his chest and disappeared after two minutes when he rested. An electrocardiogram and X-Ray film of his chest were examined at the Southern General Hospital, Glasgow, but no abnormality was found.

The pain was brought on by less and less effort until, in December, 1956, he had a similar attack of pain while at rest. This lasted for three minutes, being quickly relieved by trinitrin. He described attacks of nocturnal paroxysmal cardiac dyspnoea. The patient had been confined to bed since that time. A second electrocardiogram showed no change, but X-Ray examination of the chest now showed slight enlargement of the heart.

Since 17.2.57, the patient had had frequent attacks of angina pectoris at rest and, on 23.2.57., an attack lasted for one hour. He was admitted to hospital on 24.2.57.

Clinical Findings on Admission.

The patient was an overweight man. He was not shocked. There was no evidence of congestive cardiac failure. B.P. was 135/75 mm.Hg. The pulse was regular in rate (84/min.) and rhythm. The heart was enlarged, the apex beat being situated in the fifth left intercostal space $\frac{1}{2}$" outwith the mid-clavicular line. The heart sounds were well heard and pure.

Treatment and Progress.

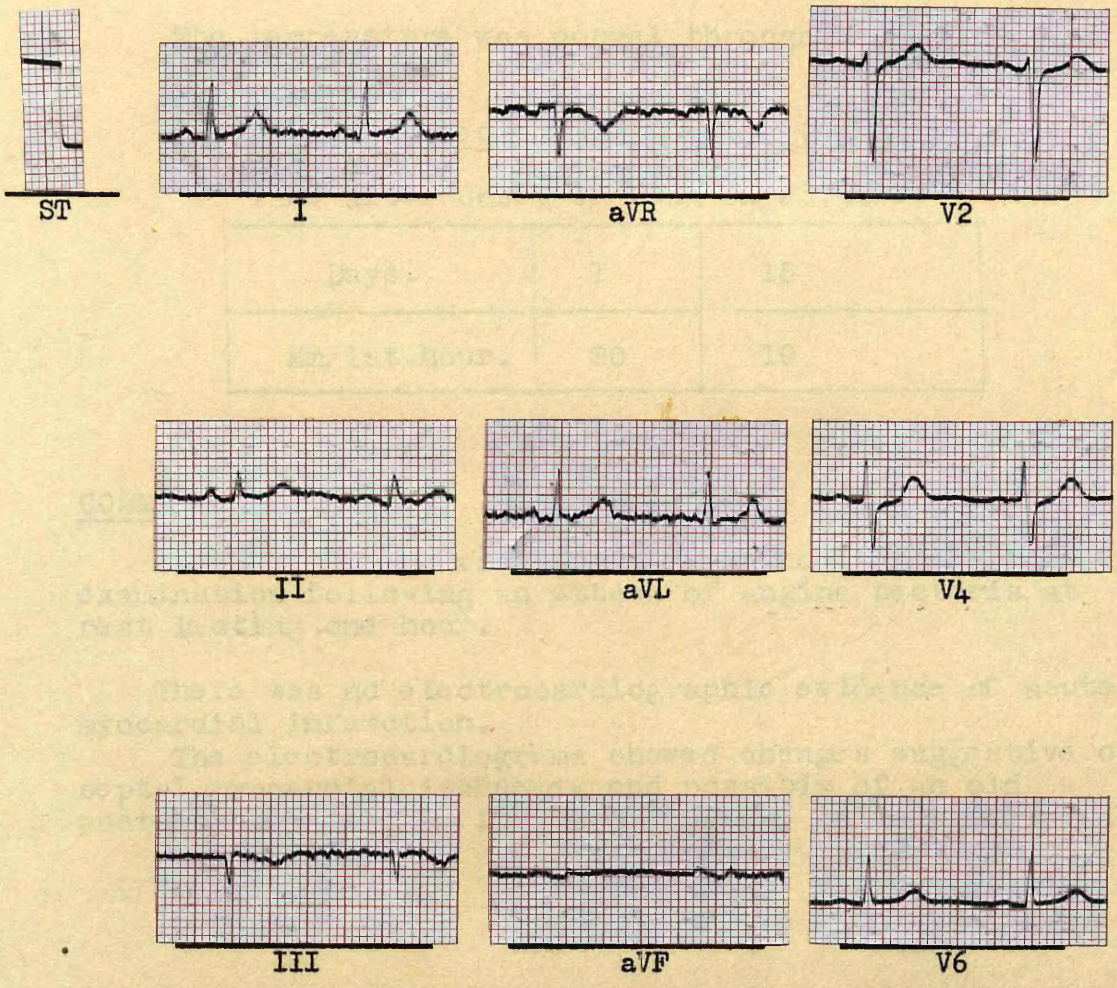
The patient settled well with rest in bed. He had one attack of severe anginal pain at rest lasting $1\frac{1}{2}$ hours on 2.3.57., but otherwise, his progress was uninterrupted and he was discharged from hospital on 17.3.57. B.P. was 140/80 mm.Hg.

Electrocardiographic Findings.

I. 24.2.57: The electrocardiogram showed no evidence of a recent myocardial infarction. The changes in a.V.F. may have been due to old posterior myocardial infarction. The slight S-T depressions in V.4 may have been due to septal ischaemia.

/2

ELECTROCARDIOGRAM CASE NO. 62



Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Anginal Pain on 23.4.57.

Hours.	24	48	72
Units.	6	8	6

Temperature Record.

The temperature was normal throughout.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Pain on 23.4.57.

Days.	1	15
Mm/1st.hour.	20	19

COMMENT:

Serum tra nsaminase activity was normal on repeated examination following an attack of angina pectoris at rest la sting one hour.

There was no electrocardiographic evidence of acute myocardial infarction.

The electrocardiograms showed changes suggestive of septal myocardial ischaemia and possibly of an old posterior myocardial infarction.

CASE NO. 63.

History of Present Illness.

A male, aged 70 years, a retired labourer, was admitted to hospital on 9.3.57., complaining of increasing breathlessness and epigastric pain of six weeks' duration. Since 1918., following an attack of influenza, the patient had had a chronic cough productive of mucoid sputum and had been subject to attacks of winter bronchitis. In 1951., he was compelled to retire from work because of increasing dyspnoea on exertion.

Following an acute upper respiratory tract infection in January, 1957., he became breathless even at rest and his ankles had become swollen. He developed a steady, severe epigastric pain which was unrelated to food and was accompanied by anorexia and nausea.

Clinical Findings on Admission.

The patient was very breathless on admission and had to be nursed in the orthopnoeic position. Marked jugular vein congestion, ankle and sacral oedema were present.

Cardiovascular System: B.P. 170/100 mm.Hg. The pulse was regular in rate (100/min.) and rhythm. The apex beat was not pslpable. The heart was enlarged, the left border as determined by percussion being 1" outwith the mid-clavicular line.

Respiratory System: There was clinical evidence of effusions at both bases and rales and rhonchi were heard throughout the lung fields. The chest was of emphysematous configuration.

Alimentary System: The liver was palpated 3" below the right costal margin and was very tender on pressure; this accounted for the pain of which the patient complained.

Treatment and Progress.

Treatment with digitalis leaf, crystalline penicillin and mersalyl was started soon after admission. The patient's condition, however, rapidly deteriorated and he died 18 hours after admission to hospital.

Permission for a post mortem examination was refused.

/2

Electrocardiographic Findings.

Electrocardiographic examination was not performed.

Serial Serum Transaminase Levels.

(12 hours after admission)
on 10.3.57.

.35 units.

Erythrocyte Sedimentation Rate (Westergren).

No examinations were performed.

Temperature Record.

No elevation of temperature was recorded.

COMMENT:

The history and clinical findings were typical of chronic cor pulmonale due to emphysema and chronic bronchitis. Serum transaminase levels were normal.

CASE NO. 64.

History of Present Illness.

A male, aged 60 years, a labourer, was admitted to hospital on 19.2.57 complaining of epistaxis of 12 hours' duration. The patient was confused and the history was obtained from his doctor, who had been called to the patient for the first time at 10 a.m. on 19.2.57. Despite packing of the nostrils with gauze bandage and sedation with Omnopon gr. 1/3 intramuscularly, the bleeding continued and the patient was admitted to hospital.

Clinical Findings on Admission.

There was profuse bleeding from the left nostril. The patient was pale but not shocked. Marked dyspnoea was present at rest and the lips were cyanosed. Slight ankle oedema was present.

Cardiovascular System: B.P. 240/150 mm.Hg. The pulse was regular in rate (130/min.) and rhythm. The heart was enlarged, the apex beat being situated $\frac{1}{2}$" outwith the mid-clavicular line in the 6th left interspace. The heart sounds were well heard. There was accentuation of the second aortic sound.

Respiratory System: On auscultation, numerous fine crepitations were heard throughout the lung fields.

Ophthalmoscopic examination showed early bilateral papilloedema.

Treatment and Progress.

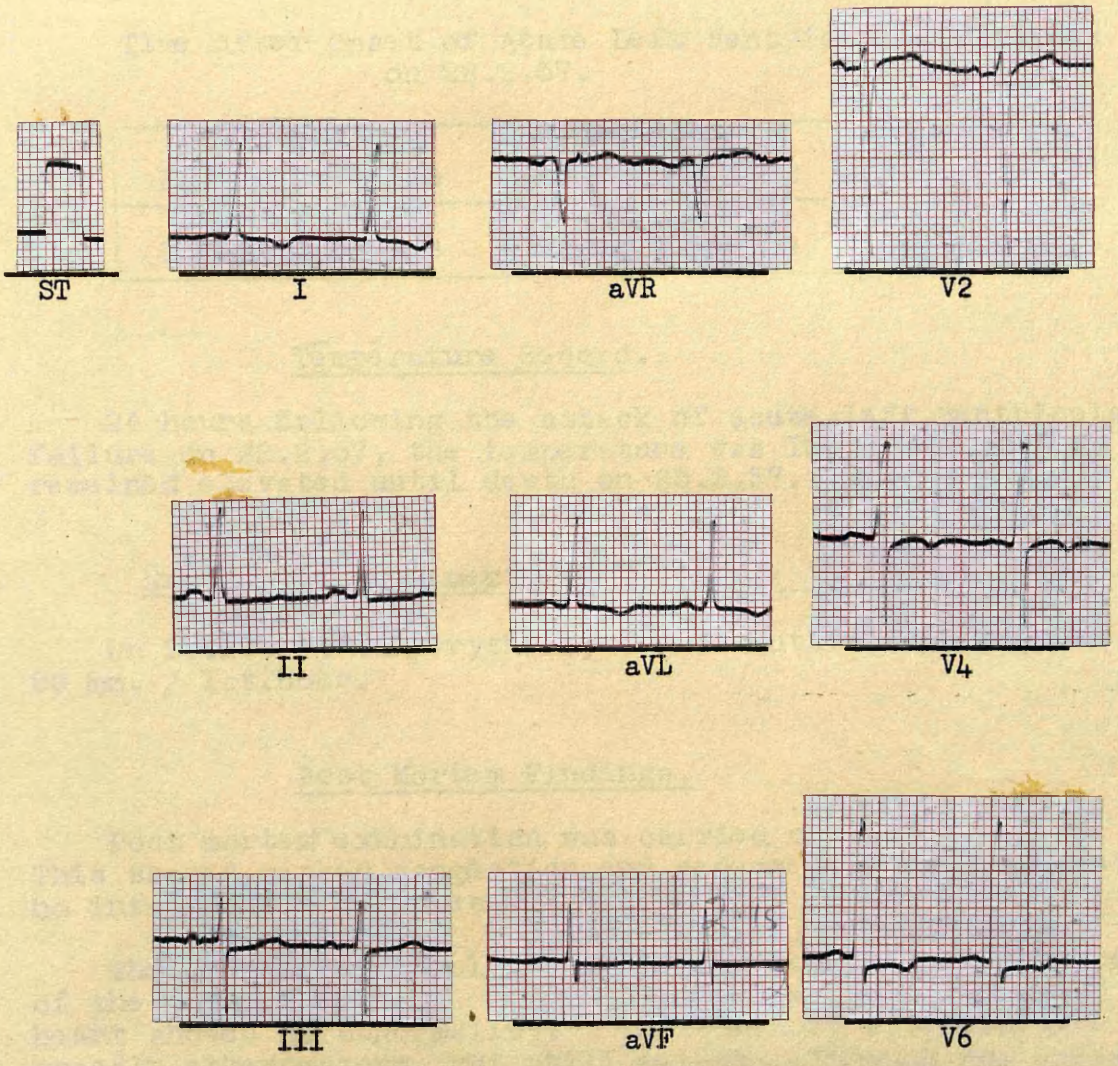
Nose bleeding was quickly controlled by firm packing of the left nostril with gauze and the blood pressure was lowered to 160/90 mm.Hg., by the injection of ansolysen, .25 mgm. intramuscularly. The blood urea was 135 mgm %.
Treatment with digitalis leaf gr. ii. t.i.d. was started.

22.2.57: B.P. 220/130 mm.Hg. The bleeding had been controlled and the patient seemed to be improving when he suddenly developed signs and symptoms of acute left ventricular failure. He was very distressed. Morphine, gr.1/4 intramuscularly and aminophylline .25 mgm. intravenously partially relieved the symptoms. Parenteral administration of ansolysen was resumed in an attempt to control the hypertension.

24.2.57: B.P. 220/140 mm.Hg. The patient remained dyspnoeic and signs of congestive cardiac failure were now present. He died suddenly on 25.2.57.

/2

ELECTROCARDIOGRAM CASE NO. 64



Electrocardiographic Findings.

I. 22.2.57: The electrocardiogram showed a basic left ventricular strain pattern but also antero-lateral ischaemia. There was no evidence of acute myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Acute Left Ventricular Failure on 22.2.57.

Hours.	24	48	72
Units.	28	26	24

Temperature Record.

24 hours following the attack of acute left ventricular failure on 22.2.57, the temperature was 100.6°F., and it remained elevated until death on 25.2.57.

Erythrocyte Sedimentation Rate (Westergren.)

On 20.2.57., the erythrocyte sedimentation rate was 20 mm. / 1st.hour.

Post Mortem Findings.

Post mortem examination was carried out on 26.2.57. This showed marked congestion and oedema of both lungs but no infarctions were present.

The heart was grossly enlarged due to marked hypertrophy of the left ventricle. The other chambers and valves of the heart showed no abnormality. The coronary arteries were grossly atheromatous, but still patent, although the anterior descending branch of the left vessel had only a small lumen in its middle portion. The myocardium was rather pale but showed no gross fibrosis or evidence of recent infarction.

No abnormality was seen in the alimentary tract.

/3

Post Mortem Findings (ctd.)

The liver, spleen, pancreas and adrenals showed marked congestion, but were otherwise normal.

Both kidneys were a little smaller in size than normal and the capsule stripped with slight difficulty. Fine granularity of the capsule was everywhere present. On section, the kidneys were congested and showed moderate destruction of the normal anatomical markings.

The ureters, urinary bladder and prostate were quite normal.

Death was considered to be due to hypertension passing into the malignant phase; left ventricular cardiac failure and pulmonary oedema.

Results of Histological Examination.

Heart Muscle: There was no evidence of myocardial infarction. Areas of ischaemic fibrosis were present.

Kidney: Marked hypertensive changes were present in the afferent arterioles of the glomeruli.

Liver: No abnormality was seen.

COMMENT:

The patient, on admission, was suffering from left ventricular failure and ischaemic heart disease, in association with malignant hypertension. There was no electrocardiographic evidence of acute myocardial infarction, although patterns indicative of left ventricular strain and antero-lateral ischaemia were present.

Post mortem examination confirmed the diagnosis. Gross atherosclerosis of the coronary arteries was present, but there was no evidence of myocardial infarction.

Serum transaminase activity was normal on serial examination.

CASE NO. 65.

History of Present Illness.

A male, aged 53 years, a company director, was admitted to hospital on 7.6.57., having had an attack of central chest pain. Since May 1956., the patient had been conscious of a gripping sensation in the retrosternal region when hurrying or when emotionally upset. He had noted that the sensation cleared away after resting, or relaxing, and that he was slightly breathless on exertion.

On 18.5.57., he was seized while at a dinner, with severe non-radiating retrosternal pain of constricting character, which lasted for three hours. This was alleviated by an injection of morphine sulphate. After an electrocardiogram had been examined, he was transferred to Perth Royal Infirmary where he was confined to bed and treated with anticoagulant drugs. After fourteen days he became restive in hospital and decided to return home to Paisley since he was feeling well. He remained symptom-free until 9.30 p.m. on 7.6.57., when he suffered a recurrence of severe, constricting retrosternal pain while at rest in bed. This pain was referred down the inner aspect of the left arm. It lasted for 30 minutes and was relieved by an injection of pethidine, 100 mgm., intramuscularly. He was admitted to hospital at 11. p.m.

Clinical Findings on Admission.

The patient was a well built man, who was symptom-free. There was no evidence of shock or congestive cardiac failure.

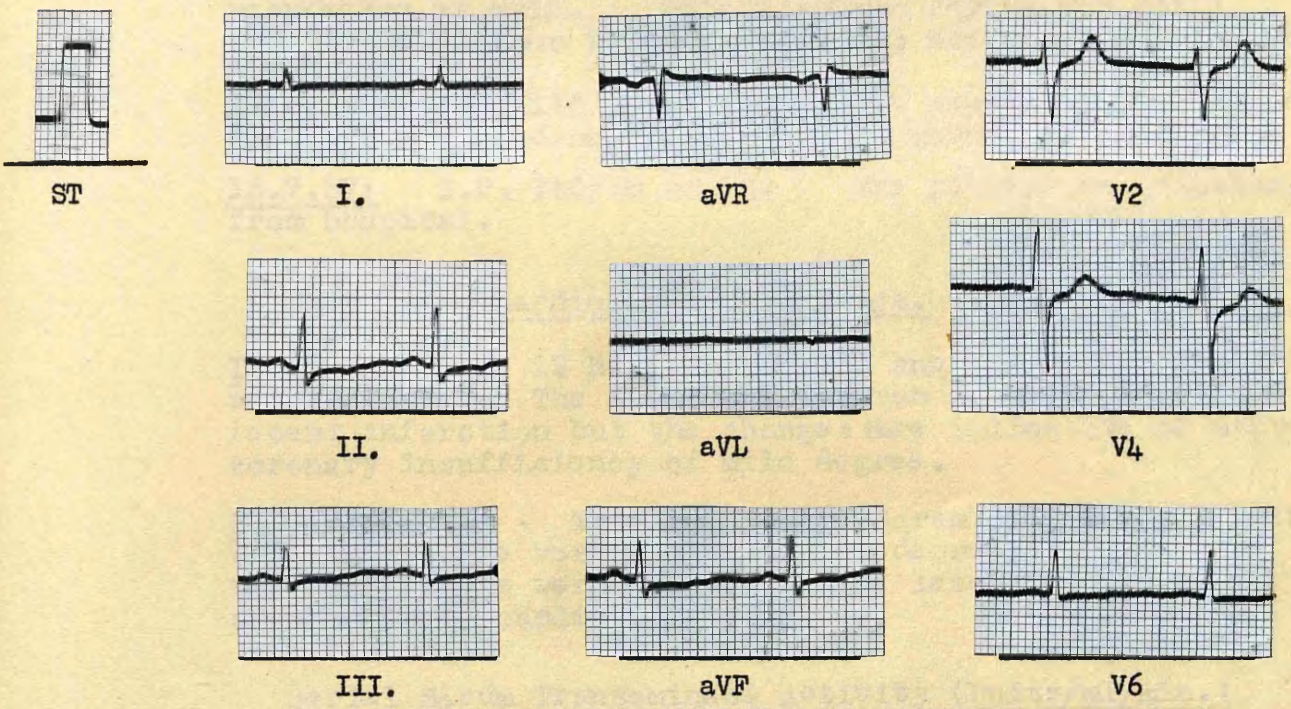
Cardiovascular System: B.P. 110/80 mm.Hg. The pulse was regular in rate (60/min.) and rhythm.; the apex beat was not felt, but the heart did not appear to be enlarged. The left border of the heart, as determined by percussion, was within the mid-clavicular line. The heart sounds were well heard, pure and of good quality.

No other abnormality was found on full clinical examination of other systems.

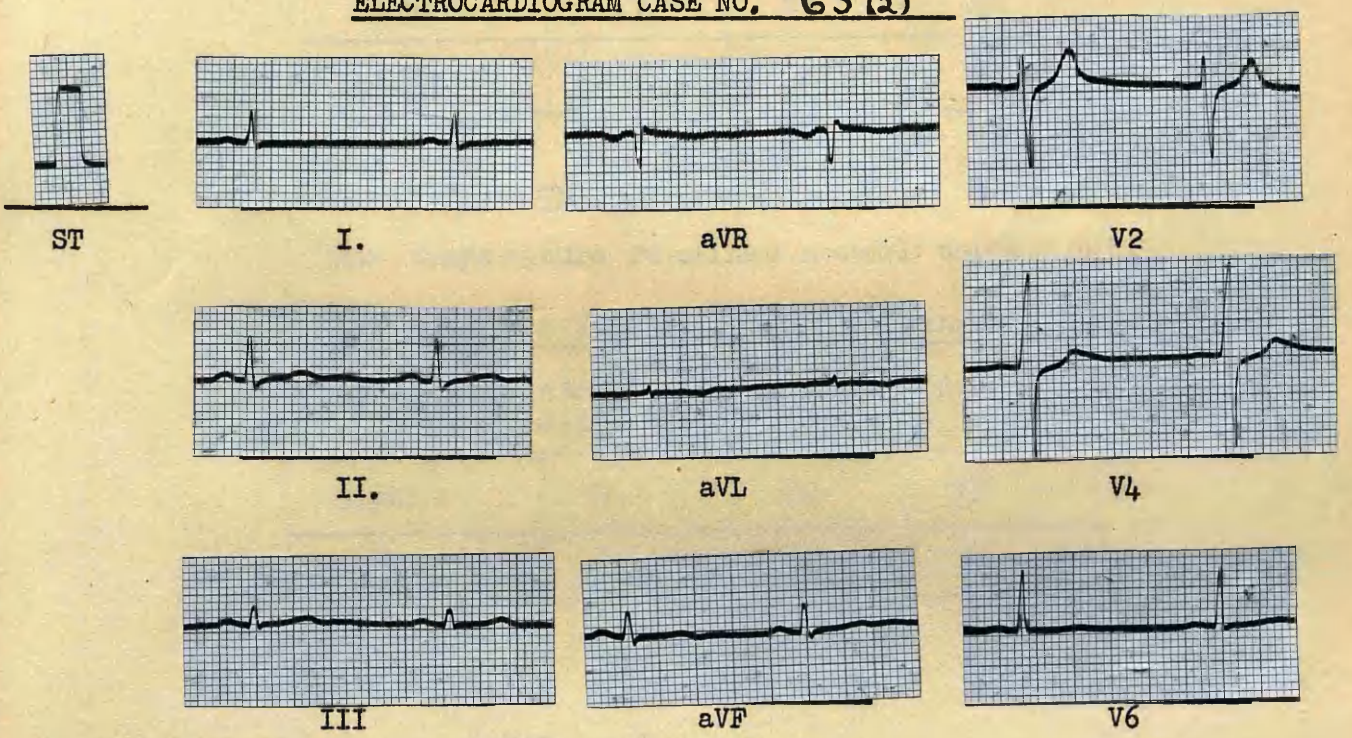
Treatment & Progress.

8.6.57: The patient was symptom-free. B.P. 105/65 mm.Hg. There was slight, but definite, jugular vein congestion and slight ankle oedema. Numerous crepitations were heard on auscultation over the base of the right lung posteriorly. The pulse was irregular due to the presence of numerous ventricular ectopic beats and protodiastolic rhythm was noted on auscultation over the mitral area. Anti-coagulant therapy was started and continued for 21 days. /2

ELECTROCARDIOGRAM CASE NO. 65 (1)



ELECTROCARDIOGRAM CASE NO. 65 (2)



Treatment with mersalyl was also started.

10.6.57: B.P. 100/65 mm.Hg. There had been no recurrence of pain. Protodiastolic rhythm was still present. Jugular venous congestion was no longer present.

2.7.57: B.P. 110/70 mm.Hg. The patient was well and there was no evidence of congestive cardiac failure.

13.7.57: B.P. 110/70 mm.Hg. The patient was discharged from hospital.

Electrocardiographic Findings.

I. 8.6.57: (12 hours following anginal pain on 7.6.57 at 9.30 p.m.) The electrocardiogram showed no evidence of recent infarction but the changes were indicative of acute coronary insufficiency of mild degree.

II. 16.6.57: The electrocardiogram showed improvement with incomplete restitution of S-T depressions. Low voltage T waves were present in all leads except V.2., suggesting myocardial fibrosis.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Retrosternal Pain on 7.6.57 at 9.30 pm.

Hours.	17	39	60
Units.	26	20	18

Temperature Record.

The temperature remained normal throughout.

Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Retrosternal Pain on 7.6.57 at 9.30 p.m.

Days.	2	10	17
mm/1st.hr.	5	3	2

COMMENT:

/over....3

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of angina pectoris at rest, lasting thirty minutes.

The electrocardiograms showed changes diagnostic of acute coronary insufficiency but there was no evidence of acute myocardial infarction.

Congestive cardiac failure of mild degree was present at the time when serum transaminase activity was measured.

CASE NO. 66.

History of Present Illness.

A male, aged 65 years, a worker in a tyre factory, was admitted to hospital on 8.3.57., complaining of attacks of breathlessness at rest. The patient had been treated in hospital from 8.2.57 until 20.2.57. Mild symptoms of angina pectoris on exertion had been present since December, 1956, and were considered to have been due to aortic incompetence of rheumatic origin and paroxysmal auricular fibrillation.

The bouts of arrhythmia were frequent, although short-lasting, and on discharge of the patient, he was advised to continue to take digitalis leaf, gr. i.b.d.

Unfortunately, he failed to continue the drug and on 6.3.57., he suffered a severe attack of paroxysmal cardiac dyspnoea; thereafter, he was very breathless at rest. He had another acute attack of dyspnoea on 8.3.57 at 4.30 p.m. and was admitted to hospital for further treatment.

Clinical Findings on Admission.

The patient was drowsy, the effect of intramuscular morphine sulphate gr. 1/2 given before admission. The lips were cyanosed, jugular vein congestion was present and the respirations were rapid and shallow. Coughing produced rust-coloured sputum.

Cardiovascular System: B.P. 140/55 mm.Hg. The pulse was irregularly regular; the rate was 100/min. The heart was enlarged, the apex beat being heaving in character and situated $\frac{1}{2}$" outwith the mid-clavicular line in the 6th left intercostal space. An aortic diastolic murmur was heard at the aortic area and was conducted down the left border of the sternum into the mitral area.

Respiratory System: There were numerous bubbling crepitations heard on auscultation over both lung bases.

Alimentary System: The liver edge was palpable 2" below the right costal margin.

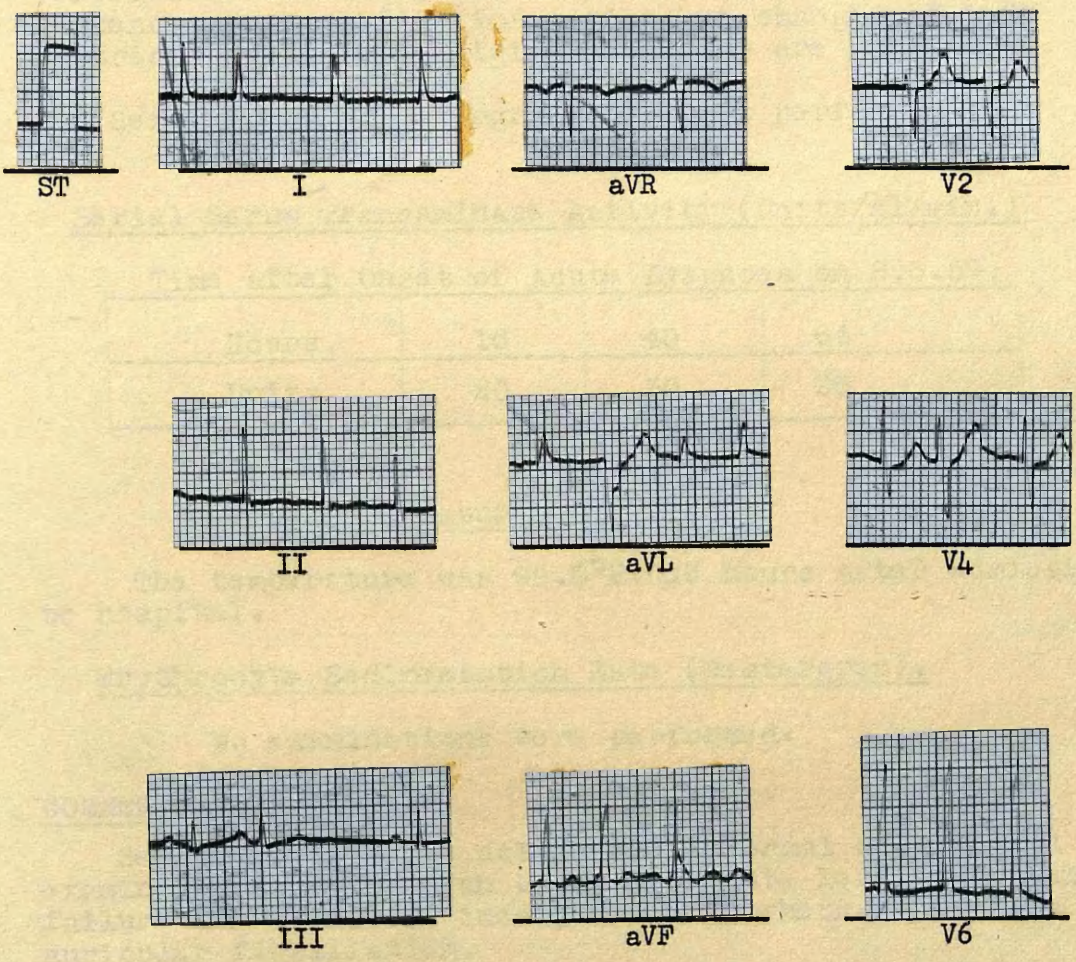
No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

The patient quickly settled following admission to hospital with rest in bed and treatment with digitalis leaf and mersalyl. He had no further attacks of

/2

ELECTROCARDIOGRAM CASE NO. 66



breathlessness and all signs of heart failure cleared. He was discharged from hospital on 2.4.57. Auricular fibrillation had become permanently established and a maintenance dose of digitalis leaf was advised.

Electrocardiographic Findings.

I. 8.3.57: (6 hours after attack of dyspnoea).

The electrocardiogram showed periods of sinus rhythm; extrasystoles, both ventricular and supra-ventricular and auricular fibrillation. There was no evidence of myocardial infarction but changes of left ventricular strain or digitalis effect are present.

Serial electrocardiograms were not performed.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Acute Dyspnoea on 8.3.57.

Hours.	16	40	64
Units.	20	30	26

Temperature Record.

The temperature was 99.8°F. 16 hours after admission to hospital.

Erythrocyte Sedimentation Rate (Westergren).

No examinations were performed.

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of acute left ventricular failure due to aortic incompetence of rheumatic origin and auricular fibrillation.

Congestive cardiac failure was present when transaminase activity was determined.

The rate of auricular fibrillation was approximately 100/minute.

CASE NO. 67.

History of Present Illness.

A male, aged 58 years, a labourer, was admitted to hospital on 27.5.57 complaining of breathlessness and chest pain on slight exertion. In 1955, the patient stopped working because he had suddenly become breathless on moderate exertion and began to have gripping retrosternal pain on exertion: the pain was referred down the left arm on one occasion. It was quickly relieved by rest and by the use of trinitrin.

Since March, 1957, the pain and dyspnoea had gradually been more easily induced until he was breathless on the slightest exertion and was subject to frequent and severe attacks of angina pectoris at rest, associated with attacks of nocturnal paroxysmal cardiac dyspnoea. He had made no response to treatment at home and was admitted to hospital for further treatment.

Clinical Findings on Admission.

The patient was a thin, anxious man who was breathless on slight exertion.

Cardiovascular System: B.P. 155/85 mm.Hg. The pulse was regular in rate (72 beats per minute) and rhythm. The heart was enlarged, the apex beat being situated in the anterior axillary line in the sixth intercostal space. The heart sounds were distant, but pure.

Treatment and Progress.

The patient was symptom-free on admission. Myocardol tab. ½ t.i.d. was given daily.

29.5.57: B.P. 150/80 mm.Hg. The patient had a severe attack of acute dyspnoea associated with severe anginal pain lasting one hour. Mersalyl and digitalis therapy was started.

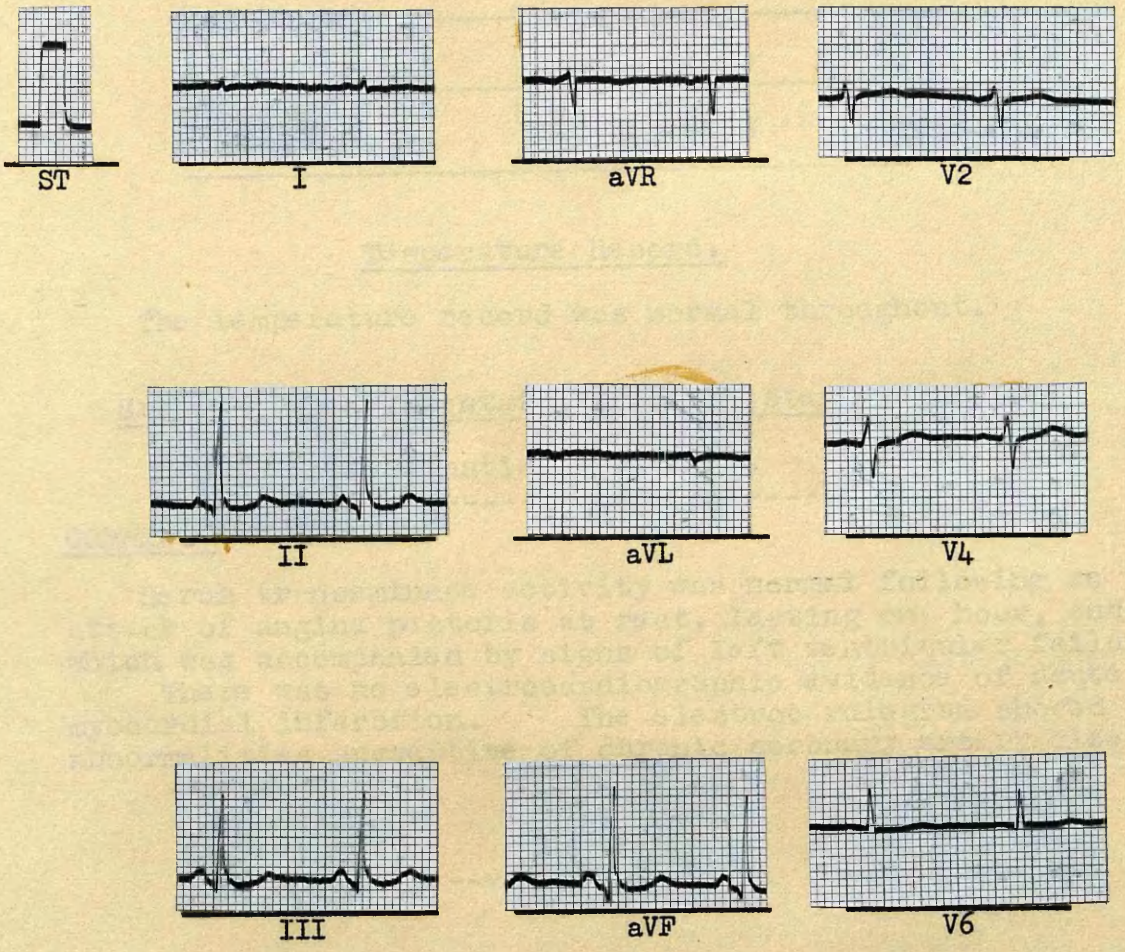
1.6.57: B.P. 140/80 mm.Hg. The patient continued to have attacks of nocturnal paroxysmal cardiac dyspnoea.

22.6.57: B.P. 150/80 mm.Hg. The patient continued to have minor attacks of dyspnoea but the anginal pain had cleared.

12.7.57: The patient was discharged from hospital.

/2

ELECTROCARDIOGRAM CASE NO. 67



Electrocardiographic Findings.

I. 31.5.57: (48 hours after acute dyspnoea and pain on 29.5.57). The electrocardiogram showed no evidence of myocardial infarction but low voltage T waves and slight S-T depression, II, III, A.V.F. suggestive of chronic coronary artery disease.

Serial Serum Transaminase Activity.(Units/ml/min.)

Time After Onset of Dyspnoea and Pain on 29.5.57.

Hours.	12	36	60
Units..	20	25	23

Temperature Record.

The temperature record was normal throughout.

Erythrocyte Sedimentation Rate (Westergren).

No examination performed.

COMMENT:

Serum transaminase activity was normal following an attack of angina pectoris at rest, lasting one hour, and which was accompanied by signs of left ventricular failure.

There was no electrocardiographic evidence of acute myocardial infarction. The electrocardiogram showed abnormalities suggestive of chronic coronary artery disease.

CASE NO. 68.

History of Present Illness.

A married woman, aged 62 years, was admitted to hospital on 3.2.57., complaining of severe retrosternal pain of three hours' duration. For three weeks before admission the patient had complained of gripping retrosternal pain and breathlessness on exertion. The pain cleared within a few minutes if she rested.

On 2.2.57 at 10 p.m., gripping retrosternal pain came on when she was lying in bed. The pain radiated through to the interscapular area and down the left arm; it subsided after three hours. She had been restless and breathless during the pain.

Clinical Findings on Admission.

The patient was overweight and of florid complexion. There was no evidence of shock or heart failure.

Cardiovascular System: B.P. 160/100 mm.Hg. The pulse was regular in rate (60/min.) and rhythm. The apex beat was not palpable, but the heart was considered to be enlarged, the left border as determined by percussion being ½" outwith the mid-clavicular line.

No other abnormalities were found on full clinical examination of other systems.

Treatment and Progress.

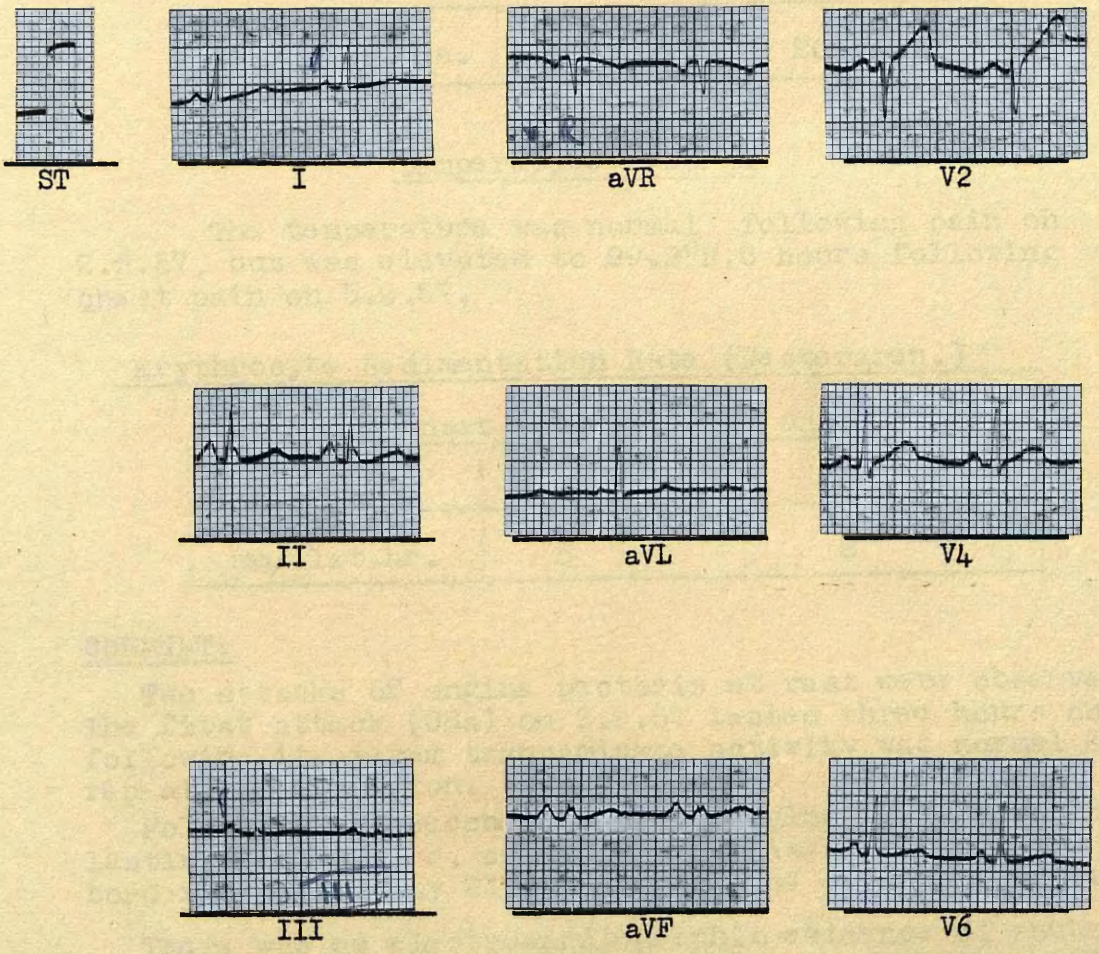
The patient was confined to bed and a low salt, 1,000 calorie diet was prescribed. She was symptom-free. On 5.2.57, she suffered another severe attack of angina pectoris at rest which lasted for three hours. The B.P. did not fall during or after this attack nor did signs of congestive cardiac failure appear. Thereafter, the patient made good progress and she was discharged from hospital on 12.3.57. B.P. was 160/100 mm.Hg. on discharge.

Electrocardiographic Findings.

I 7.2.57: (48 hours following chest pain on 5.2.57). The electrocardiogram shows no evidence of infarction. No gross abnormality was seen although low voltage is noted in A.V.F. in praecordial T waves suggesting myocardial fibrosis.

/2

ELECTROCARDIOGRAM CASE NO. 68



Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain on 2.2.57.

Hours.	10	33
Units.	23	31

Time After Onset of Chest Pain on 5.2.57.

Hours.	24.	48.	72
Units.	43	22	20

Temperature Record.

The temperature was normal following pain on 2.2.57, but was elevated to 99.2°F.6 hours following chest pain on 5.2.57.

Erythrocyte Sedimentation Rate (Westergren.)

Time After Onset of Chest Pain on 2.2.57.

Hours.	48	72
mm/ lst.hr.	3	8

COMMENT:

Two attacks of angina pectoris at rest were observed. The first attack (68a) on 2.2.57 lasted three hours and, following it, serum transaminase activity was normal on repeated examination.

Following the second attack of angina on 5.2.57 (68b)., lasting three hours, serum transaminase activity rose to borderline activity 24 hours after the onset of the illness.

There was no electrocardiographic evidence of acute myocardial infarction, the changes in the electrocardiographic patterns suggesting myocardial fibrosis.

CASE NO. 69.

History of Present Illness.

A male, aged 57 years, a checker in a foundry, was admitted to hospital on 14.2.57., complaining of severe dyspnoea of one week's duration. The patient had been working until 7.2.57 when he developed an upper respiratory tract infection and became very breathless. Following this, ankle swelling was noted and the abdomen felt "tight" and breathlessness became so severe that it was present while he rested in bed. He denied having any pain in his chest; he was admitted to hospital for further treatment.

Past History.

The patient had had respiratory symptoms for 20 years. At first they consisted of winter cough, but since 1947 he had had a cough throughout the year which was productive of a viscid mucoid spit which became mucopurulent when he had an upper respiratory tract infection. The patient had worked in the dusty atmosphere of a foundry for 35 years. His cigarette consumption was 40-50 per day. He had been examined in hospital on 28.1.57 when the diagnosis of chronic bronchitis with severe emphysema had been made. B.P. was 130/70 mm.Hg.

Clinical Findings on Admission.

The patient was very dyspnoeic and central cyanosis was present. Sacral and ankle oedema and jugular venous congestion were marked. Finger clubbing was noted. The patient was mentally confused.

Cardiovascular System: B.P. 130/70 mm.Hg. The pulse was regular in rate (100/min.) and rhythm. The apex beat was not felt. The heart sounds were pure but poorly heard.

Respiratory System: Chest expansion was very restricted and the accessory muscles of respiration were being used.

Alimentary System: The liver was palpable 2" below the right costal margin and free fluid was present.

No other abnormality was found on full clinical examination.

Treatment and Progress.

Treatment with digitalis leaf gr. ii t.i.d., and crystalline penicillin and mersalyl was started on admission and repeated intravenous injections of aminophylline 0.25 gm. seemed to relieve the dyspnoea partially,

/2

/partially, although the patient remained confused. On 15.2.57., at 9 a.m., the patient became more cyanosed and extremely breathless again and, once more, intravenous aminophylline was effective. His condition remained unchanged with treatment, and the patient died at 5 p.m. on 16.2.57. Permission for a post mortem examination was refused.

Electrocardiographic Findings.

I. 15.2.57: (5 hours following onset of extreme breathlessness.) The electrocardiogram was diagnostic of an acute transmural antero-septal myocardial infarction.

Duplicate electrocardiographic records are not available for inclusion in this study.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Extreme Dyspnoea on 15.2.57.

Hours.	24
Units.	313

Temperature Record.

Low grade pyrexia 98.8 - 99.6°F was present during the period of observation.

Erythrocyte Sedimentation Rate (Westergren).

No estimations were performed.

COMMENT: On admission, congestive cardiac failure due to chronic bronchitis and emphysema was considered to be the diagnosis. Some hours after admission, the patient became extremely breathless and cyanosed and, despite the absence of pain, myocardial infarction was suspected. An electrocardiogram, taken 5 hours after the onset of severe dyspnoea, was diagnostic of transmural myocardial infarction. Pyrexia and a minimal degree of peripheral vascular failure developed and the myocardial infarction was considered to be of poor risk type. Serum transaminase activity was at very high levels 24 hours following the attack of dyspnoea. The assay was not considered to have contributed to the diagnosis.

CASE NO. 70.

A married woman, aged 69 years, a housewife, was admitted to hospital on 4.4.57 having had a severe attack of breathlessness on 4.4.57. The patient had been dyspnoeic on exertion since 1955 but, since October 1956, it had become worse and she was unable to walk any distance without undue dyspnoea. On 4.4.57., while walking, the patient became very dyspnoeic and complained of praecordial tightness and a retrosternal sensation of heaviness. These symptoms lasted for one hour.

Clinical Findings on Admission.

The patient was overweight. There was no evidence of shock or congestive cardiac failure.

Cardiovascular System: B.P. 215/115 m..Hg. The pulse was regular in rate (88/min.) and rhythm. The heart was enlarged, the apex beat being ½" outwith the mid-clavicular line in the fifth left intercostal space. The heart sounds were of good quality. There was a loud systolic murmur at the mitral area and the second aortic sound was accentuated.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

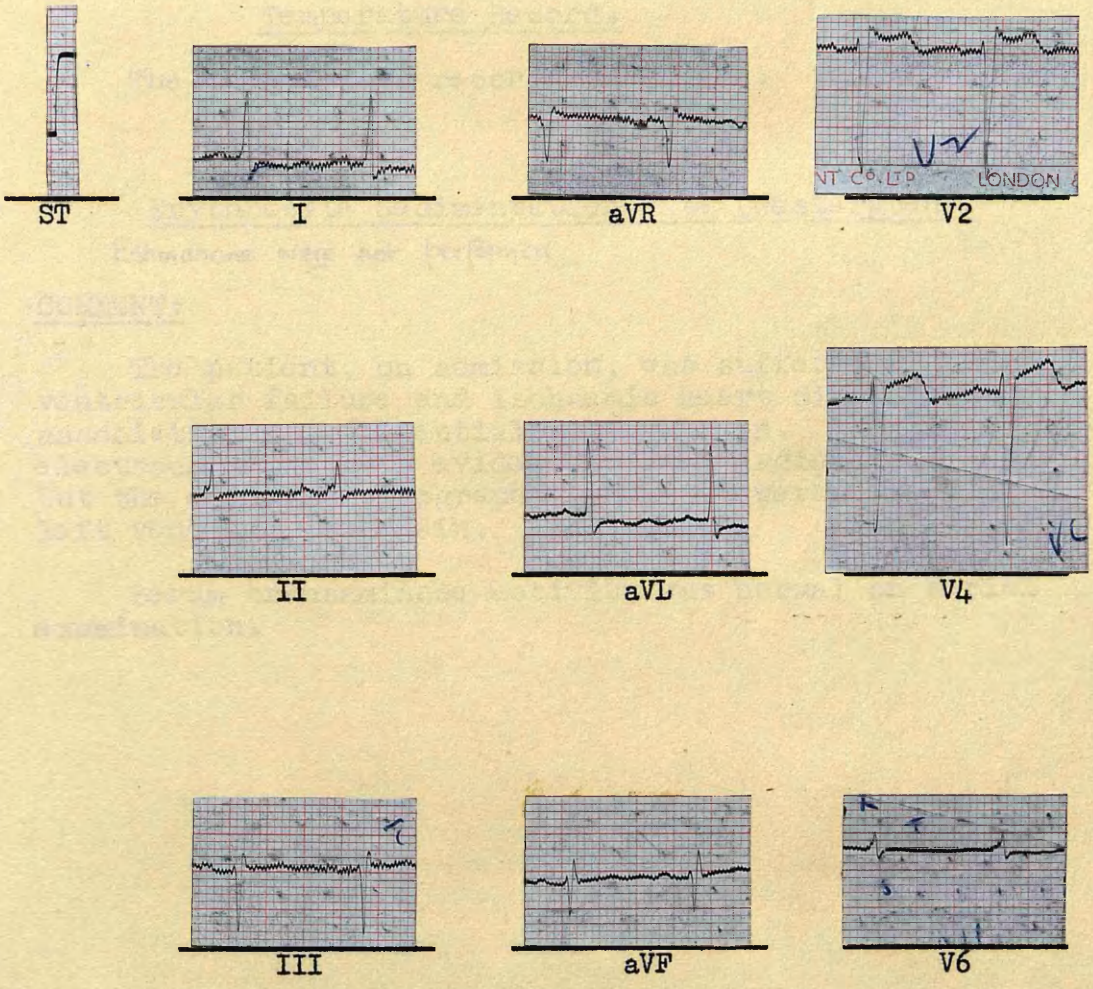
The patient was symptom-free on admission and remained so throughout her stay in hospital. No special treatment was given apart from a low salt, low calorie diet. She was discharged from hospital on 15.5.57. B.P. was 190/110 mm.Hg.

Electrocardiographic Findings.

I. 4.4.57: The electrocardiogram showed changes suggestive of left ventricular strain. There were ventricular extrasystoles. The tracing was technically poor, but there was no evidence of infarction.

/2

ELECTROCARDIOGRAM CASE NO. 70



Serial Serum Transaminase Activity (Units/ml/min.)

5.4.57	:	29 units.
6.4.57	:	26 units.
8.4.57	:	30 units.

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren).

Estimations were not performed.

COMMENT:

The patient, on admission, was suffering from left ventricular failure and ischaemic heart disease in association with essential hypertension. There was no electrocardiographic evidence of myocardial infarction but the electrocardiographic patterns were suggestive of left ventricular strain.

Serum transaminase activity was normal on serial examination.

CASE NO. 71.

History of Present Illness.

A male, aged 64 years, a dyer, was admitted to hospital on 3.11.56., complaining of severe retrosternal pain of crushing character of 2 hours' duration.

On 27.10.56., the patient, having previously enjoyed good health, began to have attacks of gripping retrosternal pain on moderate exertion which passed off in 2 minutes, when rested. At 2 a.m., on 3.11.56., he had an attack of anginal pain at rest which persisted and was still present on admission.

Past History.

In 1945., the patient was treated for a perforated peptic ulcer, but had had no dyspeptic symptoms since then.

Clinical Findings on Admission.

The patient was pale and mildly shocked. Neck veins showed congestion.

Cardiovascular System: B.P. 210/110 mm.Hg. The pulse was irregular, due to the presence of ventricular ectopic beats. The heart was enlarged, the apex beat being outwith the mid-clavicular line. The heart sounds were of poor quality; the second aortic sound was accentuated. Pericardial friction was present along the left border of the sternum from the 3rd - 5th intercostal space.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

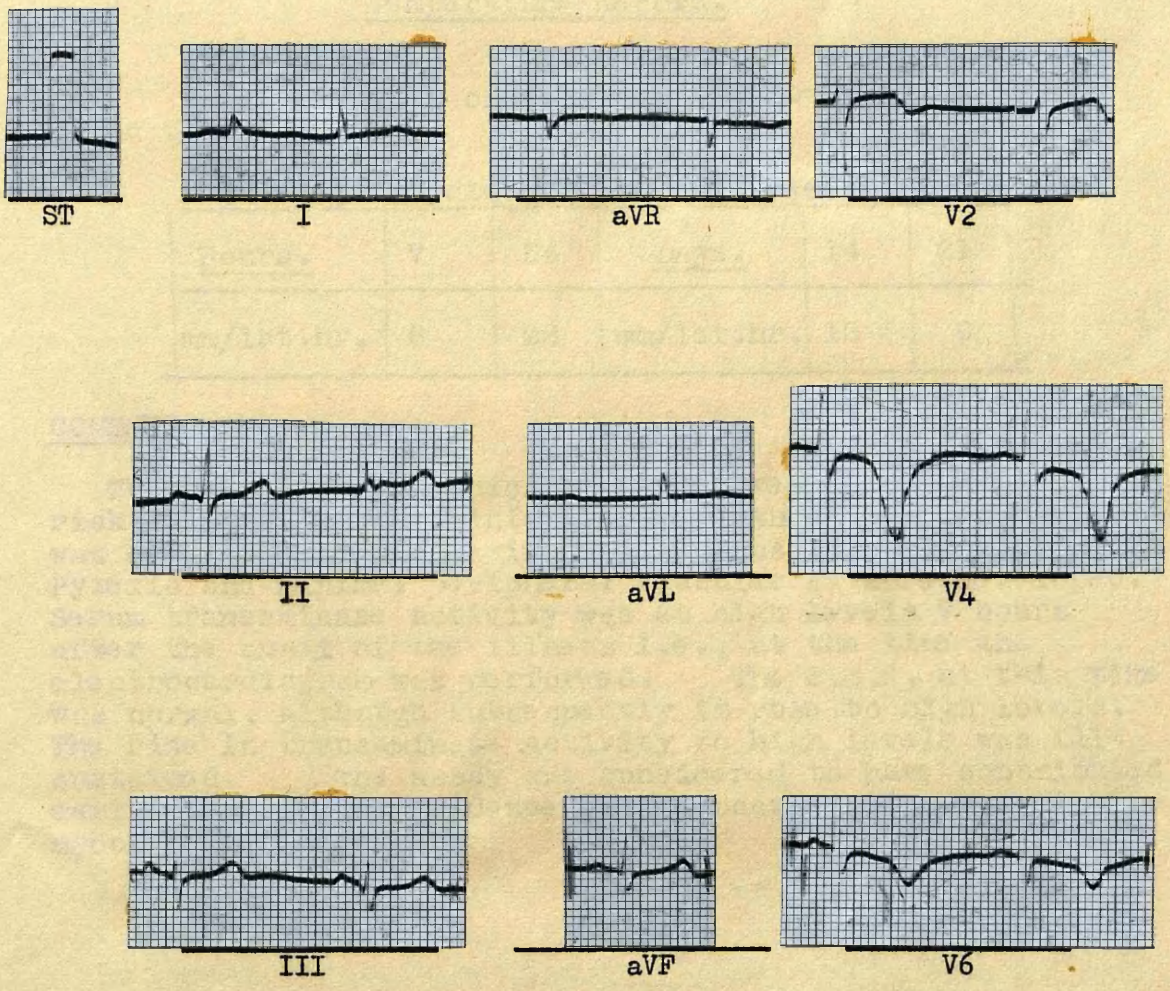
Anticoagulant therapy was started soon after admission and was continued for 21 days. The patient made an uninterrupted recovery and was discharged from hospital on 17.12.56. B.P. 150/100 mm.Hg.

Electrocardiographic Findings.

I. 3.11.56: (7 hours after the onset of pain). The electrocardiogram showed changes diagnostic of an acute intramural antero-septal myocardial infarction. Occasional ventricular extrasystoles were noted.

/2

ELECTROCARDIOGRAM CASE NO. 71



Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Pain on 3.11.56.

Hours.	7	31	54	78
Units.	55	85	48	34

Temperature Record.

A temperature of 99.6°F. was recorded 30 hours after onset of pain.

Erythrocyte Sedimentation Rate (Westergren.)

Hours.	7	54	Days.	14	21
mm/1st.hr.	6	22	mm/1st.hr.	12	9

COMMENT:

The history and clinical findings were typical of a poor risk acute myocardial infarction and the electrocardiogram was diagnostic of acute intramural myocardial infarction. Pyrexia and minimal peripheral vascular failure developed. Serum transaminase activity was at high levels 7 hours after the onset of the illness i.e., at the time the electrocardiogram was performed. The E.S.R. at this time was normal, although subsequently it rose to high levels. The rise in transaminase activity to high levels was ill-sustained. The assay was considered to have contributed early confirmatory evidence of the occurrence of acute myocardial infarction.

CASE NO. 72.

History of Present Illness.

A married woman, aged 57 years, was admitted to hospital on 29.6.57 complaining of dyspnoea of six weeks' duration.

On 17.5.57, the patient developed an influenzal-like illness with pyrexia, praecordial tightness and cough productive of white frothy sputum.

The patient retired to bed and, since then, had been dyspnoeic on the slightest exertion in bed. She had had two attacks of paroxysmal cardiac dyspnoea in the week before her admission to hospital.

Clinical Findings on Admission.

The patient was a pale, anxious woman who was orthopnoeic. Slight jugular vein congestion was present.

Cardiovascular System: B.P. 140/70 mm.Hg. The pulse was regular in rate (100/min.) and rhythm. The apex beat was not palpable. The heart sounds were pure but poorly heard.

Respiratory System: On auscultation, numerous medium crepitations were heard throughout the lung fields, especially over the base of the right lung.

Alimentary System: The liver edge was palpable 1" below the right costal margin.

Treatment and Progress.

The patient recovered quickly with treatment with digitalis leaf and a low salt, low calorie diet. On 7.7.57, the patient had an attack of paroxysmal cardiac dyspnoea lasting half an hour which responded to treatment with morphine sulphate, gr. 1/4.

Electrocardiographic Findings.

I. 7.7.57: The electrocardiogram showed no evidence of infarction. The low voltage T waves and slight S-T depression in a.V.F. were suggestive of chronic coronary artery disease.

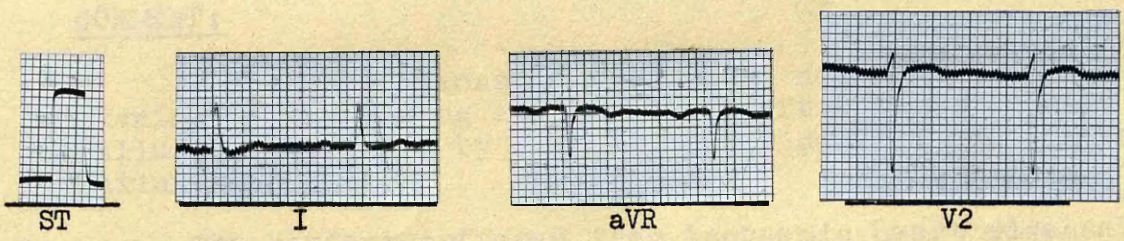
Serial Serum Transaminase Activity (Units/ml/min.)

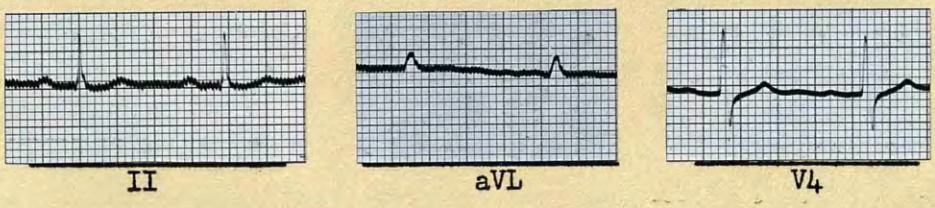
Time After Onset of Dyspnoea on 7.7.57

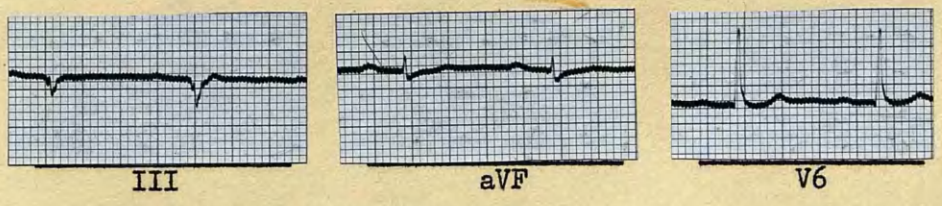
Hours.	24	48	72
Units.	20	29	20

/2

ELECTROCARDIOGRAM CASE NO. 72







Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren).

No estimations were performed.

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of left ventricular failure, accompanied by signs of early congestive cardiac failure.

The patient suffered from ischaemic heart disease.

There was no electrocardiographic evidence of myocardial infarction, but electrocardiographic changes suggesting chronic coronary artery disease were noted.

CASE NO. 73.

History of Present Illness.

A male, aged 57 years, a publican, was admitted to hospital on 26.6.57 complaining of dyspnoea and retrosternal pain on exertion. Since 1952, the patient had gradually become more and more breathless on exertion and had had dull, non-radiating retrosternal pain on exertion which was relieved by rest.

On 22.5.57, the patient suffered two severe attacks of paroxysmal cardiac dyspnoea and, although treatment with digoxin and mersalyl was started, these attacks continued in milder form until 5.6.57. At this time, the patient's face became suffused and dyspnoea at rest was still present. When no further improvement took place the patient was admitted to hospital for further investigation.

Clinical Findings on Admission.

The patient was an obese man whose face was swollen and suffused. There was an increase in neck size and marked plethora of the upper half of the body with dilated supra-clavicular veins and neck veins, very suggestive of obstruction of the superior vena cava.

Cardiovascular System: B.P. 180/100 mm.Hg. The pulse was regular in rate (80/min.) and rhythm. The apex beat was palpable in the mid-clavicular line in the 5th left inter-costal space. The heart sounds were of good quality. A soft systolic murmur was present at the mitral area.

Respiratory System: The chest was barrel-shaped and, on auscultation, numerous medium crepitations were heard throughout the lung fields.

Alimentary System: The liver was palpable 2" below the right costal margin; the liver was tender.

No other abnormality was found on full clinical examination of other systems.

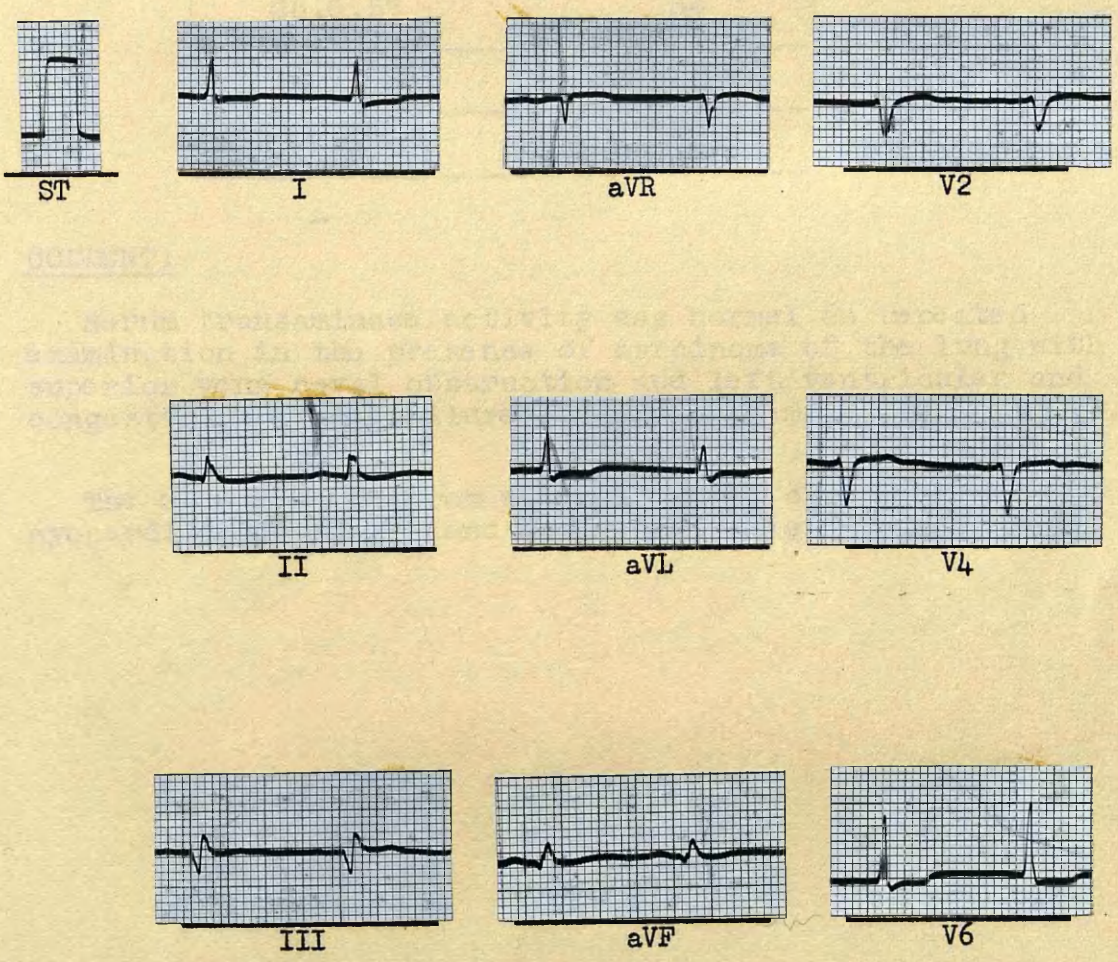
Treatment and Progress.

The patient was given a low salt, low calorie (1,000) diet and treatment with digoxin 0.25 mgm. b.d., and mersalyl 2 c.c. twice weekly. X-Ray film of the chest revealed a bronchogenic carcinoma of the base of the right upper lobe with considerable enlargement of the hilar glands of the right lung.

On 1.7.57., the patient was transferred to another hospital for radiotherapy.

/2

ELECTROCARDIOGRAM CASE NO. 73



Electrocardiographic Findings.

I. 26.6.57: The electrocardiogram showed changes of an old posterior myocardial infarction and of left ventricular strain.

Serial Serum Transaminase Activity (Units/ml/min.)

Date.	Units.
26.6.57	34
27.6.57	30
28.6.57	36

COMMENT:

Serum transaminase activity was normal on repeated examination in the presence of carcinoma of the lung with superior vena caval obstruction and left ventricular and congestive cardiac failure due to ischaemic heart disease.

The electrocardiogram was diagnostic of old posterior myocardial infarction and left ventricular strain.

CASE NO. 74.

History of Present Illness.

A married woman, aged 72 years, a housewife, was admitted to hospital on 31.5.57 complaining of severe breathlessness at rest.

The patient had been known to suffer from hypertension for many years, but led an active life until 17.5.57., when she began to become breathless on exertion. At 2 a.m., on 31.5.57, the patient had a severe attack of paroxysmal cardiac dyspnoea and was transferred to hospital for treatment.

Past History.

Since 1951, the patient had received injections of anahaemin for the treatment of pernicious anaemia.

Clinical Findings on Admission.

The patient was an elderly, obese woman. She was orthopnoeic. Slight jugular venous congestion was present.

Cardiovascular System: B.P. 150/80 mm.Hg. The pulse rate was 104/min., but the pulse was irregular due to ventricular extrasystoles. The apex beat was palpable 2 " outwith the mid-clavicular line in the fifth left intercostal space. A loud blowing systolic murmur was present in the mitral area.

Respiratory System: Numerous medium crepitations were heard on auscultation over both lung bases.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

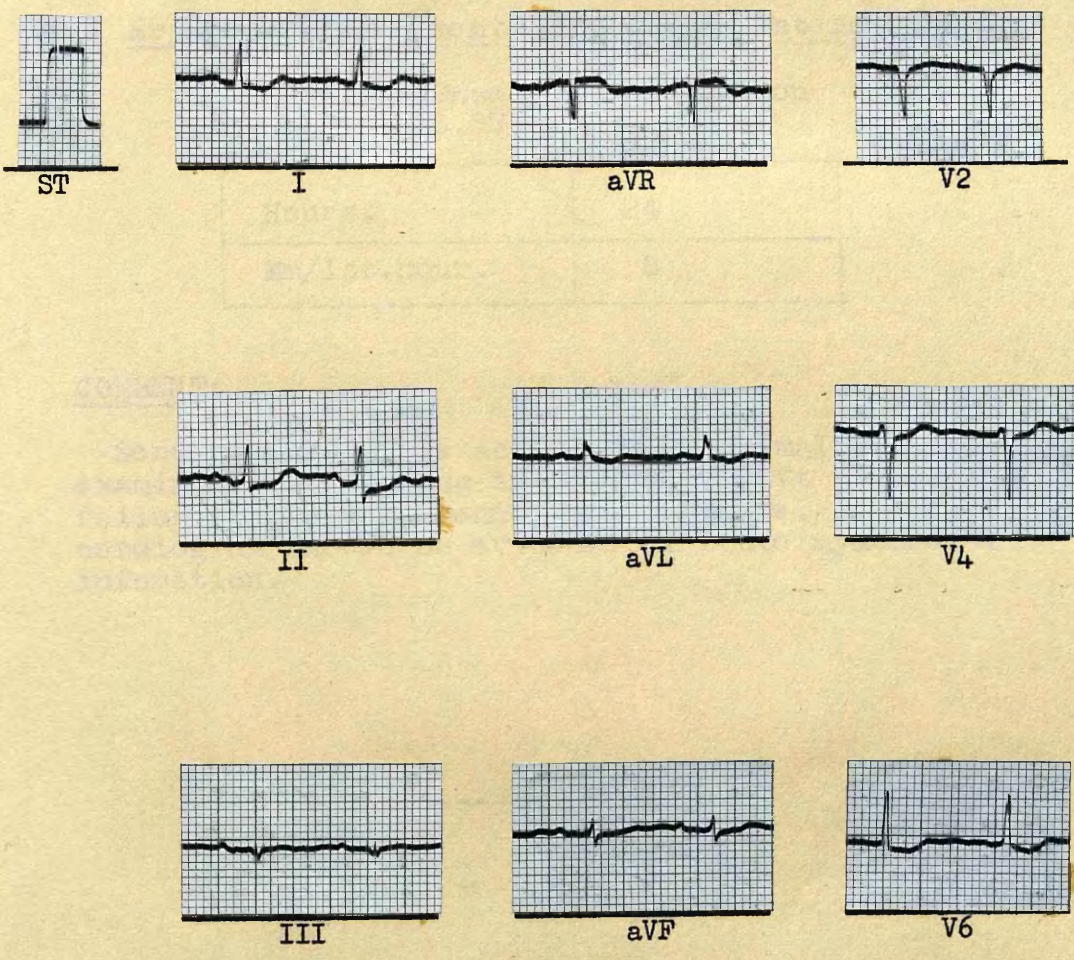
The dyspnoea quickly responded to treatment with rest in bed and digitalis leaf and the patient was discharged from hospital on 1.7.57.

Electrocardiographic Findings.

I. 5.6.57: The electrocardiogram showed no evidence of myocardial infarction. Digitalis effect masked any other changes which may have been present. Left ventricular strain was not excluded.

/2

ELECTROCARDIOGRAM CASE NO. 74



Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Dyspnoea on 31.5.57.

Hours.	10	34	58
Units.	25	32	26

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Dyspnoea on 31.5.57

Hours.	24
Mm/1st.hour.	5

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of left ventricular failure due to ischaemic heart disease. The electrocardiogram showed no evidence of acute myocardial infarction.

CASE NO. 75.

The patient, a married woman, aged 60 years, had been blind since 1945 when a retinopathy due to diabetes mellitus had been diagnosed. In 1952., the patient was in hospital for treatment of an acute pyelonephritis and stabilisation of the diabetic state.

The electrocardiogram showed changes very suggestive of antero-septal myocardial ischaemia. The patient also had joint changes, diagnostic of rheumatoid arthritis.

In 1955., she was again in hospital for treatment of a urinary infection and diabetes mellitus.

In January, 1956., she was admitted to hospital for treatment of congestive cardiac failure due to ischaemic heart disease. At this time, she complained of dysphagia and radiological examination revealed a small hiatus hernia with oesophageal reflux. An electrocardiogram again showed changes suggestive of myocardial ischaemia.

On 25.2.57, the patient was again admitted to hospital suffering from congestive cardiac failure and ischaemic heart disease and gangrene of the left foot, which had begun two days earlier. An electrocardiogram again showed the changes of antero-septal myocardial ischaemia. There was no evidence of myocardial infarction. Her condition was that of gradual deterioration despite therapy and she died on 6.4.57. Permission for post mortem examination was refused.

Serum Transaminase Activity (Units/ml/min.)

25.2.57	:	35 units.
26.2.57	:	32 units.

COMMENT:

Serum transaminase activity was normal on repeated examination 48 and 72 hours following the onset of gangrene of the foot, due to peripheral artery thrombosis. There was no electrocardiographic evidence of acute myocardial infarction. The patient had suffered from diabetes mellitus for many years and occasionally complained of symptoms due to hiatus hernia. In addition, rheumatoid arthritis was present.

CASE NO. 76.

A male, aged 64 years, a slaughterman, was transferred from a surgical unit on 13.2.57 complaining of breathlessness at rest.

He had been admitted to hospital on 2.2.57 as a case of suspected intestinal obstruction. All investigations of the alimentary tract had been negative.

For 20 years, he had been subject to attacks of bronchitis especially in the winter and had become progressively more breathless on exertion until, in December, 1955, he was forced to stop work. After thirteen weeks in bed he was able to do his heavy work in the slaughterhouse although remaining dyspnoeic on moderate exertion. In November, 1956, he was compelled to rest in bed, the slightest exertion making him breathless. On 31.3.57., he was very breathless at rest and his ankles were swollen. He had improved somewhat with rest while in the surgical unit and was transferred to a medical ward on 13.2.57.

Past History.

In 1920, the patient had had an attack of rheumatic fever.

Clinical Findings on Admission.

The patient was an elderly, obese man, whose lips and face were cyanosed. Jugular vein congestion was marked and sacral and ankle oedema were present.

Cardiovascular System: B.P. 160/ 100 mm.Hg. The pulse was regular in rate (100/min.) and rhythm. The heart was enlarged, the apex beat being 1½" outwith the mid-clavicular line in the 6th left intercostal space. The heart sounds were well heard. There was a loud blowing systolic murmur at the base of the heart, maximally heard over the aortic area but not conducted into the carotid arteries or into the axilla. The second pulmonic sound was accentuated.

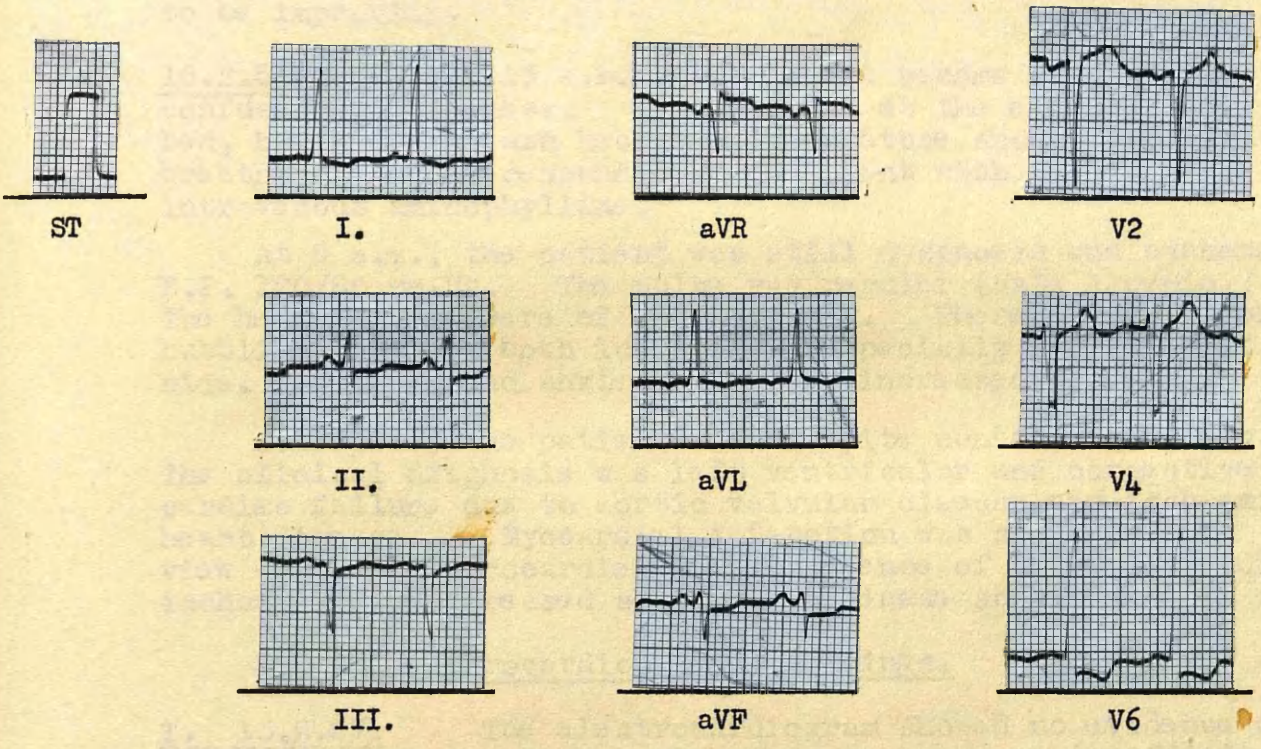
Respiratory System: Numerous rhonchi were heard on auscultation throughout the lung fields and numerous medium crepitations were heard at the bases of both lungs.

Alimentary System: The liver was palpable 2" below the right costal margin.

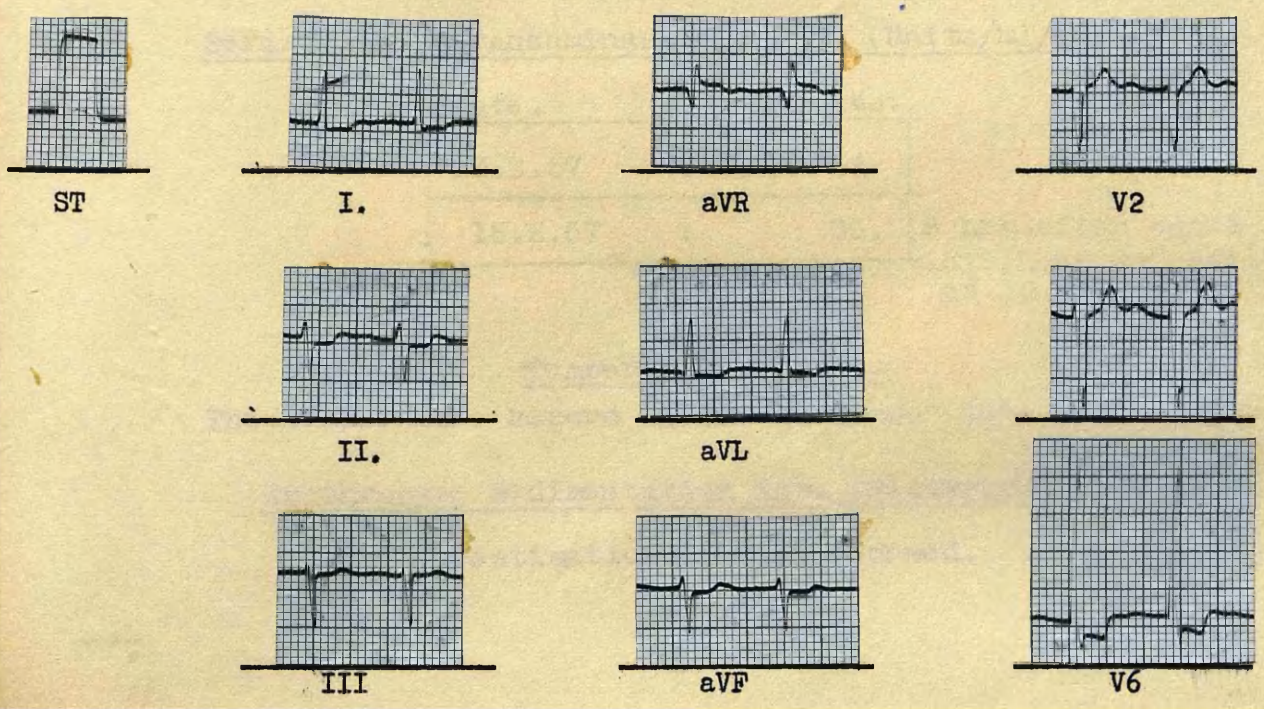
No other abnormality was found on full clinical examination of other systems.

/2

ELECTROCARDIOGRAM CASE NO. 76 (1)



ELECTROCARDIOGRAM CASE NO. 76 (2)



Treatment and Progress.

Treatment with digitalis leaf and mersalyl was started shortly after admission to hospital and the patient seemed to be improving.

16.2.57: At 2.15 a.m., the patient became mentally confused and restless. When sitting at the edge of the bed, he collapsed and became semi-comatose and extremely breathless. He responded to treatment with oxygen and intravenous aminophylline.

At 9 a.m., the patient was still dyspnoeic and cyanosed. B.P. 120/80 mm.Hg. The pulse was regular (Rate 120/min.) The heart sounds were of poor quality. There were numerous bubbling rales at both lung bases, especially on the right side. Sacral and ankle oedema had increased.

At 7 p.m., the patient died despite continued therapy. The clinical diagnosis was left ventricular and congestive cardiac failure due to aortic valvular disease and ischaemic heart disease. Myocardial infarction was suspected in view of the electrocardiographic evidence of acute myocardial ischaemia and increased serum transaminase activity.

Electrocardiographic Findings.

I. 13.2.57: The electrocardiogram showed no evidence of infarction but was diagnostic of acute coronary insufficiency and probable left ventricular strain.

II. 16.2.57 at 6.15 a.m. The electrocardiogram showed more marked changes of acute coronary insufficiency. The P - R interval was prolonged. (0.21 sec.)

Serial Serum Transaminase Activity (Units/ml/min.)

Date.		Units.	
13.2.57	:	14.	
16.2.57	:	66.	(8 hrs.after onset of dyspnoea and collapse at 10 a.m.)

Temperature Record.

The temperature record showed no temperature elevation.

Erythrocyte Sedimentation Rate (Westergren.)

No estimations were performed.

/3

Post Mortem Findings.

Post mortem examination was carried out on 18.2.57. This showed the left lung to be totally adherent to the chest wall. The right lung was adherent over the whole of the right upper lobe. Both lungs on section showed marked emphysema with a considerable degree of anthracosis in the left upper lobe. There was a circumscribed, peripherally-situated carcinoma of lung 1½" in diameter.

The heart was grossly enlarged due to hypertrophy of the left ventricle. The aortic valves showed extensive calcification and distortion. The other valves and chambers of the heart were normal. The coronary arteries were patent. The myocardium showed only patchy areas of old infarction, the largest of which was half a centimeter in diameter.

The aorta showed extensive atheroma throughout its length.

The alimentary tract showed no abnormality.

The liver and spleen showed evidence of chronic venous congestion, but no evidence of any metastases was seen.

The pancreas, adrenals, kidneys and urinary bladder showed no abnormality.

Death was considered to be due to aortic valvular disease; congestive cardiac failure; emphysema; an early carcinoma of lung was an incidental finding.

Results of Histological Examination.

Heart Muscle: On examination of sections, patchy areas of ischaemic fibrosis of the myocardium were seen but there was no evidence of acute infarction of heart muscle.

Liver: The changes of severe chronic venous congestion were present. There was no evidence of secondary tumour deposition.

Lung: The appearances were those of an alveolar cell carcinoma. Areas of necrosis were present in the tumour and at the margins of the tumour, there were small areas of pulmonary infarction.

COMMENT:

Increased serum transaminase activity was found 8 hours after an attack of severe left ventricular failure which was superimposed on congestive cardiac failure. There was electrocardiographic evidence of acute coronary insufficiency but no evidence of acute myocardial infarction.

Post-mortem examination failed to confirm the clinical

/clinical diagnosis of myocardial infarction and there was no histological evidence of acute necrosis of the myocardium in the sections of heart muscle examined. The clinical diagnosis of aortic valvular disease and ischaemic heart disease was confirmed. However, at autopsy, an alveolar cell carcinoma of lung was found which had not been suspected during life. Histological examination of lung revealed not only the appearances of carcinoma but also areas of necrosis of lung and small areas of pulmonary infarction in relation to the tumour.

There was no histological evidence of centrilobular necrosis of liver although the changes of severe chronic venous congestion of liver were present.

The finding of increased serum transaminase activity was misleading. The cause of the rise in activity to high levels remains a matter for conjecture. There was no evidence of centrilobular necrosis of liver which suggests that the liver was not the source of increased serum activity. There was no evidence of acute myocardial infarction although a careful search was made and, while it is acknowledged that a small area of myocardial necrosis may escape detection, it seems improbable in this case.

There was evidence, however, of necrosis and infarction of pulmonary tissue and the rise in serum transaminase activity was probably due to release of the enzyme from necrotic pulmonary tissues. The infarction of lung was thought to be secondary to local thrombosis of pulmonary vessels.

CASE NO. 77.

A male, aged 67 years, a retired night watchman, was admitted to hospital on 9.6.57., having complained of severe retrosternal pain on 7.6.57.

Since January 1957., the patient had had symptoms of intermittent claudication in the right leg. He was unable to walk more than 100 yards over flat ground without being forced to rest by severe pain in the right calf. On 19.5.57., the patient developed symptoms of angina pectoris and breathlessness on exertion and on 7.6.57 he had an attack of severe vice-like retrosternal pain which lasted for about eight hours. The pain radiated down the inner aspect of the left arm. When the pain was present, the patient was breathless at rest.

Clinical Findings on Admission.

The patient was a thin, tired-looking man. There was no evidence of shock or congestive cardiac failure.

Cardiovascular System: B.P. 150/80 mm.Hg. The pulse was regular in rate (100/min.) and rhythm. The apex beat was not felt. The heart sounds were pure but poorly heard.

Respiratory System: Scattered rhonchi were heard on auscultation throughout the lung fields.

No other abnormality was discovered on full clinical examination of other systems.

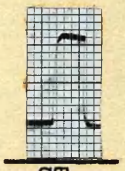
Treatment and Progress.

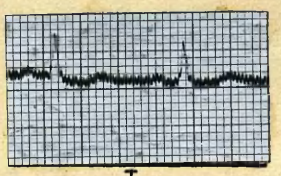
Anticoagulant therapy was started soon after admission and the patient had no further recurrence of pain until 18.6.57 when he complained of gripping pain in the epigastrium and lower retrosternal region. This pain was accompanied by abdominal distension. B.P. was 110/70 mm.Hg. Acute myocardial infarction was diagnosed. On 19.6.57 the patient appeared to be somewhat improved and, although slight epigastric pain persisted, the abdominal distension had improved. At 1.45 p.m., the patient lost consciousness for a few seconds and,on recovery,complained of pain in the right foot. On examination, the toes of the right foot were blue and cold and the pulses could not be felt in the right leg. An embolism of the right femoral artery was diagnosed. On 20.6.57., the patient still complained of slight abdominal discomfort and changes of early gangrene were present in the right foot. The patient died suddenly.

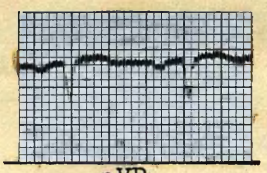
Electrocardiographic Findings.

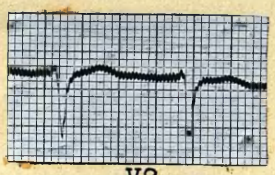
I. 9.6.57: (36 hours after the onset of pain on 7.6.57): The electrocardiogram showed changes indicative of acute /2

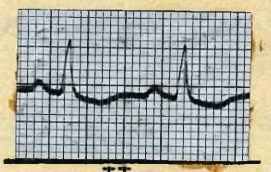
ELECTROCARDIOGRAM CASE NO. 77

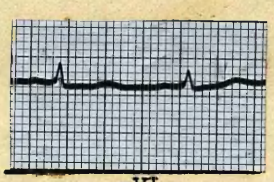

ST

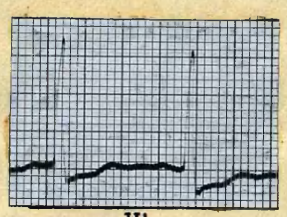

I

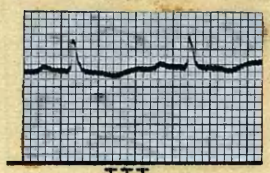

aVR

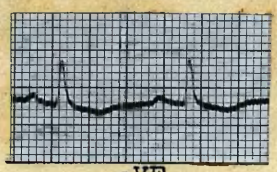

V2

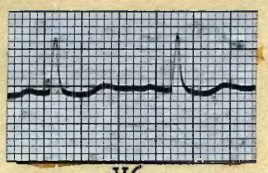

II


aVL


V4


III


aVF


V6

/acute coronary insufficiency.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Chest Pain on 7.6.57.

Hours.	36	60
Units.	27	33

Time after Onset of Epigastric Pain on 18.6.57.

Hours.	4	24
Units.	30	95

Temperature Record.

The temperature was 99.6°F on 20.6.57.

Erythrocyte Sedimentation Rate (Westergren.)

Time after Onset of Chest Pain on 7.6.57.

Days.	6
mm/1st. hour.	12.

Time after onset of Epigastric Pain on 18.6.57.

Days.	2
mm/1st.hour.	20

Post Mortem Findings.

Post mortem examination, carried out on 20.6.57, showed a considerable terminal congestion of both lung bases. The heart was considerably enlarged due to hypertrophy and dilatation of the left ventricle. The other chambers and valves of the heart showed only senile changes. The coronary arteries all showed severe /3

severe atheromatous degeneration, and the posterior vessel, almost from its commencement, was occluded by "porridgey" atheroma. On the posterior wall of the left ventricle, just below the mitral valve, there was a small patch of old fibrosis. In addition to this, however, a very much larger area of muscle showed complete infarction. This infarction was probably of 24 hours' duration. There was no mural thrombus found in either the auricle or the ventricle.

The aorta showed considerable atheromatous degeneration, but no superficial thrombosis.

In the abdomen, there was no evidence of any mesenteric embolism or thrombosis. The abdominal viscera showed only congestive changes.

No evidence of any embolism was found in the right femoral artery which was severely affected by atheromatous degeneration..

Death was considered to be due to acute myocardial infarction and atheroma.

COMMENT:

The history and clinical findings suggested that the attack of severe angina pectoris at rest, which occurred 2 days before the patient's admission to hospital, might have been due to an acute myocardial infarction. The electrocardiogram, however, showed no evidence of acute myocardial infarction although patterns characteristic of acute coronary insufficiency were present. No pyrexia or peripheral vascular failure developed following this attack of pain. The E.S.R. was slightly elevated 12 days after the attack of chest pain. Serum transaminase activity was normal on repeated examination following the attack. The first estimation was not performed until 36 hours after the onset of pain. The assay would have been more helpful had it been possible to do it in the first 24 hours following the pain, since a rise in transaminase may have occurred in this period. On the evidence obtained, the attack of prolonged, severe angina pectoris at rest, accompanied by electrocardiographic evidence of acute coronary insufficiency, did not result in increased serum transaminase activity 36 hours after the onset of pain.

On 18.6.57., the history and clinical findings were suggestive of a poor risk acute myocardial infarction and pyrexia and minimal peripheral vascular failure developed. The E.S.R. rose to abnormal levels 2 days after the onset of this illness. Serum transaminase activity rose to high levels, 24 hours after the onset of the myocardial infarction. Post mortem examination confirmed the presence of a very recent acute myocardial infarction. An /4

An electrocardiogram had not been performed. In the absence of electrocardiographic evidence, the assay was considered to have provided early and valuable confirmation of the occurrence of acute myocardial infarction. The development of severe ischaemia of the right foot was not considered to have resulted in the post infarction rise in serum transaminase activity since the ischaemia developed four hours after the serum for transaminase assay had been withdrawn.

CASE NO. 78.

History of Present Illness.

A widow, aged 60 years, was admitted to hospital on 24.1.57 having had an attack of anterior chest pain.

At noon on 23.1.57., when preparing a meal, the patient developed severe burning retrosternal pain which quickly spread into the neck and radiated round the chest wall and into the interscapular region. She felt as though her head was "bursting" and lost consciousness. The patient's family doctor found her in this state. Within two hours, the patient regained consciousness; she felt nauseated and vomited. The pain was controlled by the intramuscular injection of morphine sulphate, gr.1/4., but on 24.1.57, the retrosternal pain recurred and was referred down the left arm. The patient's doctor noted that the B.P., usually 230/130 mm.Hg., had fallen to 190/120 mm.Hg.

Past History.

The patient had previously been in hospital for treatment of severe essential hypertension in 1952 and 1953. She had been fairly well since her discharge from hospital on 19.5.53 until November 1956 when she began to complain of breathlessness and anginal pain, mainly on exertion but occasionally at rest. She had been gaining weight.

Clinical Findings on Admission.

The patient was not shocked on admission but complained of chest pain and of an ache in the neck and jaws. She was restless and apprehensive. She belched frequently. Peripheral arterial pulsations were present and equal.

Cardiovascular System: B.P. 160/105 mm.Hg. The pulse was regular in rate (88/min.) and rhythm.

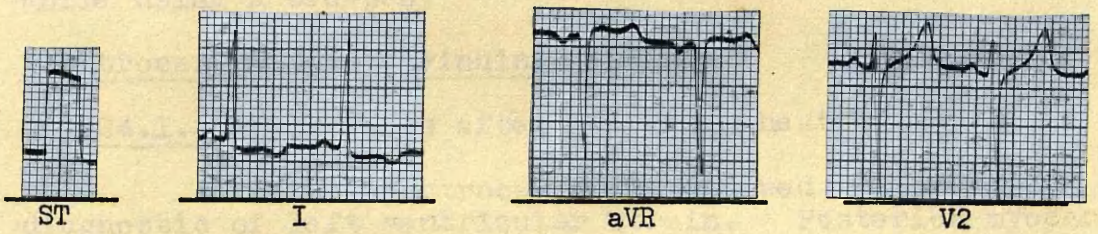
The heart was enlarged, the left border of heart as determined by percussion lying 1" outwith the mid clavicular line. The apex beat was not palpable .

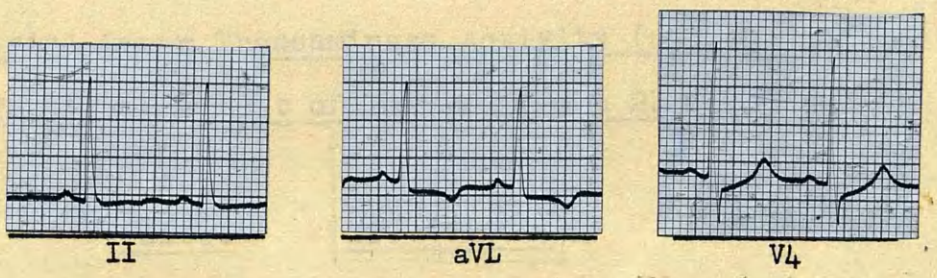
A systolic murmur was well heard at the aortic area and the second aortic sound was markedly accentuated.

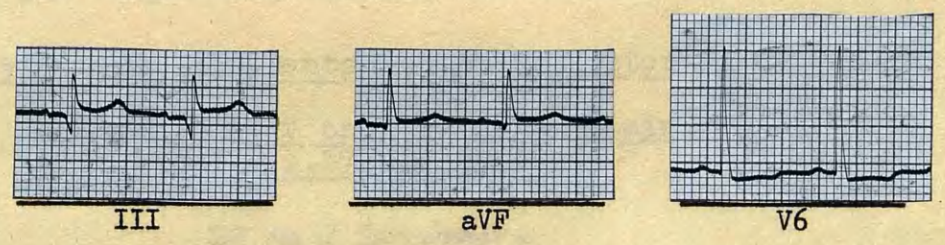
No other abnormality was found on full clinical examination of other systems.

/2

ELECTROCARDIOGRAM CASE NO. 78







Treatment and Progress.

Chest pain was alleviated by the intramuscular injection and the patient seemed to be somewhat improved. Anticoagulant therapy was not begun because of lack of electrocardiographic confirmation of infarction.

25.1.57: The patient complained of nausea and flatulence and at 2 p.m., she vomited 3 ounces of fresh blood. B.P. 140/70 mm.Hg.

At 7.15 p.m., the patient collapsed and died while using a bed-pan.

Electrocardiographic Findings.

I. 24.1.57: 17 hours after onset of chest pain on 23.1.57.

The electrocardiogram showed changes diagnostic of left ventricular strain. Posterior myocardial infarction could not be excluded. Serial tracings are necessary for the final E.C.G. diagnosis.

Serial Serum Transaminase Activity (units/ml/min.)

Time After Onset of Chest Pain on 23.1.57.

Hours.	17.	36.
Units.	106.	413.

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren).

17 hours after onset of chest pain on 23.1.57.

12 mm / 1st.hour.

Results of Histological Examination and Post-Mortem.

over. /3

Post-Mortem Findings.

Post-mortem examination was carried out on 28.1.57. This showed a haemopericardium with approximately one-half pint of blood in the sac. The source of this was a transverse rupture of the anterior half of the aorta just above the cusps. Prior to rupture the blood had dissected up the arch of the aorta to the great vessels, but the lumen of these had not been affected.

The heart was moderately enlarged due to hypertrophy and dilatation of the left ventricle. The aortic and other valves were normal, but the first part of the aorta showed a moderate dilatation. The coronary arteries all showed severe calcifying atheromatous degeneration. The main branches were patent and in the posterior vessel there was aneurysmal dilatation at a point 2 inches along the course of the vessel. Section of the heart showed that most of the chordae were ischaemic. The remainder of the heart muscle was pale, but showed no obvious infarction.

The aorta showed gross atheromatous degeneration throughout its course.

The liver was moderately enlarged. The spleen and kidneys were similarly affected, with chronic venous congestion.

No other abnormality was seen in the alimentary tract, pancreas, adrenals, urinary bladder, uterus and adnexae.

The brain and its membranes were normal.

Death was considered to be due to rupture of a dissecting aneurysm of the first part of the aorta; cardiac tamponade; atherosclerosis.

Results of Histological Examination.

Heart: Ischaemic fibrosis of the chordae tendineal was present but there was no evidence of an acute infarction of the myocardium.

Liver: Marked centrilobular necrosis of the liver was present with fatty infiltration of the surviving cells.

COMMENT:

The history and clinical findings were very suggestive of "poor risk" myocardial infarction but the electrocardiographic findings were those of left ventricular strain although posterior myocardial infarction could not be excluded. / 4.

COMMENT (ctd.)

The divergence between the history and clinical findings and the electrocardiographic patterns observed led to the decision that anticoagulant therapy should be avoided although dissecting aneurysm was not suspected until a few hours before the patient's death when haematemesis occurred.

Post-mortem examination revealed rupture of a dissecting aneurysm of the first part of the aorta, haemopericardium, which gave rise to cardiac tamponade and severe calcifying atherosclerosis of the aorta and coronary arteries.

There was no evidence of acute myocardial infarction on macroscopic or microscopic examination of the heart muscle although ischaemic fibrosis of the chordae tendineae was present. Marked centrilobular necrosis of the liver was present.

Serum transaminase activity reached high levels 17 hours after the onset of the illness and rose to very high levels before the patient's death. The erythrocyte sedimentation rate was slightly elevated 17 hours after the onset of the illness.

The cause of the great rise in serum transaminase activity in this case is difficult to explain. It is considered that centrilobular necrosis of the liver resulted in the rise of activity. Release of the enzyme from the heart muscle, rendered ischaemic by pressure from a haemopericardium, was not thought to be a likely explanation.

CASE NO. 79.

History of Present Illness.

A male, aged 58 years, a salesman, was admitted to hospital on 15.6.57 complaining of severe retrosternal pain of twelve hours' duration.

At 9.30 p.m. on 14.6.57, the patient had been suddenly seized with severe retrosternal pain while working in his garden. The pain spread into the epigastrium; it lasted for 12 hours and, before admission to hospital, it was felt in the left praecordium.

Past History.

Since 1952, the patient had complained of severe frontal headaches and breathlessness on exertion and he had been told that he suffered from hypertension.

Clinical Findings on Admission.

The patient was dyspnoeic, apprehensive and restless. He was moderately shocked. The lips were cyanosed and the jugular veins were congested.

Cardiovascular System: B.P 120/85 mm.Hg. The pulse was regular in rate (80/min.) and rhythm. The apex beat was not palpable. The heart sounds were pure but very faint.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Pain was controlled by intramuscular injection of pethidine, 100 mgm. but recurred almost daily throughout the period of observation.

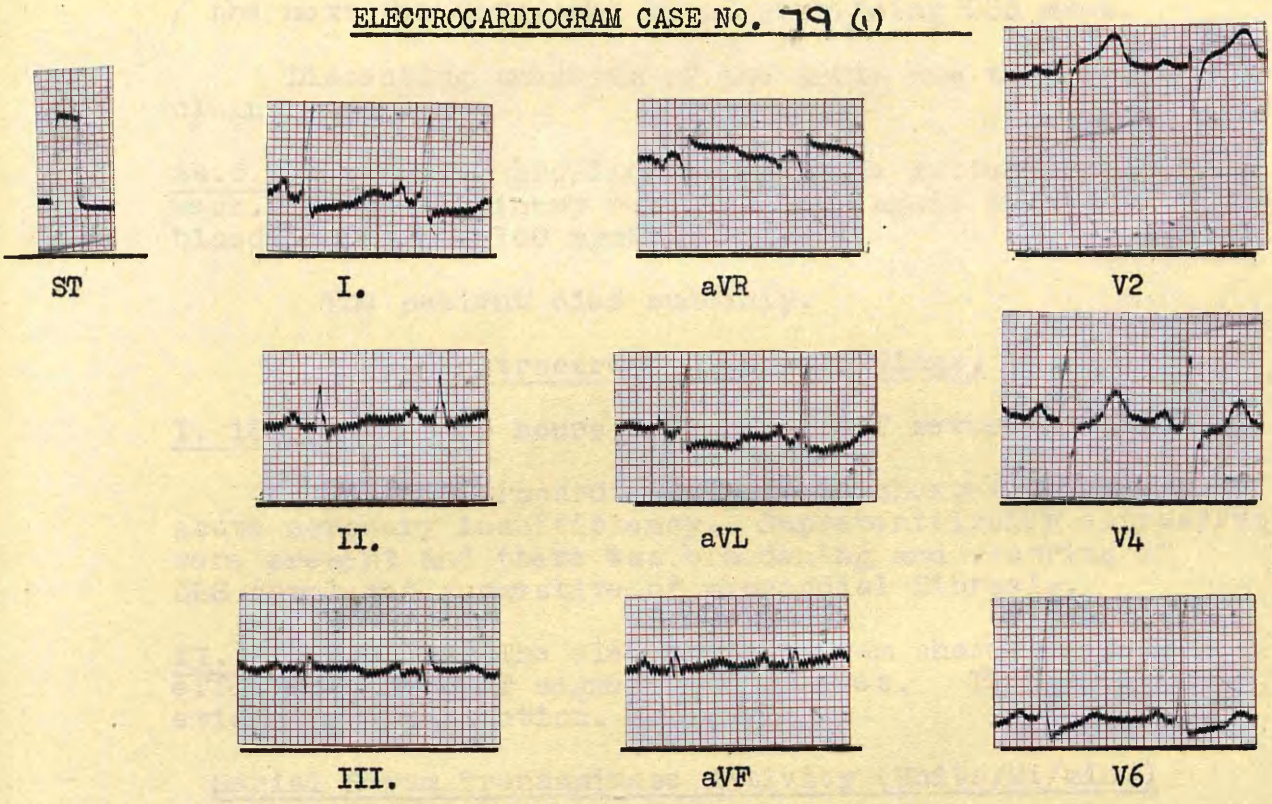
16:6:57 B.P. 110/70 mm.Hg. (Right arm.) B.P. was not recorded on the left arm.

Auricular fibrillation was present and was treated with quinidine sulphate. Normal rhythm was restored after the arrhythmia had been present for 5 hours. Signs of congestive cardiac failure viz., neck vein congestion, sacral oedema and pulmonary oedema had made their appearance.

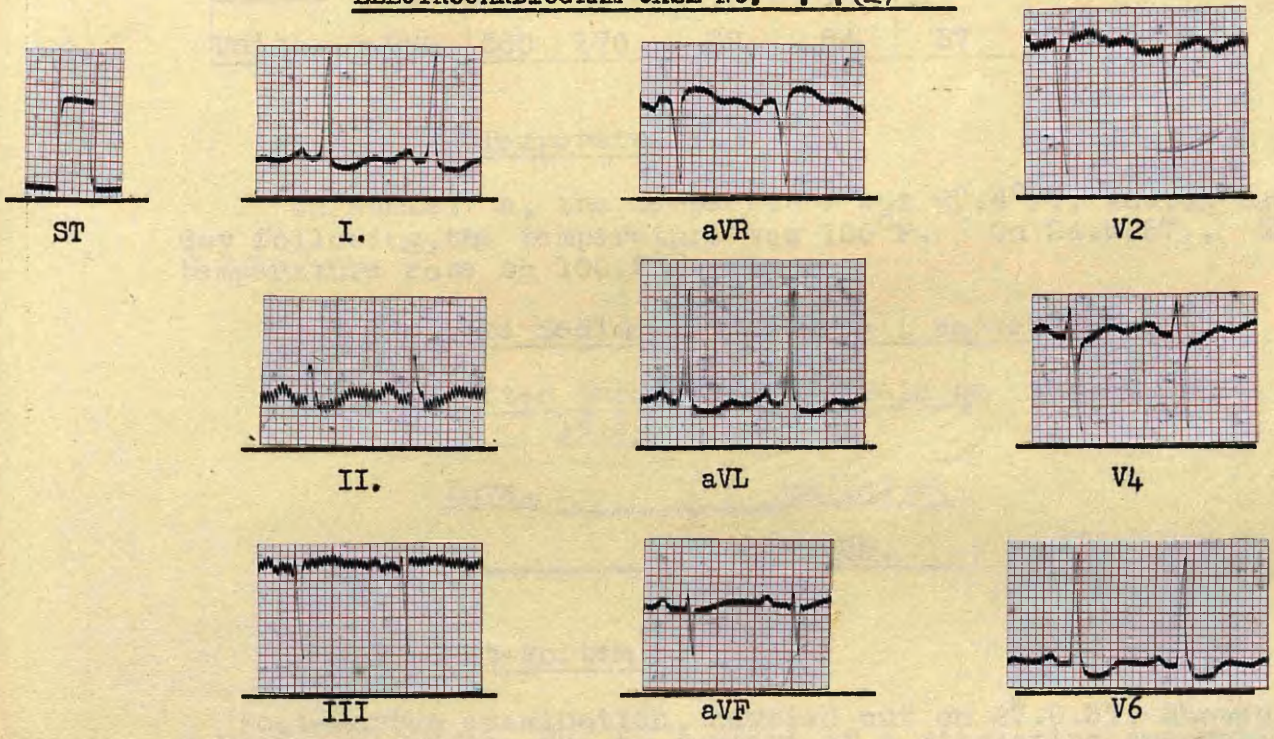
20:6:57: B.P. 200/115 mm.Hg. The patient's condition remained unchanged and treatment with digoxin was started, auricular fibrillation (apex rate 124/min.) being present.

The patient's condition gradually deteriorated. Retention of urine with albuminuria was a feature in the /2

ELECTROCARDIOGRAM CASE NO. 79 (1)



ELECTROCARDIOGRAM CASE NO. 79 (2)



/ the next few days, the blood urea being 230 mgm%.

Dissecting aneurysm of the aorta was the tentative diagnosis.

24.6.57:- B.P. 190/110 mm.Hg. The patient was very weak. Marked urinary retention was again present, the blood uria being 160 mgm%.

The patient died suddenly.

Electrocardiographic Findings.

I. 15.6.57: (13 hours after onset of severe chest pain).

The electrocardiogram showed changes indicative of acute coronary insufficiency. Supraventricular extrasystoles were present and there was broadening and slurring of QRS complexes suggestive of myocardial fibrosis.

II. 23.6.57:- The electrocardiogram showed digitalis effect on the ST-T segment and T waves. There was no evidence of infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain on 14.6.57 at 9.30 p.m.

Hours.	17	40	61	85	109	133	157
Units.	290	560	170	98	64	57	38.

Temperature Record.

On admission, the temperature was 99.4°F., and, on the day following, the temperature was 100°F. On 24.6.57., the temperature rose to 100.6°F.

Erythrocyte Sedimentation Rate (Westergren.)

Time After Onset of Chest Pain on 14.6.57.

Days.	mm/1st.hr.
6	38.

Post-Mortem Findings.

Post-mortem examination, carried out on 27.6.57, showed a haemopericardium due to rupture of a dissecting aneurysm

Post-Mortem Findings (ctd.)

/aneurysm of the aorta into the pericardial sac. The aorta at the start of the descending portion was grossly atheromatous and moderately dilated. At this point, there was a transverse rupture of the aorta and blood had tracked back to the pericardial sac. The left sub-clavian vessel had been partially occluded at its outset by the haemorrhage into the aortic wall.

The heart was considerably enlarged due to hypertrophy and dilatation of the left ventricle. The other chambers and valves of the heart were normal. On the posterior wall of the left ventricle, just below the mitral valve, there was an old infarction of the heart with some dilatation. The cardiac muscle on either side of the old infarction also showed evidence of recent infarction of some 24 - 48 hours' duration.

No abnormality was found in the alimentary tract or the viscera apart from the kidneys. These showed a moderate degree of hypertensive scarring of the cortex without much disturbance of the normal anatomical cortico-medullary ratio and pattern.

The bladder was moderately dilated, but no evidence of any stricture or prostatic enlargement was present.

Death was considered to be due to old and new myocardial infarction; dissecting aneurysm of the aorta and atheroma.

Results of Histological Examination.

Heart muscle: Sections showed marked ischaemic fibrosis of the myocardium with evidence of recent infarction.

Kidney: Sections showed arteriosclerotic scarring of the kidney but there was no evidence of infarction.

Liver: No sections were examined.

COMMENT:

The history and clinical findings on the patient's admission to hospital were very suggestive of acute myocardial infarction ("poor risk"). Serial electro-cardiograms showed no evidence of acute myocardial infarction, although changes of acute coronary insufficiency and other

/ other evidence of ischaemic heart disease were noted.

Pyrexia, congestive cardiac failure and marked peripheral vascular failure developed. Bouts of auricular fibrillation were noted although electrocardiographic proof of this arrhythmia was not obtained. Five days after admission, the tentative diagnosis of dissecting aneurysm of the aorta was made. Serum transaminase activity was at high levels 17 hours after the onset of the illness and rose to peak levels 40 hours after the onset. The erythrocyte sedimentation rate rose to high levels 6 days after the onset of the illness. The cause of this marked rise in serum transaminase activity is unknown. Post mortem examination confirmed the clinical diagnosis of dissecting aneurysm of the aorta. Haemopericardium was present and atherosclerosis was marked. The age of the infarction on the posterior wall of the left ventricle was indeterminate and it was unlikely to have occurred but 9 days previously and to have caused the transaminase activity rise observed. The fresh areas of infarction at the site of this old infarction were probably only 24 - 48 hours old and were not thought to be related to the rise in serum transaminase activity. Unfortunately, the liver was not examined histologically in this case and the possibility of a rise in transaminase activity associated with centrilobular necrosis of the liver was not explored.

CASE NO. 80.

A married woman, aged 60 years, a housewife, was admitted to hospital on 31.10.56, suffering from congestive cardiac failure and haematuria. The cause of the congestive cardiac failure was obscure. There was no clinical evidence of rheumatic heart disease or evidence of sub-acute bacterial endocarditis, and ischaemic heart disease, auricular fibrillation and renal embolism with infarction was considered the most likely diagnosis. On 5.11.56., she developed signs and symptoms of acute pulmonary infarction involving the left lung. Following treatment with digitalis and mersalyl there was some improvement in the patient's condition and the rate of fibrillation was controlled.(90-110/min.) When apparently making a good recovery from this pulmonary infarction the patient, on 14.11.56., suddenly developed a feeling of tightness and numbness in both lower legs. There was evidence of impaired circulation of both legs below the knees and the diagnosis of saddle embolus of the aorta was made. Anticoagulant therapy was started.

On 23.11.56., the circulation in the right leg had returned but early gangrene of the left foot and toes was present with secondary phlebothrombosis of the deep veins of the left leg. On 29.12.56., a left mid-thigh amputation was performed. Following operation, treatment with digitalis and mersalyl was continued and the patient did well.

On 12.1.57., however, she suddenly became very dyspnoeic and collapsed. She responded to treatment with intravenous aminophylline but signs of advancing cardiac failure re-appeared and the patient's condition slowly deteriorated.

She died on 14.1.57.

Electrocardiographic Findings.

I. 1.11.56: The electrocardiogram showed changes of auricular fibrillation with low voltage T waves in all leads, suggestive of chronic coronary artery disease. (Heart rate approximately 170-180/min.)

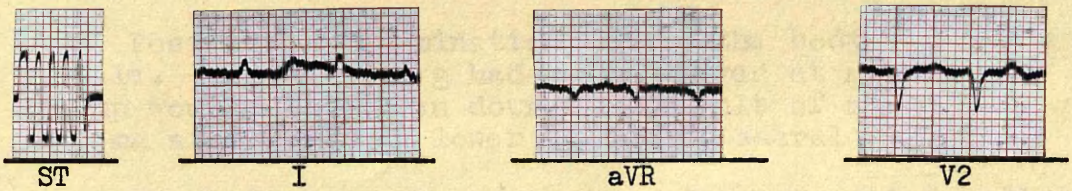
SerialSerum Transaminase Activity (Units/ml/min.)

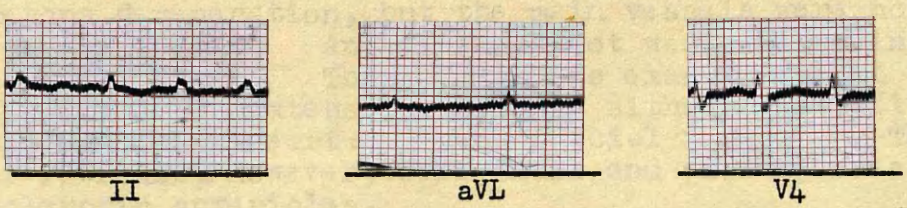
Time after Onset of Pulmonary Infarction on 5.11.56.

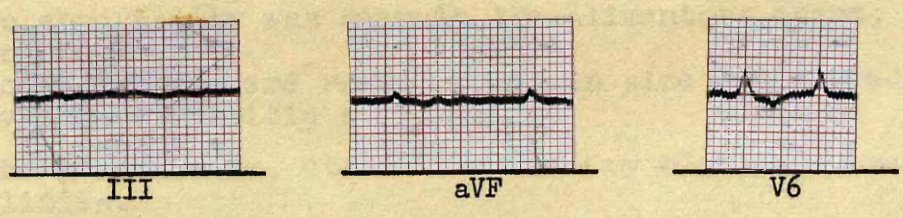
Hours.	12	24	36
Units.	35	48	34

/2

ELECTROCARDIOGRAM CASE NO. 80







Time after Onset of Embolism of Leg Arteries on 14.11.56.

Days.	6	7	8
Units.	38	43	35

Post Mortem Findings.

Post mortem examination was carried out on 15.1.57., and is as follows:-

Post-mortem examination showed the body of an elderly female. The left leg had been removed at mid thigh. The stump wound had broken down as a result of marked general oedema affecting the lower limbs and sacral area.

The left lung showed three medium sized infarctions of a week or more duration. The right lung was congested but contained no infarctions.

The heart was moderately enlarged due to dilatation of all the chambers. The coronary arteries showed marked atheromatous degeneration, but the main vessels were not occluded by thrombus. Ante-mortem clot was present in both auricular appendages. The microscopic examination of the myocardium revealed extensive fibrosis although the valves and chambers of the heart showed no special features. The areas of fibrosis, however, were small and closely related to atherosclerotic arterioles.

The aorta showed marked atheromatous degeneration.

The liver and spleen were moderately enlarged and showed evidence of long-standing chronic venous congestion.

No abnormality was seen in the alimentary tract, pancreas or adrenals.

Both kidneys were rather small in size and showed extensive pyelonephritic scarring.

The gallbladder, uterus and urinary bladder showed no abnormalities.

Death was considered to be due to myocardial degeneration; atherosclerosis; auricular fibrillation and multiple emboli.

Results of Histological Examination.

Heart: Many areas of ischaemic fibrosis were present but there was no evidence of acute infarction of the myocardium.

Kidney: Renal infarctions and scarring of the pyelonephritic type were present.

Liver and lung sections were, unfortunately, not examined.

COMMENT:

Serum transaminase activity rose to borderline levels following the onset of acute pulmonary infarction and again following embolism of the leg arteries. The site of origin of embolus in both cases was probably the ante-mortem thrombus found at post-mortem examination in the auricular appendages.

At the time of onset of acute pulmonary embolism with infarction, rapid auricular fibrillation (rate 170-180/min.) and congestive cardiac failure were present. There was no electrocardiographic evidence of acute myocardial infarction.

At the time of onset of peripheral embolism, congestive cardiac failure was present but auricular fibrillation had been controlled by digitalis therapy. No electrocardiograms were performed during this attack. It should be noted that the first transaminase assay was performed six days after the onset of the embolism. Increased serum transaminase activity following acute pulmonary infarction could be explained either as due to the release of enzyme from lung tissue or to hepatic damage in association with rapid cardiac arrhythmia. Unfortunately, by an oversight, histological examination of the liver was not performed and so these two possible explanations remain.

Following the attack of peripheral artery embolism, increased transaminase activity was probably due to the release of enzyme from necrotic skeletal muscle but again, in the absence of histological study of the liver, hepato-cellular damage cannot be excluded as the cause. There was no evidence of acute myocardial infarction on autopsy but multiple emboli were found. The presence of renal infarctions was confirmed.

CASE NO.81.

A male, aged 40 years, a hoistman, was admitted to hospital on 25.3.57 complaining of haemoptysis and pain in the left side of his chest.

The patient had previously been in hospital in May 1955, when the diagnosis of mitral stenosis of rheumatic origin with auricular fibrillation had been made. He had sustained an embolism of the left middle cerebral artery but had made a good recovery from the resulting hemiplegia.

On 24.3.57., the patient developed severe sharp pain in the left side of the neck and left praecordium which was made worse by breathing. The cough was productive of blood-stained sputum. On admission to hospital, signs of consolidation were present over the mid zone of the left lung posteriorly; X-ray film of the chest confirmed this finding. Pulmonary infarction, in association with rapid auricular fibrillation and mitral stenosis, was diagnosed. There was no evidence of sub-acute bacterial endocarditis. The patient made a good recovery with treatment with digitalis leaf and anticoagulant therapy. The very rapid auricular fibrillation present on admission was controlled within 24 hours. The patient was discharged from hospital on 19.5.57.

Electrocardiographic Findings.

I. 25.3.57: (24 hours after onset). The electrocardiogram showed rapid auricular fibrillation (170-180/min.) with partial right bundle branch block or right ventricular strain.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain on 24.3.57.

Hours.	41	55	79
Units.	43	45	35

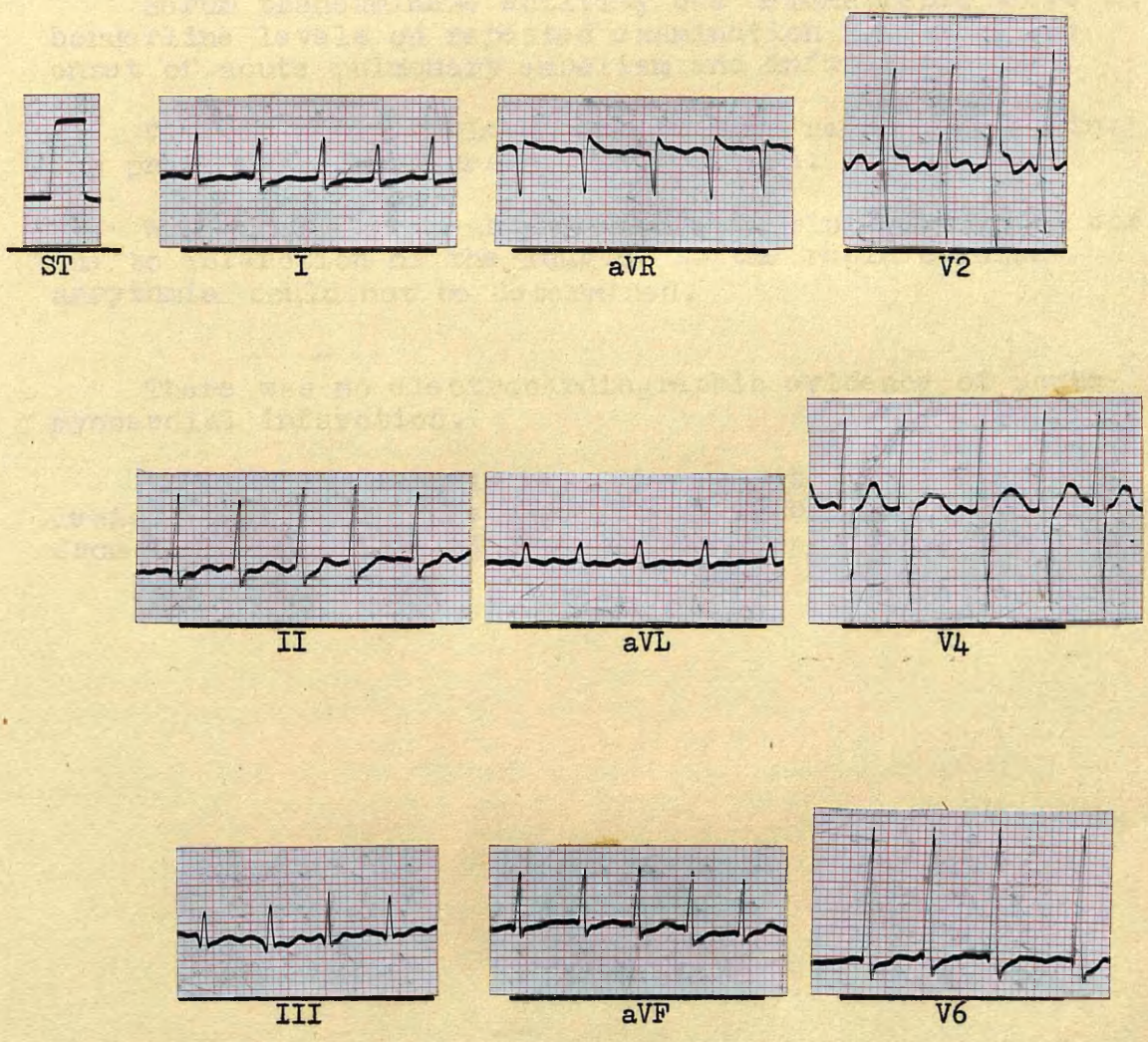
Temperature Record.

The temperature record showed a temperature of 99.2°F 24 hours after the onset of pain.

Erythrocyte Sedimentation Rate (Westergren).

ctd /2

ELECTROCARDIOGRAM CASE NO. 81



Erythrocyte Sedimentation Rate (westergren).

Time After Onset of Pain on 24.3.57.

Hours.	41
Mm/1st.hr.	15

COMMENT:

Serum transaminase activity was demonstrated to be at borderline levels on repeated examination following the onset of acute pulmonary embolism and infarction.

Very rapid auricular fibrillation (rate 170-180/min.) was present for 24 hours after admission.

Whether the increased serum transaminase activity was due to infarction of the lung or to the rapid cardiac arrythmia could not be determined.

There was no electrocardiographic evidence of acute myocardial infarction.

Rheumatic heart disease was present, the predominant lesion being mitral stenosis and the embolus probably arose from thrombus in the right auricular appendage.

CASE NO. 82.

A spinster, aged 56 years, a clerkess, was admitted to hospital on 24.3.57 complaining of breathlessness at rest.

Since March 1956, the patient had been dyspnoeic on moderate exertion and in December 1956 she developed retrosternal pain on exertion which was referred into the left wrist. Following a rest, she was less dyspnoeic on exertion but since 1.3.57 breathlessness on exertion had again been marked.

On 22.3.57, the patient became suddenly breathless while resting in bed and ankle swelling was noted. Haemoptysis was present but consisted merely of blood streaking of the sputum.

On admission to hospital, the patient was suffering from congestive cardiac failure, in association with ischaemic heart disease and hypertension (B.P. 180/120 mm.Hg.) The recent sudden increase in breathlessness was considered to have been due to pulmonary infarction, there being signs of consolidation of the lower lobe of the right lung. X-Ray examination of the chest confirmed the latter clinical finding. No site of origin of embolus was found on admission but, on 27.3.57, there was evidence of deep vein thrombosis of the right calf muscles. Treatment with digitalis leaf and mersalyl resulted in a good recovery, the radiological signs of infarction gradually clearing and the patient was discharged from hospital on 1.5.57.

Electrocardiographic Findings.

I. 24.3.57:(2 days after onset of dyspnoea on 22.3.57). The electrocardiogram showed left ventricular strain pattern. Sinus tachycardia (120/min.) was present.

II. 1.4.57: The electrocardiogram showed more obvious changes of left ventricular strain. There was clockwise rotation of the heart which suggested that right ventricular enlargement may have been present.

III. 15.4.57: The electrocardiogram showed no significant change.

Serial Serum Transaminase Activity (Units/ml/min.)

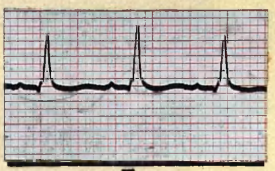
Time after Onset of Sudden Dyspnoea on 22.3.57.

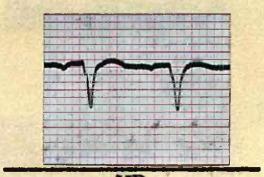
Days.	2	3	4	5	6	7
Units.	38	30	43	57	40	30

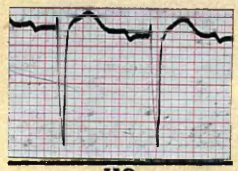
/2

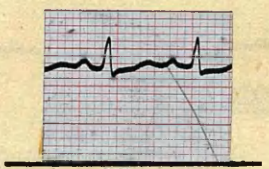
ELECTROCARDIOGRAM CASE NO. 820

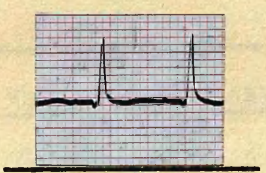

ST

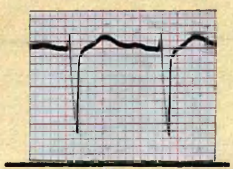

I

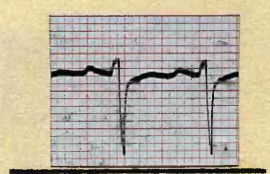

aVR

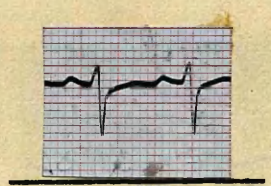

V2

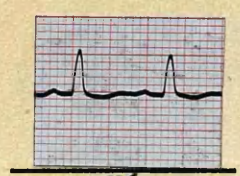

II


aVL


V4

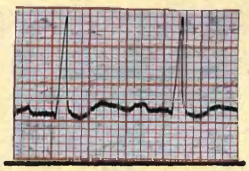

III

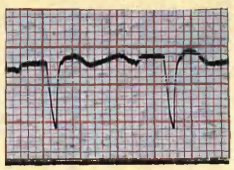

aVF

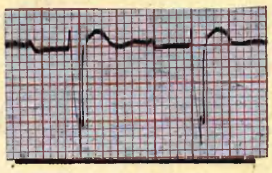

V6

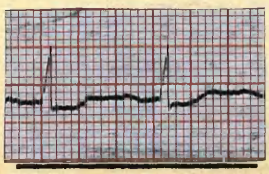
ELECTROCARDIOGRAM CASE NO. 82 (2)

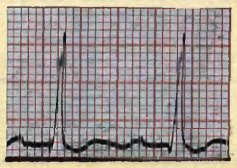

ST

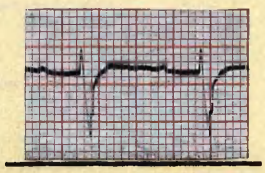

I.

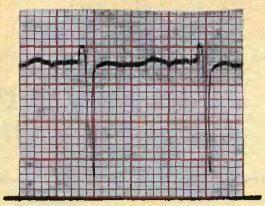

aVR

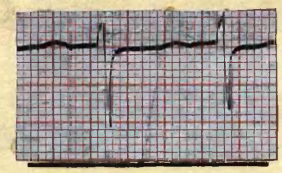

V2

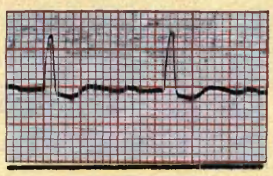

II.


aVL

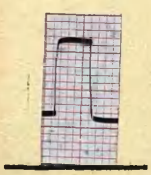

V4

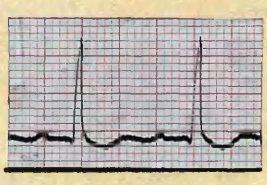

III.

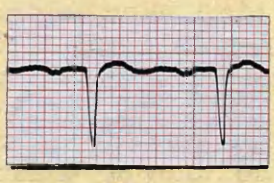

aVF

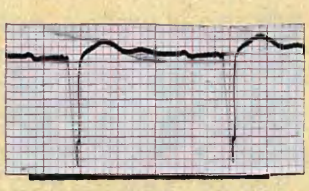

V6

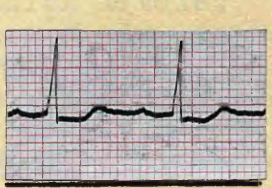
ELECTROCARDIOGRAM CASE NO. 82 (3)

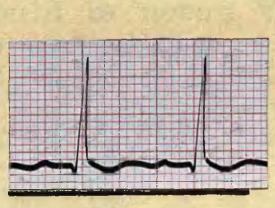

ST

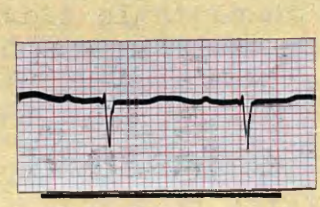

I.

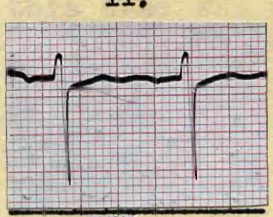

aVR

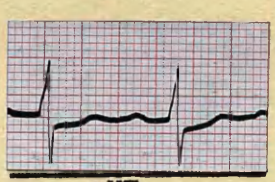

V2

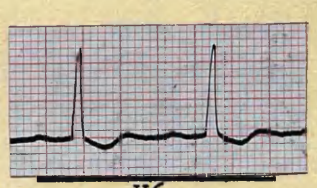

II.


aVL


V4


III


aVF


V6

Temperature Record.

An irregular pyrexia, Temp. 97.8° - 100.8°F was present for four days following admission.

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Sudden Dyspnoea on 22.3.57.

Days.	5	12	19	26	33
mm/1st.hr.	27	47	30	30	28

Liver Function Tests.

Time after onset (days)	VAN DEN BERGH. Direct: mgm/100 ml.	Indirect:	TURBIDITY. Thymol.	Zine.
2	Trace.	1.6	1	2
4.	Trace.	1.0.	1	1
5.	Trace.	0.7	1	1
6.	Trace.	0.8	1	1

COMMENT: Serum transaminase activity was normal on the second and third days following the onset of acute pulmonary infarction, secondary to phlebothrombosis of deep veins of the leg. At this time, congestive cardiac failure and hypertension of moderate degree were present. Serum transaminase activity rose to borderline levels on the fourth day after the onset of acute pulmonary infarction and on the fifth day rose to high levels. It should be noted that this significant increase in transaminase activity developed at a time when the liver function tests had returned to normal, suggesting that liver damage associated with congestive cardiac failure was not the cause of the increase. Serial electrocardiograms showed no evidence of acute myocardial infarction or of cardiac arrhythmia. The rise in serum transaminase activity in this case was considered to have been associated with acute pulmonary infarction.

CASE NO. 83.

A married woman, aged 37 years, a housewife, was admitted to hospital on 10.2.57, complaining of chest pain of sudden onset on 8.2.57.

The patient, who was known to suffer from aortic incompetence of rheumatic origin had given birth to a child on 20.1.57. On 2.2.57, she developed signs of deep vein thrombosis in the calf muscles of the left leg.

On 8.2.57, the patient complained of sudden sharp pain of moderate severity below the right scapula. The pain had become very severe and was related to coughing, breathing and movement.

On 10.2.57., haemoptysis was noted.

On admission, clinical signs of aortic incompetence with left ventricular enlargement, consolidation of the lower lobe of the right lung and phlebothrombosis of the left leg were present.

Radiological examination confirmed the cardio-respiratory findings. Treatment with penicillin and anticoagulant drugs was started soon after admission and the patient made a satisfactory recovery; she was discharged from hospital on 8.3.57.

Electrocardiographic Findings.

I. 14.2.57: The electrocardiogram showed no significant abnormality.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain on 8.2.57.

Days.	2	3	4
Units.	8	7	8

Temperature Record.

The temperature record was normal.

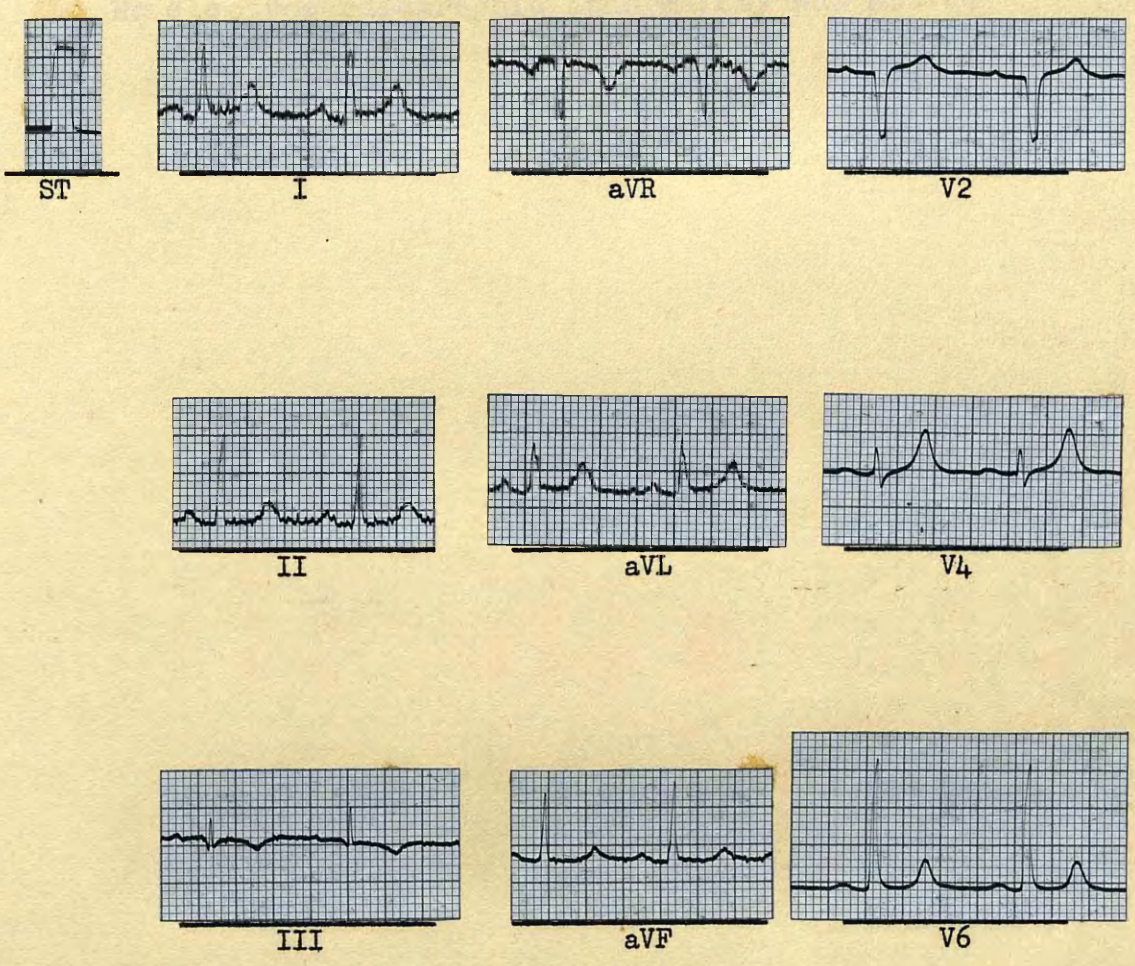
Erythrocyte Sedimentation Rate (Westergren).

Time After Onset of Chest Pain on 8.2.57.

Days.	3	12
mm/1st.hour.	17	8

/2

ELECTROCARDIOGRAM CASE NO. 83



COMMENT:

Serum transaminase activity was normal when examined on the second, third and fourth days following the onset of acute pulmonary infarction, secondary to embolism from phlebothrombosis of the leg veins.

Rheumatic heart disease was present, aortic incompetence being the dominant lesion.

No electrocardiographic abnormality was noted.

CASE NO. 84.

History of Present Illness.

A widow, aged 78 years, a housewife, was admitted to hospital on 20.2.57., complaining of breathlessness of 6 hours' duration. The patient had been in good health until 3.2.57., when she developed a crushing non-radiating pain behind the sternum, while sitting in a chair. The attack lasted for one hour. She had no further symptoms until 17.2.57., when she began to have short but severe attacks of breathlessness at rest. On 20.2.57., at 10 a.m., the patient became suddenly very dyspnoeic and cyanosed and complained of a constricting feeling in the retrosternal region. There had been no haemoptysis or chest pain, related to respiration.

Past History.

There was no relevant past history.

Clinical Findings on Admission.

The patient was an elderly, alert, overweight woman. Cyanosis of the lips was present and she was breathless at rest. There was no evidence of shock or congestive cardiac failure.

Cardiovascular System: B.P. 140/95 m..Hg. The pulse was regular in rate (94/min.) and rhythm. The heart was enlarged, the apex beat being palpable 1" outwith the mid-clavicular line. The heart sounds were faintly heard and much obscured by breath sounds. There was wide splitting of the first mitral sound.

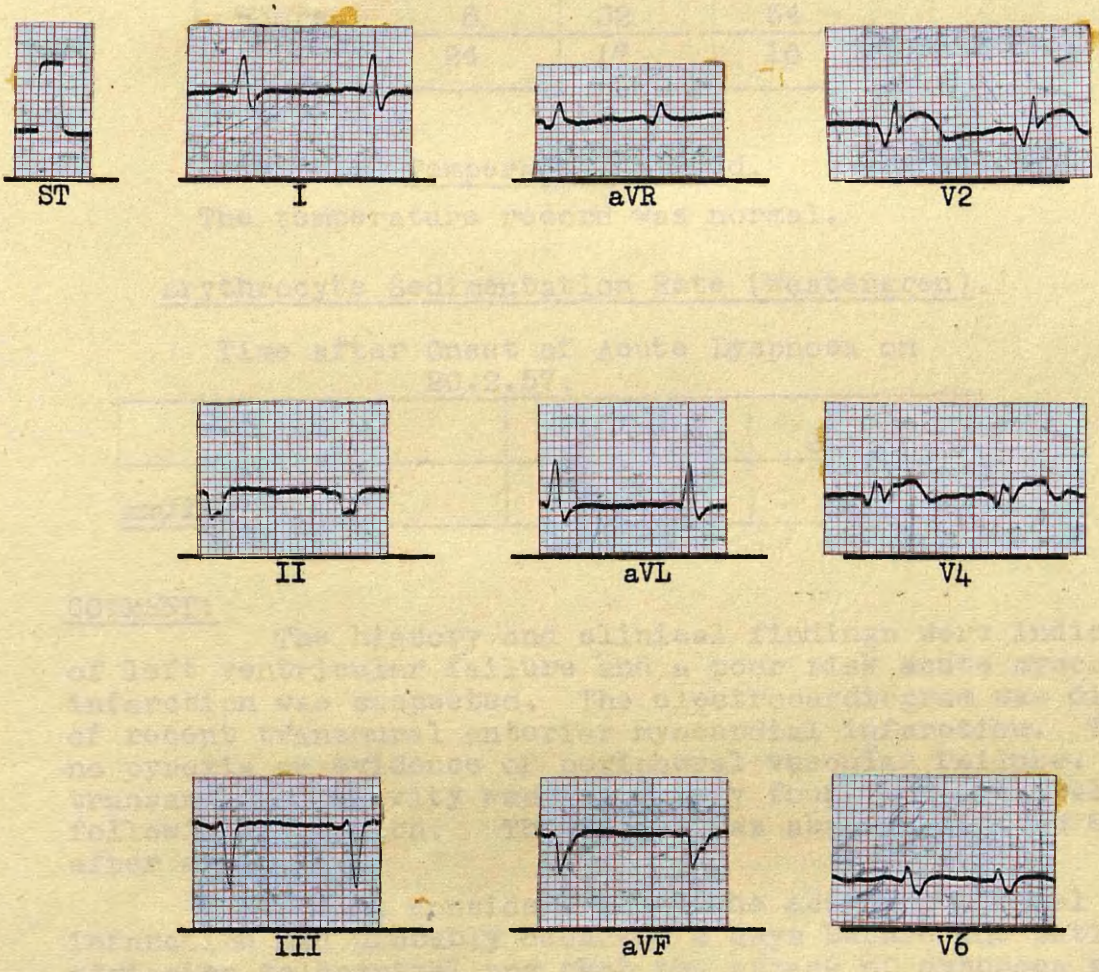
Respiratory System: The percussion note was dull over the base of the left lung and bronchial breathing and whispering pectoriloquy were present over this area.

No other abhormality was discovered on full clinical examination of other systems. There was no evidence of phlebothrombosis of the limbs.

Treatment and Progress.

Treatment with anticoagulant drugs was started soon after admission. Radiological examination of the chest revealed the presence of a pleural effusion on the left side and confirmed the heart enlargement. Following admission, the patient was very ill and mentally confused but, with mersalyl therapy, the dyspnoea and signs of effusion at the left base cleared. She was discharged from hospital on 20.3.57.

ELECTROCARDIOGRAM CASE NO. 84



Electrocardiographic Findings.

I. 20.2.57: (7½ hours after the onset of acute dyspnoea). The electrocardiogram showed changes diagnostic of recent transmural anterior myocardial infarction and of right bundle branch block.

Serial Serum Transaminase Activity (Units/ml/min).

Time after Onset of Acute Dyspnoea on 20.2.57

Hours.	8	32	54
Units.	24	17	10

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Acute Dyspnoea on 20.2.57.

8 hours.	14 days.	21 days.
mm/1st.hr. 85	29	30

COMMENT:

The history and clinical findings were indicative of left ventricular failure and a poor risk acute myocardial infarction was suspected. The electrocardiogram was diagnostic of recent transmural anterior myocardial infarction. There was no pyrexia or evidence of peripheral vascular failure. Serum transaminase activity was repeatedly found to be normal following admission. The E.S.R. was abnormally high 8 hours after admission.

It was considered that the acute myocardial infarction had probably occurred 3 days before the patient's admission to hospital and that the attack of dyspnoea which occurred on the day of admission was not accompanied by myocardial infarction. The normal serum transaminase activity was considered to be due to late

/3

/ late sampling of the serum following the onset of the myocardial infarction. Sera from other patients showed high levels of transaminase activity which suggested that the normal transaminase levels found in this case were not the result of faulty technique in the performance of the test.

CASE NO. 85.

A male, aged 33 years, an engineer, was admitted to hospital on 16.11.56.

On 6.11.56, the patient felt unwell and began to sweat profusely. On 11.11.56, he developed an unproductive cough. On 10.11.56, he began to have flitting pains in the joints, those of the knee, ankle and shoulder being affected, and he was admitted to hospital for further investigation and treatment.

Past History.

In 1951, the patient had had an attack of acute rheumatic fever, from which he had made a good recovery, there being no evidence of a cardiac lesion.

Clinical Findings on Admission.

On admission to hospital, effusions were present in both ankle joints and in the left knee joint. The patient was fevered, the temperature being 104.2°F.

The only abnormality noted on examination of the heart was a blowing systolic murmur at all areas. Signs of consolidation of the lung were present over the right middle lobe, which was confirmed by radiological examination.

Electrocardiographic Findings.

The electrocardiogram showed no significant abnormality.

Treatment and Progress.

The diagnosis of bronchopneumonia of the middle lobe of the right lung and acute rheumatic fever was made and treatment with aspirin, gr.90 daily, and penicillin was started, on admission. Penicillin therapy was stopped on 21.11.56. The pneumonic consolidation resolved completely. Aspirin therapy, gr. 30 daily, was maintained until the patient's discharge from hospital on 20.1.57, at which time there was no evidence of a cardiac lesion.

Serial Serum Transaminase Activity (Units/ml/min.)

Date.		Units.
17.11.56	:	30.
20.11.56	:	25.
27.11.56	:	20.

Temperature Record.

For 48 hours following admission, temperature recorded

Temperature Record. (ctd.)

/recorded was 100.6°F - 102°F.

Erythrocyte Sedimentation Rate (Westergren).

Date.		Mm/1st.hour.
22.11.56	:	120
2. 12.56	:	48

COMMENT:

Serum transaminase activity was normal on repeated examination during an attack of acute rheumatic fever.

Bronchopneumonia complicated the illness, but it responded quickly to penicillin therapy.

CASE NO. 86.

A male, aged 37 years, a barman, was admitted to hospital on 6.3.57, suffering from typical rheumatic fever.

Polyarthritis followed an attack of acute tonsillitis, after an interval of ten days, four weeks before admission.

The symptoms were very acute on admission but quickly responded to treatment with aspirin, gr. 90 daily.

The electrocardiogram showed no significant abnormality.

This was the patient's first attack of the disease and there was no evidence of a cardiac lesion, on the patient's discharge from hospital on 16.4.57.

Serial Serum Transaminase Activity (Units/ml/min.)

Date.		Units.
7.3.57	:	31
9.3.57	:	28
10.3.57	:	25

Erythrocyte Sedimentation Rate (Westergren.)

7.3.57 : 37 mm/1st.hr.

COMMENT:

Serum transaminase activity was normal on repeated examination during the acute phase of an attack of acute rheumatic fever.

CASE NO. 87.

A spinster, aged 22 years, was admitted to hospital on 4.2.57 suffering from congestive cardiac failure, auricular fibrillation (apex rate 130/min.) and mitral stenosis and incompetence of rheumatic origin.

The patient had been treated for attacks of congestive cardiac failure in May 1955, June 1956 and in October 1956. There was evidence of a dominant mitral incompetence and mitral valvotomy was contra-indicated.

Treatment with digitalis leaf and mersalyl was started soon after admission, and the signs of congestive cardiac failure cleared: the heart rate was 80-90 /min. when, on 20.2.57., the patient complained of sudden severe gripping pain on the left side of the praecordium which was associated with sweating and increased respiratory rate. There was no clinical or radiological evidence of pulmonary infarction and the pain was considered to be anginal in type and associated with severe mitral disease. There was no electrocardiographic evidence of myocardial infarction but changes of auricular fibrillation were present. The pain returned on several occasions but the patient's condition improved markedly and she was discharged from hospital on 22.3.57.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain on 20.2.57.

Hours.	6	30	54
Units.	10	20	24

Erythrocyte Sedimentation Rate (Westergren).

Time after Onset of Chest Pain.

Hours.	24
mm/1st.hour.	2

COMMENT:

Serum transaminase activity was normal on repeated examination following an attack of anginal pain complicating severe mitral valve disease of rheumatic origin. When transaminase assay was performed auricular fibrillation was 80 - 90/minute.

CASE NO. 88.

A male, aged 50 years, an engineer, was admitted to hospital on 12.2.57 complaining of acute breathlessness since 7.2.57.

On 7.2.57, the patient had suddenly become very breathless and found that he had to sit up throughout the night instead of lying down. He noted on 8.2.57 that his ankles were swollen for the first time and the breathlessness and oedema grew gradually worse. He was admitted to hospital for investigation and treatment.

Past History.

Since 1953, the patient had suffered from winter bronchitis and had been breathless on climbing stairs. His work record had been poor as he found it difficult to keep a job for long because of breathlessness and his recurrent "colds". The patient had had no other illnesses.

Clinical Findings on Admission.

The patient was very anxious and distressed. Marked sacral and ankle oedema and jugular vein congestion were present. He was cyanosed; he sweated and was orthopnoeic.

Cardiovascular System: B.P. 70/40 mm.Hg. The pulse was irregular in rate (140/min.) and rhythm. The heart was enlarged, the apex beat being situated 1" outwith the mid-clavicular line. The apex rate was over 160/min. The heart sounds were well heard. The first mitral sound was abrupt and forceful but no diastolic murmurs were heard.

Respiratory System: The accessory muscles of respiration were in use. The percussion note was diminished over the base of the right lung and numerous coarse and fine crepitations were heard on auscultation over both lung bases.

Alimentary System: The liver edge was palpable 2" below the right costal margin.

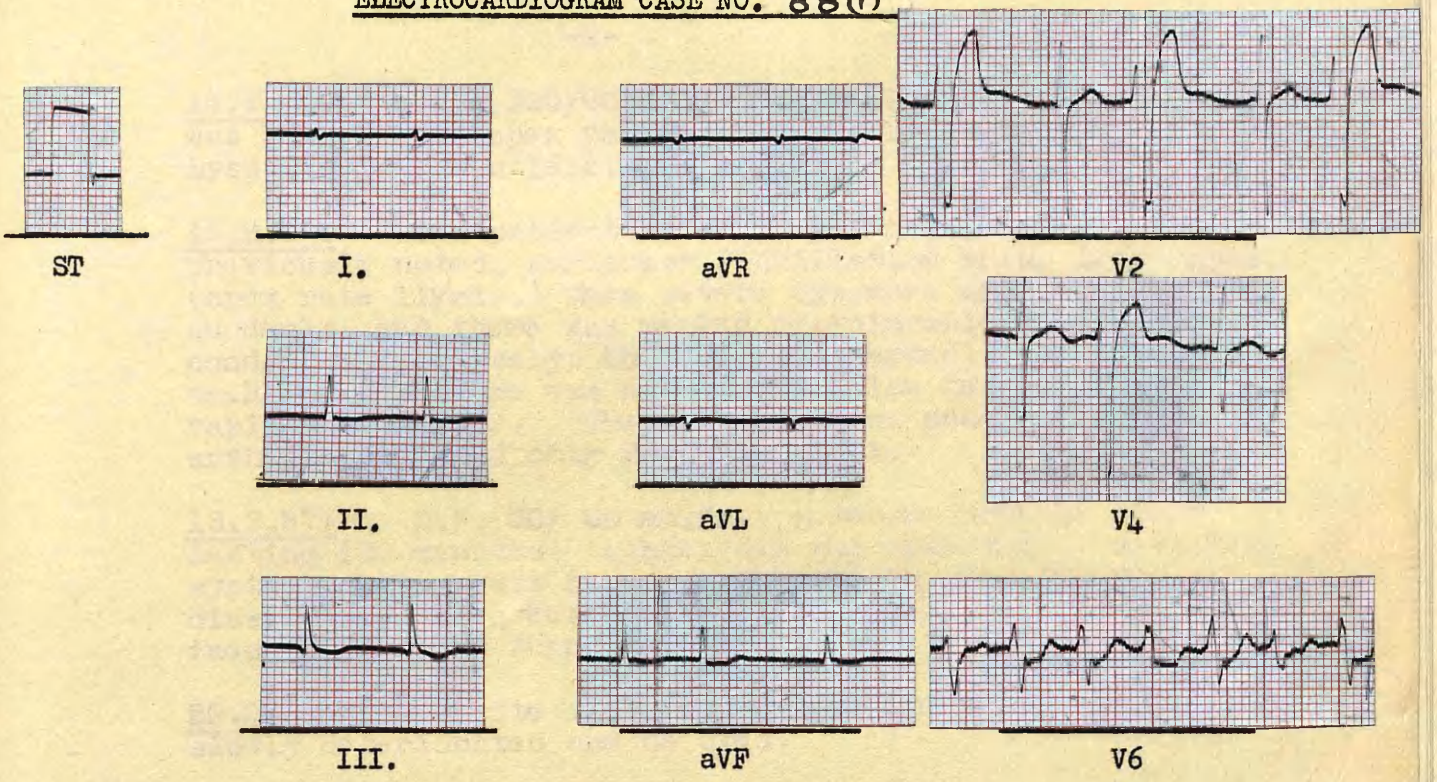
No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

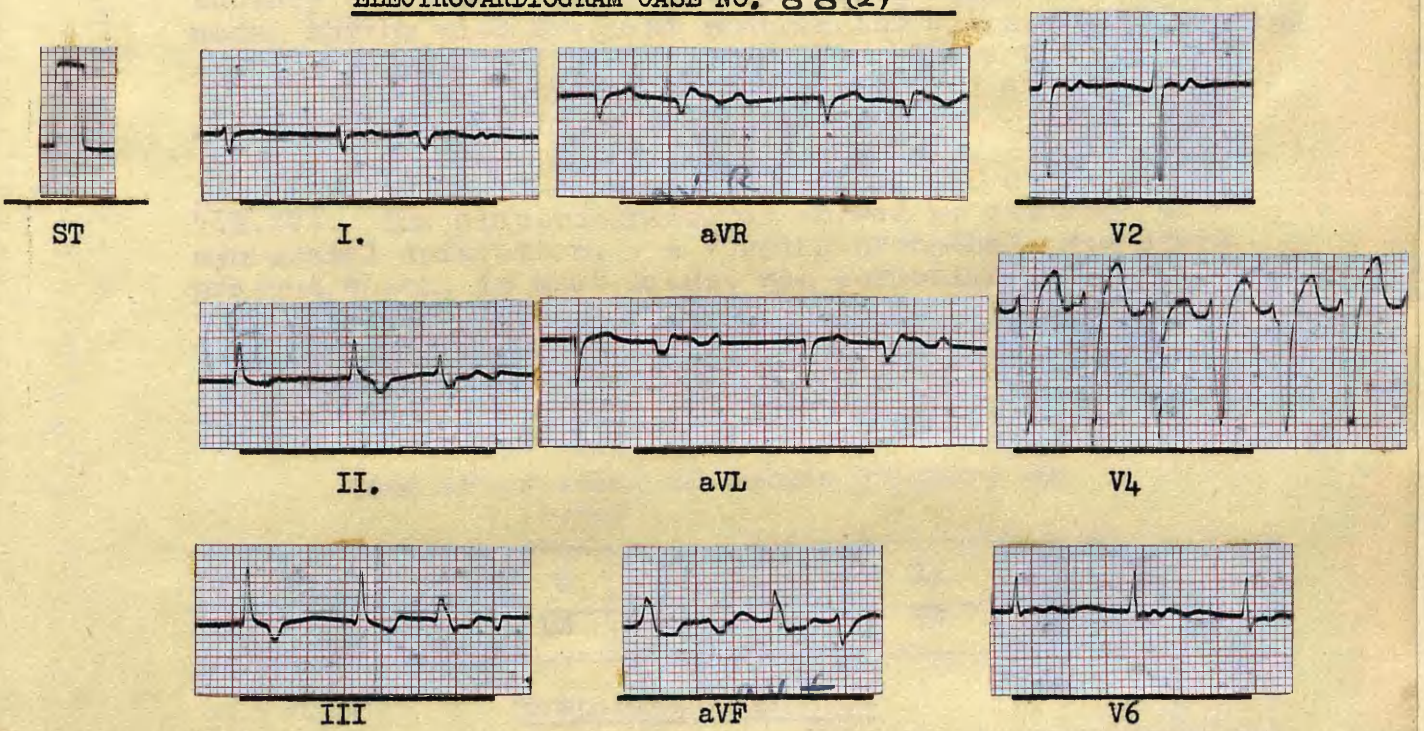
Treatment with digitalis leaf and crystalline penicillin was started immediately upon admission and, with oxygen therapy and intravenous aminophylline, there was an encouraging improvement in the patient's condition a few hours after admission. B.P. 110/70 mm.Hg. The clinical diagnosis of auricular fibrillation, congestive cardiac failure and chronic bronchitis and emphysema was made.

/2

ELECTROCARDIOGRAM CASE NO. 88(1)



ELECTROCARDIOGRAM CASE NO. 88(2)



13.2.57: B.P. 120/80 mm.Hg. Auricular fibrillation was less rapid (apex rate approximately 150/min.). Dyspnoea was also less.

16.2.57: The patient had maintained the improvement previously noted, auricular fibrillation being less rapid, (apex rate 110/min.) when severe dyspnoea reappeared suddenly, and there was marked deterioration in his condition. Mersalyl therapy was started. B.P. 90/ 70 mm.Hg. The pulse was of extremely low tension and very rapid and regular. The apex rate was uncountable. This arrhythmia lasted only for 20 minutes.

18.2.57: B.P. 90/ 60 mm.Hg. A second bout of short lasting (30 minutes) tachycardia was observed. A blowing systolic murmur was heard at the mitral area but no diastolic murmurs were heard and mitral stenosis and incompetence was suspected.

19.2.57: Despite therapy, the patient's condition slowly deteriorated and he died.

Electrocardiographic Findings.

I. 16.2.57: (9 days after the onset of dyspnoea on 7.2.57). The electrocardiogram was technically unsatisfactory but showed an arrhythmia which could be a basic nodal rhythm with frequent ventricular extrasystoles giving rise to coupling of the beats in V2. There was rapid auricular fibrillation in V6. There was no evidence of myocardial infarction.

II. 18.2.57: (11 days after the onset of dyspnoea on 7.2.57). The electrocardiogram showed no evidence of myocardial infarction. A varying arrhythmia was again present which, in most leads, was auricular fibrillation with ventricular extrasystoles but, in V4., a paroxysm of ventricular tachycardia was present.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after onset of sudden dyspnoea on 7.2.57.

Days.	6	8	10	11	12
Units.	213	236	138	77	58

Temperature Record.

Low grade pyrexia 98.6°F - 99.8°F was present during the period of observation.

/3

Erythrocyte Sedimentation Rate (Westergren)

Time after Onset of Sudden Dyspnoea on 7.2.57.

Days.	7
mm/1st. hr.	1

Post Mortem Findings.

Post mortem examination, carried out on 20.2.57, showed the following:

Post mortem examination showed the body of a rather poorly built, very cyanosed male.

Both lungs were adherent to the chest wall and showed moderate emphysema on section. In addition, both lungs were of a rubbery consistency, the result of long-standing congestion.

The heart was normal in size, but the right ventricle was moderately dilated and hypertrophied. An early mitral stenosis was present. The valve admitted the tip of one finger. The valve cusps showed extensive fibrosis, but no calcification. The left auricle was also a little dilated. No thrombus was present in the auricular appendage. The coronary arteries were patent and showed only minimal atheromatous changes. No infarcted muscle was seen in the left ventricle on section.

Examination of the abdominal organs showed no abnormality apart from long-standing chronic venous congestion in the liver. The spleen and kidneys were also congested.

The alimentary tract, pancreas and adrenals were normal.

The urinary bladder was distended and full of urine, but the prostate gland was normal.

Death was considered to be due to mitral stenosis; chronic bronchitis and emphysema; congestive cardiac failure.

RESULTS OF HISTOLOGICAL EXAMINATION.

Heart: Changes of pericarditis and of ischaemic fibrosis of some of the papillary muscles were present. There was no evidence of acute myocardial infarction. /4

Liver: Changes characteristic of centrilobular necrosis of the liver were present.

Lungs: Changes characteristic of severe emphysema and chronic venous congestion were present.

Serial Liver Function Tests:

Time after onset of sudden dyspnoea on 7.2.57. (Days)	VAN DEN BERGH		TURBIDITY.	
	Direct. mgm/100 ml.	Indirect. mgm/100 ml.	Thymol.	Zinc.
6	Pos.	1.4	-	-
8	Pos.	2.0	8	22
10	Pos.	2.4	8	26
12	Pos.	2.1.	-	-
15	Pos.	2.4	7	28

In each of these specimens the serum alkaline phosphatase activity was found to be within normal limits.

COMMENT:

Serum transaminase activity was demonstrated to be at high levels from the 6th - 12th day following the onset of congestive cardiac failure and rapid auricular fibrillation and supraventricular tachycardia. The heart rate on admission to hospital was more than 160/min. There was no clinical or electrocardiographic evidence of acute myocardial infarction. Serial tests of liver function revealed evidence of liver dysfunction but it was observed that serum transaminase activity fell towards more normal levels although convincing evidence of liver dysfunction was present.

Post mortem examination confirmed the clinical diagnosis of congestive cardiac failure and revealed that rheumatic mitral stenosis and chronic bronchitis and emphysema were present. There was no evidence of acute myocardial infarction on histological examination of the myocardium.

However, microscopic examination of the liver revealed changes characteristic of centrilobular necrosis of the liver.

/5

Therefore, increased transaminase activity in this case was due to liver necrosis consequent to rapid cardiac arrhythmia and congestive cardiac failure. No close correlation between the results of serial tests of liver function and serum transaminase activity was noted and the reason for this lack of correlation is unknown.

It should be noted that short lasting bouts of ventricular tachycardia were observed but that they did not result in a further rise in transaminase activity.

A married woman, aged 53 years, was admitted to hospital on 25.2.57 in a comatose state. Three hours before admission, she had developed a right hemiplegia and, on admission, cyanosis and coldness of the left forearm was noted. Auricular fibrillation (apex rate 90-100/min) was present. There was no evidence of mitral stenosis, there being a soft blowing systolic murmur only at the mitral area. The left radial and brachial artery pulsations could not be felt.

The electrocardiogram showed the changes of auricular fibrillation,(rate approx. 90/min.)

The diagnosis of embolism of the left middle cerebral and left brachial artery, congestive cardiac failure and auricular fibrillation of unknown aetiology was made.

Treatment with anticoagulants and penicillin was started soon after admission but the patient died 24 hours after her admission.

Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Hemiplegia and Brachial Embolism.

Hours.	12
Units.	85.

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren).

No estimations were performed.

Post Mortem Findings.

Post mortem examination was carried out on 27.2.57. This showed moderate congestion of both lungs with some brown induration of the lung tissue.

The heart was moderately enlarged due to hypertrophy of the right ventricle and left auricle. The mitral valve was stenosed, fixed and calcified, but still admitted one finger. The left auricle contained a pedunculated ball thrombus in

/2

/ in the auricular appendage. The coronary arteries showed moderate atheroma, but were still patent.

The aorta showed moderate atheroma throughout its course.

No abnormality was seen in the alimentary tract.

The liver and spleen were moderately enlarged and showed chronic venous congestion on section.

The pancreas, adrenals and right kidney showed no gross abnormality. The left kidney showed almost total infarction and a large embolism was impacted in the renal artery at the hilum of the kidney.

The Head: A large cerebral embolism obstructed the left middle cerebral artery at its outset and, related to this, there was recent infarction of almost the whole of the right cerebral hemisphere.

Death was considered to be due to mitral stenosis, congestive cardiac failure and multiple emboli.

Results of Histological Examination.

Heart: Changes characteristic of ischaemic fibrosis were present in the wall of the left atrium in association with ballthrombus formation. There was no infarction or fibrosis in the muscle of the ventricles.

Kidney: Multiple areas of infarction of kidney were present.

Liver: The appearances were normal.

Sections of brain and lung were not examined.

COMMENT: Serum transaminase activity was at high levels following the onset of embolism of the left middle cerebral, the left brachial and the left renal artery. At autopsy, mitral stenosis of rheumatic origin was found and, in the left atrium, there was a ball thrombus which had been the source of emboli. There was no evidence of myocardial infarction. Auricular fibrillation and congestive cardiac failure were present at the time of serum transaminase assay. The rise in serum transaminase activity was the result of brachial and/or renal artery embolism. It is unlikely that the relatively slow cardiac arrhythmia or acute cerebral infarction contributed to the rise in serum transaminase activity.

CASE NO. 90.

A male, aged 34 years, an aircraft engineer, was admitted to hospital on 27.2.57 complaining of breathlessness and vomiting since 20.2.57. On 18.2.57., the patient felt shivery and went to bed. On 20.2.57., he vomited and had diarrhoea. At this time, he became very breathless especially when recumbent. He had been mentally confused and very restless and was admitted to hospital for further investigation and treatment.

Past History.

There was no history of rheumatic fever. In 1955., the patient had been examined in another hospital as an outpatient, when auricular fibrillation and cardiomegaly of unknown aetiology was diagnosed. The patient had defaulted in attendance before full investigations were carried out.

Clinical Findings on Admission.

The patient was very breathless, restless and overweight. Marked malar flush, jugular venous congestion, sacral and ankle oedema were present and central cyanosis was noted.

Cardiovascular System: B.P. 120/90 mm.Hg.(Approx.) Rapid auricular fibrillation was present, the pulse rate being approximately 130-140 beats/min. The heart rate was too rapid to count accurately. The heart was greatly enlarged, the apex beat being felt in the anterior axillary line in the fifth left intercostal space. It was diffuse and heaving. The heart sounds were well heard and triple rhythm was thought to be present. No murmurs were audible but the second aortic sound was greatly accentuated.

Respiratory System: The percussion note was dull at both bases and numerous fine crepitations were heard at both lung bases.

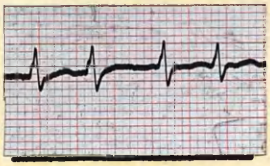
Alimentary System: The liver edge was palpable 4" below the right costal margin. The spleen was not palpable.

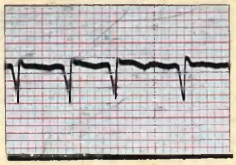
No other abnormality was found on full clinical examination of other systems.

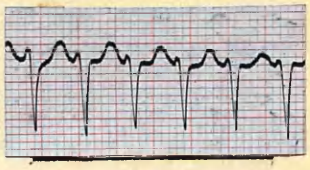
/2

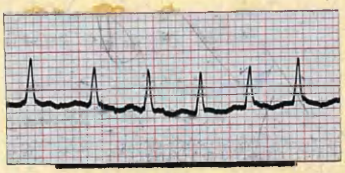
ELECTROCARDIOGRAM CASE NO. 90(1)

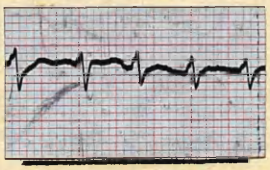

ST

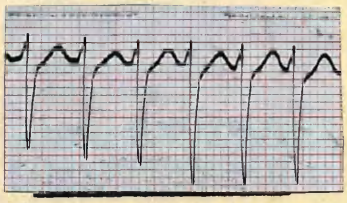

I.

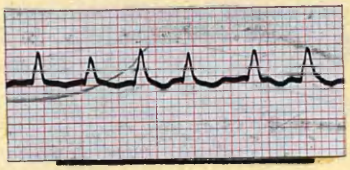

aVR

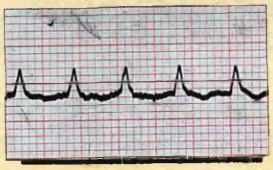

V2

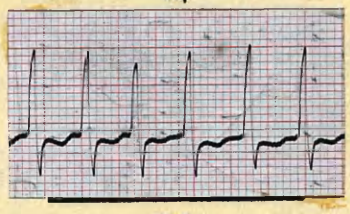

II.


aVL


V4

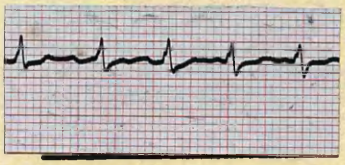

III.


aVF


V6

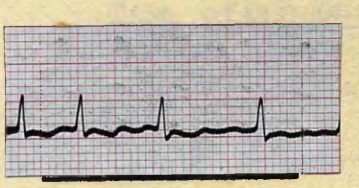
ELECTROCARDIOGRAM CASE NO. 90(2)


ST


I.

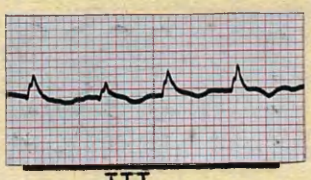
aVR

V2


II.

aVL

V4


III

aVF

V6

Treatment and Progress.

The rapid auricular fibrillation proved very difficult to control with digitalis leaf. This drug was given in a dosage of 8 grains daily for five days, then of 6 grains daily for three days before the apex rate fell below 140/ min. Congestive cardiac failure proved refractory too but, following treatment with Mersalyl, begun on 2.3.57., it gradually cleared. On 8.3.57., the patient sustained a splenic embolism with infarction but this complication cleared without special treatment. There was no evidence on full bacteriological examination of sub-acute bacterial endocarditis. Radiological examination of the heart, including chest screening confirmed marked cardiomegaly, and revealed selective heart chamber enlargements, indicating mitral stenosis and incompetence.

The patient was discharged from hospital on 30.3.57., and instructed to take a maintenance dose of digitalis leaf.

Electrocardiographic Findings.

I. 27.2.57: The electrocardiogram showed rapid auricular fibrillation (approx. 190/min.) Shallow inversions of the T wave in leads I., II., III and a.V.F, and diphasic T waves in V6 suggested coronary insufficiency or left ventricular strain.

II. 4.3.57: The electrocardiogram showed no change in pattern, but the fibrillation was shown (140-150/min.)

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Acute dyspnoea on 20.2.57.

Days.	7	8	9	10	14	15
Units.	1400	945	370	170	76	40

Temperature Record.

The temperature was normal until 7.4.57 when pyrexia (99.8°F - 100°F) was present for three days following infarction of the spleen.

Erythrocyte Sedimentation Rate (Westergren)

No estimations were performed at the time transaminase activity was measured.

Liver Function Tests.

Time after onset(days)	VAN DEN BERGH. Direct.	Indirect.
8	Pos.	2.2
9	Pos.	2.0
10	Pos.	2.2

COMMENT:

Serum transaminase activity was demonstrated to be at high levels from the 7th - 14th day after the onset of rapid auricular fibrillation, and congestive cardiac failure.

The heart lesion present was mitral stenosis and incompetence of rheumatic origin. There was no clinical or electrocardiographic evidence of acute myocardial infarction. The auricular fibrillation was very rapid (approximately 190/min) and continued at these rapid rates for three days despite adequate treatment with digitalis leaf.

The highest levels of serum transaminase activity found in this study occurred in this case. There was suggestive evidence of liver dysfunction and increased serum transaminase activity was probably due to liver damage in association with auricular fibrillation and congestive cardiac failure. There was no close correlation between the results of serial tests of liver function and serum transaminase activity.

No transaminase assays were performed following the onset of splenic infarction.

CASE NO. 91.

A male, aged 22 years, a labourer, was admitted to hospital on 19.2.57 complaining of sudden onset of severe epigastric pain.

Perforation of a peptic ulcer was diagnosed and, at operation, a perforation was found on the anterior wall of the first part of the duodenum.

Serum Transaminase Activity (Units/ml/min.)

Time After Onset i.e., just before operation was performed.

Hours.	$7\frac{1}{2}$
Units.	11.

COMMENT:

Serum transaminase activity was normal $7\frac{1}{2}$ hours after perforation of an acute ulcer of the first part of the duodenum.

CASE NO. 92.

A spinster, aged 38 years, was admitted to hospital on 19.2.57.

On admission, perforation of a peptic ulcer was diagnosed and, at operation, a perforation of a chronic pre-pyloric ulcer was found.

Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Epigastric Pain

Hours.	6
Units.	21

COMMENT:

Serum transaminase activity was normal 6 hours after the onset of perforation of a chronic pre-pyloric ulcer.

CASE NO. 93.

A male, aged 59 years, a fitter, was admitted to hospital on 21.2.57 having developed severe generalised abdominal pains on 20.2.57.

The clinical diagnosis of perforated duodenal ulcer was confirmed by the radiological finding of free gas under the right dome of the diaphragm but the patient was treated conservatively since it was judged that 24 hours had elapsed since the perforation before his admission to hospital.

Barium meal examination on 26.3.57 revealed chronic ulcer of the duodenum.

Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Abdominal Pain.

Hours.	24.
Units.	5.

COMMENT:

Serum transaminase activity was normal 24 hours after the onset of perforation of a chronic duodenal ulcer.

CASE NO. 94.

A male, aged 56 years, a labourer, had been admitted to an infectious diseases hospital on 18.1.57 suffering from diarrhoea, the stools containing blood on occasion.

He had a productive cough. There was a family history of pulmonary tuberculosis.

No organisms had been isolated from the stools when, at 5 p.m. on 25.1.57., the patient developed severe, sharp retrosternal pain. The blood pressure had fallen from 190/110 to 95/60 mm.Hg. He was transferred to a medical unit as a case of myocardial infarction.

Clinical Findings on Admission.

On admission, the patient was restless and confused; muscle twitching was noted.

Cardiovascular System: B.P. 95/60 mm.Hg. Tachycardia was present (120/min.) but the pulse was regular. The apex beat was not felt. The heart sounds were pure but rapid and distant. There was marked pericardial friction at the third left sterno-costal junction.

Respiratory System: The percussion note was dull over the left lung; on auscultation, numerous bubbling rales were heard throughout the left lung and at the base of the right lung.

Alimentary System: There was marked resistance to palpation in the upper abdomen but no true guarding or local tenderness.

Urine could not be obtained for examination even after catheterisation.

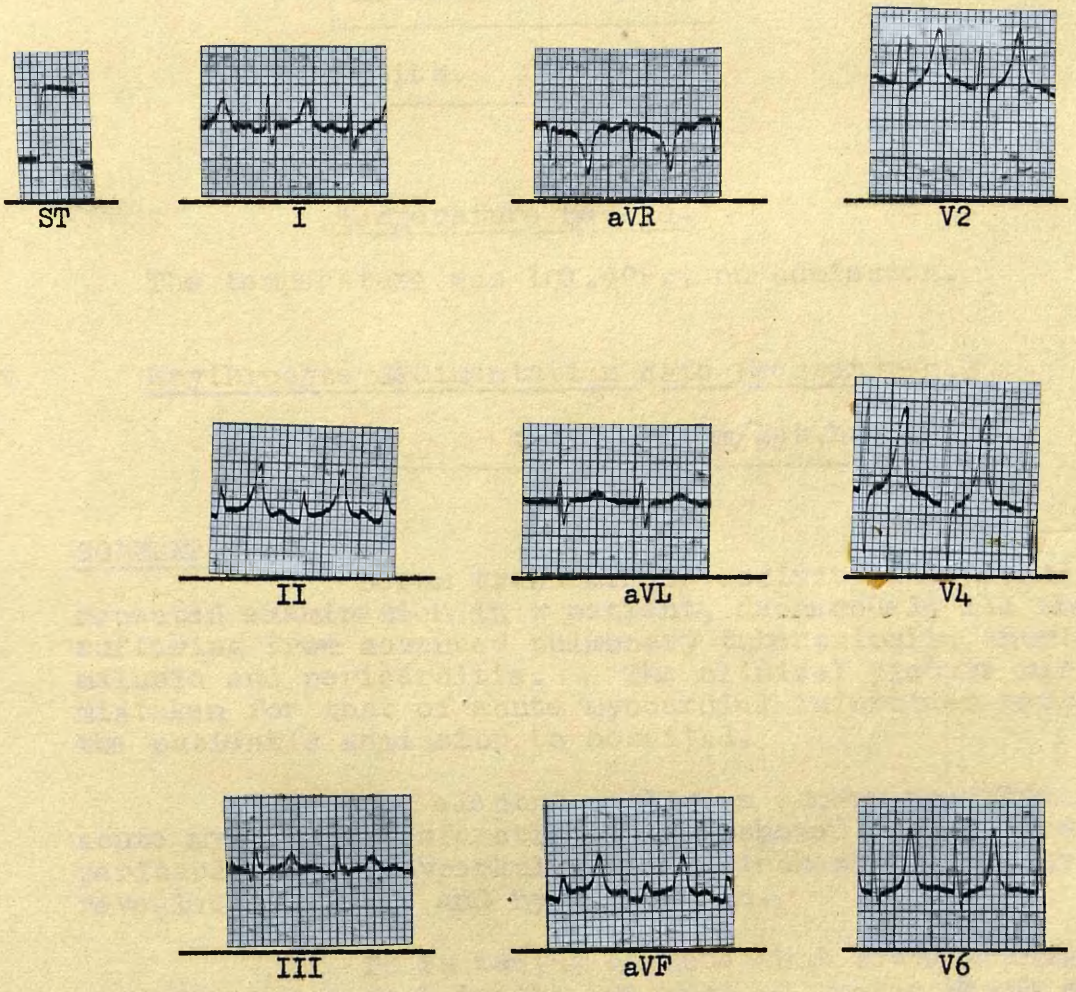
Treatment and Progress.

Radiological examination of the chest revealed changes of fibro-caseous tuberculosis in the left lung and treatment with streptomycin sulphate, gr. i daily was started. The patient was uraemic, the serum urea being 188 mgm%., and hyperkalaemia was marked, the serum potassium being 31 mgm%. Treatment with Resonium "A" was started.

The diarrhoea continued and the patient died suddenly on 26.1.57, 28 hours after admission. Permission for a post mortem examination was refused.

/2

ELECTROCARDIOGRAM CASE NO. 94



Electrocardiographic Findings.

I. 25.1.57: (3 hours after onset of chest pain.) The electrocardiogram showed changes diagnostic of hyperkalaemia and pericarditis.

Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Chest Pain.

Hours.	16.
Units.	15

Temperature Record.

The temperature was 101.4°F., on admission.

Erythrocyte Sedimentation Rate (Westergren.)

25.1.57	:	120 mm/1st.hour.

COMMENT:

Serum transaminase activity was normal on repeated examination in a patient, dangerously ill and suffering from advanced pulmonary tuberculosis, anuria, maluria and pericarditis. The clinical picture was mistaken for that of acute myocardial infarction before the patient's admission to hospital.

The electrocardiogram showed no evidence of acute myocardial infarction but it showed the changes of pericarditis and hyperkalaemia. Biochemical examination revealed uraemia, and hyperkalaemia.

It is worthy of note that serum transamina se activity was normal in the presence of anuria which suggests that renal excretion of the enzyme is not of primary importance. The gross alterations in electrocardiographic patterns present were accompanied by normal transaminase activity.

CASE NO. 95.

A male, aged 52 years, a bank teller, was admitted to hospital on 11.6.57 complaining of sudden loss of speech and weakness of the right limbs.

On 28.5.57., the patient had had severe retrosternal pain and, after electrocardiographic examination, an anterior myocardial infarction had been diagnosed. He appeared to be making a good recovery when, on 11.6.57, his wife found him trying to get out of bed and suddenly unable to speak.

Clinical Findings on Admission.

The patient was suffering from expressive dysphasia. There was no evidence of shock or of congestive failure.

Cardiovascular System: B.P. 115/80 mm.Hg. The pulse was regular in rate (78/min) and rhythm. The heart was slightly enlarged, the apex beat being situated ½" outwith the mid-clavicular line in the fifth left intercostal space. The heart sounds were pure and easily heard.

There was evidence of right hemiparesis.

No other abnormality was found on full clinical examination.

Treatment and Progress.

The diagnosis of embolism of the left middle cerebral artery from a mural thrombus, consequent to a myocardial infarction, was made and anticoagulant therapy was started and continued for 28 days. The signs of hemiparesis cleared and, with speech therapy, the dysphasia was improving when the patient was discharged from hospital on 7.8.57.

Electrocardiographic Findings.

I. 11.6.57: (14 days post-infarction.) The electrocardiogram showed changes diagnostic of recent extensive anterior myocardial infarction.

II. 30.7.57: The electrocardiogram showed minor sequential changes confirming the diagnosis.

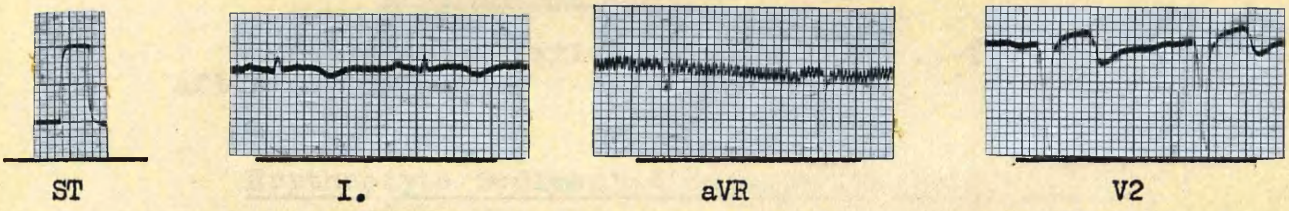
Serial Serum Transaminase Activity (Units/ml)

Time after Onset of Dysphasia on 11.6.57.

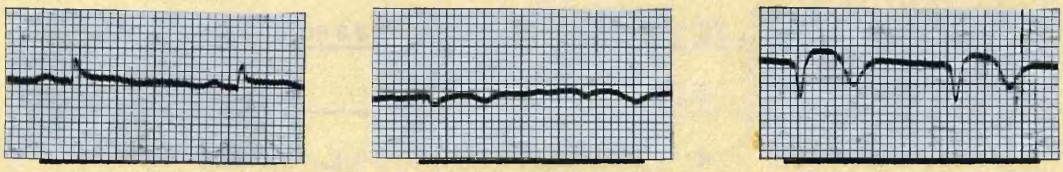
Hours.	7	31	55.
Units.	20	18	21.

/2

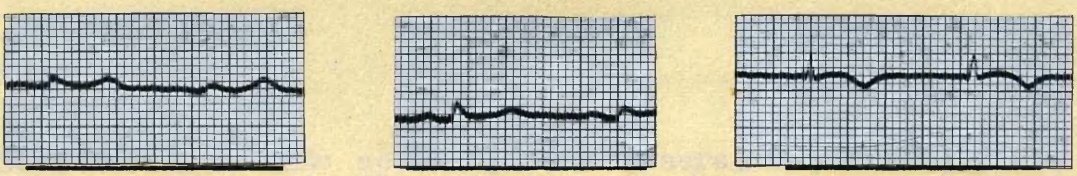
ELECTROCARDIOGRAM CASE NO. 95 (1)



ST I. aVR V2

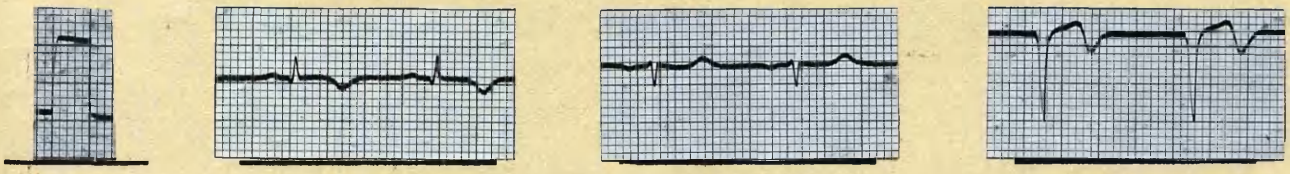


II. aVL V4

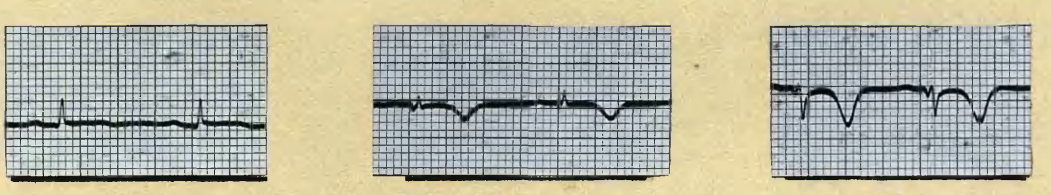


III. aVF V6

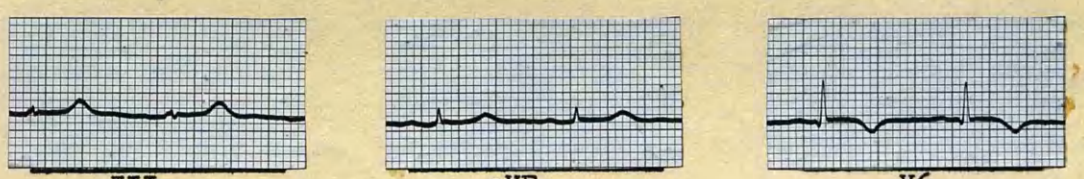
ELECTROCARDIOGRAM CASE NO. 95 (2)



ST I. aVR V2



II. aVL V4



III aVF V6

Temperature Record.

There was a pyrexia 99°F - 99.6°F., for 48 hours after admission.

Erythrocyte Sedimentation Rate (Westergren.)

Time after Onset of Dysphasia on 11.6.57

Days.	2	9	16
mm/1st.hr.	19	5	5

COMMENT:

Serum transaminase activity was measured repeatedly following the onset of cerebral embolism and was found to be normal. The site of origin of the embolus was presumed to be mural thrombus in the left ventricle since there was clinical and electrocardiographic evidence that acute myocardial infarction had occurred 14 days before the onset of cerebral embolism.

CASE NO. 96.

A woman, aged 53 years, was admitted to hospital on 21.1.57 complaining of generalised oedema. The patient had been treated, in a sanatorium, for pulmonary tuberculosis in 1954. At that time, the sputum had contained tubercle bacilli. Since then, exertional dyspnoea had been present and, in June 1956, the patient noted ankle oedema which had gradually worsened until the trunk and hands were involved.

On admission to hospital, marked generalised oedema and ascites were present. B.P. was 80/60 mm.Hg., but the heart was not enlarged and the heart sounds were pure. The percussion note was dull over the base of the left lung posteriorly and numerous coarse crepitations were heard, on auscultation, over this area.

Clinical examination of the urine revealed gross albuminuria (Esbach 16 parts) while microscopic examination showed scanty red blood cells.

23.1.57: Oliguria was noted, the daily output of urine being only 7 ounces.

An X-Ray film of the chest showed some collapse of the left thorax with considerable pleural thickening and calcification of the left chest wall and base. Examination of the plasma proteins showed that total protein was 5.2 gm/100ml. (Albumin 1.4 g: Globulin 3.0 g: Fibrinogen 0.8 g/ 100ml.)

No abnormality was found on full examination of the blood. The blood urea was normal.

The diagnosis of amyloid nephrosis, due to chronic pulmonary infection was made. The patient made no response to treatment and died on 28.1.57.

Permission for a post-mortem examination was refused.

Serum Transaminase Activity (units/ml/min.)

23.1.57 :	5 units.

COMMENT: Normal serum transaminase activity was demonstrated in a case of amyloid nephrosis secondary to long-standing tuberculous empyema. There was no evidence of uraemia. Oliguria was present when the transaminase activity was normal.

CASE NO. 97.

A male, aged 48 years, was admitted to hospital on 8.2.57., complaining of swelling of his legs and abdomen.

In 1945, the patient had had a severe attack of jaundice lasting six weeks while he was attending a venereal disease clinic for the treatment of syphilis.

In 1954., he was admitted to hospital having become jaundiced again and the diagnosis of chronic hepatitis secondary to homologous serum jaundice was made.

In August 1957, having had no symptoms apart from transient dyspepsia, he noted swelling of the ankles at night and, shortly after this, his abdomen began to swell. Mersalyl therapy had reduced the ascites but, in the fortnight before his admission, it had lost its effect and the patient was admitted for further treatment.

The main clinical findings on admission were jaundice, ascites and oedema of the sacral area and ankles.

Electrocardiographic examination revealed no significant abnormality.

Treatment with a high protein, low fat and low salt diet and thiomerin 1 cc. thrice weekly was started on 9.2.57., and there was some improvement in his condition, the ascites being reduced following satisfactory diuresis.

On 16.2.57, the patient was drowsy, nauseated and febrile and it was decided that liver failure was progressing. Thiomerin treatment was discontinued and tetracycline 500 mgm.stat. and 250 mgm. 6-hourly was started. Protein was excluded from the diet and fluids and carbohydrates (400 g./daily) only were given. Within 48 hours, great improvement was noted and this regime was discontinued on 25.2.57. The improvement, however, was evanescent and, on 7.3.57., the patient was drowsy, disorientated and febrile. The ascites had increased. Following paracentesis abdominis (68 ounces of cloudy amber fluid was withdrawn) and the re-institution of a protein-free diet and tetracycline therapy, there was temporary improvement but on 13.3.57 his condition had regressed, pyrexia being uncontrolled and a further paracentesis abdominis (75 ozs. fluid withdrawn) was required.

On 15.3.57., the patient passed a melaena stool and a blood transfusion was given. Despite continued therapy, the patient died on 18.3.57.

/2

Serial Serum Transaminase Activity (Units/ml/min.)

11.2.57	:	49 units.
20.2.57	:	55 "
8.3.57	:	60 "
10.3.57	:	75 "

Liver Function Tests.

11.2.57: Serum bilirubin: Direct -positive. Indirect- 1.2 mg/per 100 ml. Thymol Turbidity Test (Maclagan): - 15 units: Zinc Turbidity: - 36 units.

Interpretation:- These findings confirmed that the jaundice was hepatogenous.

10.3.57: Serum bilirubin: Direct -positive. Indirect - 5.2 mg/100ml. Plasma Alkaline Phosphatase: 13.1 units (King, Armstrong Method.) Zinc Turbidity Test: 38 units. Total Plasma Proteins: 6.5 g/100ml. Plasma Albumen: 1.4g/100ml: Globulin: 5.1 gm/100ml.

Interpretation. The findings indicated that the jaundice was hepatogenous.

Post Mortem Findings.

Post mortem examination was carried out on 19.3.57, as follows :-

The body was that of a man of about the stated age. The general colour of the skin was pale with a strong yellowish tinge. The abdomen was slightly distended.

Copious serous exudate was present both in the pleural cavities and in the greater sac of the peritoneum. The lungs were small and very moist. The trachea showed moderate inflammatory change with the presence of some purulent exudate. On section, the lungs showed generalised congestion and oedema, which was most marked at the bases.

The abdomen contained several pints of fluid. The ascending and transcending colon was distended with blood.

Erosion, oesophageal varices and bleeding points in the terminal segment of the oesophagus were present.

The stomach contained about half a pint of altered blood.

The liver was strikingly small and shrunken and displayed superficially

/ a coarse and nodular surface. The appearances were those of a severe hepatic cirrhosis.

The spleen was of average size and texture. No abnormality was found in the pancreas.

The kidneys showed some superficial scarring and the capsules were slightly adherent. Section disclosed some loss of cortical tissue. The remainder of the urinary tract presented no features of note.

Diagnosis: Hepatic cirrhosis; oesophageal varices with haemorrhage: ascites and hydrothorax.

COMMENT:

High levels of serum transaminase activity were demonstrated on three occasions during the terminal phase of jaundice due to cirrhosis of the liver, which was complicated by bleeding from oesophageal varices.

Tests of liver function were compatible with the diagnosis of increasing hepatogenous jaundice.

Post mortem examination confirmed the diagnosis of advanced cirrhosis of the liver with bleeding from oesophageal varices.

The increase in serum transaminase activity was presumably due both to release of enzyme from damaged liver cells and to diminished excretion of the enzyme by the liver. The course of the illness was characterised by episodes of early hepatic coma suggesting that liver damage was steadily progressing.

The results of liver function tests supported this idea.

CASE NO. 98.

A woman, aged 50 years, a factory worker, was admitted to hospital on 4.2.57 complaining of headache.

The patient had been dyspnoeic on exertion since 1956 and she had complained of occipital headache on waking for six months. The headaches became very severe on 20.1.57 and the patient's legs had become so weak on 3.2.57 that she had been unable to get out of bed.

On admission, the patient was mildly dysarthric and confused. The heart was enlarged, the apex beat being 1" outwith the mid-clavicular line in the fifth left intercostal space and the B.P. was elevated - 160/115 mm.Hg.

Signs of left hemiparesis were present and cerebral thrombosis in association with essential hypertension was diagnosed.

Serial electrocardiograms showed changes consistent with the diagnosis of left ventricular hypertrophy and strain and an old antero-septal infarction.

There was no evidence of myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min.)

4.2.57	:	30 units.
5.2.57	:	35 "
6.2.57	:	25 "

Following admission to hospital, the blood pressure rose to levels of 240/140 mm.Hg., and, on ophthalmoscopic examination, scattered recent exudates were seen in the retinae.

On 13.2.57., the patient developed signs and symptoms of left ventricular failure which failed to clear with digitalis and mersalyl therapy and, on 20.2.57., inversine therapy was started and a good hypertensive effect was attained. Despite all therapy, dyspnoea continued, the patient became confused and incontinent and left hemiplegia became complete. The blood urea remained normal throughout the illness. The patient died on 21.3.57.

Post-Mortem Findings.

Post-mortem examination was carried out on 22.3.57, as follows:-

The body is that of a woman of about the stated age. Superficially, there are no features of note.

/2

Head and Neck: The dura was under slightly increased tension, and the surface of both hemispheres showed some flattening. No extra or subdural haemorrhage was found nor was there evidence of subarachnoid haemorrhage. Section through the hemispheres disclosed a small haemorrhagic lesion (2 cm. in diameter) in the optic radiation of the right side. Section at a lower level showed the presence of a large thrombus disrupting the ventricular nucleus and extending posteriorly to involve the internal capsule and adjacent structures on the right side. The blood clot here was firm and retained its colour. Also present in the basal nuclei were many small (less than 2 mm. diameter) softenings and cystic spaces containing clear fluid. A similar group of small lesions was present on the left side, also in the ventricular and caudate nuclei and involving also the internal capsule on this side. The vessels at the base of the brain in the Circle of Willis were grossly atheromatous.

Thorax: The lungs showed the usual features of terminal congestion and oedema.

Heart: The pericardial sac was healthy. Gross hypertrophy was present in the left ventricle with some early dilation. Section of the heart disclosed an extensive area of old fibrosis and this was most marked at the base of the left ventricle and covering also the interventriculum septum. Projecting into the lumen at this site of healed infarction was a large mural thrombus undergoing organisation.

Abdomen: No abnormality was seen in the gut or its related glands. The kidneys were of average size and shape. The capsules strip readily. The surfaces showed only slight scarring. Generalised arterial degeneration was evident but section on the appearances here did not suggest that hypertension was secondary to renal disease.

Diagnosis: Malignant hypertension; myocardial infarction with no thrombosis; cerebral embolism with haemorrhage.

COMMENT: Serum transaminase activity was found to be normal on repeated examination following the onset of a cerebro-vascular accident. On admission, the diagnosis of thrombosis of the right middle cerebral artery was made but post-mortem examination after a second cerebro-vascular accident suggested that the lesion studied had probably been an embolism of the right middle cerebral artery, the site of origin of the embolus being mural thrombus in the left ventricle. The electrocardiographic diagnosis of old antero-septal myocardial infarction was confirmed at autopsy.

At the time when serum transaminase activity was normal, hypertension of severe degree was present.

CASE NO. 99.

A married woman, aged 69 years, was admitted to hospital on 24.2.57 complaining of attacks of epigastric pain and vomiting of two years' duration.

On admission, to a surgical unit, the diagnosis of acute cholecystitis was made and laparotomy was performed on 25.2.57 because of increasing pain and tenderness in the right hypochondrium. Jaundice was not present.

At operation, the gallbladder contained multiple stones and those palpable in the region of the cystic duct were easily moved into the gallbladder. No stones were palpated in the common bile duct. The fundus of the gallbladder was incised with the escape of concentrated bile and multiple stones were removed. The gallbladder was closed round a rubber tube which was brought to the surface through a separate lateral stab incision.

Serum Transaminase Activity.(Units/ml/min.)

24 hours before laparotomy on 24.2.57.
35 units.

Serial Assay of Transaminase Activity in Serum, Bile and Urine Following Operation.

25.2.57:	Serum Activity	:	30 units/ml/min.
	Bile "	:	74 " "
	Urine "	:	5 " "
26.2.57:	Serum Activity	:	30 units/ml/min.
	Bile "	:	68 " "
	Urine "	:	8 " "
27.2.57:	Serum Activity	:	24 units/ml/min.
	Bile "	:	65 " "
	Urine "	:	6 " "

The patient made a good recovery and was discharged from hospital on 30.3.57.

COMMENT: Normal serum transaminase activity was demonstrated before and after the operation of cholecystostomy.

/2

Comment: (ctd)

The patient suffered from acute cholecystitis and cholelithiasis. No gallstones were found in the common bile duct. No rise in serum transaminase activity was detected following operation but the results of serial assay of transaminase activity in serum, bile and urine suggest that the enzyme may be excreted by the liver since transaminase activity of bile was consistently higher than that of serum or urine.

CASE NO. 100.

A male, aged 66 years, a retired civil servant, was admitted to hospital on 14.2.57 complaining of attacks of throbbing epigastric pain accompanied by jaundice of 18 months' duration.

On admission, there was no jaundice or abnormal clinical findings. Combined telepaque and biligrafin examinations showed no evidence of gallbladder function or of duct outline.

The urine contained a trace of bile and liver function tests showed a weakly positive direct Van den Bergh reaction: serum bilirubin: 1.3 mgm/100ml.: Hanger flocculation test: negative.: serum alkaline phosphatase: 42 units (King & Armstrong).

These findings were suggestive of biliary obstruction. The attacks of pain were considered to be due to cholelithiasis and on 20.2.57., laparotomy was performed.

At operation, the gallbladder was thick-walled and contained many small stones. The liver was congested and its surface was granular. The common bile duct was dilated and there was a stone in its supraduodenal part. The duct was incised and the stone was removed with the escape of apparently uninfected bile. The common bile duct was closed round a T tube for drainage and cholecystectomy was performed. The patient made a good recovery and he was discharged from hospital on 20.3.57.

Serum Transaminase Activity (Units/ml/min.)

19.2.57 :	Before Operation:	45 units.

Serial Assay of Transaminase Activity in Serum, Bile and Urine, Following Operation.

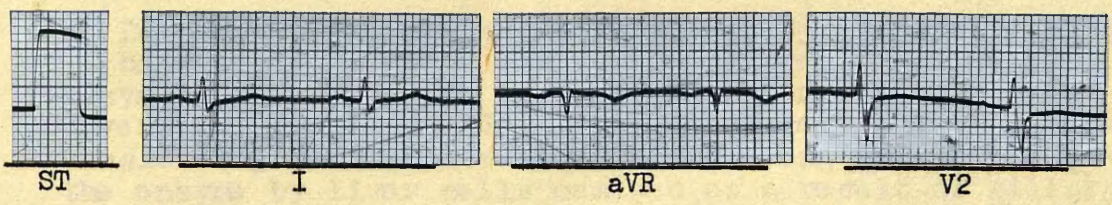
21.2.57:	Serum Activity	:	35 units/ml/min.
	Bile "	:	53 " "
	Urine "	:	9 " "
22.2.57:	Serum Activity	:	11 " "
	Bile Activity	:	24 " "
	Urine Activity	:	3 " "

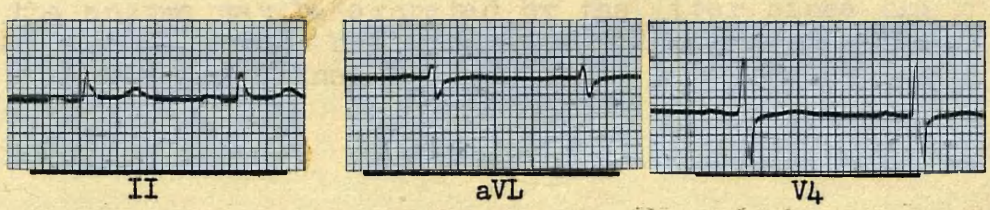
Electrocardiographic Findings.

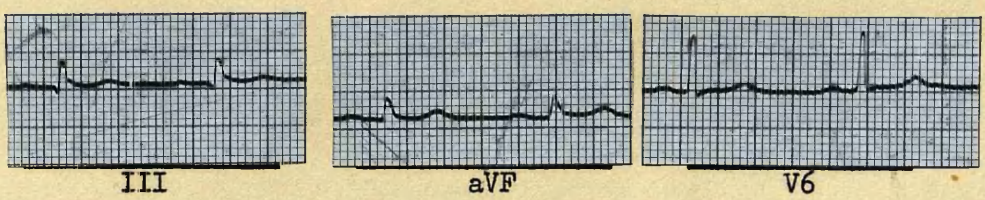
I. 15.2.57: (24 hours after onset of pain on 14.2.57). The electrocardiogram showed no significant abnormality, apart from low T waves in praecordial leads.

/2

ELECTROCARDIOGRAM CASE NO. 100 (1)







COMMENT:

Borderline levels of serum transaminase activity were demonstrated before cholecystectomy was performed. Chronic cholecystitis and cholelithiasis were present and a gallstone was removed from the common bile duct. There was no significant electrocardiographic abnormality.

A trace of bile was present in the urine. The results of liver function tests suggested that biliary obstruction was present but there was no evidence of jaundice on clinical examination.

Increased serum transaminase activity was probably due to biliary obstruction with diminished excretion of the enzyme. The presence of granularity and congestion of the liver surface, observed during the operation, raises the possibility of the rise in activity being due to release of the enzyme by liver cells damaged as a result of biliary obstruction.

No rise in serum transaminase activity was observed following the operation. The results of serial assay of transaminase activity in serum, bile and urine suggested that the enzyme may be excreted by the liver since the transaminase activity of bile was consistently higher than that of serum or urine.

CASE NO. 101.

A male, aged 55 years, a railway worker, was admitted to hospital on 13.3.57., complaining of dyspnoea on exertion of three months' duration.

The patient had been treated in hospital in December, 1954 and May 1955 for chronic cor pulmonale due to emphysema and chronic bronchitis.

In January 1957., the patient developed pleurisy over the base of the left lung posteriorly and, since then, he had become progressively breathless on exertion and had been having frequent attacks of bronchospasm. He was admitted to hospital for further investigation.

On admission to hospital, marked bronchospasm was present and the diagnosis of chronic cor pulmonale due to emphysema and chronic bronchitis was confirmed by clinical examination and X-Ray examination of the chest.

Electrocardiographic Findings.

I. 14.3.57: The electrocardiogram showed indirect evidence of right ventricular enlargement and diphasic T waves in V2 and V4., suggestive of right ventricular strain.

II. 18.3.57: The electrocardiogram showed no significant change.

III. 24.3.57: The electrocardiogram showed slight improvement in the right ventricular strain pattern.

Serial Serum Transaminase Activity.

13.3.57	:	12 units.
14.3.57	:	15 units.

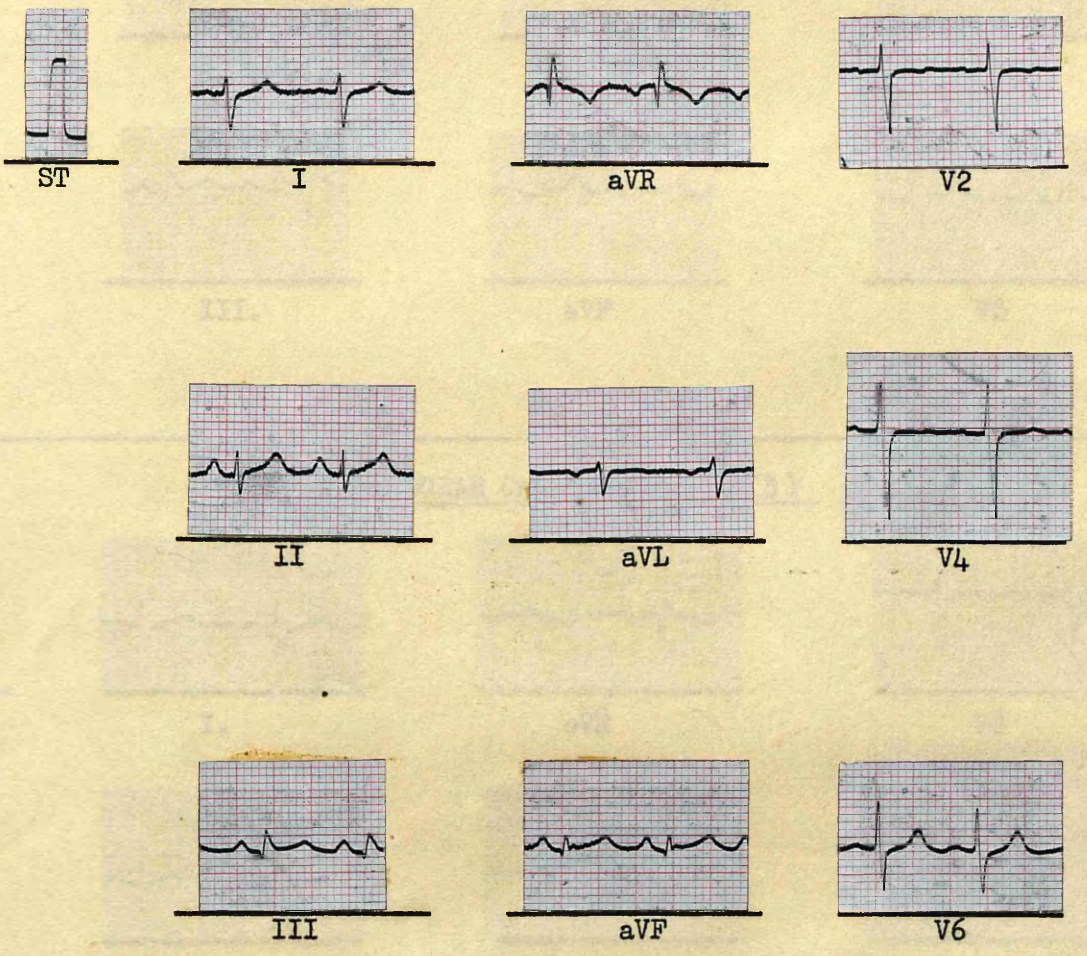
Erythrocyte Sedimentation Rate (Westergren).

18.3.57	:	3 mm/ 1st.hour.

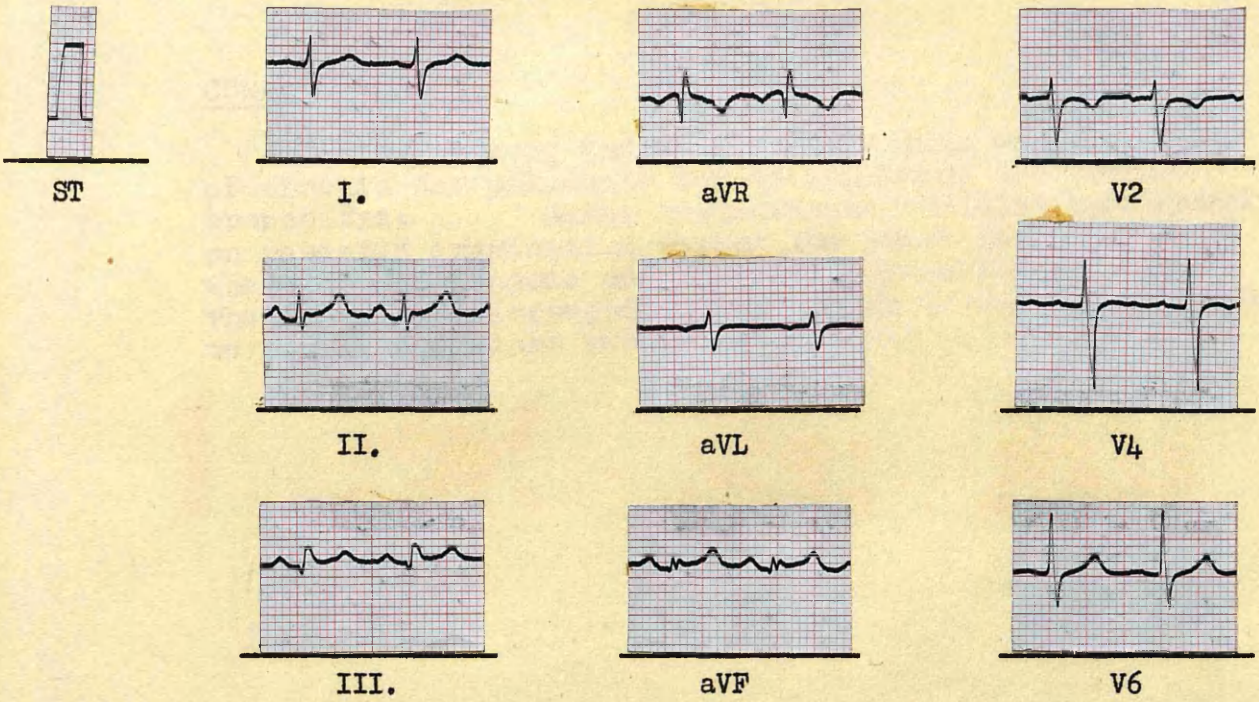
The patient was much improved symptomatically on his discharge from hospital on 5.4.57.

/2

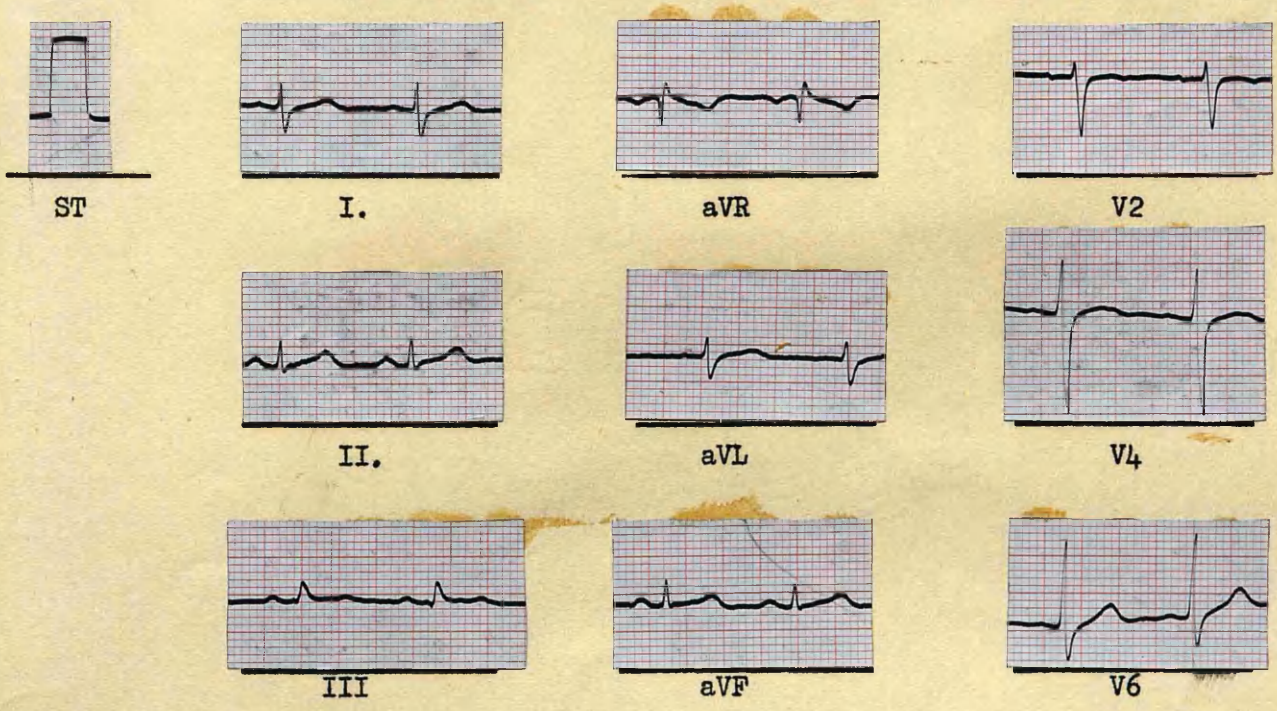
ELECTROCARDIOGRAM CASE NO. 101 (1)



ELECTROCARDIOGRAM CASE NO. 101 (2)



ELECTROCARDIOGRAM CASE NO. 101 (3)



COMMENT:

The history and clinical findings were typical of chronic cor pulmonale due to emphysema and chronic bronchitis. Serum transaminase activity was normal on repeated examination during the phase of the illness when marked dyspnoea due to bronchospasm was present. The electrocardiographic patterns, on serial examination, were those of right ventricular strain.

CASE NO. 102.

A male, aged 77 years, a retired engineer, was admitted to hospital on 24.3.57, complaining of breathlessness on slight exertion and at rest of three weeks' duration.

For 40 years the patient had had attacks of winter bronchitis and attacks of bronchospasm in association with hay fever in the summer months.

On admission, the clinical findings and the appearances in the X-ray film of the chest were compatible with the diagnosis of emphysema and chronic bronchitis complicated by severe attacks of bronchospasm.

Adrenaline, aminophylline, penicillin, given by parenteral route and oral digitalis leaf did not relieve the severe bronchospasm but, when oral prednisolone was administered on 28.3.57, there was immediate improvement which was maintained until his discharge from hospital on 21.4.57.

Electrocardiographic Findings.

I. 24 3.57: (recorded during acute dyspnoea). The electrocardiogram showed evidence of a lateral infarction of indeterminate age and also acute coronary insufficiency which could be associated with asthmatic attacks and tachycardia.

Serial Serum Transaminase Activity.

24.3.57	:	30 units.
25.3.57	:	38 units.
26.3.57	:	35 units.

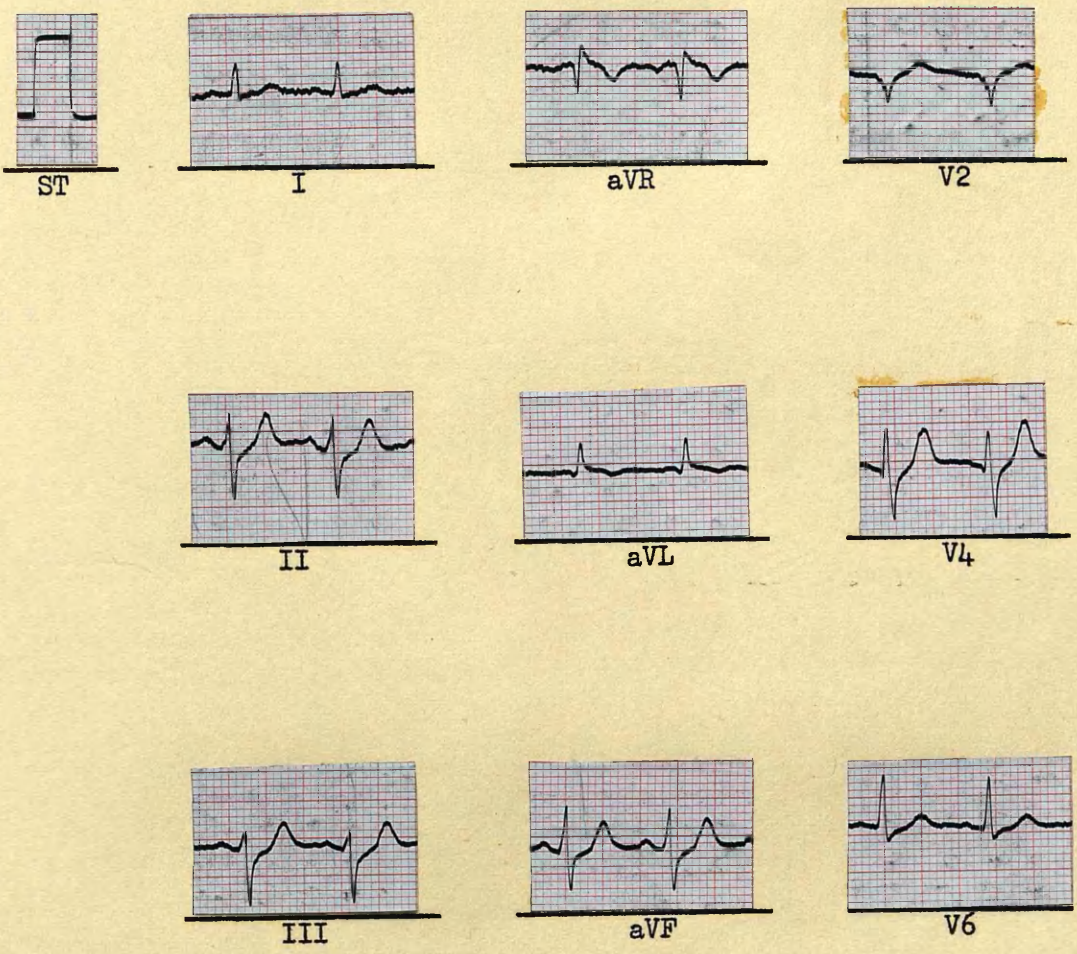
Erythrocyte Sedimentation Rate (Westergren).

25.3.57 : 17 mm/1st.hour.

COMMENT:

The final diagnosis in this case was one of asthma occurring in association with severe emphysema, chronic bronchitis and ischaemic heart disease. Bronchospasm was severe and prolonged and was relieved only by steroid therapy.

ELECTROCARDIOGRAM CASE NO. 102



The electrocardiographic patterns were those of acute coronary insufficiency and of a lateral myocardial infarction of indeterminate age. Acute myocardial infarction was not considered to have occurred.

Serial serum transaminase activity was normal during the acute phase of the illness.

The erythrocyte sedimentation rate was elevated when the serum transaminase was normal.

CASE NO. 103.

A male, aged 42 years, was admitted to hospital on 14.4.57., complaining of severe epigastric pain of three hours' duration.

Perforated peptic ulcer was diagnosed, and, at operation, a chronic ulcer in the anterior wall of the first part of the duodenum with a perforation in its centre was found.

The perforation was closed in the usual manner and the wound was closed.

Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Epigastric Pain.

Hours.	4
Units.	28.

COMMENT:

Serum transaminase activity was normal 4 hours after the onset of perforation of a chronic duodenal ulcer.

CASE NO. 104.

A male, aged 79 years, a traffic warden, was admitted to hospital on 31.3.57 complaining of generalised abdominal pain of colicky type of two days' duration.

The patient had had a gastro-enterostomy performed for duodenal ulcer in 1944.

On admission to hospital, there was evidence of his having sustained a perforation of bowel and the opinion was that a perforated peptic ulcer was the most likely diagnosis. In view of his poor general condition and the long delay in his reaching hospital it was thought inadvisable to perform a laparotomy and the patient was treated conservatively. The patient seemed to respond satisfactorily to these measures but, on 14.4.57., he developed a tender mass in the left iliac fossa which suggested a localised collection of pus. Eventually, this swelling pointed in the left iliac fossa and, on 16.5.57, the abscess was incised and a mixture of pus and faecal fluid escaped.

The patient's general condition gradually deteriorated until his death on 28.5.57.

Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Symptoms.

Hours.	48.
Units.	39.

Post Mortem Findings.

Post mortem examination revealed that a large stomal ulcer had perforated and that there was a low grade generalised peritonitis. In addition, an annular carcinoma of the transverse colon was present. There was no evidence of acute myocardial infarction.

COMMENT:

Normal serum transaminase activity was demonstrated 48 hours after perforation of a stomal ulcer. In addition, an annular carcinoma of the transverse colon was present.

CASE NO. 105.

A male, aged 49 years, a lorry driver, was admitted to hospital on 15.7.57 complaining of severe pain below the lower end of his sternum since 7.7.57 and of dyspnoea on exertion since 9.6.57.

The patient had had rheumatic fever in 1927 and had been subject to winter bronchitis with attacks of bronchospasm since 1950.

In 1955, the patient had had an attack of ulcer dyspepsia. On 9.6.57, he had stopped work because of a feeling of tightness in the chest.

At 6 p.m. on 7.7.57, the patient had developed a severe, burning pain below the lower sternum and in the epigastrium. This pain began one hour following a meal while the patient was resting. It did not radiate but was associated with intense nausea. Until 11.7.57, the pain was intermittent and was worst in the early hours of the morning. When severe, it was accompanied by vomiting; it became persistent and severe on 13.7.57 when it required omnopon, gr. 1/3 intramuscularly for its relief. During the first few days, the pain had been relieved by alkalis but, before admission, they had lost their effect. Nausea with occasional retching had become severe on 13.7.57.

Clinical Findings on Admission.

The patient complained of intense nausea. He was anxious and agitated and dyspnoeic at rest.

Cardiovascular System: B.P. 185/110 mm.Hg. The pulse was regular in rate (80/min.) and rhythm. The heart was not enlarged, the apex beat being situated in the fifth interspace 1" within the mid-clavicular line. The heart sounds were pure.

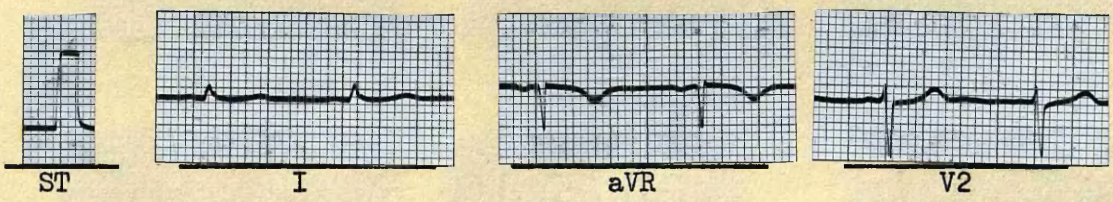
Respiratory System: The chest was barrel-shaped and the percussion note was hyper-resonant. High-pitched rhonchi was present throughout the lung fields.

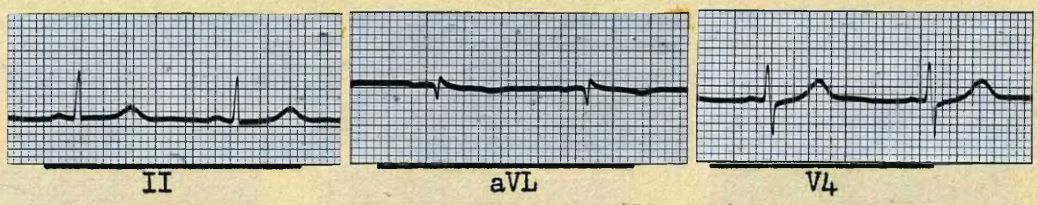
Alimentary System: There was slight guarding of the right rectus muscle in the epigastrium and also tenderness in the epigastrium.

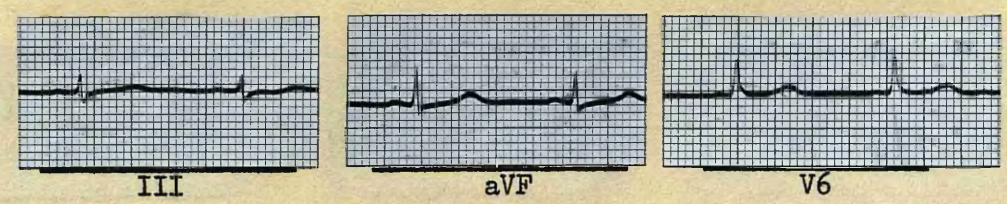
No other abnormality was found on full clinical examination.

/2

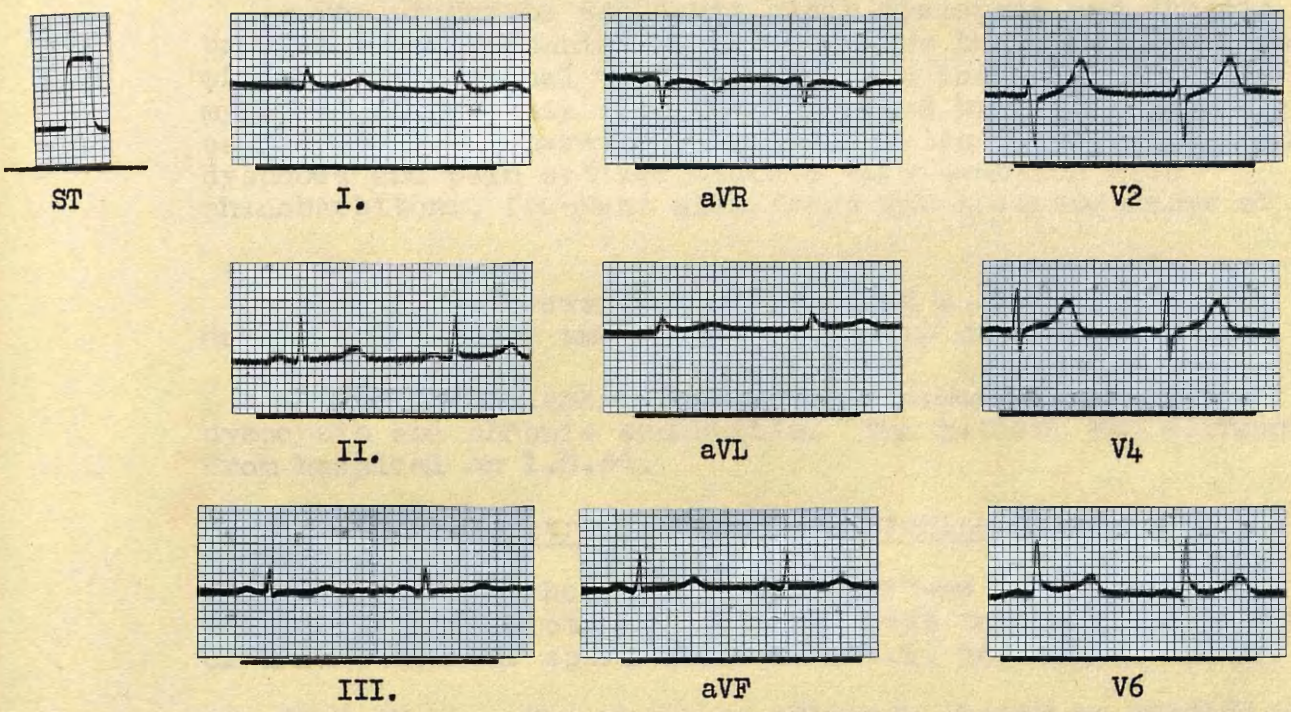
ELECTROCARDIOGRAM CASE NO. 1050)



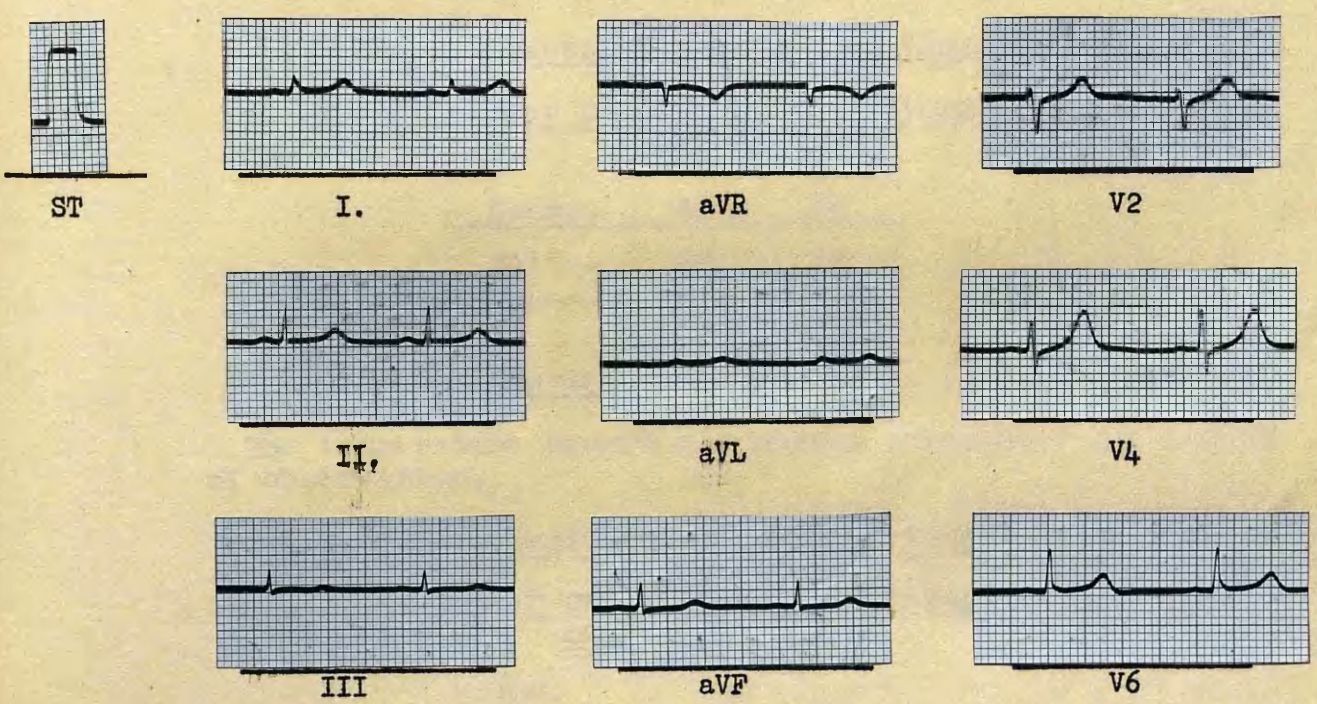




ELECTROCARDIOGRAM CASE NO. 105 (2)



ELECTROCARDIOGRAM CASE NO. 105 (3)



Treatment and Progress.

The diagnosis was acute ulcer dyspepsia and chronic bronchitis, accompanied by bronchospasm but the association of recurring sternal pain and dyspnoea indicated that myocardial ischaemia should be excluded by serial electrocardiograms. There was no fall in blood pressure and the dyspnoea and pain settled quickly with sedation with phenobarbitone, frequent milk feeds and adequate doses of

Barium meal examination revealed a small spastic duodenal cap. A small duodenal ulcer was present.

The final diagnosis was one of duodenal ulcer dyspepsia and chronic bronchitis. The patient was discharged from hospital on 1.8.57.

Electrocardiographic Findings.

I. 15.7.57. (48 hours after pain became persistent and severe). The electrocardiogram showed no definite evidence of infarction but appearances in a.V.L. were equivocal.

II. 23.7.57: The electrocardiogram showed no significant change. The appearances in a.V.L. were considered positional in origin.

III. 30.7.57: The electrocardiogram showed no change.

Serial Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Severe, Persistent Pain on 13.7.57.

Hours.	48	72
Units.	20	20

Temperature Record.

The temperature record was normal throughout the period of observation.

Erythrocyte Sedimentation Rate (Wéstergren.)

Time After Onset of Severe, Persistent Pain on 13.7.57.

Hours.	48
mm/1st.hr.	1

/3

COMMENT:

Normal serum transaminase activity was found on repeated examination during an attack of acute dyspepsia due to duodenal ulcer. Chronic bronchitis and bronchospasm were also present at this time.

CASE NO. 106.

A spinster, aged 65 years, was admitted to hospital on 7.6.57., complaining of severe epigastric pain of six hours' duration. The patient had been under observation in hospital from 6.5.57 until 27.5.57, having had an attack of lover sternal, epigastric and interscapular pain which was considered to be due to acute pancreatitis. This attack was treated conservatively, but the presence of a gallstone was noted. Following discharge from hospital on 27.5.57., the patient was well until noon on 7.6.57 when she developed severe epigastric pain which radiated through to the interscapular region.

On examination, the blood pressure was well maintained, (B.P. 140/95 mm.Hg.) and no abnormality of the cardiovascular system was found. There was marked guarding and tenderness on palpation of the epigastrium.

Treatment and Progress.

Acute relapsing pancreatitis was diagnosed and the symptoms settled with medical treatment. On 22.6.57., however, a mass was palpated in the upper abdomen and, on 24.6.57., laparotomy was performed. The gallbladder was felt to contain stones but none was palpable in the ducts. The pancreas was exposed to inspection and was enlarged and indurated. The pancreas was paler in colour than normal and the appearance was consistent with the diagnosis of acute recurrent pancreatitis. The fundus of the gallbladder was incised and one large gallstone and innumerable small seed stones were removed. The bile appeared normal. A drainage tube was sutured into the gallbladder and brought to the surface through a separate incision. The main wound was closed in layers.

The patient's post-operative course was uneventful. There was considerable drainage of bile. The drainage tube was removed on 4.7.57 and the patient was allowed home on 7.7.57.

No electrocardiograms or Erythrocyte Sedimentation Rate estimations were performed.

Temperature Record.

The temperature was 99.6°F on the day of admission and thereafter, was normal.

/2

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Severe Pain on 7.6.57.

Hours.	24	48
Units.	30	25.

Transaminase Activity in Serum, Bile and Urine Following Operation on 24.6.57.

25.6.57 :-	Serum Activity -	23 units.
	Bile " -	45 "
	Urine " -	5 "
28.6.57 :-	Serum Activity -	28 units.
	Bile " -	40 "
	Urine " -	3 "

Liver Function Tests.

22.6.57:- No abnormality was shown.

Serum bilirubin: Direct - negative. Indirect: 0.3mgm/100ml.
Hanger Flocculation : negative.
Serum Alkaline Phosphatase: 10.1 units (King, Armstrong.)
Total Plasma Protein: 6.8 gm/100ml. Plasma Albumin: 4.6gm/100ml.
Plasma Globulin: 2.2 gm/100ml.

COMMENT:

Normal serum transaminase activity was found when examined 24 and 48 hours after operation for pancreatitis when the acute symptoms had subsided. At operation, necrosis and haemorrhage was not found in the pancreas, the appearance of the organ being typical of recurrent interstitial pancreatitis, and there was no obstruction of the common bile duct although gallstones were present in the gallbladder. Tests of liver function before laparotomy was performed revealed no abnormality. Inflammatory changes in the pancreas may, therefore, occur with normal serum transaminase activity.

The presence of higher levels of transaminase activity in the bile than in the serum suggests that the enzyme may be excreted by the liver. The insignificant levels of transaminase activity in the urine as compared with those in the serum and bile suggest that this route of excretion is not an important one.

CASE NO. 107.

A married woman, aged 47 years, was admitted to hospital on 18.3.57 complaining of severe abdominal pain of four hours' duration. 20 hours before admission, the patient had complained of severe burning continuous pain behind the lower end of sternum which lasted for two hours and which cleared spontaneously. At noon on 18.3.57, while doing light housework, the patient was seized with severe burning pain behind the lower end of sternum which rapidly spread downwards across the abdomen; the pain was referred into the interscapular region and it was continuous but there were spasms of pain of great severity lasting for ten minutes.

There was no relevant past history.

Clinical Findings on Admission.

The patient was pale and shocked. The lips and finger tips showed cyanosis. There was no jaundice.

Cardiovascular System: B.P. 130/70 mm.Hg. The pulse was regular in rate (90/min.) and rhythm. The heart was not enlarged and the apex beat was palpable in the fifth interspace $\frac{1}{2}$" within the mid-clavicular line.

Alimentary System: The abdomen was rigid, the rigidity being most marked in the upper half of the abdomen. Rebound tenderness was present. Bowel sounds were present. Liver dullness was not diminished.

No abnormality was found on full clinical examination of other systems.

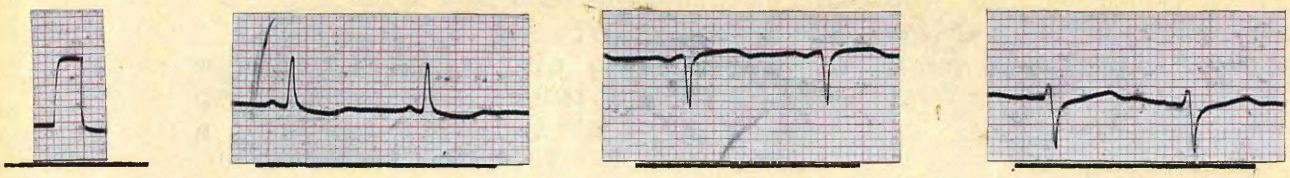
A tentative diagnosis of acute pancreatitis was made and the patient was transferred to the surgical wards.

Treatment and Progress.

19.3.57: The patient's condition was obviously deteriorating and a laparotomy was performed at 1 p.m. The serum amylase before operation was at high levels. (286 Wohlgemuth units/ml): normal less than 10 units). At operation, the peritoneal cavity contained abundant blood-stained fluid and patchy fat necrosis of the omentum was noted. The pancreas was exposed and was found to be the site of haemorrhage and necrosis. One gallstone was felt in the gallbladder while another was felt at the foramen of Winslow. This latter stone was presumed to be in the common bile duct and was fragmented during manipulations to return it to the gallbladder.

/2

ELECTROCARDIOGRAM CASE NO. 107(1)

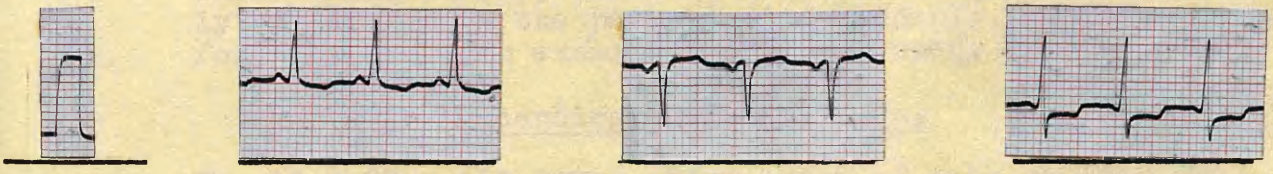


ST I. aVR V2

II. aVL V4

III. aVF V6

ELECTROCARDIOGRAM CASE NO. 107 (2)



ST I. aVR V2

II. aVL V4

III aVF V6

Cholecystostomy with removal of a mulberry calculus was performed. The gallbladder area and pancreas were drained and both tubes were brought to the surface through a lateral stab incision.

The patient's general condition was good and she made good progress, being allowed up on 29.3.57.

3.4.57: The patient developed a pancreatic fistula.

17.4.57: The wound was explored and another drainage tube was inserted at the site of the fistulous opening. Once again, the patient's condition improved following operation.

4.5.57: The patient had developed diabetes mellitus, requiring insulin treatment and she was passing frequent pale, unformed stools with a high fat content. Steatorrhoea and diabetes mellitus due to pancreatic insufficiency was diagnosed.

15.5.57: Despite low fat diet, diarrhoea had continued and hypopotassaemia, hypochloraemia and hypoalbuminaemia had developed. A macrocytic anaemia (Hb - 40%) was present.

17.5.57: Despite repeated blood transfusions and intravenous therapy directed at correcting severe electrolyte imbalances, the patient died suddenly. Permission for a post mortem examination was refused.

Electrocardiographic Findings.

I. 18.3.57: (30 hours after onset of pain on 17.3.57). The electrocardiogram showed the changes of acute coronary insufficiency.

II. 19.3.57: (45 hours after onset of pain on 17.3.57). The electrocardiogram showed more marked changes of acute coronary insufficiency. There was no evidence of myocardial infarction.

Serial Serum Transaminase Activity (Units/ml/min).

Time after Onset of Epigastric Pain on 17.3.57.

Hours:	24	48	72	96	120	144	168
Units:	462	237	71	58	54	40	35

/3

Temperature Record.

The temperature was 99°F on the day following admission and it was normal for the first week when transaminase estimations were performed.

Erythrocyte Sedimentation Rate (Westergren).

No estimations were performed.

Serial Tests of Liver Function.

Hours after onset of pain.	VAN DEN BERGH. Direct; Indirect mgm/100ml.		TURBIDITY. Thymol:	Zinc.
24	Pos.	2.0	3	9
48	Pos.	2.0	3	9

COMMENT:

Serum transaminase activity was increased to high levels for six days after the onset of acute haemorrhagic pancreatitis, associated with gallstones. At laparotomy, the pancreas was necrotic , haemorrhagic and omental fat necrosis was found. Gallstones were present, in the common bile duct and gallbladder.

The presence of positive Van Den Bergh reaction, raised serum bilirubin levels and slightly increased zinc turbidity indicated co-existing liver dysfunction. Serial electrocardiograms, taken 30 and 45 hours after the onset of the illness, showed the changes of acute coronary insufficiency. Unfortunately, further electrocardiographic studies were not made and acute subendocardial myocardial infarction was not finally excluded in this case. This is a possible explanation of the rise in serum transaminase activity in this case. However, the presence of pancreatic necrosis and bile duct obstruction suggested that these were probably the causes of increased serum transaminase activity although the mechanism of the rise in activity remained conjectural.

CASE NO. 108.

History of Present Illness.

A widow, aged 70 years, was admitted to hospital on 1.5.57 complaining of pain in the right side of her chest of 24 hours' duration.

For a year, the patient had been breathless on exertion and the dyspnoea was associated with a sense of constriction below the mid-sternal region. This was relieved by rest.

In March 1957., the dyspnoea on exertion became more severe and retrosternal pain, referred into both shoulders, was present on exertion, relieved by resting. The patient was advised to restrict her activity and was treated with digitalis leaf and phenobarbitone with good effect.

On 30.4.57., while sitting in her garden, she suddenly developed pain in the region of the 9th right costal cartilage. The pain was sharp and made worse by coughing and deep breathing. Blood streaking of the sputum had been noted on one occasion.

There was no relevant past history.

Clinical Findings on Admission.

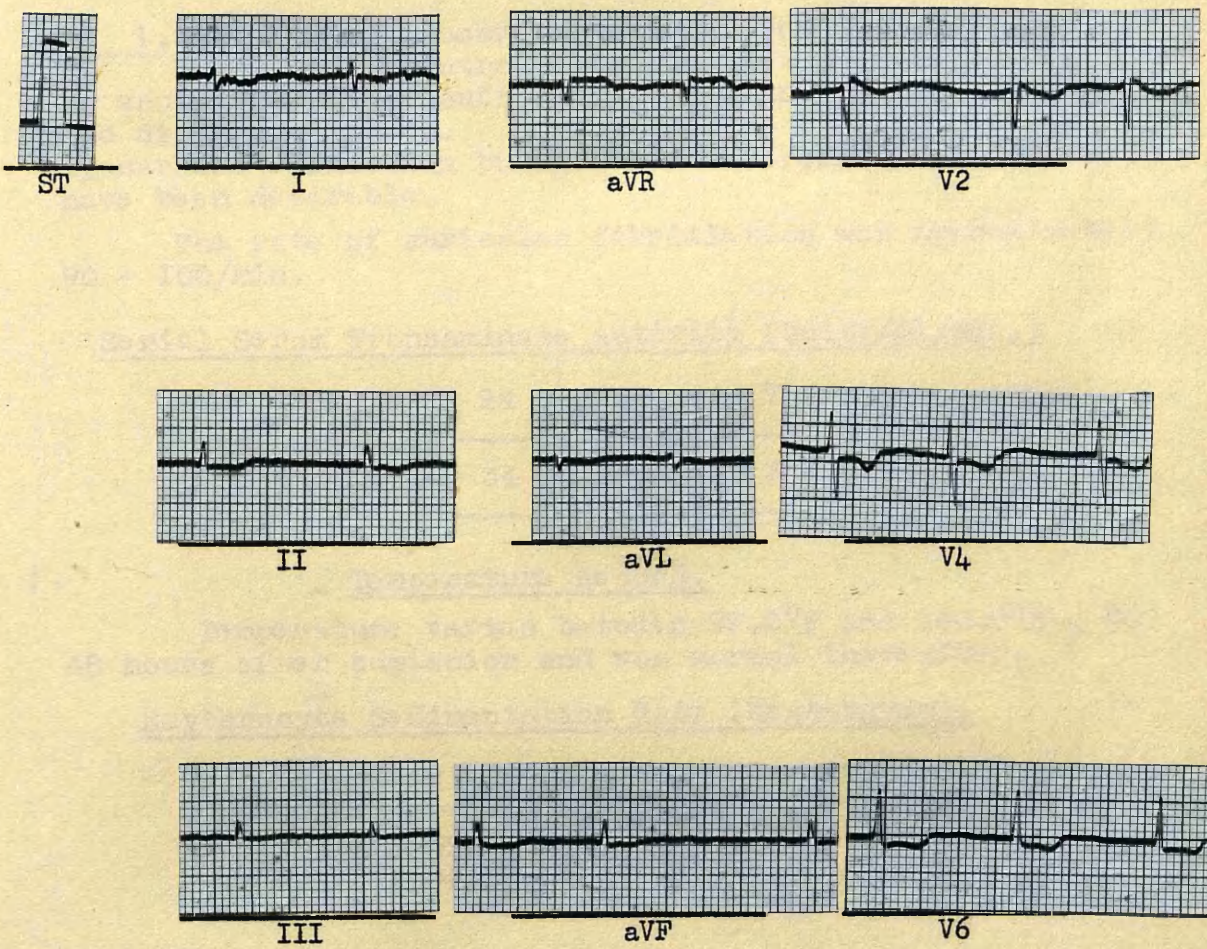
The patient was an elderly woman. There was no evidence of shock or congestive cardiac failure.

Cardiovascular System: B.P. 190/80 mm.Hg. The pulse was irregularly regular (90/min.) The heart was considerably enlarged, the apex beat being 2" outwith the mid-clavicular line in the fifth interspace. Soft systolic murmurs were present at all areas but no diastolic murmurs were heard. There was no evidence of phlebothrombosis of the leg veins.

Respiratory System: Expansion of the right side of the chest was limited. The percussion note was dull over the lower half of the right lung. The air entry was diminished in this area and numerous fine and medium crepitations were heard. Pleural friction was present in the right infra-axillary region.

No other abnormality was found on full clinical examination of other systems.

ELECTROCARDIOGRAM CASE NO. 108



Treatment and Progress.

Acute pulmonary infarction in association with auricular fibrillation and ischaemic heart disease was diagnosed.

Anticoagulant therapy was started shortly after admission and continued for 21 days. Digitalis therapy was continued i.e., digitalis leaf, gr. i b.d.

Serial X-Ray films of chest showed changes consistent with the diagnosis of pulmohary infarction.

The patient made an uninterrupted recovery and was discharged from hospital on 2.6.57.

Electrocardiographic Findings.

I. 1.5.57: (24 hours after onset of pain in chest). The electrocardiogram showed changes diagnostic of acute coronary insufficiency and auricular fibrillation, and digitalis effect. There was no evidence of recent myocardial infarction but serial electrocardiograms would have been desirable.

The rate of auricular fibrillation was approximately 90 - 100/min.

Serial Serum Transaminase Activity (Units/ml/min.)

Hours.	24	48	72
Units.	34	26	38

Temperature Record.

Temperature varied between 99.2°F and 100.6°F., for 48 hours after admission and was normal thereafter.

Erythrocyte Sedimentation Rate (Westergren).

Days.	1	15	21	28
mm/1st hr.	32	33	21	15

COMMENT:

Serum tra nsaminase activity was normal on repeated examination following the onset of acute pulmonary infarction. The site of embolus was presumed to be thrombus in the right auricular appendage, there being no evidence of phlebothrombosis elsewhere. Auricular fibrillation (90-100/min.) and ischaemic heart disease were present. The electrocardiograms showed auricular fibrillation, digitalis effect and changes diagnostic of acute coronary insufficiency. There was no evidence of recent myocardial infarction and serial electrocardiograms were not performed.

CASE NO. 109.

History of Present Illness.

A male, a gardener's labourer, aged 52 years, was admitted to hospital on 4.2.57 having fainted at work.

Since 2.2.57., the patient had felt unwell and had developed a slight cough and generalised aches and pains. He had also complained of a sharp pain situated to the left of the middle of the sternum, which was constant, of moderate severity and seemed to be accentuated by breathing.

On 4.2.57., while working, this pain became worse and the patient fainted.

There was no relevant past history.

Clinical Findings on Admission.

The patient was a thin, nervous individual of limited intelligence.

Cardiovascular System: B.P. 130/80 mm.Hg. The pulse was regular in rate (80/min.) and rhythm. The heart was not enlarged, the apex beat being situated 1" within the mid-clavicular line. The heart sounds were soft but pure.

No abnormality was found on full clinical examination of other systems.

Treatment and Progress.

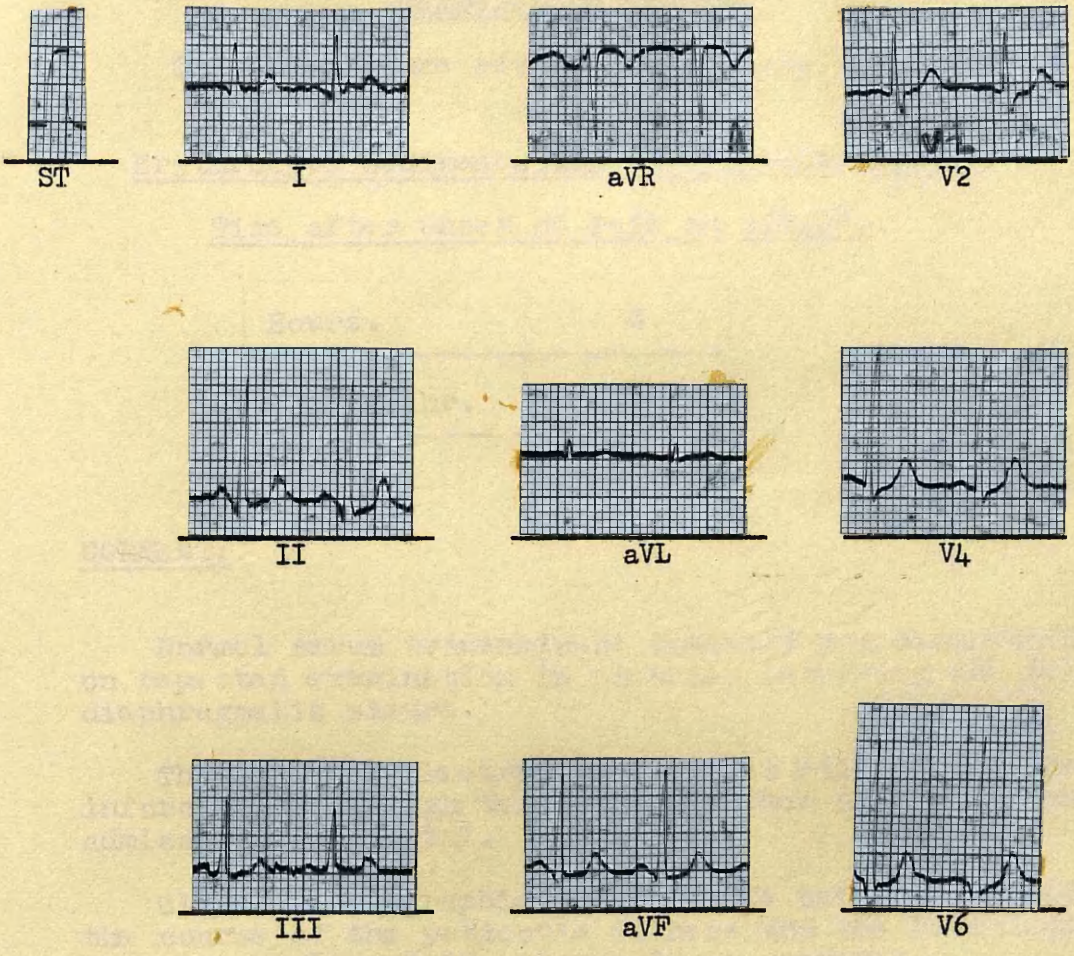
The patient had no symptoms following admission to hospital. History-taking was almost impossible because of the patient's limited intelligence. On admission, myocardial infarction was suspected, but serial X-Ray films showed changes consistent with the diagnosis of a recent left diaphragmatic pleurisy. No special treatment was given and the patient was discharged on 13.2.57.

Electrocardiographic Findings.

I. 7.2.57: The electrocardiogram showed S-T depressions in II, III, a.V.F., V4, V6., which were probably due to tachycardia. Appearances in a VL were equivocal but were probably positional in origin. No evidence of recent infarction was present but serial tracings would have been desirable.

/2

ELECTROCARDIOGRAM CASE NO. 109



Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Severe Pain with Collapse on 4.2.57.

Hours.	6	24	48
Units.	20	20	20

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren.)

Time after Onset of Pain on 4.2.57.

Hours.	6.
mm/1st.hr.	2

COMMENT:

Normal serum transaminase activity was demonstrated on repeated examination in pleurisy involving the left diaphragmatic pleura.

There was no electrocardiographic evidence of myocardial infarction, although this was suspected on the patient's admission to hospital.

Electrocardiographic studies were not complete but the course of the patient's illness and the radiological findings confirmed the diagnosis of pleurisy.

CASE NO. 110.

A male, aged 60 years, a labourer, was admitted to hospital on 13.2.57 complaining of loss of power of his right limbs with loss of speech of six hours' duration.

The patient had suddenly developed these symptoms while working. There was no relevant past history.

The clinical findings on admission were those of marked dysphasia and right hemiplegia. No cardio-vascular lesion was found apart from this and the blood pressure was normal. (B.P. 130/80 mm.Hg.) There was no serological evidence of syphilis.

The final diagnosis was thrombosis of the left middle cerebral artery with hemiplegia. The patient's recovery was incomplete. He was discharged from hospital on 21.5.57.

Electrocardiographic Findings.

Duplicate tracings were not available for inclusion.

The electrocardiogram showed no significant abnormality.

Serial Serum Transaminase Activity(Units/ml/min.)

Time after Onset of Hemiplegia on 13.2.57.

Hours.	6	23	47
Units.	5	10	8

Temperature Record.

The temperature record was normal for 48 hours after admission.

Erythrocyte Sedimentation Rate (Westergren).

No estimations performed.

COMMENT:-

Serum transaminase activity was measured repeatedly following the onset of cerebral thrombosis and normal levels of activity were demonstrated.

CASE NO. 111.

A male, aged 36 years, a hoistman, was admitted to hospital on 18.1.57 complaining of generalised swelling of the lymph glands of four weeks' duration.

On admission, pyrexia 100°F was present. There was generalised lymphadenopathy, the glands being painless, mobile and rubbery. The liver was enlarged, the liver edge being 3" below the right costal margin and irregular; there was no jaundice. No abnormality was found on full clinical examination of other systems.

A biopsy was performed on an axillary lymph node and histological examination of the gland revealed changes consistent with the diagnosis of early lymphadenoma.

Because of obvious liver involvement, serial serum transaminase estimations were performed. The patient was transferred to a radiotherapeutic centre, where he responded well to treatment.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Admission to Hospital.

Days.	5	6	7
Units.	30	25	33

COMMENT:

Serum transaminase activity was normal on repeated examination in a case of lymphadenoma in which there was clinical evidence of involvement of the liver in the disease process.

CASE NO. 112.

A female, aged 65 years, suffered from steatorrhoea, confirmed by fat balance studies, following partial pancreatectomy for carcinoma of the Ampulla of Vater.

The patient's general condition was good following treatment and, at the time when transaminase estimations were performed, the results of liver function tests were normal.

Serum Transaminase Activity.

17.11.56	: 7 units/ml.

COMMENT:

Normal serum transaminase activity was demonstrated in steatorrhoea due to pancreatic insufficiency, a result of partial pancreatectomy.

CASE NO. 113.

A male, aged 62 years, was admitted to hospital on 4.10.56 suffering from hyperparathyroidism.

Parathyroidectomy was performed on 21.11.56 and a parathyroid tumour was removed from the lower pole of the right lobe of the thyroid.

Histological examination showed the tumour to be a simple parathyroid adenoma.

Serum Transaminase Activity (Units/ml/min.) on 27.11.56. (6 days after the operation)

Days.	6
Units.	12.

COMMENT:

Serum transaminase activity was found to be normal six days after the removal of a parathyroid adenoma which had resulted in hyperparathyroidism.

CASE NO. 114.

A male, aged 71 years, a retired clerk, was admitted to hospital on 26.7.56 because of increasing breathlessness at rest

The patient had been treated in hospital for congestive cardiac failure from 7.3.56 until 4.7.56. He had relapsed and was again admitted for treatment.

The electrocardiogram taken on 6.3.56 had shown changes diagnostic of left bundle branch block. On 29.11.56 there was no change, there being no evidence of recent infarction.

Duplicate tracings were not available for inclusion in this study.

Treatment with digitalis leaf and mersalyl resulted in great improvement and the patient was discharged on 15.1.57.

At the time transaminase estimations were performed, the patient was suffering from congestive cardiac failure.

Serum Transaminase Activity (Units/ml.)

30.11.56	:	8 units.
1.12.56	:	10 units.

COMMENT:

Serum transaminase activity was normal on repeated examination in the presence of congestive cardiac failure due to ischaemic heart disease.

The electrocardiogram showed no evidence of acute myocardial infarction, but was diagnostic of left bundle branch block.

CASE NO. 115.

A married woman, aged 46 years, was admitted to hospital on 13.11.56., complaining of jaundice of six months' duration. On clinical examination, the only abnormalities found were jaundice and hepatomegaly. After thorough investigations, the diagnosis of primary hepatogenous jaundice, probably due to post hepatitis cirrhosis, was made. The patient was discharged from hospital on 23.11.56., the jaundice having lessened slightly.

Serum Transaminase Activity (Units/ml/min).

14.11.56	50 units.

14.11.56: Liver Function Tests.

Serum bilirubin: Direct :-	Positive +
Indirect:-	5.5. mgm per 100 ml.
Serum Total Cholesterol:	502 mgm. per 100 ml.
Plasma Alkaline Phosphatase:	41.1 units (King-Armstrong Method.)
Plasma Total Protein	8.2 gm. per 100 ml.
Plasma Albumin.	3.4. .....
Plasma Globulin.	4.8 .....
Albumin/Globulin.	0.71 : 1.
Blood Urea:	29 mgm. per 100 ml.
Thymol Turbidity Test: (Maclagan) -	23 units.
Zinc Turbidity Test: -	48 units.

Urine:	Bilirubin (Fouchet)	: Negative.
	Urobilinogen (Ehrlich)	: Positive +
	Urobilin (Schlessinger)	: Positive +
	Bile Acids (Hay)	: Negative.
	Albumin	: Negative.

Interpretation of Liver Function Tests.

Although the hypercholesteraemia and markedly increased alkaline phosphatase are suggestive of jaundice due to extrahepatic biliary obstruction, the hypoalbuminaemia and hyperglobulinaemia, grossly increased turbidities and the absence of bilirubin with excess of urobilin in the urine are in keeping with primary hepatogenous jaundice, probably a post hepatitis cirrhosis, judging from the high phosphatase and thymol turbidity levels.

Comment /over....2

COMMENT:

Borderline serum transaminase activity was demonstrated in a case of jaundice due to hepatic cirrhosis, the result of infective hepatitis.

The results of liver function tests were compatible with this diagnosis.

CASE NO. 116.

A retired master butcher, aged 66 years, was admitted to hospital on 15.11.56., complaining of swelling of the left ankle and leg of two months' duration. The swelling had gradually become worse. The patient complained of some pain in his left thigh. He had always suffered from constipation and recently had lost weight and had difficulty in starting micturition.

On examination after admission, pitting oedema of the left leg was present. The skin of the leg showed mottled cyanosis and there was tenderness and redness over the line of the left saphenous vein.

No abnormality was found on full examination of other systems. P.R. examination revealed no abnormality.

23.11.56: The patient complained of severe breathlessness during the night and he was mentally confused.

24.11.56: The electrocardiogram showed changes consistent with antero-lateral myocardial ischaemia but no evidence of myocardial infarction.

28.11.56: Icterus of conjunctivae was noted and oedema of right leg was now present. The jaundice deepened progressively and the patient became confused. He died on 13.12.56.

Serum Transaminase Activity (Units/ml/min.)

28.11.56 : 24 units.

28.11.56. Liver Function Tests.

Serum bilirubin: Direct - Positive.
Indirect - 1.5 mg per 100ml.

Serum Total Cholesterol: 361 mg per 100 ml.
Plasma Alkaline Phosphatase: 27.6 units(King-Armstrong Method.)

Plasma Total Protein:	7.8 gm. per 100 ml.
Plasma Albumin :	3.3 .....
Plasma Globulin ;	4.5 .....
Albumin/Globulin :	0.74 : 1.
Blood Urea :	46 mgm. per 100 ml.
Thymol Turbidity Test	(Maclagan) - 1 unit.
Zinc Turbidity Test :	- 2 units.

/2

Urine:

Bilirubin (Fouchet)	:	Weak Positive.
Urobilinogen (Ehrlich)	:	Positive.
Urobilin (Schlessinger)		Positive.
Bile Acids (Hay)	:	Negative.
Albumin	:	Trace.

Interpretation of Liver Function Tests.

Slight jaundice is present. It is difficult on the above findings to distinguish between primary hepatogenous jaundice (not due to infective hepatitis) and incomplete obstructive jaundice with secondary liver damage. Although the alkaline phosphatase is not increased into the zone considered characteristic of obstructive jaundice and there is excess urobilin in the urine, the normal turbidities make the second of the two alternative diagnoses more likely.

Post Mortem Findings.

Post mortem examination revealed an adenocarcinoma of the pelvic colon with innumerable metastatic tumours in the liver which weighed 1625 gm. The lower part of the inferior vena cava, the common iliac, external iliac and internal iliac veins were occluded by antemortem thrombus. There was hypertrophy of the left ventricle of the heart but no evidence of myocardial infarction.

COMMENT:

Normal serum transaminase activity was demonstrated when obstructive jaundice and thrombosis of the veins draining the lower limbs was present. The results of liver function tests were considered to be more suggestive of obstructive than of hepatogenous jaundice.

Post mortem examination revealed multiple metastases in the liver, which had derived from an adenocarcinoma of the pelvic colon. There was no evidence of acute myocardial infarction. Thrombosis of the inferior vena cava and other veins draining the lower limbs was confirmed.

CASE NO. 117.

A married woman, aged 47 years, was admitted to hospital on 1.11.56, for investigation of thyrotoxicosis and auricular fibrillation.

The patient had been examined in 1953 when operative removal of a large nodular goitre was advised. In October, 1956, she returned to hospital complaining of a change in her voice.

Examination on admission to hospital revealed a large nodular goitre, some exophthalmus and auricular fibrillation with mild congestive failure. An electrocardiogram on 3.11.56 showed auricular fibrillation (rate 80-90/min.) but no evidence of myocardial ischaemia. Duplicate records were not available for inclusion in this thesis.

The B.M.R. was raised (+ 72% and + 68%) and the results of radioactive iodine studies indicated thyrotoxicosis. The patient was discharged from hospital on 23.11.56., arrangements having been made for her treatment with radioactive iodine.

Serum Transaminase Activity (Units/ml/min)
Auricular Fibrillation (rate 90/min.)

14.11.56	:	10 units.
16.11.56	:	17 units.

COMMENT:

Normal serum transaminase activity was demonstrated on repeated examination in a patient suffering from thyrotoxic nodular goitre, auricular fibrillation and congestive cardiac failure. Auricular fibrillation was slow. (Heart Rate - 90 - 100/min.)

CASE NO. 118.

A married woman, aged 69 years, was admitted to hospital on 15.11.56., complaining of pain in the right hypochondrium and jaundice of 7 weeks' duration.

On admission, examination of the patient revealed on palpation of the abdomen a large craggy mass which was felt in the gallbladder area. The patient was jaundiced. There was evidence of loss of weight.

No other abnormality was found on full clinical examination.

A laparotomy was performed on 23.11.56 and a neoplastic mass was discovered in the upper abdomen, which involved the gallbladder, the duodenum and the transverse colon and which, posteriorly, seemed to be fixed to the pancreas. The lesion was considered to be a carcinoma of the gall-bladder with wide local spread. Excision was impossible. The patient was discharged home on 11.12.56.

21.11.56: Serum Transaminase Activity - Units/ml/min.

40 units.

21.11.56: Liver Function Tests.

Serum bilirubin:	Direct:	Positive -
	Indirect:	10 mgm per 100 ml.
Serum Total Cholesterol:		282 mgm. per 100 ml.
Plasma Alkaline Phosphatase:		63.2 units (King Armstrong Method.)
Plasma Total Protein:		6.4 mgm. per 100 ml.
Plasma Albumin:		3.3 .. .. ..
Plasma Globulin:		3.1 .. .. ..
Albumin/Globulin:		1.06: 1.

Blood Urea was 23 mgm. per 100 ml.

Thymol Turbidity Test (Maclagan):	1 unit.
Zinc Turbidity Test:	2 units.

Urine.	Bilirubin: (Fouchet) :	Positive.
	Urobilinogen:(Ehrlich):	Negative.
	Urobilin (Schlesinger):	Negative.
	Bile Acids (Hay) :	Positive.
	Albumin :	Positive.

/2

Interpretation of Liver Function Tests.

The slight hypercholesteraemia, greatly increased alkaline phosphatase and normal turbidity tests, together with the presence of bilirubin, without excess of urobilin in the urine, suggests that the jaundice is due to extra-hepatic biliary obstruction.

COMMENT:

Serum transaminase activity was demonstrated to be at the upper limit of normal in the presence of obstructive jaundice, shown at operation to be due to carcinoma of the gallbladder. The result of liver function tests indicated that the jaundice was due to extra-hepatic biliary obstruction.

CASE NO. 119.

A farmer, aged 67 years, was admitted to hospital on 17.11.56 complaining of gradually deepending jaundice, associated with pruritis of six weeks' duration.

On clinical examination, deep jaundice was present and the gallbladder was easily palpable suggesting the presence of obstructive jaundice of neoplastic origin.

On 23.11.56, an exploratory laparotomy was performed which showed the cause of obstruction to be a small carcinoma of the head of the pancreas which was obstructing the common bile duct. Liver biopsy confirmed the diagnosis of early obstructive jaundice. There was no evidence of secondary spread of the tumour and a preliminary cholecystostomy was carried out. Within a few days of this operation, the pruritis disappeared and the jaundice began to lessen.

On 12.12.56, the operation of pancreatic duodenectomy was performed. After a stormy convalescence, the patient was discharged from hospital on 5.2.57. Histological examination of the head of the pancreas showed a poorly differentiated adenocarcinoma of pancreas.

20.11.56: Serum Transaminase Activity (units/ml/min)

18 units.

20.11.56: Liver Function Tests.

Serum bilirubin: Direct-Positive ++.	Indirect:23.2 mgm/100 ml.
Serum Total Cholesterol:	248 mgm per 100 ml.
Plasma Alkaline Phosphatase:	31 units (King-Armstrong Method).
Plasma Total Protein:	5.5 gm per 100 ml.
Plasma Albumin:	2.5 .....
Plasma Globulin:	3.5 .....
Albumin/Globulin:	0.72 : 1.
Blood Urea:	43 mgm. per 100 ml.
Thymol Turbidity Test)Maclagan)	: 1 unit.
Zinc Turbidity Test:	: 4 units.

Urine:		
	Bilirubin (Fouchet)	: Positive ++
	Urobilinogen(Ehrlich)	: Negative.
	Urobilin(Schlesinger)	: Negative.
	Bile Acids (Hay)	: Positive.
	Albumin:	: Positive.

Interpretation of Liver Function Tests.

Although the cholesterol is normal, the alkaline phosphatase is not elevated to the extent considered characteristic of obstructive jaundice and there is marked hypo-albuminaemia, yet the normal turbidity tests and the absence of excess urobilinuria make the findings more suggestive of extra-hepatic biliary obstruction than of hepatogenous jaundice.

COMMENT:

Serum transaminase activity was normal in the presence of obstructive jaundice which was shown at operation to be due to carcinoma of the head of the pancreas. The results of liver function tests were equivocal but suggested a diagnosis of extra-hepatic biliary obstruction rather than hepatogenous jaundice.

CASE NO. 120.

A married woman, aged 43 years, had had a parathyroidectomy performed for hyperparathyroidism on 24.8.56. At operation, a simple adenoma of the parathyroid gland was removed from the right lower lobe of the thyroid gland.

She made a good recovery but was having occasional attacks of mild carpo-pedal spasm due to osteomalacia following parathyroidectomy when serum transaminase estimations were performed.

Serum Transaminase Activity.

8.12.56	6 units/ml.

COMMENT:

Serum transaminase activity was normal in osteomalacia which followed the removal of a parathyroid adenoma.

CASE NO. 121.

A spinster, aged 35 years, was admitted to hospital on 16.12.56 complaining of increasing nervousness, loss of weight and undue prominence of the eyes of six months' duration.

On examination, slight exophthalmos was noted, the thyroid gland was slightly enlarged; the patient perspired freely and she was hyperkinetic, and excitable.

B.P. 150/80 mm.Hg. Tachycardia (rate 116/min.) was present but the pulse was regular. The heart was not enlarged but a soft systolic bruit was present at the mitral area.

The patient had no symptoms referrable to the cardio-vascular system. The electrocardiogram showed sinus tachycardia (120/min.).

The clinical diagnosis of hyperthyroidism was confirmed by B.M.R. and radioactive iodine studies. Treatment with carbimazole 5 mgm t.i.d. was started and the patient was discharged from hospital on 19.12.56.

Serum Transaminase Activity.

15 units/ml/min.

COMMENT: Normal serum transaminase activity was demonstrated in a patient suffering from exophthalmic goitre. Sinus tachycardia (rate 120/min.) was present.

CASE NO. 122.

A male, aged 64 years, a chartered accountant, was admitted to hospital on 2.12.56., complaining of severe substernal pain of 3 hours' duration.

On 22.11.56., while hurrying home from work, the patient had developed substernal pain of constricting character which lasted for half an hour; it did not, however, force him to stop walking. On several occasions, since that time, he had had similar attacks of pain usually following exertion.

At midnight on 2.12.56., he was seized with severe gripping substernal pain, which radiated into the left arm and neck. The pain was associated with dyspnoea. He called on his family doctor at 3 a.m., who gave him an injection which relieved his pain.

There was no relevant past history.

Clinical Findings on Admission.

The patient was an elderly man, who looked ill.

Cardiovascular System: B.P. 100/70 mm.Hg. The pulse was regular in rate (100/min.) and rhythm. The apex beat was diffuse and was situated within the mid-clavicular line in the fifth left intercostal space. The heart sounds were faint, but pure.

Respiratory System: On auscultation, numerous medium crepitations and expiratory rhonchi were heard over the base of the left lung posteriorly.

No other abnormality was found on full clinical examination of other systems.

Treatment and Progress.

Anticoagulant therapy was started soon after admission, and was continued after the patient's discharge on 7.1.57. B.P. on discharge, was 120/70 mm.Hg.

Electrocardiographic Findings.

Duplicate electrocardiographic records are not available for inclusion in this study.

I. 3.12.56: (10 hours after the onset of pain on 2.12.56). The electrocardiogram showed changes diagnostic of an acute transmural antero-septal myocardial infarction.

II. 16.12.56: The electrocardiogram showed sequential changes confirming the diagnosis.

/2

Serial Serum Transaminase Activity (Units/ml/min.)

Hours.	10	34	58	82
Units.	116	120	51	27

Temperature Record.

The temperature was 98.8°F on day of admission.

Erythrocyte Sedimentation Rate (Westergren).

No estimations were performed.

COMMENT:

The history and clinical findings were indicative of a good risk myocardial infarction and the electrocardiogram was diagnostic of transmural myocardial infarction 10 hours after the onset of the illness. Pyrexia was absent, and there was minimal peripheral vascular failure. Serum transaminase activity was at high levels 10 hours after the onset but the assay was not considered to have contributed to the diagnosis.

CASE NO. 123.

A male, aged 64 years, was admitted to hospital on 14.11.56, complaining of frequency and difficulty in micturition and increasing loss of energy.

On admission, retention of urine was present and enlargement of the prostate was felt on rectal examination.

The patient was suffering from uraemia (blood urea 160 mgm per 100 ml).

The patient's symptoms were relieved by emergency prostatectomy and he made a good recovery.

Serum Transaminase Activity (Units/ml/min.)

14.11.56	:	19 units.

COMMENT:

Normal serum transaminase activity was demonstrated in a case of uraemia, secondary to prostatic hypertrophy, with retention of urine. This suggests that the renal pathway of excretion of the enzyme is not of great importance.

CASE NO. 124.

A male, aged 68 years, a retired labourer, was admitted to hospital on 26.4.57., complaining of vomiting of red blood.

On admission, the patient required blood transfusions and, on examination, slight icterus of conjunctivae, hepatomegaly and splenomegaly were present. After full investigation, the diagnosis of bleeding from oesophageal varices due to cirrhosis of the liver was made. The patient made a fairly good recovery and was transferred to a convalescent home on 2.6.57.

Serum Transaminase Activity (Units/ml/min.)

27.4.57	:	22 units.
3.5.57	:	16 units.

27.4.57: Liver Function Tests.

Serum bilirubin: Direct - Weak positive.
Indirect - 1.6 mgm per 100 ml.

Hanger Flocculation test:- ++++
Plasma Alkaline Phosphatase: 27 units (King-Armstrong Method)
Plasma Cholesterol: 138 mgm per 100 ml.
Plasma Total Protein: 5.5. gm. per 100ml.
Plasma Albumin; 2.8 .....
Plasma Globulin: 2.7 .....
Blood Urea: 44 mgm per 100 ml.

Interpretation of Liver Function Tests.

The findings suggested hepatogenous rather than obstructive jaundice.

COMMENT:

Normal serum transaminase activity was demonstrated on repeated examination in a case of jaundice due to cirrhosis of the liver in which bleeding occurred from oesophageal varices.

CASE NO. 125.

A spinster, aged 51 years, a housekeeper, was admitted to hospital on 11.1.57., complaining of jaundice and breathlessness on exertion of 1 month's duration.

On admission to hospital, the patient was obviously jaundiced and splenomegaly was present. Marked anaemia with reticulocytosis was present. (Hb: 48%: P.C.V.21%: M.C.H.C: 33g%.: Reticulocytes 16%.) The blood film showed macrocytosis, poikilocytosis and anisocytosis. Sections and smears of the sternal marrow showed a totally hyperplastic marrow due to normoblastic activity although erythroblastic activity was present. Coomb's Test (direct anti-human globulin test) was repeatedly positive while no abnormality was found on repeated examination of the fragility of the red blood cells. The patient was considered to be suffering from auto-immune haemolytic anaemia and her response to oral cortisone was very satisfactory. She was discharged from hospital on 16.2.57 to continue on a maintenance dose of cortisone.

Serum Transaminase Activity (Units/ml/min.)

12.1.57	:	16 units.
13.1.57	:	25 ".

Results of Liver Function Tests. (12.1.57)

Serum bilirubin: Direct - positive. Indirect: 8.7 mgm per 100 ml. Serum Cholesterol: 143 mgm per 100 ml.
Serum Alkaline Phosphatase: 12 units (King Armstrong)
Hanger Flocculation Test: + + + +

Electrophoresis of the plasma proteins showed a diffuse increase in the gamma globulin fraction.

Urine: Bile pigments (Fouchet) : negative.
Urobilinogen (Ehrlich) : strongly positive.

COMMENT:

Serum transaminase activity was normal on repeated examination in a case of haemolytic anaemia in which jaundice was a feature.

CASE NO. 126.

A male, aged 56 years, a clerk, was admitted to hospital on 10.1.57., suffering from bronchopneumonia of the base of the right lung. On examination, the liver was moderately enlarged, there was slight icterus of conjunctivae and signs of peripheral neuropathy were found in the lower limbs. The patient had been addicted to alcohol for many years and a diagnosis of hepatic cirrhosis with peripheral neuritis, probably due to alcohol, was made. The patient made a good recovery and was discharged from hospital on 20.2.57.

Serum Transaminase Activity (Units/ml/min).

21.1.57	:	52 units.

21.1.57: Liver Function Tests.

Serum bilirubin: Direct - Positive.
Indirect - 2.5 mgm%
Serum Alkaline Phosphatase - 14 units (King Armstrong Method)
Thymol Turbidity Test (Maclagan) - 3 units.
Zinc Turbidity Test - 11 units.

Interpretation of Liver Function Tests.

The findings were considered suggestive of hepatogenous jaundice.

COMMENT: A high level of serum transaminase activity was demonstrated in a case of jaundice due to cirrhosis of the liver. The results of liver function tests supported the clinical diagnosis.

CASE NO. 127.

A male, aged 31 years, a labourer, was admitted to hospital on 9.1.57., complaining of pain in the right side of the upper abdomen and of deepening jaundice of one month's duration.

On examination, the patient was deeply jaundiced; the liver was markedly enlarged and its surface was irregular. The diagnosis of obstructive jaundice was made and an exploratory laparotomy was performed on 12.1.57. Massive hepatic tumour was found. Examination of the biopsy specimen showed changes consistent with the diagnosis of primary hepatoma.

11.1.57: Serum Transaminase Activity: 72 units/ml/min.

11.1.57: Liver Function Tests.

Serum Bilirubin: Direct: Strongly positive.
Indirect: 17.3 mgm per 100 ml.

Serum Alkaline Phosphatase: 90.7 (King Armstrong Units).

Thymol Turbidity Test (Maclagan) : 1 unit.

Zinc Turbidity Test. : 4 units.

The liver function tests were characteristic of obstructive jaundice.

COMMENT:

Serum transaminase activity was found to be at high levels in obstructive jaundice due to primary tumour of liver. The liver function tests showed changes typical of obstructive jaundice.

CASE NO. 128.

A male, a labourer, aged 60 years, was in hospital from 2.1.58 until 4.2.58., suffering from congestive cardiac failure due to severe emphysema and chronic bronchitis of many years' duration. The degree of respiratory insufficiency was very severe and the congestive cardiac failure was unresponsive to drugs.

Electrocardiographic Findings.

The electrocardiographic findings on serial examination were those of right ventricular hypertrophy and strain, but duplicate tracings are not available for inclusion.

Serum Transaminase Activity.

The serum transaminase activity was measured during attacks of acute bronchitis.

20.2.58:	Serum transaminase activity:	16 units.
21.2.58:	" " " :	22 "
22.2.58:	" " " :	26 "

COMMENT:

The history and clinical findings were typical of chronic cor pulmonale due to severe emphysema and chronic bronchitis. The electrocardiographic patterns were those of right ventricular hypertrophy and strain. During attacks of acute bronchitis, marked by severe dyspnoea and bronchospasm, serial serum transaminase activity was normal.

CASE NO. 129.

A married woman, aged 44 years, was admitted to hospital on 22.3.57 complaining of increasing breathlessness on exertion and of retrosternal pain of three months' duration.

The patient had been known to have mitral stenosis of rheumatic origin since 1953 but she had been symptom-free until December 1956 when she began to be breathless on exertion. This symptom had grown worse and on 13.3.57., the patient began to have attacks of breathlessness at rest, which were accompanied by a gripping, aching sensation in the retrosternal region which was not referred and which was not closely related to exertion. This pain, which might last for several hours, was unresponsive to trinitrin.

The diagnosis of mitral stenosis and incompetence was confirmed on clinical and radiological examinations. There was no evidence of auricular fibrillation or other arrhythmia. Pulmonary oedema was present on admission but responded to treatment with digitalis leaf. The patient was discharged from hospital on 13.5.57.

Electrocardiographic Findings.

Duplicate tracings are not available for inclusion.

Serial electrocardiograms showed no evidence of myocardial infarction, but showed "pulmonary" P waves and evidence of right ventricular enlargement.

Serial Serum Transaminase Activity (Units/ml/min.)

Time after Onset of Acute Dyspnoea and Praecordial Pain on 24.3.57.

Hours.	24	48
Units.	12	24

Temperature Record.

The temperature record was normal.

Erythrocyte Sedimentation Rate (Westergren.)

25.3.57	:	4 mm/1st.hr.

COMMENT: /2

Case 129 (ctd)

COMMENT:

Serum transaminase activity was normal on repeated examination in mitral stenosis and incompetence of rheumatic origin. Pulmonary oedema was present when the assay was performed.

CASE NO. 130.

A male, aged 36 years, a dyer, had been in hospital on four occasions since 1956, suffering from recurrent attacks of haemoptysis due to auricular fibrillation and mitral stenosis and incompetence of rheumatic origin. Unfortunately, the patient also suffered from aortic stenosis and incompetence of rheumatic type of a degree that precluded the operation of mitral valvotomy.

On 13.5.57., the patient was re-admitted having suffered renal embolism with infarction of the left kidney which had given rise to pain in the left renal angle and macroscopic haematuria. There was no evidence of sub-acute bacterial endocarditis.

Serial electrocardiograms showed no evidence of myocardial infarction, but showed auricular fibrillation (rate 80-90/min.) and right axis deviation.

The patient responded well to treatment with digitalis and anticoagulants and he was discharged from hospital on 14.6.57.

Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Pain in Left Renal Angle on 13.5.57.

Hours.	12	36
Units.	16	22

COMMENT:

Serum transaminase activity was normal on repeated examination following the onset of renal artery embolism. Auricular fibrillation (rate 80-90/min.) and combined mitral and aortic valve lesions of rheumatic origin were present.

CASE NO. 131.

A male, aged 47 years, was admitted to hospital on 10.3.57 suffering from right homonymous hemianopia due to thrombosis of the left posterior cerebral artery, in association with severe hypertension. (B.P. 220/140 mm.Hg)

The patient had been known to suffer from essential hypertension since June, 1956, when he had been treated in hospital for dysphasia and right hemiplegia due to thrombosis of the left middle cerebral artery. The patient also suffered from diabetes mellitus, the glycosuria being easily controlled by restriction of diet.

Electrocardiographic Findings.

The electrocardiogram showed evidence of left ventricular strain but no evidence of myocardial infarction.

The patient made a partial recovery from his illness and he was discharged from hospital on 28.3.57.

Serial Serum Transaminase Activity. (Units/ml/min)

Time After Onset of Cerebral Thrombosis on 9.3.57.

Hours.	24	48
Units.	24	30

COMMENT:

Serum transaminase activity was demonstrated to be normal on repeated examination following the onset of cerebral thrombosis. Essential hypertension of severe degree was also present at this time. The patient was known to suffer from diabetes mellitus of mild degree, glycosuria being easily controlled by restriction of diet.

CASE NO. 132.

A married woman, aged 39 years, was admitted to hospital on 10.3.57, complaining of attacks of epigastric pain of 20 hours' duration.

For a year, she had complained of attacks of upper epigastric pain, unrelated to food. On 9.3.57., an attack of pain started which radiated into the left flank and was accompanied by severe nausea and vomiting.

On admission to hospital, there was no jaundice but rigidity and tenderness were present in the epigastrium and left hypochondrium. A clinical diagnosis of acute relapsing pancreatitis was made and laparotomy was performed 24 hours after the onset of the illness. At operation, free fluid was present in the abdominal cavity. The pancreas was very oedematous and hard. The peritoneum was also oedematous and bile-stained with a few foci of fat necrosis. The gallbladder was distended and tense with multiple small stones and stones were also palpated in the cystic and common bile duct. The common bile duct was dilated. It was opened and several small cholesterol stones were washed out of it, along with purulent material. Following effective clearing of the common bile duct, the gallbladder was removed. The patient made an uninterrupted recovery.

Serum Transaminase Activity (Units/ml/min.)

Time After Onset of Abdominal Pain.

Hours.	24.
Units.	38

COMMENT:

Acute pancreatitis may occur without increase in serum transaminase activity.

CASE NO.133.

A married woman, aged 27 years, was admitted to hospital on 23.11.56, suffering from bronchopneumonia of the lower lobe of the right lung.

On admission to hospital, the patient had had severe pleural pain for 12 hours. There was clinical evidence of consolidation of the lower lobe of the right lung and coarse pleural friction was present over this area.

An X-Ray film showed consolidation of the lower lobe of the right lung.

The patient was treated with penicillin and made a good recovery. She was discharged from hospital on 15.12.56.

Serum Transaminase Activity (Units/ml/min)

Hours.	12	36	48
Units.	23	18	25

COMMENT:

Acute bronchopneumonia and pleurisy were associated with normal serum transaminase activity.

Case No. 134.

A girl, aged 15 years, after full investigation in hospital was found to be suffering from Vitamin D resistant rickets. A massive daily dose of calciferol, (400,000 I.U.) was required for the control of this condition.

The patient did not always co-operate by taking Vitamin D regularly and when serum transaminase activity was measured, plasma alkaline phosphate was high, suggesting that the rickets was not fully controlled. (20 King Armstrong Units).

Serum Transaminase Activity.

30.11.56 :	14 units/ml.

CASE NO. 135.

A married woman, aged 47 years, had had the operation of parathyroidectomy performed for the removal of a simple parathyroid adenoma on 22.5.56.

The history was unusual. The patient had suffered from coeliac disease since the age of 15 years. In 1955, she complained of generalised aching of the bones and, at that time, steatorrhoea was confirmed by fat balance studies. Her symptoms responded well to treatment with a gluten free diet and calciferol 50,000 I.V. daily, but it was observed that hypercalcaemia developed with this maintenance dose of Vitamin D. The patient complained of pains in the loins and back in March 1956 and once again hypercalcaemia was noted accompanied by low levels of serum phosphate. After full investigation of bone metabolism, hyperparathyroidism was diagnosed and exploration of the neck revealed a parathyroid adenoma, which was removed.

The patient made a good recovery from the operation and the biochemical findings became normal. She has maintained good health on a gluten free diet.

Serum Transaminase Activity.

14.11.56	:	14 units/ml.
28.11.56	:	10 units/ml.

VOLUME II.

APPENDIX III.

TABLE I.

Serum and Urine Transaminase Activity in Controls.

TABLE I.

Control.	Sex.	Age	SGOT ACTIVITY. units/ml/min.	Physical Condition.
1.	M	23.	7, 10.	Resting: after exercise.
2.	M	23.	13, 17.	Resting: after exercise.
3.	M	23.	11, 15.	Fasting: after hearty meal.
4.	F	36.	16, 12, 13.	Normal.
5.	F	32.	26, 35, 28.	Normal.
6.	F	25.	+5(U)15.	Normal.
7.	F	41.	+3(U)10.	Normal.
8.	M	25.	29, 30, 35.	Normal.
9.	M	37.	14, 10.	Normal.
10.	M	20.	9.	Torn cartilage (R. knee.)
11.	M	15.	5.	Torn cartilage (R. knee.)
12.	F	40.	10.	Prolapsed lumbar disc.
13.	M	41.	11.	Torn ligaments of ankle.
14.	M	52.	22.	Ganglion of wrist.
15.	M	59.	31.	Sebaceous Cyst.
16.	F	46.	32.	Varicose Veins.
17.	M	60.	14.	Hallux Rigidus.
18.	M	48.	12.	Carpal Tunnel Syndrome.
19.	F	55.	15.	Osteoarthritis of Knee.
20.	M	65.	10.	Cervical Spondylosis.
21.	F	23.	16.	Flat Feet.
22.	F	62.	10.	Hallux Valgus.
23.	F	39.	22.	Bruised Ankle.
24.	M	45.	12.	Prolapsed lumbar disc.
25.	M	39.	10.	Bruised Shoulder.

+ (U):- Transaminase Activity of Urine.

TABLE II.

Serial Serum Transaminase Activity in 39 attacks of Acute Transmural Myocardial Infarction in which a Rise in Activity was Demonstrated.

	TIME AFTER CLINICAL ONSET.						
Case No.	0-6 hrs. Units.	6-24 Units.	24-48 Units.	48-72 Units.	72-96 Units.	96-120 Units.	1 wk. Units.
1.	-	90	176	328	135	66	50
3.	-	-	-	238	199	-	-
5.	17	247	140	91	51	35	30
9.	-	-	-	-	-	84 (6 days)	30
11a.	-	-	158	87	36	-	-
12.	10	186	164	82	24	-	32
13a.	-	-	-	-	80	60	-
14.	-	-	62	36	17	-	12
15.	-	60	65	56	29	25	-
17.	33	171	93	60	25	25	-
20a.	-	50	130	250	140	80	35
21.	-	85	135	90	50	30	25
22.	37	198	208	150	72	35	-
23.	33	-	200	153	80	69	35
25c.	-	100	116	-	80	49	30
26.	-	-	193	139	94	66	37
27.	-	128	235	146	113	57	40

TABLE II. (ctd).

	TIME AFTER CLINICAL ONSET.						
Case No.	Hrs. 0-6 Units.	Hrs. 6-24 Units.	Hrs. 24-48 Units	Hrs. 48-72 Units	Hrs. 72-96 Units	Hrs 96-120 Units	1 week Units
28.	-	-	-	-	-	57	45
31a.	-	85	84	60	28	19	-
31b.	37	107	54	-	49	30	-
34.	30	240	200	493	-	-	-
35.	-	120	190	-	-	-	-
36a.	-	-	120	60	35	-	-
37.	-	98	65	-	-	-	-
40.	-	-	-	65	25	-	-
41.	30	77	40	25	-	-	-
42a.	-	135	180	84	38	-	-
42b.	-	82	36	-	-	-	-
44.	-	90	173	62	50	25	-
45.	-	126	100	76	32	-	-
46.	27	66	105	58	-	34	-
47a.	-	-	110	63	22	-	-
47b.	-	75	46	-	-	-	-
48.	-	24	55	56	37	-	-
50.	-	183	274	118	73	59	34
55.	-	-	-	-	90	-	-
59.	-	120	-	-	-	-	-
69.	-	313	-	-	-	-	-
122.	-	116	120	51	27	-	-

TABLE III.

Serial Serum Transaminase Activity in 6 attacks of Acute Intramural Myocardial Infarction in which a Rise in Activity was Demonstrated.

Case No.	TIME AFTER CLINICAL ONSET.						
	0 - 6 Units	H 6 -24 Units	O 24-48 Units	U 48-72 Units	R 72-96 Units	S 96-120 Units	1 week Units
7.	-	73	38	-	23	40	21
25a.	25	55	19	35	-	-	-
25b.	-	55	80	43	30	-	-
39.	25	-	58	50	30	-	-
43.	-	-	56	21	11	-	-
71.	-	55	85	48	34	-	-

TABLE IV.

Serial Serum Transaminase Activity in 5 Attacks of Acute Myocardial Infarctions in which the Electrocardiogram was not diagnostic of Acute Infarction but in which a Rise in Activity was demonstrated.

Case No.	TIME AFTER CLINICAL ONSET. HOURS						
	0 - 6	6-24	24-48	48-72	72-96	96-120	1 week
	Units	Units	Units	Units	Units	Units	Units
6.	-	83	209	-	-	-	-
10.	-	60	32	32	34	-	30
11b.	36	60	86	40	34	-	-
19b.	-	51	60	40	20	15	-
24.	-	-	220	117	-	-	-

TABLE V.

Serial Serum Transaminase Activity in Cases of Myocardial Infarction Diagnosed on Clinical Grounds, in which a Rise in Activity was Demonstrated.

Case No.	TIME AFTER CLINICAL ONSET.						
	0-6 Units	6-24 Units	24-48 Units	48-72 Units	72-96 Units	96-120 Units	1 week Units
2	30	-	110	-	-	-	-
13b.	-	620	-	-	-	-	-
20b.	30	90	60	45	32	-	-
36b.	-	75	-	-	-	-	-
38.	30	73	-	-	-	-	-
77.	30	95	-	-	-	-	-

TABLE VI.

Attacks of Acute Myocardial Infarction in which Increased Serum Transaminase Activity was not Demonstrated.

Case No.	TIME AFTER ONSET OF SEVERE SYMPTOMS WHICH OCCASIONED ADMISSION TO HOSPITAL.						
	0-6 Units	6-24 Units	24-48 Units	48-72 Units	72-96 Units	96-120 Units	1 wk. Units
4.	23	-	-	-	-	-	-
8.	-	-	-	35	40	35	35
16.	25	-	23	26	21	23	20
18.	30	-	-	-	-	-	-
19a.	-	-	-	17	12	9	7
29.	-	34	23	20	22	-	-
49.	-	45	30	25	-	-	-
51.	-	15	21	19	-	-	-
54.	-	30	19	20	-	-	-
56.	-	35	30	32	-	-	-
84.	-	24	17	10	-	-	-

TABLE VII.

Serial Serum Transaminase Activity Following Attacks of Angina Pectoris at Rest.

Case No.	TIME AFTER CLINICAL ONSET. HOURS 0-6 Units.	6-24 Units	24-48 Units	48-72 Units	72-96 Units	96-120 Units.	1 week. Units.
2.	29	31	22	22	43	26	25
7.	21	20	20	22	-	-	-
8.	40	35	35	29	-	-	-
11.	-	18 20	-	-	-	-	-
25d.	-	16	19	20	-	-	-
25e.	-	42	31	24	-	-	-
25f.	30	-	35	25	23	-	-
26	-	17 20	16	17	23	27	-
30a	-	2 0	20	-	-	-	-
30b.	16	35	19 23	-	-	-	-
32.	-	26	31	24	-	-	-
33.	-	27	23	30	18	-	-
52.	-	30	25	32	-	-	-
53.	-	23 31	28	-	-	-	-
57.	-	33	28	-	-	-	-
58a.	-	20	16	-	-	-	-
58b.	16	28	-	-	-	-	-
60	-	24	19	-	-	-	-
61.	18	20	20	-	-	-	-
62.	-	6	8	6	-	-	-
65.	-	26	20	18	-	-	-
67.	-	20	25	23	-	-	-
68a.	-	23	31	-	-	-	-
68b.	-	43	22	20	-	-	-
77.	-	-	27	33	-	-	-

TABLE VIII.

CARDIOVASCULAR CONDITIONS OTHER THAN ACUTE MYOCARDIAL INFARCTION AND ANGINA PECTORIS AT REST IN WHICH SERUM TRANSAMINASE ACTIVITY WAS MEASURED.

CONDITION.	NO.	CONDITION.	NO.
Ischaemic heart disease.	6	Uraemic Pericarditis.	1
Left Ventricular Failure.	4	Cerebral Infarction.	4
Congestive Cardiac Failure.	3	Acute Pulmonary Infarction.	6
Essential Hypertension.	4	Other thrombo-embolic conditions.	6
Chronic cor pulmonale.	4	Dissecting Aneurysm of the Aorta.	2
Acute Rheumatic Fever.	2	Cardiac Arrhythmia.	10.
Chronic Rheumatic Valvular Disease of Heart.	8		

TABLE IX.

DISEASES OUTWITH THE CARDIOVASCULAR SYSTEM IN WHICH SERUM TRANSAMINASE ACTIVITY WAS MEASURED.

CONDITION.	NO.	CONDITION.	NO.
Peptic Ulcer.	1.	Diabetes Mellitus.	2
Perforation of Peptic Ulcer.	5.	Thyrotoxicosis.	2
Hiatus Hernia.	2.	Cholelithiasis.	5
Steatorrhoea.	2.	Acute Pancreatitis.	3
Pulmonary Tuberculosis	2.	Jaundice due to Neoplasm.	4
Pleurisy and Bronchopneumonia.	3.	Jaundice due to Hepatic Cirrhosis.	4
Neoplasm of Lung.	2.	Haemolytic Anaemia.	1
Metabolic Bone Disease.	3.	Lymphadenoma.	1
		Uraemia.	2
		Oliguria.	1

TABLE X.

The Results of Liver Function Tests and Serum Transaminase Assay Following Acute Transmural Myocardial Infarction.

Case No.	Time After Onset-HRS.	VAN DEN BERGH. Direct - Indirect.		TURBIDITY. Thymol.	Zinc.	SERUM TRANSAMINASE ACTIVITY. (Units.)
1.	65	Pos.	1.8	1	2	328
3.	53	Neg.	0.7	-	-	179
	80	"	1.3	-	-	147
5.	4	Neg.	1.0	2	12	17
	40	"	1.1	2	13	140
	52	"	1.0	1	10	91
11a.	14	Neg.	1.0	1	4	62
	35	"	0.9	1	4	158
	83	Trace.	0.9	1	3	36
12.	3	Neg.	0.6	2	-	10
	9	"	0.6	2	-	86
	21	Pos.	1.7	1	5	186
15.	7	Neg.	0.9	1	4	48
	24	"	0.5	1	3	60
	47	"	0.5	1	5	65
	74	"	0.5	1	5	56
	85	"	1.0	1	5	29
17.	2	Neg.	1.4	2	5	33
	22.	-	-	1	1	171
	46	-	-	1	1	93
	70	-	-	1	1	60
26.	30	Neg.	1.2	2	4	193
	54	"	1.3	1	3	139
27.	37	Neg.	1.0	1	16.	235
	59	"	1.5	1	15	146
	84	"	0.7	1	15	113
	107	"	1.0	1	16	57
	134	"	0.5	2	19	40
31a.	15	Neg.	2.2	2	8	85
	38	"	1.4	-	-	84
	61	"	1.4	-	-	60
	83	"	0.8	1	4	28
31b.	½	Neg.	0.5	3	3	37
	14.	"	0.6	1	3	107
	86.	"	1.1	2	3	49
	111.	"	0.9	3	8	30
48.	16	Neg.	0.5	1	12	24
	48	"	0.7	1	14	56
	72	"	0.5	2	12	37
69.	24.	Neg.	0.9	4	25	313

TABLE XI.

The Results of Liver Function Tests and Serum Transaminase Assay Following Acute Intramural Infarction.

Case No.	Time after Onset. Hours.	VAN DEN BERGH. Direct	Indirect.	TURBIDITY. Thymol.	Zinc.	SERUM TRANSAMINASE ACTIVITY. Units
7.	3	Neg.	0.7	1	3	-
	18	"	0.5	1	4	73
	42	"	0.6	1	4	38
	80	"	0.6	-	-	23
8.	126	Neg.	0.5	-	-	35
	174	"	0.5	-	-	20
16.	6	Neg.	1.5	2	11	25
	28.	"	1.2	-	-	23
25b.	12	Neg.	1.0	1	3	55
	36	Pos.	0.9	1	3	80
	84	Neg.	1.4	3	10	30

TABLE XII.

The Results of Liver Function Tests and Serum Transaminase Assay in Attacks of Acute Myocardial Infarction in which the Electrocardiogram was not Diagnostic.

Case No.	Time after Onset-Hrs	VAN DEN BERGH. Direct	Indirect	TURBIDITY. Thymol.	Zinc.	SERUM TRANSAMINASE ACTIVITY-Units
10.	2	Neg.	0.5	1	1	-
	42	"	0.5	-	-	32.
11b	24	Trace.	0.7	1	7	60
	48	"	0.7	1	7	86
	72	"	0.7	1	7	40

TABLE XIII.

Degree of Peripheral Vascular failure.	Respiration.	Pulse.	Blood Pressure.	Mental state.	Cyanosis.	Extremities.	Oliguria.
Minimal. (+)	Normal.	Thready & Rapid.	Slight fall.	Restless & apprehensive.	Lips or Extremities or both	Pale & Cool.	None.
Moderate (++)	Rapid & shallow.	Thready & Rapid.	80/60 - 60/40.	Apprehensive & confused.	" " " "	Cold & clammy.	Questionable.
Marked. (+++)	Often Cheyne-Stokes or sighing.	" "	60/40 - 40/20.	Confused to stuporose.	" " " "	Cold & clammy.	Slight.
Extremely marked (++++).	Often Cheyne-Stokes or sighing.	Rapid, slow or unobtainable.	40/0 - 20/0.	Stuporose to comatose.	Extremities mottled (Extensive)	Cold & clammy.	Moderate (often albumen red cells & casts.)

TABLE XIV.

Normal Serum Transaminase Activity.

Authors.	No.of Normals studied.	Range. Units/ml.	MEAN ± S.D.Units/ml
Wroblewski et al. (1955)	500.	5 - 40	22 ± 7
Kattus et al. (1956)	11.	16 - 24.	20.
Steinberg et al. (1955)	20.	10 - 33.	-
Chinsky et al. (1956)	15.	7 - 40	20 ± 8
Nydick et al. (1955)	75.	10 - 40.	25 ± 7
Baron et al. (1956)	-	7 - 25.	-
Present Series.	25.	5 - 35.	17 ± 8

TABLE XV.

Maximum Serum Transaminase Activity and Electrocardiographic Findings in 45 attacks of Acute Myocardial Infarction. (Transmural).

CAse No.	Serum Transaminase. Time after Onset(Hrs)	Maximum Activity.	Electrocardiographic Findings.
1.	65.	328.	Extensive transmural acute antero septal infarction.
3.	64.	238.	Moderately extensive acute transmural antero septal infarction.
5.	16.	247.	Very extensive acute transmural antero septal infarction.
9.	144.	84.	Extensive transmural antero septal infarction.
11a	35.	158.	Fairly extensive transmural recent antero septal infarction. Old posterior infarction.
12.	21.	186.	Extensive transmural acute antero septal infarction.
13a	96.	80.	Very extensive acute transmural antero septo lateral infarction.
14.	38.	62.	Extensive acute transmural antero septo lateral infarction.
15.	47.	65.	Extensive acute transmural antero septal infarction.
17.	22.	171.	Serial ECG: - posterior lateral infarction, probably extension of old posterior infarct.
20a	54.	250.	Extensive acute antero-septa lateral infarction.
21.	27.	135.	Acute transmural posterior infarction. Auricular fibrillation.
22.	41.	208.	Extensive acute transmural posterior infarction.
23.	26.	200.	Very extensive acute transmural antero-septo-lateral infarction.
25c.	36.	116.	Fairly extensive acute transmural antero-septal infarction.

Case No.	Serum Transaminase. Time after Onset(hrs)	Serum Transaminase. Maximum Activity.	ELECTROCARDIOGRAPHIC FINDINGS.
26.	30.	193.	Extensive Acute transmural posterior infarction.
27.	37.	235.	Extensive acute transmural antero-septal infarction.
28.	120.	57.	Acute transmural posterior myocardial infarction.
31a.	15.	85.	Extensive transmural antero-septal infarction.
31b.	14.	107.	Acute transmural posterior infarction.
34.	48.	493.	Acute transmural antero-septal infarction. Supraventricular tachycardia.
35.	26.	190.	Acute transmural posterior myocardial infarction. Auricular fibrillation.
36a.	27.	120.	Acute, probably transmural, septo-lateral infarction.
37.	22.	98.	Acute transmural posterior myocardial infarction.
40.	72.	65.	Acute transmural posterior infarction.
41.	17.	77.	Acute transmural antero-septal infarction. Old transmural posterior infarction.
42a.	39.	180.	Acute transmural antero-septal infarction.
42b.	24.	82.	Lateral extension of previous antero-septal infarction.
44.	33.	173.	Acute transmural posterior infarction.
45.	19.	126.	Acute transmural antero-septal infarction.

TABLE XV.. (ctd).

\+ indicates those cases in which normal or borderline levels of serum transaminase activity were found.

	Case No.	Serum Transaminase. Time after Onset(hrs)	Maximum Activity.	ELECTROCARDIOGRAPHIC FINDINGS.
	46.	44.	105.	Acute transmural antero-septal infarction.
	47a.	33.	110.	Acute transmural posterior infarction.
	47b.	24..	75.	Recent transmural anterior infarction.
	48.	48.	56.	Acute transmural posterior infarction.
	50.	44.	274.	Recent transmural antero-septal infarction.
	55.	80.	90.	Acute transmural antero-septal infarction.
	59.	19.	120.	Acute transmural antero-septal infarction.
	69.	24.	313.	Acute transmural antero-septal infarction.
	122.	34.	120.	Acute transmural antero-septal infarction.
+	19a.	72.	17.	Acute transmural extensive antero-septo-lateral infarction. Possible old posterior infarction.
+	29.	14.	34.	Fairly extensive acute transmural posterior infarction.
+	49.	13.	45.	Recent transmural antero-septal infarction. Probable old posterior infarction.
+	51.	48.	21.	Recent transmural antero-septal infarction. Old posterior infarction.
+	56.	24.	35.	Recent extensive antero-septo-lateral infarction.
+	84.	8.	24.	Recent transmural anterior infarction. Right bundle branch block.

TABLE XVI.

Maximum Serum Transaminase Activity and Electrocardiographic Findings in 9 Attacks of Acute Intramural Myocardial Infarction.

Case No.	Serum Transaminase. Time After Onset(hrs)	Maximum Activity.	ELECTROCARDIOGRAPHIC FINDINGS.
7.	18	73	Extensive acute intramural antero septo lateral infarction.
25a.	15	55	Recent intramural antero-lateral infarction.
25b	36	80	Acute intramural antero-septal infarction.
39.	32	58	Acute intramural anterior infarction.
43.	32	56	Acute intramural septo-lateral infarction.
71	31	85	Acute intramural antero-septal infarction.
+ 8.	78	40	Fairly extensive intramural antero-septal infarction.
+ 16.	52	26	Extensive acute intramural antero-septo-lateral myocardial infarction.
+ 54.	24	30	Intramural lateral infarction probably of some days' duration. Chronic antero-lateral coronary insufficiency.

+ indicates those cases in which normal serum transaminase activity was demonstrated.

TABLE XVII.

Maximum Serum Transaminase Activity and Electrocardiographic Findings in 6 attacks of Acute Myocardial Infarction in which the Electrocardiogram was not Diagnostic, at any time, of Acute Infarction.

Case No.	Serum Transaminase. Time after Onset(hrs)	Maximum Activity.	ELECTROCARDIOGRAPHIC FINDINGS.
6.	38	209	Highly suggestive of an acute intramural extensive posterior myocardial infarction. Heart block (2:1).
10.	18	60	Left bundle branch block: minor sequential changes possibly indicative of infarction.
11b.	48	86	Suggestive of a recent posterior myocardial infarction. Supra-ventricular tachycardia (160/mins.) Electrocardiogram incomplete.
19b.	48	60	Probably lateral extension of a previous antero-septo-lateral infarction.
24.	25	220	Left bundle branch block. Changes suggestive of septal infarction but no significant sequential change.
+ 18.	5	30	Acute coronary insufficiency; old anterior myocardial infarction.

+ indicates a case in which normal serum transaminase activity was demonstrated.

TABLE XVIII.

SHOWING THE IMPORTANCE OF EARLY ESTIMATION OF SERUM TRANSAMINASE ACTIVITY FOLLOWING ACUTE TRANSMURAL MYOCARDIAL INFARCTION.

Time after Onset of Infarction. Hours.	No.of cases examined.	No.of cases showing diagnostic levels of serum transaminase.
0 - 6	9	-
6 - 24	27	26.
24 - 48	31	29.
48 - 72	27	25.
72 - 96	28	12.
96 -120.	19	9.
One Week.	13	-

TABLE XIX.

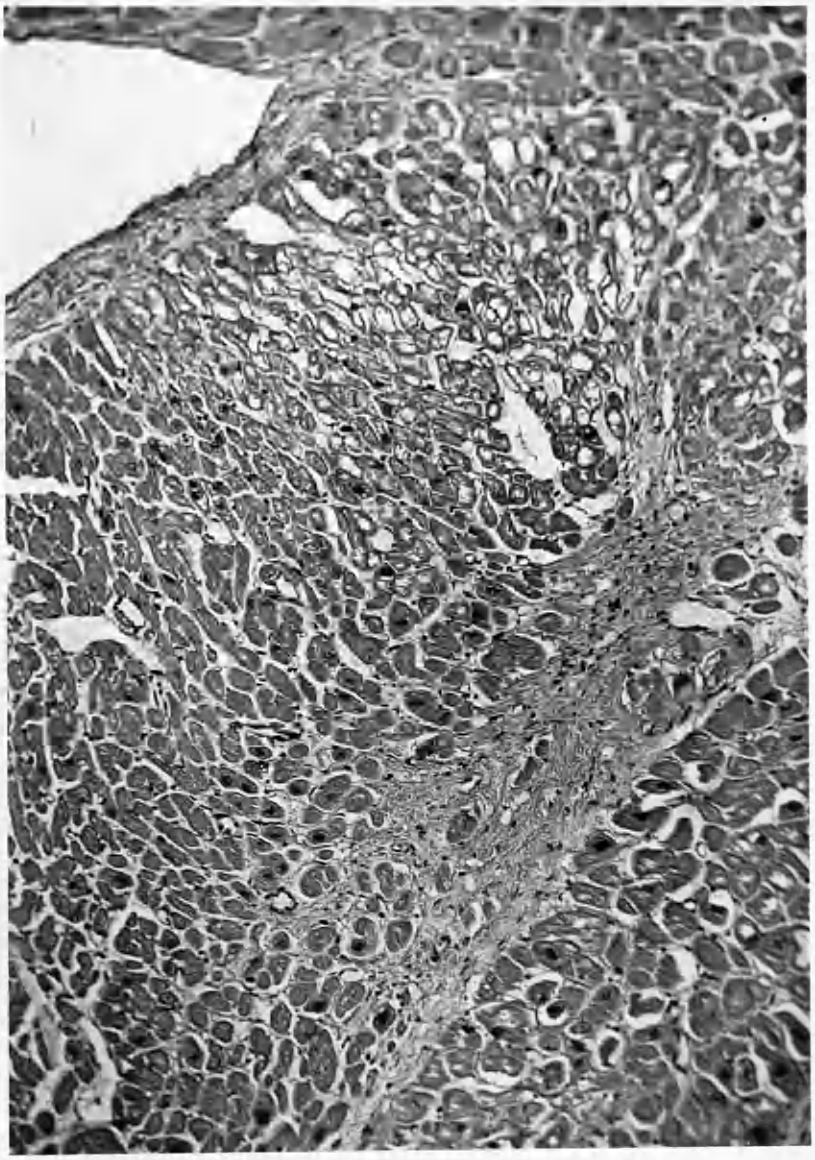
SHOWING THE IMPORTANCE OF EARLY ESTIMATION OF SERUM TRANSAMINASE ACTIVITY FOLLOWING ACUTE INTRAMURAL MYOCARDIAL INFARCTION.

Time after onset of infarction. (Hrs.)	No.of cases examined.	No.of cases showing diagnostic levels of serum transaminase.
0 - 6	2	--
6 - 24	4	4
24 - 48	6	4
48 - 72	5	--
72 - 96	5	--
96 - 120	1	--
One Week.	1	--

VOLUME II

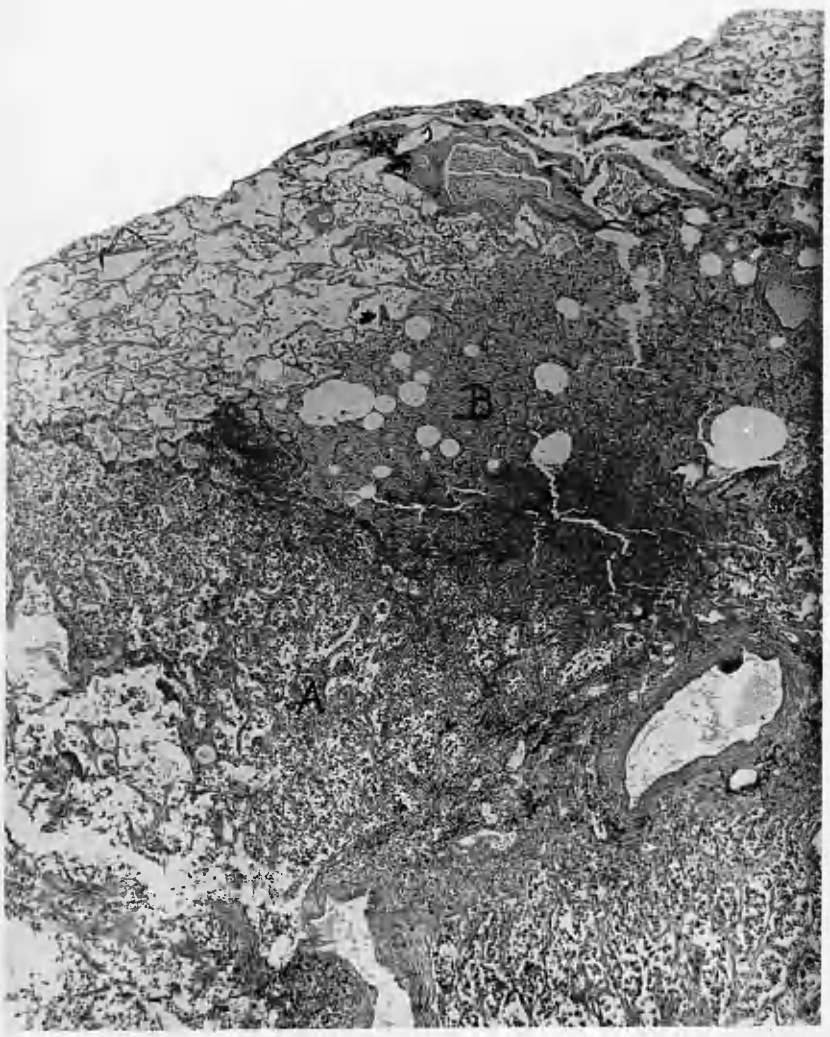
APPENDIX IV.

PLATE I.



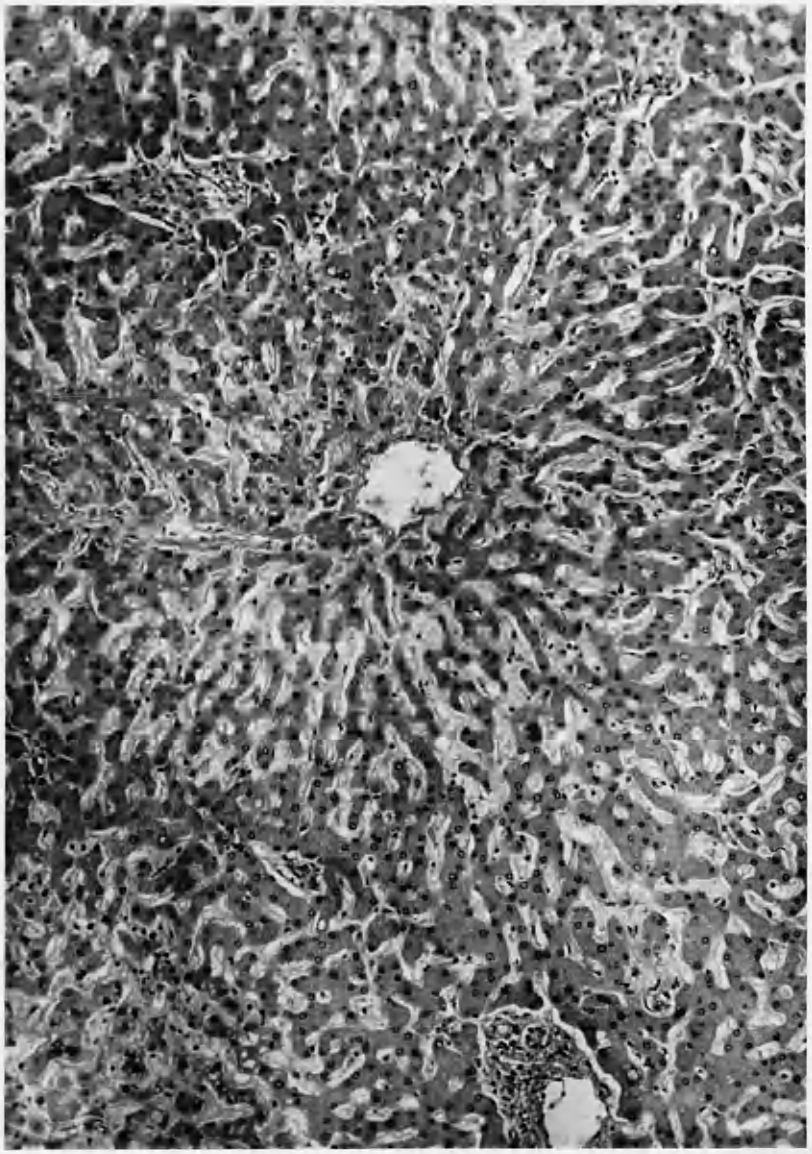
A representative histological section of heart tissue from Case 76. An area of ischaemic fibrosis of the myocardium with surrounding muscle cell hypertrophy is present. There is no evidence of recent myocardial infarction.

PLATE II.



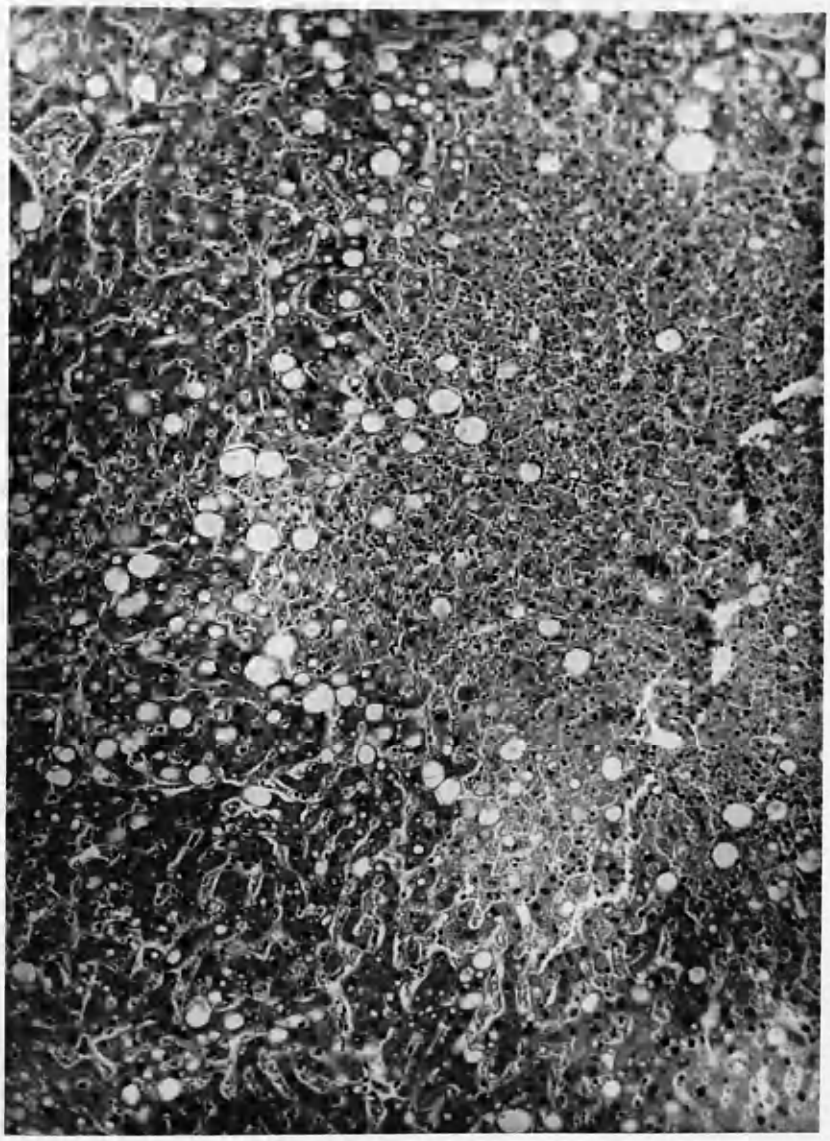
A histological section of lung from Case 76., showing an alveolar cell carcinoma (A) with marginal areas of acute pulmonary infarction. (B).

PLATE III.



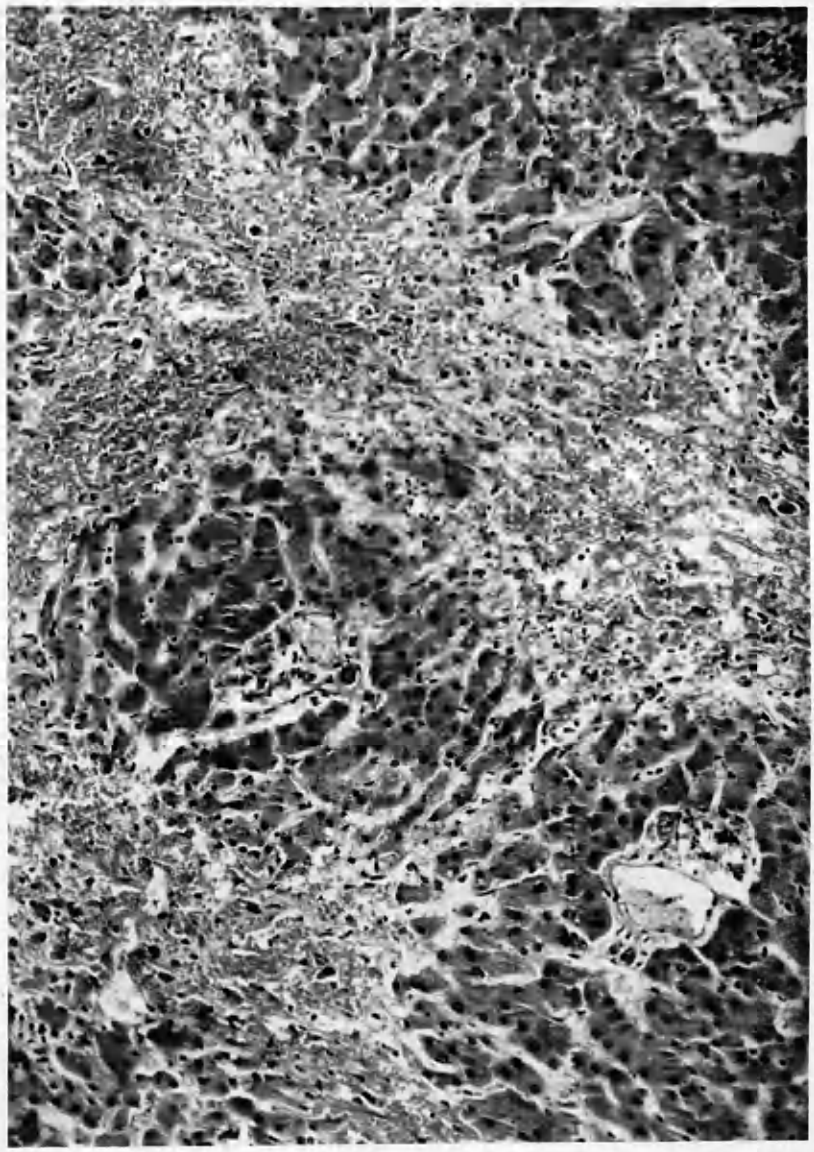
A representative histological section from Case 76. The changes of severe chronic venous congestion are present. There was no evidence of secondary carcinoma of the liver.

PLATE IV.



A representative histological section of liver from Case 78. Massive necrosis of liver is present and there is fatty infiltration of the surviving liver cells.

PLATE V.



A representative histological section of liver from Case 88. The changes of severe centrilobular necrosis of liver are present.
