THE RELATIONSHIP

BETWEEN

GALL BLADDER DISEASE

AND

CORONARY ARTERY DISEASE

BY

T. D. V. Lawrie, B.Sc., M.B., Ch.B., F.R.F.P.S.

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

I N D E X.

INTRODUCTION.

The present work was begun towards the end of 1947, and had its main purpose to determine whether there was any evidence of an etiological relationship between gall bladder disease and coronary artery disease.

Over the past three hundred years these two conditions have aroused a great deal of interest and argument. As the knowledge about each of these increased, it became evident that the symptoms and signs of these two diseases were often much alike, that, even today, with the great advances in the ancillary methods of diagnosis, such as electrocardiography and radiology, they are frequently mistaken for each other. This similarity in symptoms and signs led to the suggestion that there might be an etiological association between the two diseases. With the advent of surgical treatment of gall bladder disease, the idea has gained ground that operative treatment of gall bladder disease leads to an improvement of any accompanying coronary artery disease, and some are so convinced, as to advocate surgical treatment of the gall bladder in patients presenting symptoms and signs only, of coronary artery disease.

Up to date no attempt appears to have been made to study all the aspects of the problem and conclusions have been reached on a survey of clinical cases alone, a series of post mortem reports, or on a few electrocardiographic changes following operation. This work has attempted to study the problem from all aspects and can be divided into five parts :-

1. Historical survey of literature.
2. Study of post mortem reports.
3. Investigation of series of cases clinically.
4. A biochemical study.
5. An electrocardiographic study of coronary artery disease, and gall bladder disease, before and after operation.

In Part 1 the literature relating to coronary artery disease is reviewed first, followed by a review of gall bladder literature, and lastly the literature relating to the association or relationship of the above.

Part 2 consists of a study of the protocols of 2,269 post mortems carried out at the Royal Infirmary, Glasgow, between 1929 and 1933. The post mortem reports of this period were chosen on the advice of Professor Montgomery and Dr. Dick, of the Institute of Pathology, Royal Infirmary, Glasgow. They considered this to be part of a period, when cases were fully reported, and consequently would provide a suitable basis for a post mortem study. Many of these post mortems were carried out by the late Professor Shaw Dunn. It was hoped that post mortem figures would give the most accurate information possible, as to the incidence of coronary artery disease,and gall bladder disease, in the various age groups and sexes, and as to how frequently they occurred together.

Part 3 consists of a clinical survey of 250 patients. 108 were primarily cases of gall bladder disease, and 100 primarily cases of coronary artery disease. These cases were gathered from the wards of Professor Burton, Mr. Dunbar and Mr. Stevenson, surgeons to the Royal Infirmary, Glasgow, and from Dr. Wright's wards, Medical Out-patient Department, and the Cardiology Department of the Royal Infirmary, Glasgow. At the same time another 42 cases were investigated for evidence of, either gall bladder disease or coronary artery disease, but these did not satisfy the criteria for diagnosis of either disease. They were classified as equivocal cases. The criteria for diagnosis of gall bladder disease are discussed in the first section of Part 3. The criteria for the diagnosis of coronary artery disease are discussed in the section on the electrocardiography of coronary artery disease.

Cholesterol seemed to offer a common ground of etiology in gall bladder disease and coronary artery disease, consequently serum cholesterol levels in each group, and in the equivocal series were estimated. This constituted Part 4. In all, 406 estimations were made, and of these 233 were the result of my own work, the remainder being done by the Biochemistry Department, Royal Infirmary, Glasgow, under the charge of Dr. Eaton. Before the work was undertaken valuable assistance as to methods of estimation was given by Dr. Tompsett, formerly of this Department. On his advice the

233 estimations were done by a modification of Bloor's technique (1) Dr. Eaton's staff used another modification of Bloor, which gave closely comparable results.

Part 5 was devoted to a study of the electrocardiography of coronary artery disease, and gall bladder disease, before and after operation. In the former group there were 85 cases with chest lead electrocardiograms, and 15 with standard limb lead electrocardiograms. In the latter group there were 200 chest lead electrocardiograms and 363 standard limb lead electrocardiograms (obtained from the files of the Cardiology Department, Royal Infirmary, Glasgow). The 42 cases in the equivocal series had chest lead electrocardiograms, bringing the total number of electrocardiograms studied to 378 standard limb leads, and 327 chest lead electrocardiograms. (The chest lead electrocardiograms comprise standard limb leads, unipolar limb leads, and six praecordial leads).

In conclusion, I should like to thank the members of the Royal Infirmary staff - Professor Burton, Mr. Dunbar, Mr. Stevenson, Dr. Eaton, Dr. Tompsett, Dr. Calder, and Dr. Haase for their help, and permission to use their cases, and in particular to Dr. J.H. Wright for his guidance and helpful criticism in writing this thesis.

REFERENCES :

1. Bloor, W.R., et al : J. Biol. Chem. 24 : 227 : 1916.

Ibid. 25 : 577 : 1916.

Ibid. 26 : 417 : 1916.

Ibid. 29 : 7 : 1917.

HISTORICAL REVIEW.

It is evident that, by the end of the sixteenth century, the coronary arteries had been seen and even portrayed, e.g. the drawings of Leonardo de Vinci (1452-1519) and the illustrations of Vesalius (1514-1564) (1); but it is probable that they had no clear conception of their function as nutrient vessels of the heart. The accumulation of data regarding the anatomy, physiology, and pathology of the coronary arteries progressed slowly, possibly due to the teaching handed down from the time of Hippocrates, that the heart, the ruler over all other organs, was not affected by disease. In the seventeenth and eighteenth centuries pathologists were mainly concerned with the grosser lesions of the heart, such as pericarditis, intra-cardiac thrombi, and congenital malformations, and these were sometimes described in great detail. They did not, however, completely overlook the coronary arteries. Vieussens of Montpellier (2) (1641-1716) described fairly accurately the course of the coronary vessels. Several writers referred to ossification in the walls of these vessels, e.g. Drelincourt (1633-1697) and Bellini (1643-1704) (3). Lancisi of Rome (1654-1720) (4) described such pathological arteries as a cause of cardiac enlargement. De Senac (5), in 1749, referred to calcified coronary arteries, associated with aneurysm of the left ventricle. Morgagni (6) recorded cases of coronary artery

disease with clinical symptoms resembling those of angina pectoris and coronary thrombosis.

As Herrick (7) points out, these writers, although recognising calcification and ossification of the coronary vessels, diffuse enlargement, or aneurysmal dilatation of the heart, and the occurrence of symptoms like those of angina pectoris, or coronary thrombosis, did not appear to realise the function of the coronary arteries as the nourishing vessels of the heart, nor did they appreciate, that changes in the heart's size, contour, and mechanical efficiency were, in part, due to inability of the diseased coronary vessels to provide adequate nourishment to the myocardium.

The next landmark in the history of coronary artery disease was the classical description of angina pectoris, in 1768, by William Heberden (8). Fourteen years later he reported his findings in 100 cases, the first description of a large series. As Herrick says "He is the pioneer clinician of the coronary arteries".

In spite of his excellent description of the symptoms of angina pectoris, Heberden's views as to the pathogenesis were hazy. Other English physicians of the same period - Fothergill, Jenner, Hillier, and Parry (9) - are reported to have discussed the subject frequently. Jenner and Parry (10) believed that the ossification of the coronary arteries found, at post mortem, in patients, who had had angina pectoris,

was the essential pathological lesion. They are said to have refrained from publishing their views because of a possible harmful effect on John Hunter, who suffered from angina pectoris. Jenner (11), who confidently predicted it would be so, found in the heart of John Hunter, at post mortem examination, extensive ossification of the coronary arteries.

Parry (12), seemed to have a clear conception of ischaemia of the heart muscle as the cause of angina pectoris. Allan Burns of Glasgow (13) adopted the coronary artery theory of Parry, and was probably the first to try to prove it experimentally, at least by analogy, by producing pain in a ligatured limb, when exercised.

This view of the nature of angina pectoris was not universally accepted. According to Herrick (14), such outstanding men as Allbutt, Wenkebach, Schmidt, and Vaquez favoured the so-called aortic theory of anginal pain. Corvisart, who was regarded as an outstanding clinician, and was the author of the most popular book on cardiology in the early nineteenth century, did not make any definite mention of angina pectoris; and Laennec, in 1819, did not give much attention to coronary artery disease or angina pectoris either. He tended to magnify the influence of the nerves, as did some notable English physicians, such as Hope and Stokes.

A possible explanation for this apparent neglect of the importance of the coronary arteries in the nineteenth century is given by Herrick (15). In 1819 Laennec published this work on auscultation, and this began a period of what could be called "A period of physical signs", i.e. inspection, palpation, percussion, and auscultation. Naturally the physical diagnosis of heart murmurs, and valvular disease claimed more attention from the physician than the diagnosis of coronary artery disease, because of the paucity of physical signs in the latter condition.

In the middle of the nineteenth century, with the advent of Virchow and his cellular pathology, it was recognised by him, Cohnheim, and Weigert (16), amongst others, that obstruction of the coronary arteries was a frequent cause of degenerative and atrophic processes, which led to myocardial fibrosis, dilatation of the heart, and cardiac failure.

Not only was observation applied to the slowly developing type of coronary artery disease. Cohnheim (17) carried out experiments on dogs, producing acute coronary occlusion. As a result of these experiments this form of occlusion was regarded as nearly always fatal. Later this conclusion was challenged and other investigators, carrying out similar experiments, reported that some animals survived the damage of acute occlusion. Clinicians, however, seem to have been somewhat slow to grasp the significance of these experiments, even although a few cases were reported in which, at post

mortem examination, a myocardial infarct was found, these patients previously having had angina-like symptoms. Such post mortem findings were apparently regarded, at that time as pathological curiosities.

Rene Marie (18) and Maximilian Sternberg (18) described two conditions respectively, parietal aneurysm and myocardial infarct, and recognised them as due to coronary occlusion. They seem, however, to have been pre-occupied with the pathological features, and to have overlooked the fact that some histories of such cases revealed symptoms now considered characteristic of acute coronary occlusion.

The first case of coronary occlusion correctly diagnosed, during life, was that reported by Dr. Adam Hammer of St. Louis in 1878 (19). Hammer, who was born in 1818, in Boden, Germany, was educated at Heidelberg University. After the failure of the Revolution in Germany in 1848,he emigrated to America, and settled in St.Louis. His case was that of a man, aged 34 years, who suddenly collapsed, while sitting in his chair. On examination he presented the usual signs of collapse, but apparently had no pain. His pulse rate originally was 40 beats per minute, but this became slower, and reached the level of eight beats per minute. As Hammer himself said "What impressed me par ticularly about this case and attracted my attention in the highest degree was the sudden appearance and steadily progressive course of the

collapse". "I thought that only a sudden, progressively increasing, disturbance in the nutrition of the heart itself, such as cutting off of the supply of nourishment, could produce such changes as this case showed, and that such an obstruction could be produced only by a thrombotic occlusion of, at least, one of the coronary arteries". "From lack of ground for any other satisfactory explanation I was carried away by this thought". Post mortem examination confirmed the clinical diagnosis. Apart from its historical interest this case shows a few interesting features, namely -

(1) Early age of onset,

(2) Painless type of myocardial infarct,

(3) Occurrence of what was probably heart block.

Other notable American contributions on coronary artery disease came from George Dock (20) and James B. Herrick (21). It is to the latter that credit must go for pointing out the clinical features of coronary occlusion in his paper "Clinical features of sudden obstruction of the coronary arteries". The paper which was read before a meeting of the Association of American Physicians in May 1912 and published in December, 1912, evoked little discussion. As Herrick said "There was no repercussion for six years". It had fallen like a "dud". A similar fate befell the paper of Obrastzow and Straschesko published two years earlier (1910) in a German Journal. Herrick's second paper was read in 1918.

It was more convincing than his original paper, and great weight was added to it by the experimental work of Fred Smith on ligation of the coronary arteries in dogs. The electrocardiograms from those experimental animals, and from one of Herrick's patients showed a striking similarity.

Since these articles by Herrick, Hammer, Obrastzow and Straschecko, in the earlier part of the century, the literature on coronary artery disease has become voluminous. Chronic coronary disease and coronary occlusion are now very common conditions, known to every practising doctor. The main advances in the knowledge concerning coronary artery disease centres round the electrocardiographic diagnosis and perhaps the most outstanding names in this respect are Pardee (22), Parkinson and Bedford (23), and Wilson (24).

The literature concerning gall bladder disease is older than that of coronary artery disease. At the beginning it is almost entirely confined to reporting the discovery of gall stones at post mortem examination. Gentile da Foligno was the first physician reputed to have described gall stones. According to Tosoni (28), he performed the first recorded autopsy, at Padua, in 1341, and during this autopsy, he found many gall stones. Although he was a distinguished physician of his time, and published many works, none of these contain an account of gall stones. Marcellas Donato (26), refers to Foligno's discovery thus "In the gall bladder many stones were

seen". "Gentile himself testifies, in a certain woman, whose viscera were removed, so that the body could be embalmed, they found in the duct of the gall bladder, at its mouth, a stone tending to green, from which the moderns might remark that there was jaundice present".

The next account of gall stones was probably that of Antonio di Pagolo Benivieni (27). He was a physician, who practised medicine in Florence, during the time when Lorenzo de Medici, Savanarola, and Marchiavelli lived there. In 1505 his "de Obditis causis morborum" was published by his brother Gerolamo, three years after he died. This work consisted of post mortem reports, primarily carried out with a view to finding out the exact cause of death. Amongst other conditions such a fibrinous pericarditis, abscess of the hip joint, and senile gangrene, he described the finding of many gall stones, of varied size and shape, in the gall bladder of a certain noblewoman, who had frequently, during life, complained of pain, arising in the neighbourhood of the liver.

Matteo Realdo Colombo (28), who was born in Cremona in 1516, and practised in Venice and Padua, where he succeeded Vasalius in the chair of anatomy, was a distinguished anatomist, and one of the discoverers of the pulmonary circulation. He later went to Pisa, as a professor, then to Rome, as a physician, to Pope Paul IV. In 1556 he was

present at the autopsy on "Ignatius of Loyola" and his book, "De re anatomica libri XV", which first appeared in 1559, and reported the finding of "stones of various shapes, and of various colours in the gall bladder, as well as in the kidneys, ureters, bladder, intestines, haemorrhoidal veins, and umbilicus".

A very good description of gall stones and the various pathological conditions of the gall bladder and bile ducts, associated with stones, was given by Jean Fernel (29). Felix Platter (30) states that calculus and sand in the liver were the cause of severe dull pains in the hypochondrium.

William Fabry (31), the father of "German surgery", who changed his name of Guilhelmus Fabricius described, with illustration, in his "Centuries of surgical cases", which was the authoritative surgical book of its day, gall stones of enormous size. The book was published some time between 1606-1646.

Daniel Sennert (32), in his "Medicinae Practicae", reviews the previous literature, mentioning such people as Fallopius, Colombus, Kentmann, Antonio Benivieni, Vesalius, Belloarmatus Senesis, Caellius Rodiginus, Rondeletius, Matthiolus, Gabriel, Fallopius and Felix Platter, all of whom had described gall stones. Sennert was of the opinion that gall stones had the same mode of formation as stones in the kidney, and were recognised with difficulty unless at autopsy,

because the signs are quite the same as in scirrhus of the liver. He also admitted that the cure of calculus in the liver was difficult.

Francis Glisson (33), described calculi in the biliary tract, especially of oxen. He also described what appears to be the small, thickened, shrunken gall bladder of chronic cholecystitis. He also mentions the fact that he knew very many people who expelled stones, similar to those which he found in the biliary passages, in great quantity through the intestine.

Lorenz Heister (34), whose name will always be associated with the gall bladder because of his description of the valves in the cystic duct, describes the post mortem on a man, who died of a mortal wound of the head, at the public examination of whom, upon opening the abdomen, many angular stones were found in the gall bladder.

Giovanni Battista Morgagni (35), gives a bibliography of previous literature on this subject in his book "The seats and causes of disease" (translated by Benjamin Alexander 1769). He lists the work of the following, Gentilis, Nicolus, Benivienius, Vesalius, Curtius, Fallopius, Fernelius, Stephanus, Columbus and Coiterus. He, like previous observers, found gall stones were commoner in the elderly and in those, especially women, who did little work or moving about. He, therefore, considered age, sex and mode of life

to be important factors in the production of biliary calculi.

It will be seen from the above review that up to the end of the nineteenth century, the main interest was centred upon, and most importance attached to, the formation and presence of gall stones. The systematic study of cholelithiasis, however, dates from the time of Naunyn's publication in 1892 (36), when he brought forward his well-known view that gall stones were always secondary to a catarrhal inflammation of the gall bladder.

The next era in the history of gall bladder disease is the one connected with the introduction of surgical treatment for gall stones and cholecystitis. The advent of surgical treatment was rather important for it prompted further investigation into the clinical picture of gall bladder disease in general - up till that time the diagnosis of gall bladder disease had mainly depended on an attack of biliary colic plus jaundice. Altogether the surgery of the gall bladder and bile ducts is only about 70 years old. As early as 1733, according to Rowlands (37), Petit described an operation for cholecystostomy, but the fear of peritonitis was so great that the operation was not performed until 1867, after the pioneer work on antisepsis by Lister. In 1867 J.S. Bobby (37), exploring for a supposed ovarian cyst found and opened a gall bladder distended with mucus and extracted about 50 small stones, closed the gall bladder, and dropped it back into position. In 1878 Marion Sim (37) performed a

cholecystostomy in a very late case of jaundice, due to gall stones, but the patient died. In 1879 Keen (37), had a similar experience. In the same year, however, Lawson Tait (37) successfully removed a large stone from a gall bladder, and a small one from the cystic duct. Since that time the importance of gall bladder disease as a cause of ill health has become gradually more fully recognised. For many years a positive diagnosis was not made unless jaundice developed, after numerous attacks of what is now known as a biliary colic. Moynihan (38) drew attention to the "inaugral symptoms" of gall stones or what we now recognise as chronic cholecystitis (he actually credits Kraus as being the first to point out the importance of these prodromal symptoms). It was then recognised that jaundice was not a necessary accompaniment of gall stones, and was only found where a stone had entered the common duct, or where a secondary hepatitis had developed.

In the opinion of Sir D.P.D. Wilkie (39), great credit is due to Sir James McKenzie for directing attention to the varied reflex symptoms, to which gall bladder disease may give rise, and to him, and his teaching, we owe, in large measure, the notable advance in the modern diagnosis of such disease.

A brief account of the historical aspects of both coronary artery, and gall bladder disease have been given. As the clinical picture associated with each condition became

better known it was recognised that the two conditions could simulate one another very closely. Not only so but the increasing frequency of surgical treatment of gall bladder disease led many people to believe that there was a definite association between the two conditions, and that surgical treatment of the gall bladder disorder led to improvement in the cardiac condition.

As early as 1809 Allan Burns (40) commented on the occurrence of abdominal symptoms in cardiac disease. In his introduction to "Observations in diseases of the heart" he said "The heart from the intricacy of its structure, and from its incessant action is liable to many diseases and these, from the importance of the function of this organ, are at all times highly alarming".

"Some of these are extremely insidious in their commencement, are attended with obscure and perplexing symptoms, and in their results are almost uniformly and speedily fatal."

"These have often the appearance of being produced by a morbid state of some other organ than of the heart but in their results they are almost uniformly and speedily fatal."

"It becomes, therefore, a matter of much importance with the medical practitioner to be able to distinguish diseases of the heart from affections of other parts; and to know the facts which regulate his prognosis".

Of the other organs, which may give rise to symptoms, and signs, suggestive of coronary artery disease, one of the

most important is the gall bladder, both in acute, and chronic cases. In the majority of cases, however, it is possible to distinguish between the two conditions, but, in a few patients, it may be impossible, even with the extra methods of investigation, to decide whether the gall bladder or the coronary arteries are the cause of the symptoms and signs. Pain and flatulent dyspepsia, and to a lesser extent icterus, are the symptoms and signs which give rise to confusion. On the one hand the pain of gall bladder disease may be referred to the front of the chest and thus simulate pain of cardiac origin, or the pain of acute coronary disease may be referred to the abdomen thus simulating gall bladder disease. It has been suggested that the pain in the latter type of coronary occlusion may be transmitted along sympathetic fibres having their origin lower than usually taken by cardiac pain (T1-4). Other suggestions offered are :-

(1) The pain is due to reflex spasm of the abdominal arteries.

(2) The abdominal pain in coronary occlusion results from congestion and dilatation of the liver with drag on the suspensory ligaments. Levine (41) favours the latter explanation, in some cases at least, pointing out the observation of an engorged liver found at operation on a case of coronary

(2) contd.

occlusion. Libman (42) was of the opinion, that liver congestion occurs in those cases in which there is involvement of the right ventricle, whilst Fishberg (43) thinks that it may occur when the inter-ventricular septum is affected. These latter opinions do not appear to be generally held.

(3) Distension of the stomach as a result of air swallowing or reflex atony of the stomach and intestine.

(4) Acute spasmodic contraction of the oesophagus and stomach.

On the other hand, some light on the production of chest pain by gall bladder disease, and its mode of action, is given by the experiments of Von Bergmann (44) many years ago. He suggested that a viscero-visceral reflex, initiated by some source of upper abdominal stimulation, such as the gall bladder, might cause a tonic shortening of the oesophagus, and pull the cardiac end of the stomach up through the hiatal orifice. He and his co-workers were able to induce a reflex shortening of the oesophagus in the experimental animal by vagal stimulation, electrically, by merely handling the lobes of the liver, by dilating the gall bladder, by dilating the cystic duct, or by stretching the walls of the stomach.

They suggest that such reflexes may occur clinically. They also state that symptoms of a reflex nature occur such as cardiospasm or tachycardia, or episodes of paroxysmal auricular fibrillation, or anginoid or actual anginal pain may be thus produced. They maintain that the anginal pain is a true angina, due to reflex vasoconstriction of the coronary arteries. A reflex casoconstriction of the coronary arteries, resulting in a marked decrease in coronary flow, was shown by Von Bergman and his associates when the oesophagus or the stomach at the hiatal orifice was dilated by means of a balloon. This effect was obviated by vagal section or atropine.

J.H. Wright (45), has found that abdominal coronary cases can be divided into four groups :-

(1) The most important, because it is the most frequent, is the flatulent dyspeptic type. Flatulent dyspepsia is a cardinal symptom of gall bladder disease, hence the difficulty in distinguishing the two conditions in some cases.

(2) The second type consists of those, who complain of epigastric fullness or pain, coming on when they exert themselves, immediately after a meal. In many cases the patient is pre-occupied with the fact that the pain follows a meal. His medical

(2) contd.

examiner may also be misled, and consequently think of some intra-abdominal condition, such as gall bladder disease.

(3) The third type is that of acute indigestion (nausea and vomiting), following an unusually heavy meal. Again a diagnosis of gastritis or cholecystitis might be made.

(4) The fourth type is that where the abdominal pain is so acute as to simulate an acute abdomen. In some such cases a laparotomy may be done. Sometimes the abdominal pain of coronary occlusion may be further complicated by the development of jaundice. Gairdner, as J.H. Wright points out, did not seem to be aware of this, when he wrote, "It occasionally happens that the very intense, and sickening pain of biliary calculus presents a degree of resemblance to angina and its accessories; and the author has even observed cases in which the diagnosis remained doubtful until the yellow tinge of the conjunctivae, appearing after an interval of hours, relieved the apprehension of the physician".

Following that brief review of the inter-relationship of gall bladder disease and coronary artery disease, a description of the literature reporting cardio-vascular disorders in gall bladder disease will now be given.

In 1907 David Riesman (46), who was reporting two cases, which displayed a systolic murmur at the apex, and increased cardiac dullness, during or directly following a gall stone colic, gave a brief resume of the preceding literature on the same subject.

In 1866 Martineau (46), reported a case of ulcerative endocarditis, resulting from disease of the gall bladder. In the same year Netter and Martha (46), reported a case of multiple hepatic abscesses, with gravel in the gall bladder, and ulcerative endocarditis of the mitral valve. They considered both conditions of common origin, for they found the same organism in both situations. In 1892 Leva (46) reported two cases of ulcerative endocarditis, resulting from disease of the gall bladder. The following year Oddo, of Marseilles (46), reported the case of a man, who had had biliary colic over many years, suddenly developing a typical attack of biliary colic and jaundice. Two days later a feeble, arrhythmic pulse, with signs of pericarditis, developed, and he died a few days later. Netter and Martha (46) report Lays (1864), Murchison (1868), Jacoud (1872), Roudot (1883) and Malibran (1884) as describing cases, which, the

various authors thought, showed an etiological connection between gall bladder and coronary artery disease, but Netter and Martha did not think that any etiological connection had been proven.

Riesman (46), also reports the classification of cardiac disturbances, due to gastro-hepatic disease, by Tessier, as follows :-

(1) Intensification of the second heart sound.

(2) Doubling of the second heart sound.

(3) A tricuspid murmur.

(4) Complete tricuspid incompetence with venous pulsation.

Quincke (46), recognises a systolic murmur, and intensification of the pulmonic second sound in icterus, but thinks them no more frequent than in other states attended by anaemia.

Two years after Riesman's article, Babcock (47) published a fairly comprehensive article on "Chronic cholecystitis as a cause of myocardial incompetence", in which he reviews some of the previous literature, mainly French. According to Babcock, Gangolphe described nine cases - four of cholelithiasis, two of emotional jaundice, two of hepatic cancer, and one of cholangitis, in which cardiac murmurs occurred. Fabre reported eight cases of jaundice, with the heart affected in five (in which way the heart was affected, is not stated). Rendu described a case of jaundice in which a systolic murmur

developed, another case of colic and icterus, in which there was marked arrhythmia, and another, of catarrhal jaundice, with gallop rhythm, but no other arrhythmia.

It is obvious from the above articles that the earlier physicians were mainly concerned with cardiac enlargement, changes in the heart sounds,and the occurrence of heart murmurs, in what, most porbably, was gall stone colic, with or without an accompanying acute cholecystitis. In short, the above signs are similar to those which are now recognised as occurring in any non-specific febrile or toxic condition. The reports on the occurrence of ulcerative endocarditis, in association with gall bladder disease, are very interesting, but again can be regarded as coincidental findings, e.g. ulcerative endocarditis has been reported in association with pyaemia and septicaemia, occurring in such varied conditions as osteomyelitis, puerperal sepsis, suppurative otitis media, and pyelonephritis.

Probably the first really comprehensive account, although only based on a few cases, of the supposed relationship between gall bladder disease and coronary artery disease was that referred to above, "Chronic cholecystitis as a cause of myocardial incompetence" by Babcock in 1909.

According to Babcock, one in ten, have gall bladder disease,while one in thirteen have gall stones, but they are all not recognised clinically, partly due to ignorance of the

symptomalogy, and partly due to the obscurity of the symptoms themselves. He then goes on to describe the symptoms of gall bladder disease, probably one of the earliest descriptions of the clinical picture of cholecystitis. Referring to the symptoms, he says "Prominent among these is indigestion or stomach trouble, with or without epigastric discomfort, distension and uneasiness coming on several hours after a meal, and accompanied, or relieved by, the eructation of gas. Not uncommonly these occur during the night-time, often waking the individual from sleep toward morning, and they are sometimes associated with palpitation. Sometimes the symptoms are relieved by food, soda, or water. Pain is not an essential symptom, even when gall stones exist. In some instances slight colicky pains are felt. Attacks of congestion of the liver may be admitted. In some cases also, there is pain in the right shoulder, considered rhuematic, or in the back, near the inferior angle of the scapula. Ewald's area of cutaneous hyperaesthesia, in the right back low down, is generally discoverable".

He then points out the various disorders of the heart, which may date from an attack of biliary colic, or acute cholecystitis, viz. arrhythmias, praecordial oppression without dyspnoea, dilatation, and valvular incompetence. These disorders may be maintained by recurrences of the acute disturbances.

The number of cases reported were 13, and he divided them into four groups, on clinical grounds -

(1) Five cases of pronounced cardiac incompetence, showing considerable dilatation, with arrhythmia, and feebleness of heart's action, with murmurs, i.e. objective and subjective evidence of serious heart disease.

(2) Two cases, which were characterised by attacks of pain that were called angina pectoris, or were anginoid in character.

(3) Three cases of intermittence of the pulse, of long standing, and very intractable, but no marked subjective symptoms of myocardial inadequacy. Two cases were much benefited by operation.

(4) Two cases of valvular disease, in which cardiac competence was destroyed, either by outspoken attacks of hepatic colic, or distressing symptoms thought referable to the stomach, at first, but subsequently attributed to gall bladder because a Riedl's lobe was palpated.

He starts his discussion by raising the query, "What is the explanation of the effect of gall bladder disease on the heart, and why do not all persons with chronic cholecystitis

develop cardiac symptoms"? He suggests that, as far as the second part of the question is concerned, the previous state of the myocardium may be a determining factor, viz. a healthy heart muscle may endure such a disturbing influence, as an attack of biliary colic, or acute cholecystitis, and recover quickly from its derangement of function. A myocardium already the seat of structural disease, however, is seriously affected by conditions of strain, or by illness which otherwise would prove harmless. Therefore, since chronic infection of the gall bladder manifests itself chiefly in persons, at or past middle age, when presumably the heart is no longer so able to resist attacks, there are furnished the conditions capable of producing the symptom-complexes reported in his 13 cases.

He advances several theories for the explanation of the harmful effects on the heart, of some cases of gall bladder disease.

(1) The circulation in the blood of bacteria, or their toxins.

(2) The depressing influence of bile constituents on the myocardium.

(3) Disturbance of the splanchinc circulation, and secondarily, of the systemic circulation, and heart.

(4) A reflex inhibition through irritation of the vagus.

He admits that it is quite possible that a different explanation is applicable to different cases, and moreover, that there must be a predisposing cause residing in the heart miscle, i.e. chronic myocarditis, in consequence of which, the heart is unfavourably affected by influences, which a healthy myocardium would be able to resist.

Regarding the first theory proposed above, he thinks that acute cholecystitis is capable of setting up a parenchymatous infection of the heart. He then argues that in the same manner, but more slowly, a chronic cholecystitis may induce a chronic myocarditis. He also thinks that cholaemia has a definite depressing effect on the heart. He quotes the work of Stewart and King, who claim to have shown that biliverdin has a toxic effect on the myocardium, while the bile salts have the effect of raising blood pressure. Babcock thinks that in chronic cholecystitis, whenever there is a mild but prolonged cholaemia, shown by slight icterus, there is a prolonged toxic effect on the heart together with a raised blood pressure caused by bile salts.

The third factor, of splanchnic disturbances, he does not comment on.

Regarding the disastrous effect of biliary colic on the heart, he thinks that this is due to the stimulation of the filaments of the pneumogastric nerve, arising in the wall of the gall bladder. This is a more likely explanation because,

in his opinion, the formation of gall stones tends to protect the heart from the toxic effects of biliverdin, by preventing its absorption into the blood. In chronic cholecystitis, on the other hand, without colic or subjective distress, the harmful effect on the heart muscle must be ascribed to the circulation in the blood of biliverdin, and possibly to bacterial toxins, to which may be added the prolonged "Blood pressure raising influence" of the bile salts.

Graham, Cole, Copher, and Moore (48), claim to have observed brilliant results, in cases of heart disease, following cholecystectomy. They state that suspected cases of angina pectoris have received complete, and permanent relief following cholecystectomy, after it had been determined that there was a pathological gall bladder. They also claim that the myocardium may be seriously damaged by acute cholecystitis, and patients, who already have a chronic myocarditis, may show a marked arrhythmia, and even evidence of decompensation, as a result of an attack of acute cholecystitis. They also claim similar beneficial results of gall bladder surgery, in cases of chronic arthritis, and of goitre. From their writings they would appear to regard the gall bladder, as a focus of infection, and point out the value of cholecystography as a means of diagnosing latent gall bladder disease, in those pathological conditions, which may be ascribed to a hidden focus of infection, such as chronic arthritis.

Wilkie (49), in describing the distant toxic effects of gall bladder disease, has this to say :-

(a) Cardiac symptoms : "In many cases of gall bladder, disease breathlessness, palpitation, and cardiac arrhythmias are present. In some cases the cardiac disturbances would appear to be reflex in origin, and in others, e.g. obese and flabby subjects, a fat laden heart may account for symptoms, but in a few cases a definite toxic myocarditis is almost certainly present. In a number of cases, where the factor of obesity was not present, I have removed an infected gall bladder, which was causing relatively little in the way of local symptoms, but was associated with marked evidence of myocarditis. The results, in these cases, have been most gratifying, and in these cases, the patients have been restored from chronic invalidism to a life of activity."

Other distant toxic effects, which benefit from gall bladder surgery, according to him, are articular manifestations (so-called rheumatoid arthritis), fibrositis, nephritis, and nephrosis.

Wilkie, therefore, appears to favour focal sepsis and nervous reflexes as explanations for the harmful effects of gall bladder disease on the heart.

Willius and Brown (50), in a post mortem study of 86 cases of coronary artery disease, noted gall bladder disease to be present in 24 cases. Schwarz and Herman (51), observed an increased incidence of heart disease, in gall bladder, as opposed to non-gall bladder cases in all decades from the third to eighth, inclusive. Bean (52), noted an incidence of 17.5 per cent of gall bladder disease, in 269 cases of myocardial infarct, while Campbell (53) states that the majority of ten cases of infarct, which he investigated, had gall bladder disease. Rolleston and McNee (54) suggest that heart disease favours the formation of gall stones, by tending to make life more sedentary, leading ultimately to stagnation of bile.

Fitz-Hugh and Wolferth (55), comment on the growing conviction, amongst internists and surgeons, that disease of the gall bladder may initiate, or aggravate actual heart disease (especially so-called coronary artery disease). This conviction is based largely on cardiac improvement following gall bladder surgery. The successful removal of gall stones, preferably by cholecystectomy, they point out, has been followed by -

(1) Restoration of cardiac compensation in a few cases of congestive heart failure.

(2) Restoration of normal rhythm in certain cases of strain, or paroxysmal auricular fibrillation, or paroxysmal tachycardia.

(3) Marked amelioration, and sometimes apparent cure, of a more or less incapacitating syndrome of angina pectoris or what, at first, seemed to be a major attack of coronary occlusion.

They admit, however, that group (3) may actually have been pure gall bladder cases, in which chest symptoms were predominant.

They describe six cases exhibiting cardiac symptoms, chiefly anginoid in character, but for the most part not of the effort type, but all found to have abnormal electrocardiographic tracings, of the nature of inverted T waves, in one or more leads. Following operation, in periods ranging from six to nine months, the electrocardiogram returned to normal. They refuse to speculate, as to the nature of the myocardial disturbances responsible for the remarkable electrocardiographic changes. They conclude that gall bladder disease may injure the myocardium, and the process to a certain extent is reversible. In their opinion the majority of cases of coronary and myocardial disease, with sumptoms and signs (electrocardiographic), suggestive of these disorders, who have associated gall stones, are usually greatly benefited by judicious and skilful surgery. They also state :-

(1) Many cases of gall stones fail to present electrocardiographic or other evidence of cardiac disease.

(2) That not all patients with associated gall stone disease, and heart disease, are benefited by gall bladder surgery.

(3) Occasionally a catastrophic coronary occlusion may occur during a bout of smouldering calculus cholecystitis or choledochitis, as well as during, or soon after operation for relief of the latter conditions.

Laird (56), analysed 65 consecutive cases of gall bladder disease admitted to hospital. The study was essentially a clinical one, but also consisted of radiological examination of the gall bladder, electrocardiogram, blood area, and blood Wassermann. The assessment of the cardiovascular system was arrived at, after consideration of the symptoms of cardiac insufficiency, clinical and electrocardiographic findings, and the patients' response to a standardised exercise test (no details given). The diagnosis of gall bladder disease was based on symptoms and clinical findings, together with evidence of gall bladder dye function. Doubtful results with oral dye were repeated with intra-venous dye. His conclusions were as follows :-

(1) Disease of the gall bladder was commoner in females than in males - 8 : 1.

(2) Gall bladder cases occurred between the third and sixth decades, but mainly in the fifth and sixth decades.

(3) In 77 per cent of gall bladder cases a cardiac lesion was present. 100 per cent of the males were affected, and 73 per cent of the females.

(4) Obesity occurred in 37 per cent of cases. The incidence of heart disease, however, was greater than 37 per cent. If obesity is a factor, then it is not the whole explanation of the cardiac lesion in gall bladder cases.

(5) Foci of sepsis were at least as common in gall bladder cases, with normal hearts, as in those with evidence of cardiac damage.

(6) The cardiac lesion was temporary in some cases, permanent in others. Some of the latter showed an unsustained amelioration after operation.

(7) The incidence of heart disease, in cases of gall bladder disease, was uninfluenced by the presence of jaundice.

(8) Coronary artery thrombosis occurred in 12 per cent of gall bladder cases.

(9) The electrocardiogram was inconsistent in many cases of myocardial insufficiency, when compared with the clinical condition of the patient, but was of great value in cases, in which coronary artery thrombosis had occurred.

(10) Operation produced a cure of gall bladder symptoms, in 78 per cent of cases, and also seemed to ameliorate the cardiac manifestations, when present. Pulmonary embolism occurred in five per cent.

(11) There was some evidence to suggest that the longer the disease of the gall bladder is permitted to exist, the greater is the possibility of cardiac manifestations making their appearance.

(12) The impression was gained, that infection of the gall bladder was a definite etiological factor in the production of myocardial lesions, commonly found in these cases, that the presence of obesity, although almost certainly a factor in some cases, does not always explain the cardiac damage.

H.R. Miller (57), gives three reasons for claiming that more than an accidental association exists between disease of the heart and of the gall bladder.

(1) Anginal pain and myocardial incompetence, signalised by heart failure, will undergo improvement, and disappear upon removing a diseased gall bladder.

(2) Electrocardiographic abnormalities, which are characteristic of myocardial damage, induced by coronary artery disease, may disappear after extirpation of a diseased gall bladder.

(3) Concurrence of gall bladder disease and cardiac affection, notably coronary artery disease, is apparently much greater than we would expect, even when due allowance is made for the natural or predictable incidence of the disease, in question, at various ages.

Miller (57), in his article, proposes to discuss clinical, as well as anatomic and physiologic evidence,which may be marshalled to support the hypothesis of a common mechanism. As regards incidence, coronary artery and gall bladder disease appear to be increasing. This, he attributes to improved methods of diagnosis and increased survival of the population. Gall bladder disease,in the very old, is more frequent than is generally accepted. As regards diagnosis, the majority of cases can be easily distinguished. The autonomic reactions such as shock, meteoriam, increased salivation, and vertigo are known to accompany sudden involvement of both gall bladder and

coronary arteries.

In commenting on the pain associated with these conditions, he lists the pathways commonly involved as follows, thoracic, 1 - 4 (left), sympathetic nerves transmit pain impulses from the heart. At these levels the afferent somatic nerves are brought into action; these, together with the visceral fibres, refer pain into the complementary related dermatomes, viz. left infraclavicular, pectoral region, and inner aspect of the left arm. The gall bladder innervation is mainly thoracic, 8 - 10 on the right side, but may include 1 - 12, on the right side, and 5 - 10, on the left side.

Clark (58) also comments on the frequent association of cholecystitis and gall stones, and coronary artery disease. He appears to regard the former as aggravating the latter by reflex means.

He also states that acute inflammatory conditions of the gall bladder and duodenum create stimuli, which reflexly act through autonomic pathways, to restrict or in some other manner alter the coronary blood, supply, so that existing minor deficiencies in the coronary circulation become manifest. It seems probable, he suggests, that people with acute duodenal or gall bladder disease, whose electrocardiograms show the transient changes he describes (R-T elevation in lead I, with diphasic T waves in leads II and III, reverting to normal in two years, following an attack of acute

cholecystitis) do have minor alterations in their coronary circulation. He believes that gall bladder disease is an aggravating factor in heart disease.

Flint (59), in a short annotation, entitled "The cholecystitic heart", (a term coined by Moynihan) states that the irritable heart in cholecystitis is due to the presence of bile salts in the blood stream.

Millar (60), in discussing gall bladder and cardiac pain, comes to the following conclusions :-

(1) Clinically there may be a great resemblance between gall bladder pain, and cardiac pain. Both may occur in the same patient and be recognisable as such.

(2) Surgical treatment of the gall bladder may relieve both gall bladder and cardiac pain.

(3) Post mortem results show that subjects with diseased gall bladders have a higher degree of arterial degeneration than those in a control group.

It is evident from the preceding remarks that a large number of investigators, both surgical and medical, are in favour of theory that the gall bladder, when the seat of an infection, has an adverse effect on the heart. The literature concerning the other viewpoint, viz. that the association is purely incidental is much less voluminous.

White (61), however, points out that cardiospasm, pylorospasm, hiatus hernia, gall bladder disease and 'irritable colon', commonly occur in persons, who have heart disease, particularly of the hypertensive, or coronary type. That this association is purely incidental, he argues, depends primarily on two factors, both common denominators -

(1) The ageing process.

(2) A type of individual or manner of life.

In the case of gall bladder disease and coronary atherosclerosis of high degree, in particular, they occur twice as commonly together as separately but gall bladder disease is more common in women, while coronary heart disease is more common in men. Furthermore, the youngest cases of either condition are uncomplicated.

The second connection between the above gastro-intestinal symptoms and heart trouble, White goes on to say, is that of provocation of symptoms. Extra systoles, paroxysmal, tachycardia, and auricular fibrillation can be excited reflexly by gastro-intestinal disorders, even in a normal heart. Sometimes serious disorders of function, such as angina pectoris and congestive heart failure, can be prevented, or relieved, in a cardiac patient, by treating the digestive upset. The opposite, of course, holds good too, viz. the sufferer from gastro-intestinal disorders may be relieved by treating his cardiovascular state.

Wolferth (62) states that the etiological relationship between the two conditions may be summarised as follows :-

(1) Evidence exists that gall bladder disease and coronary artery disease co-exist more often than would be expected from the incidence of the two diseases separately.

(2) Removal of gall bladder, in some cases, has a beneficial effect on the myocardium, as shown by -

(a) Abolition of arrhythmias.

(b) Restoration of cardiac compensation.

(c) Relief of anginal pain.

(d) The disappearance of abnormalities in the electrocardiogram.

(e) The reason for the increased co-existence of gall bladder disease and coronary artery disease has not yet been determined.

REFERENCES :

1. Leonardo da Vinci, and Vesalius : Diseases of the Coronary Arteries and Cardiac Pain, edited by R.L. Levy, The Macmillan Company, 1936, p.17.
2. Vieussens : Ibid. p.18.
3. Drelincourt and Bellini : Ibid. p.19.
4. Lancisi : Ibid. p.19.
5. De Senac : Ibid. p.19.
6. Morgagni, B.G. : Ibid. p.19.
7. Herrick, J.B. : Ibid. p.19.
8. Heberden, W. : Commentaries on the History and Cure of Disease, Boston, Wells and Lilly, 1818. p.292.
9. Fothergill, J., Jenner, E., Hillier and Parry, C.H. : Diseases of the Coronary Arteries and Cardiac Pain, edited by R.L. Levy, The Macmillan Company, 1936, p.19.
10. Jenner, E. and Parry, C.H. : Ibid. p.19.
11. Jenner, E. : Ibid. p.19.
12. Parry, C.H. : Ibid. p.20.
13. Burns, A. : Observations in the Disease of the Heart, 1809.
14. Herrick, J.B. : Diseases of the Coronary Arteries and Cardiac Pain, edited by R.L. Levy, The Macmillan Company, 1936, p.21.
15. Herrick, J.B. : Ibid. p.21-22.

16. Virchow et al : Ibid. p.22.

17. Cohnheim : Ibid. p.22.

18. Marie, R., and Sternberg, M. : Ibid. p.23.

19. Hammer, A. : Wein Med. Wehnschr, 28 : 102 : 1878.
(Eng. Trans. by Major, R.H.)

20. Dock, G. : Notes on the Coronary Arteries, Ann Arbor, The Inland Press, 1896.

21. Herrick, J.B. : J.A.M.A. 59 : 2015 : 1912.

22. Pardee, H.E.B. : Arch. Int. Med., 26 : 244 : 1920.

23. Parkinson, J. and Bedford, D.E. : Heart 14 : 195 : 1927-1929.

24. Wilson, F.N. : Diseases of the Coronary Arteries and Cardiac Pain, The Macmillan Company, 1936, p.281.

25. Tosoni : Quoted by Major R.H., Classic Description of Disease, Charles C. Thomas, Third Edition, p.635.

26. Donato, M. : De Medica Historia Mirabili Libri Sex, Mantua Parsius, 1586. p. 269.
(Eng. Trans. by Major, R.H.
Classic descriptions of disease).

27. Benivieni, A. di P. : De obditis causes morborum, 1505. Ibid. p.636.

28. Colombo, M.R. : De re anatomica libri 15 : 1572.
Ibid. p. 638.

29. Fernel, J. : Io. Fernelii ambiani, universa medicina, 1581. Ibid. p. 639.

30. Platter, F. : Praxeos, Tomus Sicundus, de doloribus 1646, p.477. Ibid. 640.

31. Fabry, W. : Opera quae extant omnia. Observationum Centuria IV, Fraufurt, Dufour, 1682, p.320. Ibid. p.641

32. Sennert, D. : Medicinae practical, Venice, 1650. p.747. Ibid. p.642.

33. Glisson, F. : Anatomia Hepatitis, London, Du Gardi, 1654, p.88. Ibid. p.642.

34. Heister, L. : Medical Chirurgical and Anatomical Cases and Observations. Translated by George Wirzman, London, Reeves, p.10, 1755. Ibid. p. 64.

35. Morgagni, B.G. : The Seats and Causes of Disease. Translated by Benjamin Alexander, M.D. London. Millar and Cadell, 11 : 225 : 1769. Ibid. p.644.

36. Naunyn : Klinic der Cholelithiasis, Leipzig, 1892, quoted by Burton, J.A.G., Glasgow, Med. J. 121 : 14 : 1934.

37. Rowlands, R.P. : Lancet 2 : 1075 : 1929.

38. Moynihan, B.G.A. : B.M.J. 2 : 1599 : 1908.

39. Wilkie, D.P.D. : B.M.J. 2 : 767 : 1932.

40. Burns, A. : Observations in the Diseases of the Heart, 1809.

41. Levine, S. : Clinical Heart Disease, 1936, p.140.

42. Libman, E. : Trans. Assoc. Amer. Phys. 34 : 138 : 1919.

43. Fishberg, A. : Heart Failure, Henry Kimpton, 1937, p.620.

44. Van Vergmann, G., and Golder, M. : Functionelle Pathologie, eine Clinische Sammlung von Ergebnissen und Anschaunngen einer Arbeitsrichtung, Berlin, Julius Springer, 1932, p.70, quoted by Gilbert, N.C., Med. Clin. N. Amer., 32 : 213 : 1948.

45. Wright, J.H. : Trans. Med. Chirurg. Soc. Edin., p.153, 1938.

46. Riesman, D. : J.A.M.A. 48 : 1589 : 1907.

47. Babcok, R.H. : J.A.M.A. 52 : 1904 : 1909.

48. Graham, E.A., Cole, W.H., Copher, C.H., and Moore, S. : Diseases of the gall bladder and bile ducts, Lea and Febinger Company, 1933. p. 169.

49. Wilkie, D.P.D. : (same as before) B.M.J. 2 : 767 : 1932.

50. Willius, F.A., and Brown, G.E. : Amer. J. Med. Sci., 168 : 165 : 1924.

51. Schwartz, M., and Herman, A. : Ann. Int. Med. 4 : 783 : 1931.

52. Bean, W.B. : Amer. Heart J. 14 : 684 : 1937.

53. Campbell, S.B. : B.M.J. 1 : 781 : 1936.

54. Rolleston, H. and McNee, J.W. : Diseases of the Liver, Gall Bladder and Bile Ducts, 1929, p.767.

55. Fitz-Hugh, T. Jr., and Wolferth, C.C. : Ann. Surg. 101 : 478 : 1935.

56. Laird, S.M. : Brit. Med. J. 1 : 884 : 1938.

57. Miller, H.R. : Amer. Heart J. 24 : 579 : 1942.

58. Clark, W.E. : Amer. Heart J. 29 : 631 : 1945.

59. Flint, H.L. : Brit. Med. J. 2 : 819 : 1920.

60. Millar, C.H. : Lancet, 1 : 767 : 1932.

61. White, P.D. : Heart Disease, Third Edition,
The Macmillan Company, 1945, p.556.

62. Wolferth, C.C. : J. Mt. Sinai Hosp. 8 : 1121 : 1941.

POST - MORTEM INVESTIGATION.

Although a possible relationship between coronary artery disease and gall bladder disease was mooted as early as 1878, it was nearly fifty years later before the post-mortem aspect of the subject was studied. Willius and Brown (1), in a post-mortem examination of eighty-six cases of coronary artery sclerosis, found evidence of gall bladder disease in twenty-four. Tennent and Zimmerman (2) found a significant association between heart disease and gall bladder disease, in a study of 1,600 post-mortem reports, when subjected to biometric assessment, using Yule's formula*. This series of post-mortems included cases of carcinoma of the gall bladder, and obstruction of the common bile duct, as well as cholecystitis. Miller (3) stated that a series of 350 consecutive post-mortems revealed a "striking coincidence" of coronary artery disease and gall bladder disease. Brockbank (4), in a series of 1,347 post-mortems, found that a cardiac lesion occurred twice as often, when associated with gall bladder disease. Mills (5), from a study of 533 post-mortems, was of the opinion, that the presence of cardiac disease favoured the occurrence of cholelithiasis.

The largest series, to date, is that of Walsh, et al, (6). A study of the protocols of 2,737 post-mortems, on persons over the age of twenty years failed to reveal evidence of any close association between gall bladder disease and coronary artery disease. Their figures suggest a slightly increased tendency for gall bladder disease and coronary artery disease to occur

together, but statistical tests showed that the increasing incidence of gall bladder disease and of coronary artery disease, after twenty years of age, was no more than the increment expected with the mounting numbers in each group. Nevertheless, they feel that the coincidence of the two conditions in the same individual is not to be accounted for by age alone, and suggested that there remains some factor, or factors, which need further elucidation.

Breyfogle (7), in a statistical study of 1,493 post-mortems, concludes that there is a positive association, regardless of age and sex, between gall bladder disease and coronary artery disease, where the latter is regarded as the direct cause of death or the primary contributing factor towards death.

A more detailed study of Walsh's and Breyfogle's figures will be made later.

In the present investigation, 2,269 post-mortem reports, representing the total post-mortem examinations performed in Glasgow Royal Infirmary, in a period of approximately four and a half years, 1929-1933, were examined. The cases were classified according to the method employed by Walsh, et al, as it seemed to be a simple, yet efficient, method of assessment.

The cases were divided into the following groups :-

1. (a) Those with no evidence of coronary disease, i.e. normal coronary arteries.

(b) Those which showed some evidence of atherosclerosis, but in which the vessel remained patent, and the myocardium healthy. In this group the degree of atherosclerosis was so slight as to be considered non-significant, and consequently was labelled 'minimal atherosclerosis'.

(c) Those cases which showed a moderate to severe degree of atherosclerosis; they were labelled coronary artery disease.

2. (a) Those cases with no evidence of gall bladder disease, i.e. normal gall bladder.

(b) Those cases which showed evidence of cholesterolosis, but no stones.

(c) Those cases of gall bladder disease which showed evidence of thickening of the wall of the gall bladder, with or without stones in the gall bladder.

The above scheme is open to the criticism that it lacks absolute standards. Pathologists differ as to what constitutes normal blood vessels, minimal atherosclerosis or definite atherosclerosis, nor are they agreed as to whether gall bladder disease is present or not in certain cases. Nevertheless, the results in a large series should be reasonably accurate.

The following table gives the distribution, in age and sex groups, of the various sub-divisions described above :-

	Normal coronary arteries.				Minimal Atherosclerosis.				Coronary artery disease.			
Age Group in years.	20-39.	40-59.	60.	Total.	20-39.	40-59.	60.	Total.	20-39.	40-59.	60.	Total
Males.												
Normal gall bladder	332	371	119	822	26	100	96	222	23	126	123	272
Minimal cholesterolosis	0	4	1	5	0	2	1	3	0	2	2	4
Gall bladder disease	10	16	18	44	5	16	28	44	1	35	55	91
Females.												
Normal gall bladder	157	176	55	388	13	59	35	107	2	55	41	98
Minimal cholesterolosis	2	3	0	5	1	2	0	3	0	3	3	6
Gall bladder disease	24	40	18	82	1	19	12	32	0	14	27	41

Total number of post-mortems ..... 2,269.

Normal coronary artery.....	1,346	(59 per cent).
Minimal atherosclerosis.....	411	(18 per cent).
Coronary artery disease.....	512	(23 per cent).
Normal gall bladder.....	1,909	(84 per cent).
Minimal cholesterolosis.....	26	(1 per cent).
Gall bladder disease.....	334	(15 per cent).
Total number of males.....	1,517	(67 per cent).
Age 20-39 years.....	392	(25.8 per cent).
40-59 years.....	682	(45.6 per cent).
60 and over.....	443	(28.6 per cent).
Total number of females.....	752	(33 per cent).
Age 20-39 years.....	200	(26.5 per cent).
40-59 years.....	361	(46.5 per cent).
60 and over.....	191	(27 per cent).

As regards coronary artery disease, the incidence in males was 24 per cent while the incidence in females was 19 per cent. The age incidence in both sexes showed an increase with advancing years :-

Males.

Age 20-39 years.....	6.1 per cent.
40-59 years.....	25 per cent.
60 and over.....	41.3 per cent.

Females.

Age 20-39 years..... 1 per cent.

40-59 years..... 19.9 per cent.

60 and over..... 37.2 per cent.

As regards gall bladder disease the incidence in males was 11.9 per cent, while the incidence in females was 20.9 per cent. The age incidence in both sexes showed an increase with advancing years :-

Males.

Age 20-39 years..... 2.8 per cent.

40-59 years..... 11.1 per cent.

60 and over..... 21 per cent.

Females.

Age 20-39 years..... 12.5 per cent.

40-59 years..... 20.2 per cent.

60 and over..... 30 per cent.

Coronary artery and gall bladder disease occurred together in 132 cases, (6 per cent). 91 of these were males (70 per cent), and 41 were females, (30 per cent). If these figures are sub-divided into the three age groups, it will be seen that the co-existence of the two conditions is negligible in the youngest age group, increases appreciably in the middle age group, and is highest in the oldest age group. These facts apply to both sexes.

The figures are as follows :-

Males.

Age 20-39 years.....	1	per cent.
40-59 years.....	34	per cent.
60 and over.....	65	per cent.

Females.

Age 20-39 years.....	0	per cent.
40-59 years.....	34	per cent.
60 and over.....	66	per cent.

These figures indicate that the co-existence of the two conditions in this series is not striking, and is dependent on age, but independent of sex.

The incidence of gall bladder disease, in the coronary artery disease group, was 25 per cent, compared with an incidence of 9.5 per cent in the normal coronary artery group. This would suggest a tendency for gall bladder disease to occur in association with coronary artery disease. On further analysis, there was found to be a slightly greater incidence in females, 28 per cent, as compared with 24 per cent in males. Further analysis in terms of age groups again shows an increasing frequency with age. The figures are as follows :-

Males.

Age 20-39 years.....	1.6	per cent.
40-59 years.....	36.3	per cent.
60 and over.....	62.1	per cent.

Females.

Age 20-39 years.....	0	per cent.
40-59 years.....	24	per cent.
60 and over.....	76	per cent.

The incidence of coronary artery disease in the gall bladder disease group was 38 per cent, as compared with an incidence of 19 per cent in the normal group. This would tend to support the view that coronary artery disease and gall bladder disease occur more often together than separately. Further analysis, in terms of age and sex groups, again reveals that the association increases with age in both sexes. The figures are :-

Males.

Age 20-39 years.....	1.6	per cent.
40-59 years.....	38.4	per cent.
60 and over.....	60	per cent.

Females.

Age 20-39 years.....	0	per cent.
40-59 years.....	33.3	per cent.
60 and over.....	66.6	per cent.

The following tables are useful as a comparison between the three groups of post-mortems, (a) Author, (b) Walsh, et al, (c) Breyfogle :-

	(a)	(b)	(c)
Total number of post-mortems.....	2,269	2,737	1,493
	%	%	%
Males.....	1,517 (67)	1,757 (64)	885 (59)
Females.....	752 (33)	980 (36)	608 (41)
Age Group.			
Males.			
20-39 years.....	392 (25.8)	293 (17)	141 (16)
40-59 years.....	692 (45.6)	729 (41.6)	328 (36.7)
60 and over.....	433 (28.6)	726 (41.4)	333 (47.3)
Females.			
20-39 years.....	200 (26.5)	212 (21.6)	158 (26)
40-59 years.....	361 (46.5)	297 (31.3)	192 (31.5)
60 and over.....	191 (27)	346 (47.1)	198 (42.5)
	%	%	%
Incidence of coronary artery disease.	23	21	10.8
Males.....	24	37	15
Females.....	19	24	3
Incidence of gall bladder disease.	15	17	24.3
Males.....	11.9	12	23
Females.....	20.6	22	18
Co-existing gall bladder and coronary artery disease.....	6	5	5.3

	(a) %	(b) %	(c) %
Incidence of gall bladder disease in the coronary artery group.	25	21	48
Males.....	24	16	54
Females.....	28	33	70
Incidence of gall bladder disease in the normal coronary artery group.....	9.4	11.5	-
Males.....	5	8	-
Females.....	17.2	16	-
Incidence of coronary artery disease in the gall bladder group.....	38	27	23
Males.....	27	15	-
Females.....	12	11	-
Incidence of coronary artery disease in the normal gall bladder group.....	19	19	14
Males.....	14.2	22	10.8
Females.....	5	7	1.8

The results of my investigations and those of Walsh, et al, are essentially the same, if allowance is made for the slight differences in numbers in the various age groups in both sexes. Such differences, however, are to be expected in post-mortem series from two different countries. On the other hand Breyfogle's series shows slight differences. It contained a greater number of females, a lower incidence of coronary artery disease, and a greater incidence of gall bladder disease in males than in females - the latter finding is contrary to the results of all other investigators. His series, too showed a greater incidence of gall bladder disease. These four differences would suffice to explain the discrepancies in his series, compared with the other two.

Summary and Conclusions.

The above results were subjected to statistical analysis and the following conclusions were drawn :-

1. There was no significant difference in the incidence of coronary artery disease and gall bladder disease in the two sexes, in spite of the clinical impression that the former occurs more frequently in males, while the latter occurs more frequently in females.
2. In both groups the incidence increased with age, in both sexes.
3. There appears to be a relationship between coronary artery disease and gall bladder disease, as shown by -

3. (contd.)

   (a) An increased incidence of coronary artery disease in the gall bladder group, compared with a normal group.

   (b) An increased incidence of gall bladder disease in the coronary artery group, compared with a normal group.

4. This relationship is insignificant in the younger individuals, but increases with age.

5. It is not considered that sex played a significant part in the increased incidence of gall bladder disease in the coronary artery group. In males there appears to be an increased incidence of coronary artery disease in the gall bladder group.

* YULE'S FORMULA.

$$Q = \frac{N - \frac{(A) + (B)}{(AB)}}{2\ ((AB) - (A) - (B)) + N + \frac{(A) + (B)}{(AB)}}$$

Where N = total number of necropsies.

A = total number of necropsies, in which coronary artery disease was observed.

B = total number of necropsies, in which gall bladder disease was observed.

AB = total number of necropsies in which coronary artery disease and gall bladder disease were observed.

Q = co-efficient of association.

If Q = 1 there is complete positive association.

If Q = less than 1, there is a complete dissociation.

REFERENCES :

1. Willius, F.A., and Brown, G.E. : Amer. J. Med. Sci., 168 : 165 : 1924.
2. Tennent, T.R., and Zimmerman, H.M. : Yale J. Biol. and Med., 3 : 495 : 1931.
3. Miller, C.H. : Lancet 1 : 767 : 1932.
4. Brockbank, E.M. : Rolleston and McNee, Diseases of Liver, Third Edition 1929, p. 767.
5. Mills, F.A. : Ibid. p. 767.
6. Walsh, B.J., Bland, E.F., Taquini, A.C., and White, P.D. : Amer. Heart J., 21 ; 689 : 1941.
7. Breyfogle, H.S. : J.A.M.A., 114 : 1434 : 1940.

CRITERIA FOR THE DIAGNOSIS

of

GALL BLADDER DISEASE

and

CORONARY ARTERY DISEASE.

One of the greatest problems of the present investigation was, what would, at first glance, appear to be the easiest to deal with, namely to decide when a patient was suffering from gall bladder disease or coronary artery disease.

Either of these diseases may be present without causing symptoms to the patient, or producing any of the signs, which have come to be regarded as diagnostic of their presence. Occasionally a patient may have symptoms, or present signs, suggestive of the presence of one or other disease, and subsequent investigations prove that no such disease had existed. Notwithstanding these limitations, a fair degree of accuracy in diagnosis was obtained, and this will become evident in later discussions, especially with regard to gall bladder disease.

The following were regarded as the desirable requirements for the investigation of a patient thought to be suffering from gall bladder disease :-

1. Characteristic history.
2. Characteristic signs.
3. Characteristic radiological signs.
4. Confirmation by the surgeon, at operation, whenever possible.

A history was considered characteristic, when the patient complained of flatulent dyspepsia, accompanied by recurring

attacks of right subcostal pain or discomfort, nausea or vomiting, and aversion to greasy foods. The most characteristic signs were right subcostal tenderness and/or rigidity, jaundice, and biliuria. A palpable gall bladder was rare.

In spite of characteristic symptoms or signs, radiological confirmation of the presence of gall bladder disease was considered essential, particularly in those cases, which did not undergo operation.

Radiological examination consisted of :-

1. A straight X-ray of the right upper quadrant of the abdomen.
2. Visualisation of the gall bladder, after the ingestion of sodium tetra-iodophenolphthalein.

Straight X-ray of the abdomen may, in a minority of cases, reveal the presence of radio-opaque gall stones, or the outline of a gall bladder thickened by inflammatory processes. Visualisation of the gall bladder with dye may be necessary, in some of these cases, to determine whether the radio-opaque calculi are biliary, or renal. In the same way radio-translucent gall stones may be visualised.

In some cases a 'non-functioning' gall bladder was obtained, after the ingestion of dye, indicating obstruction in the cystic duct, usually due to stone preventing dye from entering the gall bladder and becoming concentrated.

The above radiological findings were accepted as evidence of gall bladder disease.

Difficulty arose in those cases where the concentration of dye in the gall bladder was poor, the so-called 'poorly functioning gall bladder'. This might have arisen in several ways :-

1. Insufficient absorption of dye from the intestine.
2. Impaired hepatic function, with diminished excretion of the dye into the bile ducts.
3. Deficient concentration of the dye in the gall bladder, because of disease, usually a cholecystitis.

Several methods are suggested for confirming the presence of a 'poorly functioning gall bladder' radiologically

1. Doubling the oral dose of the dye, to ensure absorption of an adequate amount into the blood stream.
2. Administration of the dye intravenously, thereby eliminating the possibility of deficient absoprtion from the gut.

The latter method was not employed because it was not considered to be completely devoid of danger, particularly in patients suffering from coronary artery disease. In order to eliminate impaired hepatic function one should,

strictly speaking, have liver function tests performed, but this unfortunately was not done in this investigation.

Wherever possible a second radiological investigation was carried out, within 10 - 14 days, if a 'poorly functioning gall bladder' was obtained from the first radiological examination. In some instances a 'normally functioning gall bladder' was obtained. The radiologist usually accepts the latter finding, and reports the gall bladder as being radiologically normal. It is possible, however, that some of these cases, particularly if they give a suggestive history, have a mild cholecystitis still present during the first radiological examination, but, after an interval of two weeks, the inflammatory process has subsided sufficiently to give a normal radiological picture.

At the beginning of this thesis it was decided, in view of the above difficulties, to carry out a preliminary investigation, in a group of 57 cases, comparing clinical diagnosis, radiological diagnosis, and operative findings, in order to assess the relative values of clinical and radiological diagnosis.

The clinical diagnosis in all these cases was gall bladder disease, and this was confirmed at operation. The history and physical signs in all were characteristic. In 53 out of these 57 cases, radiological investigation revealed changes, indicative of gall bladder disease but, in four, no

radiological evidence of gall bladder disease was obtained. In 21 cases radiological examination showed a 'non-functioning gall bladder', and, at operation, gall stones were found in 20. The exact location of the stones was not given in the operation notes, but it is tempting to postulate that they had blocked the cystic duct. In the remaining case the gall bladder did not contain any calculi, but was so small and shrunken, from previous inflammation, as to appear incapable of any function at all. In 19 cases radiological examination revealed a 'poorly functioning gall bladder'. In four of these cases chronic cholecystitis was found at operation, and in the remaining 15 cases gall stones were also found. In the remaining 17 cases of this series, gall stones were demonstrated radiologically. These results indicate that a high standard of accuracy, in the diagnosis of gall bladder disease, can be obtained, if the measures suggested above are used.

The diagnosis of coronary artery disease is discussed, in detail, in the section of electrocardiography, and requires little comment meantime.

There was little difficulty in reaching a firm diagnosis in the straightforward case of either gall bladder disease, or coronary artery disease, but there was real difficulty in deciding, whether gall bladder disease was complicated by coronary artery disease or coronary artery disease was

complicated by gall bladder disease, because the symptoms and signs, in each condition, can closely resemble one another. Pain and flatulent dyspepsia are symptoms found in both diseases. The pain of gall bladder disease, which is usually felt in the right subcostal region, may be referred to the front of the chest, and thus simulate coronary artery disease; whilst the pain of coronary artery disease is often referred to the upper abdomen thus simulating gall bladder disease. In addition left ventricular failure, secondary to coronary artery disease, may give rise to right subcostal discomfort and tenderness, due to engorgement of liver.

In the series of patients with gall bladder disease, electrocardiography was sometimes helpful in confirming the presence of coronary artery disease. In some cases, however, the clinical picture and electrocardiograms were equivocal, and one was left in doubt about the presence of coronary artery disease.

Similarly in the patients with primary coronary artery disease, radiological examination was helpful in determining the presence of gall bladder disease, but sometimes the clinical picture and radiological findings gave equivocal results. This was particularly so in those cases of coronary artery disease, in whom radiological examination demonstrated a 'poorly functioning gall bladder'. Wherever possible a

a repeat radiological examination was sought, but on a few occasions the general condition of the patient prevented this.

During the time when the series of gall bladder disease and coronary artery disease cases were being collected, a further 42 patients examined had symptoms and signs suggestive of either gall bladder or coronary artery disease, but a firm diagnosis could not be made. These constituted an 'equivocal group'.

GALL BLADDER DISEASE.

CLINICAL SURVEY.

108 patients suffering from gall bladder disease were investigated, and, of these, 93 were females, and 15 were males. The age and sex incidence is given below :-

Age Group.	Females.	Males.
20 - 29 years,	1	0
30 - 39 years,	11	1
40 - 49 years,	28	4
50 - 59 years,	29	5
60 - 69 years,	20	5
70 and over,	4	0

The highest incidence of gall bladder disease, in both sexes, is in the fifth, sixth, and seventh decades, with the maximal incidence in the sixth decade, in both sexes.

The associated diseases found in the 108 gall bladder cases, in this series were :-

Duodenal ulcer in five cases.

Valvular disease of heart in two cases.

(1 case of mitral disease)

(1 case of mitral and aortic disease)

Anaemia in three cases.

Thyrotoxicosis in two cases.

Diabetes mellitus in two cases.

Renal glycosuria in one case.

Congenital heart disease in one case.

The case of congenital heart disease seems to be worth while reporting. She was a middle-aged woman, of small, slight build, who had led a sheltered life, since childhood, because of breathlessness on exertion, and who was known to have had a heart murmur, since early childhood. Physical and radiological signs were in keeping with an inter-atrial septal defect; her electrocardiogram had changes indicative of coronary artery insufficiency. At operation, empyema of the gall bladder was found and from this staphylococcus aureus was cultured. She was given penicillin, 1 mega unit twice daily, for the first two weeks following operation. She made an uneventful recovery. When seen about twelve months later, she was feeling somewhat better but her activities were still much reduced. Her post-operative electrocardiogram, however, showed definite evidence of improvement (see Fig. 4, Appendix 3).

Three patients were anaemic, the cause being different in each case :-

1. Post-haemorrhagic (excessive menstrual loss, and also at the menopause).
2. Iron deficiency, probably due to dietetic deficiency.
3. Familial haemolytic anaemia.

The first patient's operation was postponed, because she was found to have a haemoglobin of 40 per cent. After a

course of iron therapy, a cholecystostomy was performed, but about 12 months later, on follow-up, she was found to have a haemoglobin, again of 40 per cent. In spite of one month's intensive iron therapy it remained unchanged, so she was referred to the gynaecologist.

The second patient had a haemoglobin of 60 per cent, associated with mitral and aortic disease.

The third was admitted to hospital, at the same time as her son, both suffering from acute cholecystitis and familial haemolytic anaemia.

A fourth case was under treatment for megalocytic anaemia (pernicious anaemia); she was well controlled by liver therapy, and her blood count was normal.

Disease of the appendix was less frequent than expected. 11 patients had had appendicectomy some time prior to gall bladder operation; in three cases, the appendix was removed during the gall bladder operation.

The coincidental occurrence of peptic ulcer and gall bladder disease, in this series, was not great, but the low incidence may be partly due to the fact, that the cases were not routinely X-rayed for peptic ulcer, unless the clinical picture suggested that it be done.

The 108 cases were analysed for the incidence of myocardial insufficiency, coronary artery disease, hypertension, and obesity, and menopausal symptoms. The results were as follows :-

Gall bladder disease and myocardial insufficiency = 70 cases (64 females, 6 males).

Gall bladder disease and hypertension = 45 cases (40 females, 5 males).

Gall bladder and coronary artery disease = 14 cases (12 females, 2 males). (The presence of coronary artery disease was confirmed by electrocardiogram).

Gall bladder and ?coronary artery disease = 15 cases (13 females, 2 males).

Gall bladder and obesity = 63 cases (60 females, 3 males).

Gall bladder and menopausal symptoms = 21 cases.

Gall bladder disease, with hypertension, and menopausal symptoms = 16 cases.

Gall bladder disease, with hypertension, and obesity = 29 cases.

Gall bladder disease, with hypertension, and myocardial insufficiency = 37 cases.

Gall bladder disease, with obesity, and myocardial insufficiency = 45 cases.

Gall bladder disease, with menopausal symptoms and myocardial insufficiency = 16 cases.

Several patients gave a history of recurring bouts of palpitation but their description of symptoms was not sufficiently accurate to determine whether paroxysmal tachycardia was indicated.

Paroxysmal tachycardia did occur in six cases, two of which had menopausal symptoms.

The number of gall bladder cases with myocardial insufficiency, without hypertension, obesity or menopausal symptoms was five.

It is evident from the above figures that myocardial insufficiency is a very frequent finding in gall bladder disease, its incidence being 65 per cent. Of the total of 70 cases, in this series, 64 were females and six were males. The age and sex incidence were as follows :-

Females.

20 - 29 years,	0 cases
30 - 39 years,	3 cases
40 - 49 years,	14 cases
50 - 59 years,	25 cases
60 - 69 years,	17 cases
70 plus,	4 cases

Males.

20 - 29 years,	0 cases
30 - 39 years,	0 cases
40 - 49 years,	1 case

Males. (contd.)

50 - 59 years,	2 cases
60 - 69 years,	3 cases
70 plus,	0 cases

In both sexes, it is evident that the incidence of myocardial insufficiency increases with age, but it shows a greater preponderance, in females, as compared with males. The reason for such a sex inequality is not apparent, at first sight, but a more detailed analysis of the other known causes of myocardial insufficiency, viz. coronary artery disease, hypertension, obesity, and menopause may shed some light on this problem.

Coronary artery disease.

The diagnosis of coronary artery disease in the gall bladder disease group, presents some difficulty. In some cases a history, typical of coronary artery disease, was obtained, together with an electrocardiogram, indicative of coronary artery insufficiency. In the remainder a typical history was obtained, but the chest lead electrocardiogram was within normal limits, or showed equivocal changes.

Number of cases, with positive electrocardiogram = 14 (12 females, 2 males).

Number of equivocal cases of coronary artery disease = 15 (13 females, 2 males).

Total = 29.

Group with positive electrocardiogram.

Females.		Hypertension.
20 - 29 years,	0 cases	0 cases
30 - 39 years,	1 case	1 case
40 - 49 years,	3 cases	1 case
50 - 59 years,	7 cases	6 cases
60 - 69 years,	1 case	0 cases
70 years plus,	0 cases	0 cases
Males.		
20 - 29 years,	0 cases	0 cases
30 - 39 years,	0 cases	0 cases
40 - 49 years,	0 cases	0 cases
50 - 59 years,	1 case	0 cases
60 - 69 years,	1 case	1 case
70 years plus,	0 cases	0 cases

Equivocal group.

Females.		Hypertension.
20 - 29 years,	0 cases	0 cases
30 - 39 years,	1 case	0 cases
40 - 49 years,	4 cases	0 cases
50 - 59 years,	4 cases	2 cases
60 - 69 years,	2 cases	1 case
70 years plus,	2 cases	1 case

Males.		Hypertension.
20 - 29 years,	0 cases	0 cases
30 - 39 years,	1 case	0 cases
40 - 49 years,	1 case	1 case
50 - 59 years,	0 cases	0 cases
60 - 69 years,	0 cases	0 cases
70 years plus,	0 cases	0 cases

The overall female incidence was 27 per cent, and the male incidence was also 27 per cent. It would appear that coronary artery disease, although occurring frequently in cases of gall bladder disease, is not the cause of the greater incidence of myocardial insufficiency, in females with gall bladder disease.

Hypertension, however, was present in 14 of the 29 cases, which suggests that hypertension plays an important part in the production of coronary artery insufficiency. The percentage incidence of hypertension, in the sexes, was essentially equal, viz. 48 per cent in females, and 50 per cent, in males.

Hypertension.

The incidence of hypertension, in the gall bladder disease group, was 47 cases out of total of 108. 38 were females, nine were males. Of the 38 females, seven had menopausal symptoms and this raised the possibility that

these were examples of menopausal vasomotor instability. Two cases were post-eclamptic, so that it was estimated that 29 had idiopathic hypertension (31 per cent). The distribution of cases, excluding the seven females with menopausal vasomotor instability was :-

Females.	
20 - 29 years,	0 cases
30 - 39 years,	2 cases
40 - 49 years,	5 cases
50 - 59 years,	19 cases
60 - 69 years,	12 cases
70 years plus,	3 cases
Males.	
20 - 29 years,	0 cases
30 - 39 years,	0 cases
40 - 49 years,	3 cases
50 - 59 years,	6 cases
60 - 69 years,	0 cases
70 years plus,	0 cases
Females (with idiopathic hypertension).	
20 - 29 years,	0 cases
30 - 39 years,	0 cases
40 - 49 years,	3 cases
50 - 59 years,	12 cases

Females (with idiopathic hypertension). (contd.)

60 - 69 years,	12 cases
70 years plus,	3 cases

The two cases, in the 30 - 39 years group, were examples of renal hypertension, following eclampsia. When these two cases and the cases of "menopausal vasomotor instability" are removed from the list, it will be seen that the incidence of hypertension increases with age. The incidence of idiopathic hypertension was 31 per cent, in females, and 27 per cent, in males.

Hypertension, therefore, occurs as often as coronary artery disease, in patients with gall bladder disease. The sex incidence is essentially the same.

Obesity.

The incidence of obesity, in the gall bladder series, was 63 cases out of 108, i.e. 58 per cent; 60 were females and three were males. The age and sex incidence were as follows :-

Females.

20 - 29 years,	1 case
30 - 39 years,	5 cases
40 - 49 years,	18 cases
50 - 59 years,	21 cases
60 - 69 years,	12 cases
70 years plus,	3 cases

Males.

20 - 29 years,	0 cases
30 - 39 years,	0 cases
40 - 49 years,	2 cases
50 - 59 years,	0 cases
60 - 69 years,	1 case
70 years plus,	0 cases

Of the number who had obesity and evidence of myocardial insufficiency, a total of 45, 41 were females, and four were males, i.e. 46 per cent were females, 26 per cent were males. It would appear, therefore, that obesity, could account for the greater incidence of myocardial insufficiency in females than in males. The higher age groups, 40 years onwards, again show the maximal incidence.

Menopause.

Of this series 21 were considered to have symptoms, indicative of the endocrine imbalance, associated with the menopause. Seven of these had hypertension, 16 had evidence of myocardial insufficiency. This group also helps to account for the increased incidence of myocardial insufficiency amongst the females.

Other conditions.

Amongst the other causes of myocardial insufficiency, which one must mention, in the gall bladder disease group, are several, which do not have a high incidence, but nevertheless

must be taken into account, as possible causes of cardiac insufficiency. These are, valvular disease of the heart, anaemia, thyrotoxicosis, and congenital heart disease. In this series of 108 cases they totalled seven.

In reviewing the above findings the following conclusions are drawn :-

1. Myocardial insufficiency is frequently found in patients suffering from gall bladder disease.
2. There are several causes of myocardial insufficiency, which may occur singly or in combination. The most important are coronary artery disease, and hypertension, but obesity, menopause and other conditions (listed above) may also be present.
3. The causes of myocardial insufficiency are found to a very large extent in the older age groups.
4. An ageing process would appear to play an important part in the high incidence of myocardial insufficiency in gall bladder disease but whether this is the main factor remains to be seen.

Post-operative follow-up.

In the present series 55 cases were operated on, and of these six died. The remaining 49 were followed up for a

period of not less than six months. In addition of a small group of 12 cases, who had undergone an operation for gall bladder disease between 9 - 12 years ago, were followed up.

Of the 49 cases, who were followed up for a period of at least six months, eight had no cardiovascular insufficiency before operation. None of them developed symptoms afterwards. They were all in the younger age groups.

Of the remaining 41 cases, five developed pulmonary embolism as a post-operative complication, and one case developed phlebitis of the leg. The five cases of pulmonary embolism were not included in the assessment of the cardio-vascular state, following operation, because of this incidental complication. Thus 36 cases are left, out of the 41 remaining cases, who had evidence of myocardial insufficienc before operation. Of these 36 cases, 18 were considered to show no significant change in their cardiovascular state, either as regards improvement or deterioration. 13 were considered to show improvement following operation, while five were considered to be worse. Of the latter five cases, one developed cerebral haemorrhage, a few weeks after leaving hospital, one developed what appeared clinically to be a coronary occlusion, also a few weeks after leaving hospital, one was unable to report after six months because she was confined to bed; she died a few months later from "heart

disease". One reported nine months after operation, with evidence of congestive cardiac failure, secondary to hypertension and coronary artery disease, and the last patient had developed severe symptoms of menopausal upset, and felt worse after operation than before. Some patients with coronary artery disease improved, others remained unchanged, a few appeared to get worse.

It is obvious then that operations for gall bladder disease, in patients with myocardial insufficiency, fail to produce an improvement in every case. Furthermore, it does not necessarily follow that, because a patient's heart condition improves following cholecystostomy or cholecystectomy, the gall bladder was the cause of the heart disease. During operation they have a chronic infective lesion removed or dealt with, which usually relieves their dyspeptic symptoms, and gives them a sense of well-being, which they did not have before operation. Furthermore, during the post-operative period, and for several months afterwards, they lead a restricted life, during which time the majority pay strict attention to the quantity and quality of their food. As a result of their dieting, an appreciable number lose a fair amount of weight, which will tend to help their cardiac state. In addition the amount of exertion following operation is usually very much curtailed and this, no doubt, has a very beneficial effect on the cardiac state. Thus operative treatment, by imposing a

series of conditions, more by accident than by design, viz. rest in bed, strict attention to diet, and curtailment of activities for some months following operation, will almost certainly produce improvement in the cardiac state irrespective of the type of operation.

As regards gall bladder symptoms following operation, 16 patients still complained of some flatulent dyspepsia, Right subcostal discomfort, nausea and vomiting. In three cases symptoms were sufficiently severe to warrant a second operation (the original operation in all three cases was a cholecystostomy).

The causes of death were as follows :-

1. Haemorrhage from a duodenal ulcer (confirmed at post mortem).
2. Fatty infiltration of the myocardium (post mortem diagnosis).
3. Haematemesis from gastric ulcer (confirmed by post mortem examination).
4. Intestinal obstruction due to adhesions (died following operation to relieve the obstruction).
5. Pulmonary embolism (confirmed by post mortem examination).
6. Duodenal haemorrhage (cause not determined).

The immediate mortality rate in this series was 12.5 per cent. It is estimated that four others would be dead within 12 months of operation, 1.20 per cent mortality.

In the small group of 12 cases, who were followed up after period of 9-12 years, following operation, the results are more difficult to assess because they were not seen in the immediate post-operative period. The electrocardiographic changes, however, are discussed more fully in the appropriate chapter.

Of the 12 cases, two claimed no improvement in their cardiovascular symptoms following operation. Seven noted improvement, following operation, but this was not maintained; two of them developed diabetes mellitus and hypertension, four developed hypertension, one developed electrocardiographic evidence of coronary artery disease. Clinically 10 of the 12 had coronary artery disease, which manifested itself after operation for gall bladder disease.

No definite conclusions can be drawn from this small series but it would appear that the progress of coronary artery disease and the development of hypertension are not materially altered by surgical treatment of a diseased gall bladder. It is probable that these 12 cases had some coronary artery disease and hypertension before operation. Surgical treatment of their gall bladder disease did appear

to ameliorate the symptoms in seven of these cases, but only for the time being, the two conditions appearing to progress gradually after operation. It would appear then that disease of the gall bladder has no etiological relationship to coronary artery disease or hypertension, but, when they co-exist, the gall bladder disease appears to be capable of aggravating the coronary artery disease, and when the diseased gall bladder is treated surgically the patients improve.

CORONARY ARTERY DISEASE

CLINICAL SURVEY

The coronary artery disease group was analysed in a similar fashion to the gall bladder disease group, and the results were as follows :-

Total number of cases	=	100
Number of males	=	60
Number of females	=	40

Females.

20 - 29 years,	0 cases
30 - 39 years,	1 case
40 - 49 years,	9 cases
50 - 59 years,	14 cases
60 - 69 years,	14 cases
70 plus,	2 cases

Males.

20 - 29 years,	0 cases
30 - 39 years,	3 cases
40 - 49 years,	25 cases
50 - 59 years,	24 cases
60 - 69 years,	8 cases
70 plus,	0 cases

Gall Bladder Disease.

13 patients were considered to have definite evidence of gall bladder disease, based on post mortem examination or clinical investigation and radiological examination. The age and sex distribution was as follows :-

Females.

20 - 29 years,	0 cases
30 - 39 years,	0 cases
40 - 49 years,	0 cases
50 - 59 years,	4 cases
60 - 69 years,	3 cases
70 plus,	0 cases

Males.

20 - 29 years,	0 cases
30 - 39 years,	0 cases
40 - 49 years,	1 case
50 - 59 years,	5 cases
60 - 69 years,	2 cases
70 plus,	0 cases

In addition there were three cases, who were regarded as doubtful or equivocal cases of gall bladder disease, one female and two males.

Hypertension.

The total number of cases in this group were 38, 18 females and 20 males. The age and sex distribution was as follows :-

Females.

20 - 29 years,	0 cases
30 - 39 years,	1 case
40 - 49 years,	5 cases
50 - 59 years,	9 cases

Females. (contd.)

60 - 69 years,	3 cases
70 plus,	0 cases

Males.

20 - 29 years,	0 cases
30 - 39 years,	1 case
40 - 49 years,	9 cases
50 - 59 years,	7 cases
60 - 69 years,	3 cases
70 plus,	0 cases

The incidence of hypertension in females was 45 per cent, in males 33 per cent.

Obesity.

The total number of cases in this group were 35, of which 20 were females, and 15 were males, i.e. an incidence of 51 per cent in the females and 22 per cent in the males. The age and sex distribution was as follows :-

Females.

20 - 29 years,	0 cases
30 - 39 years,	1 case
40 - 49 years,	4 cases
50 - 59 years,	11 cases
60 - 69 years,	5 cases
70 plus,	0 cases

Males.

20 - 29 years,	0 cases
30 - 39 years,	2 cases
40 - 49 years,	4 cases
50 - 59 years,	5 cases
60 - 69 years,	4 cases
70 plus,	0 cases

ASSESSMENT OF THE COMBINED GROUPS

OF

GALL BLADDER DISEASE

AND

CORONARY ARTERY DISEASE

Having gathered together the two series, it is now possible to add them together and find the overall incidence of the co-existence of coronary artery disease and gall bladder disease, and the incidence of hypertension and obesity in the combined groups.

Total number of cases = 208.

Number of cases of coronary artery disease, in the gall bladder disease group = 15.

Number of equivocal cases of coronary artery disease, in the same group = 15.

Number of cases of gall bladder disease in the coronary artery disease group = 13.

Number of equivocal cases of gall bladder disease, in the same group = 3.

The overall percentage of the co-existence of gall bladder disease and coronary artery disease, in 208 cases was 13.5. The figure, which was obtained in the post mortem series, was 16 per cent, i.e. a fairly close agreement between the clinical and post mortem series. If the equivocal cases are included, the percentage rises to 21, which probably means that some equivocal cases did not have coronary artery or gall bladder disease, as the case may be.

Hypertension was found in 85 out of 208 cases, i.e. 41 per cent; 29 were males, an incidence of 14 per cent, while 56 were females, an incidence of 27 per cent.

Obesity was found in 98 out of 208 cases, i.e. 40 per cent; 18 were males, an incidence of 8 per cent, while 80 were females, an incidence of 40 per cent.

It is obvious then that in the two series of gall bladder and coronary artery diseases the two conditions occur not infrequently together, but, in addition, hypertension and obesity are frequently present, especially in the females.

Conclusion.

1. Gall bladder disease occurs more frequently in females (5 : 1) than males, while coronary artery disease occurs more frequently in males (2 : 1) than females.
2. The maximal age incidence was essentially the same, in both groups, about 90 per cent occurring in fifth, sixth and seventh decades.
3. Gall bladder disease occurs more commonly in association with other diseases, than alone. These conditions are coronary artery disease, hypertension, and obesity. Other diseases which are frequently found with gall bladder disease are peptic ulcer, diabetes mellitus, thyrotoxicosis, valvular disease of the heart.
4. Myocardial insufficiency is frequently found in patients suffering from gall bladder disease. The most common causes of myocardial insufficiency are coronary artery disease and/or hypertension and obesity.
5. Hypertension and obesity are the most common causes of myocardial insufficiency in female patients with gall

5. (contd.)

bladder disease. Hypertension is just as frequently found in association with gall bladder disease, as is coronary artery disease. Hypertension and obesity were more common in females than males.

6. Some patients with myocardial disease improve following operation. This applies to some cases of coronary artery disease, hypertension, or obesity. Some with coronary artery disease or hypertension remain unchanged, while a few seem to get worse following operation.

7. It is not certain, by any means, that improvement of the cardiac condition following operation is entirely due to the operation on the diseased gall bladder.

8. 66 per cent of cases were relieved of gall bladder symptoms, up to six months after operation. The mortality rate was 12.5 per cent. Pulmonary embolism occurred in 8.8 per cent of the cases undergoing operation.

9. In a group of cases, about 12 per cent of the total of 250 cases examined clinically, it was not possible to decide whether the patient had gall bladder disease, coronary artery disease, or both.

EQUIVOCAL SERIES.

While the above 208 cases were being gathered, another 42 cases were investigated, as possible examples of gall bladder disease or coronary artery disease. In 29 of these cases it was found impossible to put a definite label on each individual case, but the results of the investigations of these cases were as follows :-

? Coronary artery disease,	= 5
? Gall bladder disease,	= 22
? Coronary and gall bladder diseases,	= 3
Duodenal ulcer,	= 7
Appendicitis,	= 2
Carcinoma of head of pancreas,	= 1
Carcinoma of ascending colon,	= 1
Paroxysmal tachycardia (stimulating coronary disease),	= 1

Out of a total of 250 cases investigated it was not possible, at the time of the investigation, to give a definite diagnosis in 30 cases, i.e. 12 per cent. Even with the aid of ancillary diagnostic methods, such as chest lead electrocardiography and X-ray investigation, an appreciable number remained without a definite diagnosis. There is little doubt, however, that if these cases were followed up, for some years, then a more definite diagnosis might be made. As this was not considered an essential part of this thesis, these cases were not followed up.

C H O L E S T E R O L

BIOCHEMISTRY AND PHYSIOLOGY.

Cholesterol is the predominant steroid in animals, and is found in all the cells of the body, in varying concentrations. It is not a single substance, but a mixture of two or more steroids, which differ in physico-chemical and biological properties (1). Chemically it is related to other compounds, viz. the bile acids, vitamin D, the sex hormones, the adrenal hormones, and certain carcinogenic agents. In spite of much investigation, the physiology and biochemistry of cholesterol in animals (including humans) is still imperfectly understood.

Cholesterol appears to be derived from two sources, endogenous and exogenous, and the endogenous seems capable of supplying the body's needs, when the exogenous supply fails.(2). It is believed that there is continuous formation and destruction of cholesterol in the tissues, and that a positive or negative balance may occur, depending on whether formation or destruction is greater. According to Peters and Van Slyke (3), ingested cholesterol is estrified, by pancreatic cholesterase, with the fatty acids liberated from fats or phospholipids. These esters are then adsorbed in the small intestine, along with the rest of the products of fat digestion. In the light of recent advances of our knowledge of fat digestion and adsorption, cholesterol seems to pass into the portal venous system, and also into the lymph channels, whence it goes by way of the thoracic duct into the blood stream. In the blood, cholesterol exists in two forms,

free and ester. The ester form acts as a means of transportation of fatty acids. The concentrations of cholesterol and phospholipids in the blood stream parallel one another, and maintain a "rather constant ratio" (4).

There is still considerable doubt as to which organs are concerned in the synthesis and destruction of cholesterol, these functions having been attributed to the adrenals, spleen, liver, thyroid, pancreas and hypophysis. According to Cantarow and Trumper (5), there is evidence to suggest that cholesterol metabolism is regulated by the activity of the reticulo-endothelial system, rather than by any one organ. Two divergent theories have been advanced, -

(a) The reticulo-endothelial cells control the normal disposition of lipids, removing cholesterol from the blood when it is present in excess, storing it, and returning it to the blood when it is low.

(b) The reticulo-endothelial system synthesizes cholesterol, and variations in the concentration of this substance in the blood are dependent upon its variable synthesis by the reticulo-endothelial cells.

Bills (6), however, states that endogenous cholesterol originates in the cells in which it occurs. There is fairly general agreement that acetic acid and acetone can serve as building blocks for cholesterol.

Cholesterol is chiefly eliminated in the intestinal secretions in the forms of cholesterol and beta-cholesterol (7). The former is converted into coprosterol by the action of anaerobic bacteria. The intestinal mucosa, and not the bile, appears to be the main source of cholesterol. The amount of cholesterol excreted in the faeces exceeds that excreted in the urine, a little is lost in desquamation of the skin, and in the milk.

The liver appears to play an important role in the intermediate metabolism of cholesterol (8). It seems to have the capacity for storing cholesterol, and liberating it into the blood and bile at a relatively constant and equal ratio. In animals fed with cholesterol, it accumulates only in the liver, and largely in the ester form, suggesting that the liver disposes of cholesterol, and esterification is an important part of the process (9). The liver is believed to act as a regulator of the relationship between free cholesterol, and cholesterol esters in the blood. In humans the proportion of free to total cholesterol remains constant in health and in most diseases. Only in hepatic dysfunction does the ratio depart from normal, and then it is almost invariably the ester fraction in blood that suffers (60-80 per cent of the plasma cholesterol is in the ester form).

According to Cantarow and Trumper (10), normal bile contains 20-200 mg per cent of cholesterol - bile cholesterol

exists only in the free state, and its concentration is normally below that of the blood. There seems to be no consistent relationship between the level of plasma cholesterol and bile cholesterol. In animals it is possible to raise the blood cholesterol without a corresponding increase in bile cholesterol, and also to increase the cholesterol elimination in the bile without any alteration in the level of blood cholesterol. In humans the lack of relationship between plasma and bile cholesterol is emphasised by the fact that in the nephrotic syndrome and diabetes mellitus, where there are extremely high plasma cholesterol values, the concentration of bile cholesterol may be low, whilst in pernicious anaemia a low plasma cholesterol may be associated with a high biliary cholesterol. In the late months of pregnancy there is both a hypercholesterolaemia, and an increase in the cholesterol content of hepatic and gall bladder bile, and this may be a factor in the causation of cholelithiasis in multipara.

The influence of several physiological states on serum cholesterol, as summarised by Peters and Van Slyke (11) are as follows :-

1. Age : The concentration of total cholesterol does not vary significantly with age. Serum cholesterol levels have reached stable values as early as the second

1. (contd.) : month of life. Adult levels do not change appreciably as life advances.

2. Sex : Cholesterol levels are equal in both sexes.

3. Race : No difference in Indians, Europeans, Americans, Eskimos.

4. Effect of diet : The reports of various investigators are rather conflicting. Some report no change after a fatty meal, others do. Some report no change after feeding cholesterol, others do.

5. Diurnal variations : Cholesterol appears to be unaffected by ordinary meals and activities.

6. Obesity : It appears to be unassociated with abnormalities in serum lipids.

7. Endocrines : Male hormones appear to have no effect. Certain workers report a fluctuation of cholesterol near the menses but this is not confirmed by other workers.

8. Effect of pregnancy : It is generally agreed that plasma cholesterol increases during pregnancy. The increment amount to 50-100 per cent. It begins after the second month. Some say that the esters are especially increased, others that the increment is entirely composed of free cholesterol.

REFERENCES :

1. Cantarow, A., and Trumper, M. : Clinical Biochemistry, Fourth Edition, W.B. Saunders Company, 1949, p.141.
2. Cantarow, A., and Trumper, M. : Ibid. p.143.
3. Peters, J.P., and Van Slyke, D.D. : Quantitative Clinical Chemistry, Vol. I, Part I, Second Edition, Bailliere, Tindall, and Cox, London, 1946, p.402.
4. Peters, J.P., and Van Slyke, D.D. : Ibid. p.387.
5. Cantarow, A., and Trumper, M. : Clinical Biochemistry p.143
6. Bills : Physiol. Rev., 15 : 1 : 1935, quoted by Cantarow and Trumper p.144.
7. Cantarow, A., and Trumper, M. : Clinical Biochemistry p.144
8. Cantarow, A., and Trumper, M. : Ibid. p.143.
9. Cantarow, A., and Trumper, M. : Ibid. p.144.
10. Cantarow, A., and Trumper, M. : Ibid. p.457.
11. Peters, J.P., and Van Slyke, D.D. : Quantitative Clinical Chemistry, Vol. I, Part I, Second Edition, Bailliere, Tindall, and Cox, London, 1946, p. 475-508.

CHOLESTEROL IN REGLATION TO ATHEROSCLEROSIS.

SUMMARY OF EXPERIMENTAL WORK.

Atherosclerosis has shown a relative increase because of the lengthening span of life. It is not, however, a disease of senescence alone, it is an important disease of young adults. Using a palpable radial artery as a guide, males under 35 years of age have an incidence of 5-10 per cent, females 1-2 per cent (1). In World War I it was found, as an incidental post mortem observation, that it occurred in 30 per cent of those at 20 years of age, in over 45 per cent at 25 years, and over 80 per cent at 50 years. In these studies the atherosclerosis was chiefly located in the left coronary artery (2).

Careful anatomical examination, however, shows that the earliest age of atherosclerosis begins in infancy. Recent studies have shown that these early fatty lesions are pathological and the antecedents of the later full blown atherosclerosis (3). The early atheromatous plaques occur in five per cent of infants under six months, and in almost 100 per cent of children over eight years (4).

To Aschoff and his school (5) goes the credit for being the first to recognise cholesterol as the fundamental chemical constituent of the lesions of atherosclerosis. Anitschkow (5) found that lesions resembling human atherosclerosis could be produced in rabbits by feeding them pure cholesterol dissolved in vegetable oil. A similar result

was obtained in chicks by Katz (6). Feeding large amounts of cholesterol to rabbits and chicks raises their serum cholesterol tenfold or more, and is associated with extensive deposits in many organs (6). In rabbits it has been found possible to produce similar changes by feeding small amounts of cholesterol over many months, without raising the serum cholesterol (5). In man, however, it has not been possible so far to produce a hypercholesterolaemia by feeding cholesterol.

Several views have been expressed on the genesis of atherosclerosis due to cholesterol feeding.

1. Anitschkow (5) (Virchow, Aschoff) believe that the lipid is extracellular at first, entering the intima directly from the plasma, wherever the internal elastic lamina has been torn. In the intima the lipid then undergoes precipitation and secondary calcium deposition occurs. They point out that focal lesions of the arterial wall and hypertension predispose to the condition by weakening the internal elastica.
2. Duff (7) contends that the primary changes are necrosis of muscle cells of the media, and swelling of the ground substance of the intima. Lipid infiltration is a secondary phenomenon, and the lipid is extracellular at first. Later wandering cells appear, becoming foam cells and still later

2. (contd.)

fibroblasts. Infiltration of lipid occurs at sites of local injury, either in the intima or media.

3. Leary (8) in his earlier work described the first change as mucoid degeneration of the intima, with deposition of extracellular isotropic lipid. This is followed by the appearance of foam cells containing anisotropic lipid, the foam cells arising from monocytes. In later reports (9), however, he contends that -

(a) Lipid accumulation is the primary change in atheroma, and precedes any degeneration.

(b) The lipid is intracellular from the start.

His view is that cholesterol-laden foam cells, originating from the Kupffer cells of the liver, and the reticulo-endothelial system of the adrenals, bone marrow, and spleen, are liberated into the blood stream, after cholesterol feeding. He states that they penetrate the endothelium of systemic vessels and accumulate under the endothelium, forming atheromatous plaques. "Chemotaxis" is the mechanism for focal penetration, and local mechanical stresses help to determine the precise distribution of lesions.

4. Hueper (10), believes that the lesions result from macromolecular substances in the circulating blood stream, which form a film over the vessel lining, and interfere with nutrition and oxygenation of the vessel wall. Endothelial cells engulf this material and proliferate to form plaques. Such endothelial cells may migrate to the media. He attributes localisation to static mechanical forces, resulting from posture, and to decreased flow in the vasa vasorum, occurring through hypertonus or hypotonus of the blood vessel wall. This view assumes that the endothelium is phagocytic.

5. Katz (11), believes that vascularisation of the arterial walls is a determining factor in the development of atheroma. Foam cells in these vasa, either coming from distant sites or locally, may accumulate and interfere with intimal nutrition. Foam cells apparently originate in the reticulo-endothelial system and travel through veins to the arterial circulation and lodge in the vasa-vasorum. Lesions develop -

   (a) Where there are intimal vasa to become obstructed.

   (b) Where the number of vasa is critical for the local needs. Portions of the aorta which are uninvolved might be free of atheroma either because -

5. (contd.)

(b) (contd.)

1. There are no intimal vasa.
2. There are many intimal vasa, so that obstruction of a few does not seriously interfere with local nutrition.

Katz (11), summarises the various conclusions, regarding the pathogenesis of atherosclerosis, as follows :-

1. Role of cholesterol :

The essential primary constitutents of atheroma are cholesterol, and its esters, and calcium. In human atherosclerosis, however, two difficulties arise -

1. The absence of hypercholesterolaemia in most cases of atherosclerosis in man.
2. The absence of alimentary hypercholesterolaemia in man.

The range of cholesterol levels in normal individuals varies from 132-392 mg per cent, but the level in any one individual is constant. Consequently 150 mg per cent may be normal for one individual, 300 mg per cent be high for the same individual, but still be within the normal range (12).

In man the lack of correlation between atherosclerosis and serum cholesterol levels has been shown (13).

In xanthomatous diseases, coronary atheroma is found in those with elevated serum cholesterol, but not in those with

normal serum cholesterol levels (14). Recently it has been claimed that patients with coronary sclerosis have a definitely elevated serum cholesterol and that the levels show wider fluctuations than normal (15). Furthermore, the mean level of blood cholesterol is higher in cases with atherosclerosis obliterans of the legs that in controls, although the range of values is the same in both (16).

Serum cholesterol levels reflects a balance between the rate at which cholesterol enters the blood from depots, from sites of synthesis, or exogenous sources, and that at which it leaves the blood to be excreted, destroyed or stored. Thus the rate of transport, rather than absorption and excretion, determine serum cholesterol levels (17). Furthermore, the serum cholesterol level may vary with shift of cholesterol from red blood cells to plasma (e.g. with variation of acid - base balance). A rise of whole blood cholesterol may mean a transfer from tissues to blood or from red blood cells to plasma (18). The thyroid and pituitary glands may regulate the shift from tissues to blood in man as in experimental rabbit atheroma (19). Evidence in animals suggests that the total body cholesterol does not change after thyroidectomy but that there is a change in its distribution (20). On this basis, if cholesterol is a major factor in human atherosclerosis, it is not the level of this substance in the serum, which is important, but rather the rate

of its transport. High rates of cholesterol exchange may be balanced so that the serum cholesterol level is average, high, or conceivably low (21).

2. Dietary factors influencing cholesterol metabolism.

(a) Cholesterol : There is little direct knowledge of the effect of long term cholesterol feeding in man but Katz and Dauber (22) think that the normal serum levels may include an element of alimentary cholesterol, also that the long term consumption of cholesterol in moderate quantities may favour the development of atheroma without hypercholesterolaemia. They suggest that the dietary cholesterol may prove to be one of the more readily controllable of the several factors involved in human atherosclerosis.

(b) Fat : Natural food sources of cholesterol contain neutral fats and lecithin also. Fat persons tend to have a higher fasting serum cholesterol level than lean ones. They show a rise in serum cholesterol after eating lard, butter and vegetable fats (23).

(c) Protein : In plasma, cholesterol is combined with euglobulin and fibrinogen (24). Serum proteins and cholesterol tend to deviate in certain conditions, e.g. lipoid nephrosis, plasmaphoresis,

(c) (contd.)

and after haemorrhage (25). Protein in the diet may, therefore, affect the production of lesions by cholesterol, by altering serum cholesterol levels.

3. Endogenous factors affecting tissue cholesterol levels.

There is clear evidence from experiments that the thyroid gland plays an important part in the development of cholesterol atherosclerosis. There is no direct correlation of basal metabolic rate with serum cholesterol, and it is evidently some other property of the thyroid secretion than its calorigenic effect that is involved (26). In experimental atherosclerosis the pituitary thyrotropic hormone has an antagonistic action to the thyroid hormone (27).

The pancreas probably also plays a part, e.g. the association of diabetes and atherosclerosis. Atherosclerosis, however, is not related to the severity of the diabetes (28). The blood sugar level, or administration of insulin, has no relation to the serum cholesterol level (28). The latter is raised in coma.

The sex glands may operate in an indirect way through the pituitary gland.

4. Local cell metabolism of cholesterol.

Cholesterol is present in all body cells. Cholesterol esterase is present throughout the body as well as in blood. Cholesterol - dehydrocholesterol has been suggested to play the part of an oxidation - reduction system in cell

metabolism (29). There is evidence that cholesterol is synthesised from multiple small molecules such as acetic acid (30).

Thannhauser (29), outlines the possible disturbances in cholesterol intermediary metabolism which may lead to local accumulation in cells :-

(a) Retention and storage in local cells due to -

1. Dinimished destruction of cholesterol.
2. Decreased excretion.
3. Lack of esters or phospholipid.

(b) Increased synthesis of cholesterol by cells generally, or by the reticulo-endothelial cells.

He accepts the latter as a basis in xanthomatosis. Primary xanthoma is due to intracellular over-production, while in secondary xanthomatosis, e.g. diabetes, the lesions are due to retention and storage.

5. Exeretory factors.

Cholesterol is excreted into the large intestine (31). It is also excreted by the liver in the bile but this cholesterol is re-absorbed (30). Colon bacilli in the large intestine may destroy cholesterol to a varying extent. (30)

6. Factors influencing the localisation of lesions.

Atheroma occurs as localised plaques, most often in the descending aorta, at the origin of the intercostal arteries, in the abdominal aorta particularly at points of branching

such as the bifurcation, and in the coronary arteries. Those who have adopted the view that imbibition from the plasma is the basic mechanism for atheroma have offered varied explanations. The following are the chief views (32) -

(a) Lipid infiltrating diffusely into the vessel wall gravitates or is massaged by the vessel pulse through the intimal spaces and is trapped in those sites which are immobile or where scarring has occurred and collects there to form atherosclerosis.

(b) Lipid infiltrates diffusely into the intima in systole and is expressed in diastole by the elastic recoil of the internal elastic lamina except hwere -

1. The elastica is damaged or torn.
2. The intima is too thick.
3. The intima undergoes some chemical change which makes it bind the lipid.

(c) Lipid infiltration occurs in greater amounts in those regions where stress and stretching injure the ground substance of the intima or have damaged the media or the elastica.

All these hypotheses are based on the assumption that the lipid deposit is on a purely mechanical basis of preferential filtration. Duff (7) claims that the first

visible microscopic change is degeneration and necrosis and only later does extracellular lipid appear, to be followed still later by foam cells. Careful histologic studies have shown that the earliest lesions are subendothelial foam cells containing anisotropic lipid or cholesterol (9). No positive experimental evidence of infiltration has been produced.

Hirsch (4), advanced the view, against the theory of infiltration, that lipid is produced locally in the lesion. According to this worker the continuous cibration and agitation of the arterial wall, more marked at the sites of eddies, breaks up the internal elastic lamina and destroys the complex organisation of the intima. Local metabolic derangements result in the local production of cholesterol within branching stellate cells, which he suggests may be a type of vascular nerve cell. Calcium, and hyalive material are locally produced simultaneously as a result of deranged metabolism.

If cholesterol enters the arterial wall by some method other than diffuse infiltration, other explanations of its entrance and localisation must be sought for. Leary (9), states that foam cells are present in the earliest microscopic lesions, i.e. the lipid in intracellular rather than extracellular from the start.

The studies of Winternitz (33), and associates have

disclosed an intramural internal circulation anastomosing with the adventitial vasa. The intimal vasa are most numerous at the origin of branching arteries and generally increase in number with age. Intimal vasa are always found in association with intimal atherosclerotic lesions so that the association has seemed more than fortuitous. They claim to have seen frequent intramural haemorrhages from these vasa and have advanced the hypothesis that such haemorrhages with the disintegration of R.B.C. and liberation of their lipid content and cholesterol serve as starting points for atherosclerosis.

Katz and Dauber's (34), view combines some of the evidence of Leary and Winternitz. Clusters of foam cells within intimal vasa have indicated the importance of both intimal blood supply and cholesterol foam bearing cells. The localisation of foam cells is determined by the presence of intimal vasa their number and distribution. At points of branching the presence of intimal vasa, permits the development of lesions.

7. The rate of tension and strain.

Increased arterial pressure may accelerate intimal thickening, and may affect the vascularity in its favoured location and thus may hsten the occurrence of atheroma. This may account for the greater frequencey of atherosclerosis in hypertensive patients.

More recently Katz and his co-workers (35), have been using dogs as experimental animals in the production of atheromatous lesion. It requires prolonged feeding with cholesterol plus thiouracil to produce serum cholesterol levels up to 2000 mg per 100 cc, in dogs, and consequently atheromatous lesions, apparently because of the great vascularity of the dogs aorta. They demonstrated that atheromatosis develops in areas of diminished vascularity (produced by cauterisation) in a relatively short time with only a moderately raised blood cholesterol. From these experiments they conclude that the nourishment of the wall of the blood vessels is an important factor in the production of atheromatous lesions.

Summarising the above material in the relation of serum cholesterol to atheroma, it may be said that the relationship was first noted in 1911 by Anitschkow in experiments with rabbits. The only other animals in which experimental hypercholesterolaemia induces atheromatous degeneration are chickens and dogs.

The work of Hueper leaves no doubt that the presence in the blood stream of macromolecular substances such as polyvingl alcohol or methyl cellulose does induce a reaction in the blood vessels indistinguishable from atheroma, the foreign material taking the place of cholesterol. Recently the physical state of the lipids in human subjects has been

studied by Moreton (36). By dark field microscopy and high speed centrifugation he found that normal serum contains few visible particles and that these resist separation by a centrifugal force of 22,500 G. for one hour. In the serum of patients with sustained hyperlipaemia large colloid particles are visible and are readily removed by a centrifugal force of 5,000 G. for one hour. Comparison of the macro-molecular substances used by Hueper, with the particles found in hyperlipaemic serum showed that they were similar in size and separability. Moreton, therefore, concluded that it is the size of the particle which determines the cellular reaction of the tissues to the lymph seeping through the intima from the vessel lumen. For a few hours after each fatty meal particles of the necessary size are present in the circulating blood and presumably in intimal tissue fluid. It is suggested that the neutral fat is locally metabolised while the more resistant cholesterol accumulates and excites 'foam cell' reaction. Duff, however, objects to the above view in that the flow of lymph normally occurs from the vasa vasorum in the artery walls towards the intima and not vice versa as suggested by Moreton and Hueper.

Leary, as stated above, believes that the cholesterol enters the intima from the lumen inside foam cells, which are reticul-endothelial cells detaining lipid material and

are derived from the sinusoids of liver, spleen and bone marrow. 'Chemotaxis' was the mechanisms suggested for focal penetration but Gordon suggests that cells of a larger size, such as those lipaphages, tend to get bumped from the axial stream of the blood to the periphery and so into touch with the endothelian by the kinetic energy of the moving red cells.

The above remarks form a brief survey of the modern concepts of the pathogenesis of atherosclerosis in terms of deranged cholesterol metabolism. Some people, however, maintain the infection plays an important part in the production of atherosclerosis, others that mural thrombi are the main forerunners of atherosclerosis and that cholesterol deposition is a secondary phenomenon. Even amongst the protagonists there is still a difference of opinion as to whether the cholesterol enters the intima from the lumen of the vessels or via the vasa vasorum in the vessel wall, whether the cholesterol is primarily intracellular (foam cells) or extracellular in the earliest lesion of atherosclerosis. Experimental animals such as rabbits, chickens and more recently dogs have had innumerable experiments performed on them with cholesterol feeding, with or without thiouracil, with or without thyroid, with or without nearly all the members of the Vitamin B complex and yet no answer to the above questions have been found.

REFERENCES :

1. Sydenstricker, E. : in Cowdry, E.V. Arteriosclerosis. The MacMillan Company, New York, 1933 (Chap. 5).
2. French, A.J., and Dock, W. : J.A.M.A. 124 : 1233 : 1944.
3. Leary, T. : Arch. Path. 21 : 419 : 1936.
4. Hirsch, S. : Cardiologia 5 : 122 : 1941.
5. Anitschkow, N. : in Cowdry, E.V. Arteriosclerosis, Chap.10.
6. Katz, L.N., and Dauber, D.V. : J. Mt. Sinai Hosp. 12 : 386 : 1946.
7. Duff, G.L. : Arch. Path. 22 : 161 : 1936.
8. Leary, T. : Arch. Path. 21 : 459 : 1936.
9. Leary, T. : Arch. Path. 32 : 507 : 1941.
10. Hueper, W.C. : Medicine 20 : 397 : 1941.
11. Katz, L.N., and Dauber, D.V. : J. Mt. Sinai Hosp. 12 : 391 : 1946.
12. Katz, L.N., and Dauber, D.V. : Ibid.
13. Lande, K., and Sperry, W.M. : Arch. Path. 22 : 301 : 1936.
14. Thannhauser, S.J., and Magendantz, M. : Ann. Int. Med. 11 : 1662 : 1938.
15. Steiner, A., and Domanski, B. : Arch. Int. Med. 71 : 397 : 1943.
16. Barker, N.W. : Ann. Int. Med. 13 : 685 : 1944.
17. Sperry, W.M. : J. Mt. Sinai Hosp. 9 : 799 : 1942.
18. Weinhouse, S. : Arch. Path. 35 : 438 : 1943.

19. Katz, L.N., and Dauber, D.V. : J. Mt. Sinai Hosp. 12 : 392 : 1946.

20. Fleishman, W., and Shumaker, H.B. : Bull. Johns Hopkins Hosp. 71 : 175 : 1942.

21. Katz. L.N., and Dauber, D.V. : J. Mt. Sinai Hosp. 12 : 392 : 1946.

22. Katz, L.N., and Dauber, D.V. : Ibid. p.393.

23. Feinblatt, H.M. : quoted by Katz and Dauber p. 394.

24. Bloor, W.R. : Flat Metabolism, Stanford Univ. Press, 1932, Vol. I, p.267.

25. Katz, L.N., and Dauber, D.V. : Ibid. p.394.

26. Katz, L.N., and Dauber, D.V. : Ibid. p.394.

27. Bruger, M., and Fitz, F. : Arch. Path. 25 : 637 : 1938.

28. Hunt, H. : New Eng. J. Med. 201 : 654 : 1929.

29. Thannhauser, S.J., and Magendantz, H. : Ann. Int. Med. 11 : 1662 : 1938.

30. Bloch, K., and Rittenberg, D. : J. Biol. Chem. 145 : 625 : 1942.

31. Bloor, W.R. : Fat. Metabolism p. 268.

32. Katz, L.N., and Dauber, D.V. : p. 396.

33. Winternitz, M.C., Thomas, R.M., and Le Compte, P.M. : Amer. Heart J. 14 : 399 : 1937.

34. Katz, L.N., and Dauber, D.V. : p.397.

35. Katz, L.N., Schlichter, J.G., and Meyer, J. :
Amer. J. Med. Sci. 218 : 603 : 1949.

36. Moreton, J.R. : Science 107 : 371 : 1948.

SERUM CHOLESTEROL IN CORONARY ARTERY DISEASE.

BIOCHEMICAL REVIEW.

In the clinical approach to the question of the relationship of cholesterol to atherosclerosis, investigations, up to date, have been directed to the estimation of serum cholesterol levels in patients with coronary artery disease, to determine whether a hypercholesterolaemia is present or not.

To begin with Davis, Stern and Lesnich (1), Steiner and Domanski (2) and Lerman and White (3) all recorded raised serum cholesterol levels in patients with coronary artery disease, as compared with serum cholesterol levels in control groups. More recently similar investigations have been done on larger series, with essentially the same results.

Morrison, Hall, and Chaney (4) reported a series of 200 unselected, cases of acute coronary occlusion, whose blood cholesterol was estimated within 48 hours of hospital admission. The technique, which they employed, was a modification of the Sperry-Schoenheimer method, which is a micro-method depending on colorimetric and gravimetric methods of estimating cholesterol. The normal cholesterol value determined in a series of 30 normal cases was 150-260 mgm per cent, a range which is in agreement with that obtained by Peters and Man; the percentage of free cholesterol ranged from 20-35 per cent. In 51 of 75 cases, under 60 years of age, with proven acute coronary occlusion,

(clinical and electrocardiographic evidence) hypercholesterolaemia was found. In 52 per cent of 125 patients, over 60 years of age, with proven acute coronary occlusion, a normal cholesterol was found, i.e. 48 per cent had an elevated serum cholesterol. The average per cent of free cholesterol was 30, compared to 28 per cent in the normal, so they concluded that the mechanism for esterification of cholesterol is not involved in this disease. 75 per cent were males and 25 per cent females, but there was no significant variation in the sexes.

Boas et al (5) found the serum cholesterol raised to over 300 mg. in 71 (58 per cent) of 122 patients, with proved coronary atherosclerosis, in all of whom the disease was considered to have begun under the age of 50. Only patients with symptoms of coronary artery disease, as well as electrocardiographic evidence of myocardial damage, were included. The average value of serum cholesterol for the entire group was 316 mg. per 100 ml; in the 71 patients referred to above, the average value was 365 mg. per 100 ml, and in the remaining 51 patients it was 250 mg. per 100 ml. Other evidences of disturbed cholesterol metabolism, such as arcus senilis, xanthelasma, and xanthomatosis occurred in 37 cases. The serum cholesterol of siblings, of the above patients, was estimated in one-third of the cases and was

found to be above 300 mg. per 100 ml. The patients in this series were mainly Jewish.

Adlersberg et al (6), in an investigation of 201 patients, in all of whom there was a history of xanthoma, coronary artery disease was present in 80 cases (40 per cent). In 66 of these the serum cholesterol was estimated, and in 57 it was above 300 mg. per 100 ml. In 49 of the 80 patients (61 per cent) cardiac symptoms had appeared, before the age of 50 years. Hypertension was present in 12 of the patients with coronary artery disease. Underdahl and Smith (7) noted the presence of hyperlipaemia in eight out of 14 women, all under 40 years of age, suffering from coronary artery disease. Priddle (8), in a study of 1,089 patients, found that 69.7 per cent of patients with coronary artery disease had a hypercholesterolaemia.

Peters and Van Slyke (9), in their survey of the biochemistry of cholesterol metabolism, in their authoritative text book "Quantitative clinical chemistry", express the opinion that it has not been proved conclusively that hypercholesterolaemia is present in coronary artery disease. Cantarow and Trumper (10), in their text book of Biochemistry, quote Joslin and Rosenthal as stating that no satisfactory demonstration of an association between hypercholesterolaemia and atherosclerosis has been made. Cantarow and Trumper (11), themselves stated that critical analysis, in large numbers of

patients with atherosclerosis, fail to reveal any significant, consistent, abnormality of plasma cholesterol. Bruger (12), believes that the development of diabetes, arthritis, and arteriosclerosis is followed, and not preceded by hypercholesterolaemia. He regards the hypercholesterolaemia as a complicating rather than as an etiologic factor.

Such considerable divergences of opinion may be due to -

(1) Difference to technique of estimating serum cholesterol, employed by the individual workers.

(2) Different assessment of the normal serum cholesterol range by different workers.

(3) Differences in the age, sex, and race of the patients used for cholesterol estimation.

In Boas' series quoted above the patients were Jews mainly, and there was a fair proportion who had xanthomatosis. Jews are considered more prone to develop xanthomatous conditions, and this may explain the high incidence of hypercholesterolaemia. It may well be that atherosclerosis can develop in patients with normal serum cholesterol levels, and that those patients, with hypercholesterolaemia, will develop it more quickly, or more extensively, because of the excess cholesterol. The above workers, although they have obtained hypercholesterolaemia

in more than half their cases with coronary disease, have apparently overlooked the cause of the atherosclerosis in the remainder with normal cholesterol levels; they certainly cannot claim hypercholesterolaemia as the cause in all their cases.

The relationship of diet to hypercholesterolaemia has received a great deal of attention with inconclusive results.

Turner and Steiner (13) were unable to detect a rise in serum cholesterol two, four, and eight hours after a fatty meal plus cholesterol. Gardner and Gainsborough (14), however, reported a hypercholesterolaemia after feeding cholesterol. McQuarrie et al (15), noted striking increases in the serum lipids in children, who were receiving diets consisting, or almost entirely consisting, of proteins or fats.

On the subject of the effect of feeding cholesterol there is much controversy. Turner and Steiner (13), were unable to alter the serum cholesterol of men by varying the quantity of fat in the diet widely. Okey and Stewart (16), by giving normal women cholesterol, in the form of yolk egg, succeeded in raising serum cholesterol appreciably. This was confirmed by Steiner and Domanski (17). It has been suggested that lecithen, rather than cholesterol, may have been the active constituent of the diet. Brun (18) administered 80 gm. of olive oil and estimated the serum cholesterol by the Sperry-

Schoeheimer technique two, four, six, and eight hours after the meal; within two to six hours there was a rise of 31 mg. (10 per cent). In addition four gms. of cholesterol made no difference, and the increment consisted entirely of the ester form. The literature, although it contains several articles claiming an increase in serum cholesterol following the ingestion of lipids, is by no means unanimous. Van Slyke and Peters (19), conclude that, since cholesterol is absorbed and aids in the absorption of fat, and since it is absorbed into the thoracic duct, rather than portal blood, its concentration in the systemic blood should rise after either a fatty meal or cholesterol. The continual delivery of bile into the intestine and the constant destruction by the liver may, however, prevent its accumulation in the blood. Gertler, Garn, and White (20), in their investigation of the relationship of serum cholesterol levels to the amount of ingested cholesterol in the diet, came to the conclusion that there was no definite relationship between the two. Dock (21) has pointed out that atherosclerosis is rarely seen in people eating diets high in cereals, beans and vegetable oils but is common in those eating animal fats. Commander Steiner (22), in a post mortem study of undernourished Okinawans, who eat a predominantly vegetable diet, found very little evidence of coronary artery disease. The incidence of coronary artery disease is low amongst Mexicans, who eat a low fat diet yet

the incidence of atherosclerosis is as high as in white races (23). Kuczinzky (24), found that the Kirgis nomads, with high fat diets, had a marked incidence of atherosclerosis, while their contemporaries, living in towns, and on a mixed diet, had a lower incidence. Eskimos (25), live on high meat diets but have low blood pressures and relatively low blood cholesterol levels.

The above brief review of diet, in relation to atherosclerosis, from the racial point of view, strongly suggests that diet can play some part in affecting the level of serum lipids, but different people react differently to diet. Nevertheless a more detailed study of the diet of the various races, their serum cholesterol, and incidence of atherosclerosis would yield valuable information. It may be that, even in the same race, the 'coronary group' will react to diet in a manner different from the 'non-coronary group'.

The result of recent biochemical investigations seem to suggest that the cholesterol; phospholipid ratio plays some part in determining the colloidal stability of serum cholesterol, and its precipitation from the blood, and this may well prove to be of more importance than the actual serum cholesterol level itself. Up to date, there has been a tendency to concentrate on this single serum lipid-cholesterol, but one feels those factors, which may control the solubility of serum cholesterol, cannot be ignored.

Attempts to widen the biochemical approach to the problem have been made.

Gertler, Garn, and Lerman (26), estimated the serum cholesterol, serum cholesterol esters, and phospholipids in three groups of individuals; a group of 97 males suffering from coronary artery disease, a control group of 146 males, and a matched control group of 97 males.

The coronary artery group levels for serum cholesterol (total, free and esterified) and serum phospholipids greatly exceeded both control groups. The greatest difference was in the serum cholesterol esters, the smallest in free cholesterol.

The ratio of total cholesterol to phospholipids was greatest in the coronary artery disease group (84 plus 2) compared with (74 plus 9) in the control group, and (78 plus 1.3) in the matched control group. These findings are taken to indicate some disturbance of serum colloidal make-up in coronary artery disease.

The importance of this type of work lies in the fact that it focusses attention on an abnormality of lipid metabolism instead of on a single substance, viz. cholesterol. Further investigation along these lines might produce more facts concerning the colloidal stability of cholesterol and explain how or why cholesterol comes to be deposited in vessel wall.

In addition it revives interest in the relationship of

macromelecule s to the development of the disease. Moreton (27), in a study of chylomicrons, after fatty meals, suggested that the recurrent hyper and macro-chylomicronaemia may be responsible for the development of atherosclerosis, thus tending to substantiate Hueper's theory of the development of atherosclerosis. The most exact study to date is that of Gofman and his co-workers (28). They used an ultracentrifuge method, which produces forces many thousands or millions of times the force of gravity, to study the character and behaviour of the giant lipo-protein complex which is normally present in the sera of healthy individuals, and in patients suffering from coronary artery disease, hypothyroidism, diabetes, hypertension and the nephrotic syndrome.

They found four classes of molecules in human sera, all of varying degrees of flotation, when ultracentrifuged. One of these four is considered to be definitely correlated with atherosclerosis, showing a much higher concentration in patients with myocardial infarction than in normal human controls.

More recently an attempt has been made to correlate morphology and serum lipids. Gertler, Garn, and Sprague (29) studied 146 healthy males and 97 males, who had experienced myocardial infarction prior to the age of 40 years. They used the Sheldon system of somatotyping and estimated the

serum cholesterol, total, free and esters, and serum phospholipid.

In the healthy group cholesterol, total cholesterol, phospholipid tended to be highest in endomorphs and lowest in ectomorphs; cholesterol esters tended to be in the reverse. Hyperlipaemia, they concluded, would be most frequent in the endomorphs. The coronary artery disease group, on the other hand, were characterised by mesomorphy. The lipid val ue of coronary mesomorphs were higher than those of coronary endomorphs, i.e. the opposite from the control group.

The preceding reviews of the literature concerning the experimental and biochemical approach to the problem of the etiology of atherosclerosis may help to show how the present investigations have evolved and may help to point out the direction of future investigations.

The discovery that cholesterol formed the greater part of the deposit in vessels with atherosclerosis, and the work of Anitschhow, provided a great impetus to the experimental pathologists. Since 1913 experimental animals, of differing kinds, have been bludgeoned in many ways in an attempt to produce atherosclerosis. As a result of a vast amount of work in this field several theories have been put forward to explain the pathogenesis of atherosclerosis. In spite of the

work of the experimental pathologists the picture was far from completion.

Attention was then focussed on patients with atherosclerosis, and especially their serum cholesterol levels. Although the majority of workers have reported that the majority of patients with atherosclerosis have hypercholesterolaemia, it is obvious that some patients appear to develop atherosclerosis with normal serum cholesterol levels. This has led to a more detailed biochemical investigation into factors controlling cholesterol solubility in plasma, and into lipid metabolism generally. Already it has become obvious that the basic knowledge about cholesterol and lipids, in general, is extremely scanty, as can be seen from a perusal on the section on the physiology and biochemistry of cholesterol.

It seems to suggest, therefore, that the next phase in the approach to this problem, must be predominantly biochemical. Not only must the biochemical abnormality in atherosclerosis be discovered, if there be such a thing, and it seems almost certain that there is, but the explanation of how it comes about must also be sought.

REFERENCES :

1. Davis, D., Stern, B., and Lesnick, G. : Ann. Int. Med. 11 : 354 : 1937.
2. Steiner, A., and Domanski, B. : Arch. Int. Med. 71 : 397 : 1943.
3. Lerman, J., and White, P.D. : Amer. Soc. Clin. Invest. May 27, 1946.
4. Morrison, L.H., Hall, L., and Chaney, A.L. : Amer. J. Med. Sci. 216 : 32 : 1948.
5. Boas, E.P., and Adlersberg, D. : J. Mt. Sinai Hosp. 12 : 84 : 1945.
6. Adlersberg, D., Parets, A.D., and Boas, E.P. : Proc. Amer. Diabetes Assoc. 8 : 173 : 1950.
7. Underdahl, L.O., and Smith, H.L. : Proc. Staff Meet., Mayo Clin. 22 : 479 : 1947.
8. Priddle, W.W. : Ann. Int. Med. 35 : 836 : 1951.
9. Peters, J.P., and Van Slyke, D.D. : Quantitative Clinical Chemistry, Vol. I, Part I, Bailliere, Tindall, and Cox, London, Second Edition, 1946, p.535.
10. Cantarow, A., and Trumper, M. : Clinical Biochemistry, Fourth Edition, W.B. Saunders Company, 1949, p.159.
11. Cantarow, A., and Trumper, M. : Ibid. p.159.
12. Bruger, M. : Arch. Int. Med. 53 : 423 : 1934 (quoted by Cantarow and Trumper : Ibid. p.159.
13. Turner, K.B., and Steiner, A. : J. Clin. Invest. 18 : 45 : 1939.

14. Gardner, J.A., and Gainsborough, H. : Biochem. J. 22 : 1048 : 1928.

15. McQuarrie, I., Musted, C., and Bloor, W.R. : J. Clin. Invest. 12 : 247 : 1933 (quoted by Peters and Van Slyke p. 483).

16. Okey, R., and Stewart, D. : J. Biol. Chem. 99 : 717 : 1933.

17. Steiner, A., and Domanski, B. : Amer. J.Med. Sci. 201 : 820 : 1941.

18. Brun, G. : quoted by Peters and Van Slyke, p. 480.

19. Peters, J.P., and Van Slyke, D.D. : Quantitative Clinical Chemistry, Second Edition, p.480.

20. Gertler, H.M., Garn, S.M., and White, P.D. : Circulation 2 : 696 : 1950.

21. Dock quoted by Sprague, H.B., in his address "Thanatophagia" to the American Heart Association, 1950

22. Steiner quoted by Sprague, H.B. : Ibid.

23. Sprague, H.B. : "Thanatophagia" to the American Heart Association, 1950.

24. Kuczinzky quoted by Sprague, H.B. : Ibid.

25. Sprague, H.B. : Ibid.

26. Gertler, M.M., Garn, S.M.and Lerman, J. : Circulation 2 : 205 : 1950.

27. Moreton, J.R. : Sci. 106 : 190 : 1947.

28. Gofman, J.W., Jones, H.B., Lindgren, F.T.,Lyon, T.P., Elliott, H.A., and Strisower, B. : Circulation 2 : 161 : 1950.

29. Gertler, M.M., Garn, S.M., and Sprague, H.B. :
Circulation 2 : 380 : 1950.

SERUM CHOLESTEROL LEVELS

IN

CORONARY ARTERY DISEASE.

In the present investigation the serum cholesterol values of 92 patients with coronary artery disease, diagnosed clinically and electrocardiographically were estimated. None of these had positive Wassermann reactions. A control group of 25 cases had their serum cholesterol levels determined.

The age and sex incidence of the 92 cases with coronary artery disease was as follows :-

Below 60 years of age.

Total	=	77 cases
Males	=	62 cases
Females	=	15 cases

Above 60 years of age.

Total	=	17 cases
Males	=	5 cases
Females	=	12 cases

The distribution of the serum cholesterol levels was as follows :-

	Serum cholesterol level.	Number of cases.	Males.	Females.
Under 60 years of age.	Below 100 mg. per 100 ml.	2	2	0
	100 - 120	2	1	1
	120 - 140	2	1	1
	140 - 160	15	12	3

	Serum cholesterol level.	Number of cases.	Males.	Females.
Under 60	160 - 180	2	2	0
years of age.	180 - 200	10	9	1
(contd.)	200 - 220	7	4	3
	220 - 240	5	4	1
	240 - 260	5	2	3
	260 - 280	8	6	2
	280 - 300	8	3	0
	300 and above,	14	13	1
Over 60	Below 100 mg.			
years of age.	per 100 ml.	2	2	0
	100 - 120	1	0	1
	120 - 140	2	0	2
	140 - 160	1	0	1
	160 - 180	1	0	1
	180 - 200	0	0	0
	200 - 220	0	0	0
	220 - 240	3	1	2
	240 - 260	3	1	2
	260 - 280	1	-	1
	280 - 300	0	0	0
	300 and above,	3	1	2

Before going on to discuss the significance of these results, it is essential to establish the serum cholesterol levels, in a control series, and so determine, if there is a significant incidence of hypercholesterolaemia, in the group suffering from coronary artery disease. Immediately two problems arise,

1. What constitutes a control group, i.e. a series of patients, of comparable age group to those with coronary artery disease, but having no evidence of atherosclerosis?
2. What is the upper limit of normal of the serum cholesterol?

Regarding the control group of patients, it must be admitted that it is almost impossible to obtain a series of patients, without evidence of atherosclerosis, in an age group ranging from 20 years to 60 years plus, a defect which applies to all the other investigators. The control group of patients consisted of 25 patients, who had no clinical or electrocardiographic evidence of coronary artery disease.

In deciding whether hypercholesterolaemia is present or not, it is necessary to have a normal range of serum cholesterol, but there is a great doubt as to what constitutes a normal range, as can be seen in the following table :-

	Serum cholesterol (mgm/100cc)	Free.	Ester Form.
Bloor (original publication),	200	-	-
Bloor,	140 - 310	48 - 125	83 - 164
Ungerleider,	211	-	-
Myers and Wordell,	100 - 220	-	-
Gardner and Gainsborough,	78 - 227	5 - 94	54 - 145
Cantarow and Trumper,	139 - 240	-	48 - 96
Peters and Man,	148.5-229.7	-	-
Morrison et al,	260	-	-
Wilkinson et al,	280	-	-
Boas,	300	-	-
Van Slyke,	118 - 360	56 - 121	51 - 261

It may be argued that the estimations of serum cholesterol levels, in a group of apparently normal persons, or a control group, such as that described above, are not reliable. In a control group, no matter how carefully chosen, the possibility of latent atherosclerosis being present cannot be excluded, and a certain amount of overlap in serum cholesterol levels will probably be found. In spite of this criticism it is felt that a comparison of the two groups has some value.

The serum cholesterol levels in the control group were as follows :-

Age Group.	Serum cholesterol in mgm per 100 ml.
30 - 49 years,	124 : 222.
40 - 50 years,	123 : 150 : 152 : 170 : 182 : 186 : 190 : 216 : 226 : 306 : 330 : 370.
50 - 60 years,	143 : 148 : 172 : 195 : 216 : 220 : 246 : 280.
60 years plus,	160 : 194 : 220.

The distribution of serum cholesterol levels was as follows :-

Serum cholesterol in mgm/100 ml.	Total number.	Males.	Females.
100 - 120	0	0	0
120 - 140	2	2	0
140 - 160	4	1	3
160 - 180	3	2	1
180 - 200	5	4	1
200 - 220	3	1	2
220 - 240	3	2	1
240 - 260	1	1	0
260 - 280	0	0	0
280 - 300	1	1	0
300 plus	3	3	0

The average value of serum cholesterol, for males, in the control group, was 168 mgm per 100 ml, and, for females,

161 mgm. In the coronary artery disease group, the average figure, for males, was 213 mgm per 100 ml, and, for females, 180 mgm per 100 ml.

These figures suggest that the serum cholesterol level, on the average, is higher in the coronary artery disease group, than in the control group. In the coronary artery group, under 60 years of age, the figure, for males, was 213 mgm. per 100 ml, for females, 222 mgm. per 100 ml; over 60 years of age, the corresponding figures were 213 mgm. per 100 ml, and 203 mgm. per 100 ml. The total number studied in the coronary artery disease group is small, but there does not appear to be any significant change in levels due to age or sex groups.

In attempting to assess the incidence of hypercholesterolaemia it is noted, that some workers accept 260 mgm. per 100 ml, as the upper limit of normal, for serum cholesterol, while others accept 300 mgm. per 100 ml, as the figure. In the control group there were three patients out of 25, with a serum cholesterol over 300 mgm. per 100 ml, i.e. 13 per cent, as compared with 17 patients out of 92 with coronary artery disease. On the other hand there were 4 out of 25 cases in the control group, compared with 34 out of 92 in the coronary artery disease group, who had a serum cholesterol over 260 mgm. per 100 ml. If one regards 260 mgm. per 100 ml, as the upper

limit of normal for serum cholesterol, then a significant number of patients, with coronary artery disease, have a hypercholesterolaemia. If 300 mgm. per 100 ml, however, is regarded as the upper limit of normal, then one is not justified in drawing this conclusion.

It is obvious from these figures that the incidence of hypercholesterolaemia, in patients with coronary artery disease, is much less in the present series, than in some groups of American workers, whose results are given in the preceding section. Although the average serum cholesterol levels, in the coronary artery disease group, in this series, was higher than in the control group, it is doubtful if one is justified in concluding that a significant incidence of hypercholesterolaemia was found in patients suffering from coronary artery disease, in the present investigation.

What then is the role of cholesterol in the production of atherosclerosis? It first assumed importance, when Anitschkow (12), produced lesions in rabbits, considered to resemble those found in human atherosclerosis, by feeding them cholesterol. This work has been confirmed and amplified, and there are various theories as to how cholesterol produced atherosclerosis. New experimental animals, viz. chicks (13) and dogs (14) have been found, in whom atherosclerosis can be produced by feeding cholesterol. In these experiments, hypercholesterolaemia played a prominent part, so that it

became a matter of time, before attempts were made to find out whether a hypercholesterolaemia occurred in human atherosclerosis, e.g. coronary artery disease. Certain workers have claimed to have shown, that hypercholesterolaemia does occur in human atherosclerosis, and by analogy with the results of hypercholesterolaemia in experimental animals, argue that hypercholesterolaemia is the essential factor in the production of human atherosclerosis. It might be worthwhile considering some of the facts before accepting this conclusion.

It has been pointed out that the rabbit is a herbivorous animal, and does not normally ingest cholesterol in its food (15). The possibility arises that the experimental production of atherosclerosis in the rabbit, by feeding cholesterol, is an unnatural, and artificial process, and consequently cannot be altogether accepted, as representing the mode of production of atherosclerosis in human beings. The main difference between rabbit and human atherosclerosis are :-

1. In rabbits the arch of the aorta is predominantly involved, while in man the abdominal aorta is the main site of deposition of cholesterol.
2. The cerebral and renal arteries are rarely affected, in the rabbit, but are frequently involved in human beings.

3. In the earlier stages, the lesions, in the rabbit, resemble those of man but they do not develop the extensive fibrosis, calcification, or ulceration, which is seen in advanced human atherosclerosis, and which makes it such an important condition pathologically.
4. In rabbits, if cholesterol feeding is stopped the lesions regress, i.e. the process is reversible.
5. In the rabbit, cholesterol is extensively deposited in other organs, such as the liver, and adrenal cortex, whereas in man this does not occur, except where there is gross disturbance of fat metabolism; in man atherosclerosis can occur by itself, i.e. an isolated disease of the vascular tree alone.

It is argued that the atheroma of chicks resembles the atheroma of human beings more closely, in character, and in distribution; furthermore, the chick is omnivorous and normally ingests cholesterol, like human (16). There is, however, more extensive deposition of cholesterol in other tissues.

In view of these differences one cannot accept, without reservations, that the mode of production of atherosclerosis

in human beings and the experimental animals is the same; nor can it be concluded that they are the same disease process. In the experimental animals, a fairly gross disturbance of cholesterol metabolism is produced, but the same does not hold true in human beings, The disease in experimental animals seems to be more closely related to human xanthomatosis, than to atherosclerosis. Admittedly atherosclerosis, of severe degree, is frequently found in human xanthomatosis, but atherosclerosis can occur in human being without other evidence of xanthomatosis, i.e. it appears to be a separate disease entirely. Furthermore, Scarff (17) has pointed out, that in the Hand-Schuller-Christian disease, which is an example of the xanthomatous group of diseases, and in which cholesterol metabolism is deranged, with the production of hypercholesterolaemia, the main deposit is not in the blood vessels but in various organs, contrary to what one would expect from the experiments in animals. From investigations on human beings, a fairly strong case for hypercholesterolaemia being the essential factor in the production of atherosclerosis would appear to have been made on the following grounds :-

1. Experimental work in animals has shown that atherosclerosis can be produced by inducing hypercholesterolaemia, by feeding.

2. Certain workers claim to have shown that a large percentage of patients, suffering from coronary artery disease,with or without coronary occlusion, have a hypercholesterolaemia.
3. There is a high incidence of atherosclerosis in those conditions which have a hypercholesterolaemia, e.g. xanthomatosis, nephrosis, myxoedema, and some cases of diabetes mellitus.

Against this conclusion are the following facts :-

1. The lack of confirmation of a high incidence of hypercholesterolaemia in the present work - about three-quarters of the patients suffering from coronary artery disease had normal serum cholesterol levels.
2. In a certain group of xanthomatous condition, viz. Hand-Schuller-Christian disease, a hypercholesterolaemia exists, but the main deposits of cholesterol do not occur in the blood vessels, but in certain other tissues.
3. In the experimental rabbit Page (18) has pointed out, that the administration of potassium iodide or organic iodides has a decided effect in inhibiting the development of experimental atherosclerosis, but it does

3. (contd.)

not produce this effect by lowering the level of serum cholesterol, because in the majority of cases the hypercholesterolaemia persists.

There would, therefore, appear to be some doubt regarding the view that hypercholesterolaemia is an essential factor for the production of atherosclerosis. The above arguments, however, refer to a sustained hypercholesterolaemia, and the possibility still remains that an intermittent hypercholesterolaemia may be as important in the production of atherosclerosis, as a sustained hypercholesterolaemia. Workers differ, however, as to the effect of diet (feeding cholesterol or fats) on serum cholesterol levels. It is interesting to note that feeding cholesterol to human beings appears to have no effect on serum cholesterol levels.

Five patients suffering from coronary occlusion had serum cholesterol levels determined at four-hourly intervals thrice daily, and also daily, for four consecutive days, at the same time each day, to see if there was any variation in the serum cholesterol level. The results were as follows :-

(a) Daily serum cholesterol levels.

Patient.	1st day.	2nd day.	3rd day.	4th day.
A. S.	232	240	248	238
T. B.	162	146	150	152
W. M.	180	182	196	200
J. T.	160	156	148	162
A. B.	166	158	148	156

The serum cholesterol levels do not vary very much from day to day at the same time, but the number of estimations are small. The percentage variation in this group, lies between 6 - 11 per cent. This is considered to be within normal limits, allowance being made for technical variations.

(b) Serum cholesterol levels at four-hourly intervals.

Patient.	9. 0 a.m.	1. 0 p.m.	5. 0 p.m.
A. G.	244	282	266
J. W.	240	262	248
A. B.	156	162	150
A. P.	308	276	290
J. D.	244	280	276

These variations are considered to be within normal limits.

It would appear from the results presented above that :-

1. Hypercholesterolaemia occurs in only about one-third of patients with coronary artery disease taking 260 mgm. per 100 ml. as the upper limit of serum cholesterol. The fact that two-thirds of the patients have normal serum cholesterol values would suggest that hypercholesterolaemia is not an essential factor for the production of atherosclerosis. The incidence of hypercholesterolaemia, in coronary artery disease, is less when 300 mgm. per 100 ml. is taken as the upper limit of normal.
2. The effect of diet on serum cholesterol levels has not yet been adequately determined, especially the ingestion of high fat diet over a prolonged period.

The main obstacle towards a better understanding of the role of cholesterol, in atherosclerosis, is a lack of fundamental knowledge of the biochemistry of cholesterol, especially the factors affecting and controlling the serum cholesterol level; they are at present virtually unknown, yet they may prove to be important in the production of atherosclerosis, by virtue of their control over serum cholesterol solution in the plasma; abnormalities in the factors controlling the serum cholesterol level and solubility,

may be more important than the absolute serum cholesterol level, in regard to deposition of cholesterol in the blood vessels. It would appear then that the biochemist has an important role to play in the solution of the causation of atherosclerosis, and the answer to the problem may not be known until he has finished his researches into the physiological chemistry of cholesterol

The experimental pathologist too, in spite of the immense amount of work done, has important problems to solve. They are not agreed as to whether cholesterol enters the intima from the lumen of the vessel or via the vasa vasorum in the vessel wall; whether the cholesterol is intra or extra-cellular in the earliest stages, whether the condition is reversible, or not, in human beings.

In view of these deficiencies in our knowledge it would be premature to suggest possible cause of atherosclerosis yet it is possible to draw certain conclusions from the work which has been done.

1. The present work does not confirm the high incidence of hypercholesterolaemia in atherosclerosis, represented by coronary artery disease, previously reported by American workers. The high incidence of patients, with normal serum cholesterol levels, in the coronary artery disease group, described above, would suggest that although

1. (contd.)
cholesterol is the essential substance in the intimal deposits in atherosclerosis, a hypercholesterolaemia is not an essential factor for the production of atherosclerosis.

2. The above figures, however, show a higher average serum cholesterol level in patients with coronary artery disease than the normal group. What the significance of this is unknown.

3. The effect of diet on serum cholesterol requires more intensive investigation to exclude the possibility of intermittent hypercholesterolaemia. The above figures reported on page do not show any significant variation but the number of patients is too small to be significant.

4. The greater incidence of hypercholesterolaemia, in the Aermican series, as compared with the present one, may be due to the effect of diet. The serum cholesterol levels, in the present investigation, were estimated at a time when these patients had been ingesting a relatively low fat diet for ten years, as a result of rationing. During these ten years the Americans appear to have had a

4. (contd.)

higher intake of fat, because rationing in America was less severe. The American series may, therefore, be considered as showing the effect of prolonged feeding of a diet, with a relatively high fat content, whilst the present series represents a control group, on a relatively low fat content.

CHOLESTEROL IN RELATION TO

GALL BLADDER DISEASE

For many years cholesterol has occupied a prominent place in the biochemistry of the gall bladder, especially in pathological states, where gall stones were noted to contain cholesterol in amounts, which varied from 25-99 per cent (1). In spite of intensive investigation, the physiological role of the gall bladder, in cholesterol metabolism, has not yet been determined. In the standard text books of biochemistry, the references to gall bladder and cholesterol are entirely concerned with pathological states. Apparently there is still doubt as to whether the gall bladder excretes cholesterol or absorbs it from the bile. Normal bile contains a smaller amount of cholesterol than does plasma, the normal range being 20-200 mgm. per 100 ml. (2). Higher concentrations occur in the gall bladder, when diseased, and in some instances may reach enormous figures (2,480 mg. per 100 ml. is the highest figure recorded) (3). Furthermore, plasma cholesterol occurs in two forms, free and ester, while bile cholesterol only occurs in the free form (4). Animal experiments have shown that the concentration of cholesterol in the bile remains fairly constant even after feeding enormous amounts. Moreover, it is possible to raise the blood cholesterol without producing a corresponding increase in bile cholesterol,and also to increase the cholesterol elimination in the bile, without any alteration in the blood cholesterol concentration. It seems,

therefore, that the cholesterol contents of plasma and bile bear no obvious relationship to one another (5).

Contradictory conclusions have been published as to the effect of gall bladder disease on serum cholesterol levels, but the concensus of opinion is, that significantly high values are encountered only in gross obstruction. Fox (6), points out that the entire suppression of one day's bile output would only raise the blood cholesterol 10 mg. per 100 ml., so that in the absence of obvious jaundice, and therefore of any serious degree of obstruction, it is unlikely that blood cholesterol estimations will be of any clinical assistance. Cantarow (7), and Epstein (8) have demonstrated an increase in the plasma cholesterol in jaundice. In about 50 per cent of such cases the cholesterol esters increase with the total cholesterol and the normal ratio is retained (9). In the remainder the increase is almost entirely in the free cholesterol. This has been ascribed to interference with the absorption of fat and cholesterol from the intestines, as a result of the absence of bile. Epstein (10) and Hawkins (11), however, report that they find an elevation, in the great majority of cases of common bile duct obstruction and bile fistulae, in which little or no bile was present in the intestine. The cause of the increase in plasma cholesterol in obstructive jaundice is not clear. The view that it is a retention phenomenon

was based on the belief that cholesterol is excreted chiefly by the liver. This has been challenged, as the intestinal mucosae is now considered to be the chief site of cholesterol excretion. Further argument against this view is offered by the observation, that an increase in plasma cholesterol occurs in cases of bile fistula.

It should be pointed out, however, that hepato-cellular damage is frequently accompanied by a diminished proportion of cholesterol esters in the plasma (12). This may, or may not, be accompanied by a fall in the plasma cholesterol concentration Generally speaking the more severe the hepatic damage the greater the tendency towards hypocholesterolaemia. It has been indicated that common bile duct obstruction is usually, but not always, associated with a hypercholesterolaemia, so that the finding of a low cholesterol plasma level in common duct obstruction is of serious prognostic significance, being indicative of severe hepato-cellular damage.

Why there is a fall in cholesterol esters in hepatic disease is not known. Several theories have been advanced, viz., faulty absorption of cholesterol from the intestine, imperfect esterification of cholesterol in the liver, and deficient storage of esters in the liver. Bile salts may play a part, as it has been shown that an increased concentration of bile salts inhibits the esterification of free cholesterol. Cantarow and Trumper (13), however, state that

hypocholesterolaemia, with a diminution in the ester fraction, may occur in conditions other than hepatic disease, and that there must be a more fundamental mechanism to explain this.

Peters and Van Slyke (14), state that the most characteristic feature of all conditions causing biliary obstruction, or destruction of the parenchyma of the liver, is an increase of the ratio of free to total cholesterol, regardless of the concentration of total cholesterol. Hyperlipaemia is consistently observed in patients with complete biliary obstructions, whatever the cause. Hyperlipaemia also occurs when there is partial, or intermittent biliary obstruction, or disease of the biliary tract, with considerable icterus. One cannot infer, however, that hyperlipaemia is correlated directly with icterus, as this would imply that the formation and excretion of bile pigments is linked with the metabolism of lipids in liver.

There is still doubt as to the role of cholesterol in the formation of gall stones.

Naunyn (15), thought that primary infection in the biliary tract is the prime factor. Andrews et al, (16) and Ravdin et al (17) suggest that, in the pathologically altered gall bladder, the solubility of the cholesterol is diminished either because :-

1. There is an increase in cholesterol concentration due to over production.

2. There is a decrease in its solubility, viz. the solubility of cholesterol in bile is dependent on bile salts.

A change in the PH of bile, because of stasis, may alter its solvent effect. Another factor is re-absorption of the bile acids through the gall bladder epithelium. Cholesterol being less readily absorbed, the ratio of bile acids to cholesterol declines, with a consequent change in the stability of cholesterol. Some workers, however, contend that precipitation of cholesterol in the gall bladder does not explain fully the process of stone formation. According to Weiser and Gray (18), the presence of emulsified fat is an essential part of the mechanism, and that the excess of cholesterol collects around the fat droplets, which tend to coalesce as bile salts are removed.

Phemister et al (19), have suggested that the composition of gall stones is much influenced by stasis and infection. Stones, which are rich in cholesterol, may form in a gall bladder where stasis is mild, but with increasing chronic obstruction of the cystic duct the deposit contains decreasing amounts of cholesterol, and increasing amounts of calcium and bile pigments. Complete, or nearly complete, obstruction combined with chronic cholecystitis predisposes to the deposition of calcium carbonate.

It will be readily understood from the above review, that the effect of gall bladder disease on plasma cholesterol levels is imperfectly understood. Furthermore, the relation of plasma cholesterol levels to gall bladder disease is further complicated by the liver, which is interposed between the plasma and the gall bladder. Since the liver may be affected secondarily by gall bladder infection, any changes in plasma cholesterol levels may be related, more to the associated liver damage, than to the gall bladder disease.

REFERENCES :

1. Bodansky, M., and Bodansky, R. : Biochemistry of Disease, The MacMillan Company, 1940, p.248.
2. Cantarow, A., and Trumper, M. : Clinical Biochemistry, W.B. Saunders Company, 1949, p.457.
3. Cantarow, A., and Trumper, M. : Ibid. p.457.
4. Cantarow, A., and Trumper, M. : Ibid. p.457.
5. Cantarow, A., and Trumper, M. : Ibid. p.419.
6. Fox, F.W. : Quart. J. Med. 21 : 107 : 1927.
7. Cantarow, A.: Internat. Clinics. 1 : 272 : 1938.
8. Epstein, E.Z. : Arch. Int. Med. 58 : 860 : 1936.
9. Cantarow, A., and Trumper, M. : Clinical Biochemistry, W.B. Saunders Company, 1949, p.156.
10. Epstein, E.Z. : Arch. Int. Med. 58 : 860 : 1936.
11. Hawkins, W.B. : J. Exper. Med. 59 : 427 : 1934.
12. Cantarow, A., and Trumper, M. : Clinical Biochemistry, W.B. Saunders Company 1949, p.160.
13. Cantarow, A., and Trumper, M. : Ibid. p.161.
14. Peters, J.P., and Van Slyke, D.D. : Quantitative Clinical Chemistry Interpretation, Vol. I, Bailliere, Tindall, and Cox, 1946, p. 527.
15. Naunyn : quoted by Bodansky, M., and Bodansky, R., Biochemistry of Disease, The MacMillan Company, 1940, p. 249.
16. Andrews, E., et al : Arch. Surg. 25 : 1081 : 1932.

17. Ravdin, I.S., Riegel, C., Johnston, C.B., and Morrison, P.J. : J. Amer. Med. Assoc. 103 : 1054 : 1934.

18. Weiser, H.B., and Gray, G.R. : Arch. Path. 17 : 1 : 1934.

19. Phemister, D.B., Aronsohn, H.G., and Pepinsky, R. : Ann. Surg. 109 : 161 : 1934.

SERUM CHOLESTEROL LEVELS

IN

GALL BLADDER DISEASE

In the present investigation 154 serum cholesterol levels were examined. They were classified in the following table :-

	Serum Cholesterol Levels.	No. of Cases.	Male.	Female.
Under 60 years of age.	Below 100 mgm per 100 ml.	4	1	3
	100 - 120	8	0	8
	120 - 140	7	2	5
	140 - 160	10	0	10
	160 - 180	14	1	13
	180 - 200	11	1	10
	200 - 220	20	2	18
	220 - 240	10	0	10
	240 - 260	7	1	6
	260 - 280	10	0	10
	280 - 300	4	0	4
	300 plus	9	0	9
Over 60 years of age.	Below 100 mgm per 100 ml.	0	0	0
	100 - 120	1	0	1
	120 - 140	2	0	2
	140 - 160	3	0	3
	160 - 180	8	1	7
	180 - 200	5	0	5

	Serum Cholesterol Levels.	No. of Cases.	Male.	Female.
Over 60 years of age. (contd.)	200 - 220	5	0	5
	220 - 240	1	0	1
	240 - 260	5	0	5
	260 - 280	3	0	3
	280 - 300	3	1	2
	300 plus	4	0	4

In this series the average serum cholesterol level, for males, was 186 mgm per 100 ml, but the total number was small, 10 in all. The average serum cholesterol level in females, was 220 mgm per 100 ml; for those under 60 years of age, 106 in number, the average was 220 mgm per 100 ml, while for those over 60 years of age, 38 in number, the average was 222 mgm per 100 ml, i.e. there was no significant difference between the age groups. The number of males was so small as not to warrant any sub-division into age groups.

13 patients had a serum cholesterol level over 300 mgm per 100 ml, i.e. 8.4 per cent of the total, compared with 13 per cent for the control group, and 20 per cent for the coronary artery disease group. 33 patients had a serum cholesterol above 260 mgm per 100 ml, i.e. 20.7 per cent of the group compared with 17 per cent for the control group, and 37 per cent for the coronary artery disease group.

These figures would suggest that, in gall bladder disease, the serum cholesterol levels do not differ significantly from those in the control series, i.e. apparently 'normal individuals'. For some reason which is not understood, unless the small numbers studied account for it, the females had a higher average serum cholesterol level than the males, although they were both within the limits of normal. At this point, however, it would be interesting to note the serum cholesterol levels in those patients, who had evidence of both gall bladder disease and coronary artery disease. 34 patients were considered to satisfy the criteria.

Their serum cholesterol levels were as follows :-

Serum cholesterol levels.	No. of Cases.	Males.	Females.
Below 100	2	0	2
100 - 120	3	1	2
120 - 140	2	1	1
140 - 160	0	0	0
160 - 180	5	1	4
180 - 200	5	1	4
200 - 220	4	2	2
220 - 240	2	0	2
240 - 260	1	1	0

Serum cholesterol levels. (contd.)	No. of Cases.	Males.	Females.
260 - 280	4	2	2
280 - 300	2	1	1
300 plus	4	0	4

The number with serum cholesterol levels over 300 mgm per 100 ml was 4, i.e. 12 per cent of the group, compared with 13 per cent of the control group, 8.4 per cent of the gall bladder disease group, and 20 per cent of the coronary artery disease group. The number with a serum cholesterol level over 260 mgm per 100 ml was 9, i.e. 27 per cent of the group, compared with 17 per cent of the control group, 20.7 per cent of the gall bladder disease group, and 30 per cent of the coronary artery disease group.

Post-operative changes in serum cholesterol levels in gall bladder disease.

The post-operative follow-up of serum cholesterol levels was rather disappointing. It was hoped that serum cholesterol levels would be estimated at the end of two weeks, one month, and six months, in each patient. The follow-up proved to be more erratic than was anticipated, and the scheme suggested did not work satisfactorily. 24 patients were followed up for a period varying from two weeks to twelve months, producing 70 serum cholesterol values. The

periods of estimating the serum cholesterol levels was so erratic that it is not possible to tabulate the results, but the general trend can be recorded.

In the first two post-operative weeks 14 observations were made, 9 cases showed no significant alteration in the serum cholesterol levels, 3 showed a rise, and 2 showed a fall. After a period of 6 to 12 months following the operation, 8 cases showed no significant alteration, 6 showed a rise, 1 showed a slight rise, 3 showed a definite fall, and 2 a slight fall.

It was possible to follow up a group of 9 cases who had cholesterol estimations made before and after operation. The interval between the pre- and post-operative estimations ranged from 7 to 13 years. Of the 9 cases, 8 showed no significant change and the remaining 1 showed a rise.

It is difficult to assess the above results and still more difficult to explain why some patients show a rise, some a fall and the remainder do not change at all as regards serum cholesterol levels following the operation. No significant difference was noted in those who had a cholecystostomy or cholecystectomy performed. Perhaps the most important results are those in the small group of 9 cases, who were followed up over a long period, using the same technique of cholesterol estimations. The great

majority showed no significant change, and it may be that, if one follows gall bladder cases up for a period longer than one year, the serum cholesterol level shows no significant change.

Conclusions.

1. The serum cholesterol levels in gall bladder disease do not differ significantly from those in the control group. Hypercholesterolaemia, whether 300 mgm or 260 mgm per 100 ml, is taken as the upper limit of normal, is not a frequent occurrence.

2. In those patients, who had both gall bladder disease and coronary artery disease, only 27 per cent had evidence of hypercholesterolaemia, taking 260 mgm per 100 ml as the upper limit of normal and 12 per cent, taking 300 mgm per 100 ml as the upper limit of normal. This is not regarded as a significantly high figure, and is insufficient proof for the theory that a disturbance of cholesterol metabolism, in the nature of a hypercholesterolaemia, is the basis of the relationship between gall bladder disease and coronary artery disease. It must be pointed out, however, that serum cholesterol levels in gall bladder disease and coronary artery disease, by themselves, are not sufficient for drawing any definite conclusions about an etiological relationship, because the possibility of an excessive excretion of cholesterol in the bile, in one or both diseases, has not yet been proved or disproved.

ELECTROCARDIOGRAPHY

OF

CORONARY ARTERY DISEASE.

Electrocardiography affords great help in the diagnosis of coronary artery disease but it has its limitations. Electrocardiographic changes, which we have come to associate with coronary artery disease, are, in fact, evidence of myocardial disease which may be due to causes, other than coronary artery disease. Furthermore, coronary artery disease may be present, without there being any significant alteration in the electrocardiogram. These deficiencies are most likely to be met with, when one is using only standard limb leads, and taking only single records. Errors are less likely to occur with the use of chest lead electrocardiography, especially when it is possible to make serial recordings.

In this investigation praecordial leads, in addition to standard limb leads, and unipolar limb leads, were used in making, or confirming, a diagnosis of coronary artery disease. This was essential in both groups of conditions, which were under investigation, viz. gall bladder disease group and coronary artery disease group. In the coronary artery disease group, many cases of myocardial infarction were included, because this is almost entirely associated with coronary artery disease, and can be recognised during life, in many cases, fairly easily.

It was considered essential to this investigation that all cases should include only coronary artery disease, with an electrocardiogram characteristic of, or suggestive of myocardial ischaemia. At the very best, however, electrocardiography can

confirm coronary artery disease to be present in 75-80 per cent of cases and to confine the investigation to such a group would be to give a false estimate.

The criteria for the electrocardiographic diagnosis of coronary artery disease will be discussed under two headings :-

(a) Coronary occlusion, acute.

(b) Coronary occlusion, chronic.

Acute coronary occlusion.

The most reliable electrocardiographic evidence of acute coronary occlusion is the demonstration of sequential changes, described by Pardee (1), and Parkinson and Bedford (2). These changes begin to develop immediately after the occlusion of the coronary artery, and may require several months for their complete evolution. They affect the QRS complex, the RS-T segment, and the T wave. The changes in the standard limb leads are sufficiently characteristic for an absolute diagnosis, in most cases.

These are well known and consist of RS-T segment deviation, either elevation or depression, depending upon which lead is taken, and the site of the infarction. This RS-T segment deviation is perhaps the earliest sign, apart from a decrease in the voltage of the QRS, and, within a matter of hours to days, this segment gradually approaches the isoelectric line again, but is accompanied by the development of a gradually increasing T wave inversion, and usually a deepening Q wave, until the

characteristic picture has developed :- large Q wave, diminished R wave, isoelectric RS-T segment, which gradually slopes or shoulders into a symmetrically inverted or "cove-plane" T wave. These changes occur in Lead I, and to a lesser extent in Lead II, in a case of anterior infarction. Praecordial leads, however, have shown that this picture really results from an antero-lateral infarction, according to the new nomenclature. Similar changes occur in Lead III, and to a lesser extent in Lead II, in a case of posterior infarction.

In some cases, however, the standard limb leads give doubtful results and, it is in these, that praecordial leads have proved to be of particular value. They not only help in the diagnosis of acute coronary occlusion, but help to localise the infarct fairly accurately, as has been shown by a comparison of electrocardiographic and post mortem findings (3).

In experimental coronary occlusion, the characteristic lesion produced by ligation of a major coronary vessel shows three consecutive zones :-

(1) A central zone of transmural infarction.

(2) A marginal zone of infarction, confined to a portion of the wall, most commonly the subendocardial layer.

(3) An outlying zone of ischaemia manifested by pallor and absence of histological evidence of degeneration.

The typical electrocardiographic pattern from the central zone consists of a QS complex, i.e. a transmural infarct merely transmits intra-cavity potentials. A markedly elevated RS-T segment, with a monophasic upright T wave is obtained, when the subepicardial layer of muscle is injured but is not dead. A notched QS is obtained, when a small portion of the underlying muscle is spared. The usual finding in the marginal zone is a QR complex, which can be correlated with infarction of the sub-endocardial layer, with preservation of the epicardial layer. The initial Q wave represents the intra-cavity potential, while the impulse is circumventing the infarcted area; the R wave represents positive potentials referred to the surface electrode, as soon as the overlying intact subepicardial layer is stimulated. The typical finding over the ischaemic zone consists of a normal QRS with cove-shaped inversion of the T wave. In chest lead electrocardiography the sites of infarction are classified under three main headings :-

(1) Antero-septal.

(2) Lateral.

(3) Posterior.

The classical QRST pattern in antero-septal infarction will be described first under two headings :-

(a) QRS pattern.

(b) RS-T - T pattern.

QRS pattern.

(a) Presence of a normal R in VI or any other lead from the right anterior chest wall.

(b) A QS or abnormal QR complex in one or more of the next three leads, i.e. V2, V3, V4.

(c) Absence of an abnormal Q wave from leads V5, V6, aVL, and standard limb leads. A Q wave is considered abnormal, when the duration from onset to nadir exceeds 0.03 seconds, and when its amplitude exceeds 25 per cent of the succeeding R in every cycle, (i.e. excluding respiratory variations).

The presence of a QS deflection in VI necessitates taking leads further to the right, e.g. V3R or VE, because the changes may be due to, (a) lateral wall infarction, (b) right ventricular dilatation and hypertrophy.

RST - T Pattern.

Early in the stage of injury associated with recent infarction the RS-T segment is elevated 2-8mm. The RS-T segment ascends to a peak in a straight line, or in a curved line with upward convexity, instead of the normal concavity, completing a monophasic upright RST-T complex. The RST-T junction begins to recede and the T wave dips below the isoelectric line. The T wave ultimately becomes cove-plane

in contour, the RST junction having a slight upward convexity. After reaching maximal depth, the T wave gradually recedes. The RST junction remains isoelectric or slightly elevated, with upward convexity, for a considerable time. The T wave may finally become flat or upright, but stabilisation may occur at any stage of the evolution.

In acute antero-septal infarction sharply inverted T waves may be recorded in V5 or V6, whence they are transmitted to the left arm, then to leads, aVL and standard limb lead I. Such T waves, when unaccompanied by an abnormal Q wave or abnormal reduction in the R wave, are a manifestation of an outlying ischaemic zone, and usually undergo a rather rapid evolution with return to normal, or to a pattern more in keeping with underlying left ventricular hypertrophy.

The classical pattern described above is not found in every case (only 7 out of 20 cases in Myers series). The deviations from the classical pattern are sub-divided into five groups :-

1. Instead of a complete disappearance of the R wave, in moving from Vi to V2, or in moving from V2 to V3, there is a decrease in amplitude only.
2. A small Q wave precedes an RS complex in VI.
3. Presence of a QS complex in VI and V2, or VI, V2 and V3.

4. The presence of right bundle branch block complicating antero-septal infarction. In this case, there is an initial Q wave preceding the customary initial R wave.
5. Serial T wave changes in VI-4, without QRS variations (this is due to an intra-mural infarct).

Standard limb leads are inadequate for the detection of antero-septal infarction.

Lateral infarction.

The diagnosis of infarctions, involving the lateral aspect of the apical portion of the left ventricle is made from a study of leads V5, V6 and aVL. The criteria for V5 and V6 are the same as for the praecordial leads VI-4, which have been described. The changes in aVL are as follows :-

When a QR or QS complex is recorded in Lead aVL, determination of the cardiac position is important in the interpretation of the findings. The position of the heart may be classified into one of the two following groups :-

(a) Horizontal to semi-horizontal.
(b) Vertical to intermediate.

(a) Differentiation of normal from abnormal QR (QS) complexes in aVL in horizontal to semi-horizontal position of the heart.

In the above positions, the potential variations of the left arm are transmitted, principally, from the epicardial surface of the free wall of the left ventricle. In the great

majority of cases, especially when the apex is directed anteriorly, the lateral wall of the left ventricle faces towards the left arm, and constitutes the main source of the QRS-T pattern in aVL. In some cases, particularly when the apex is displaced backwards, the basal aspect of the posterior or postero-lateral wall may exert the predominant effect upon the potential variations of the left arm. The decision, as to whether the variation in aVL comes from the lateral aspect of left ventricle, or postero-basal wall of left ventricle, is of importance in the evaluation of QR patterns. The normal Q wave in V5, V6 and aVL measures 0.01 seconds, or less, from its onset to nadir, and is less than 25 per cent of the amplitude of the succeeding R wave. On the other hand, the normal Q wave in oesophageal leads, opposite the postero-basal wall of the left ventricle, and also in aVL, may reach 0.03 seconds, in duration, and may approach 25 per cent of the amplitude of the succeeding R wave.

Indirect evidence of the chief source of the QRS pattern in lead aVL may be obtained from :-

(1) The direction of the associated P wave, if present.

(2) The contour of the QRS complex in lead aVR.

When aVL is derived from the lateral aspect of the left ventricle, then the P wave in V5, V6 and aVL is upright. When the heart is rotated backward, so that the postero-basal aspect

faces the left arm, then more of the left atrium is directed towards aVL so that the P wave is inverted or diphasic.

When the heart is rotated, such that the postero-basal aspect is facing the left arm, rather than the lateral aspect of left ventricle facing the left arm, then the postero-basal aspect tends to face the right arm as well as the left arm, resulting in a prominent late R wave in aVL and also in aVR.

A QR complex of 0.5 millivolt or more in lead aVL, transmitted from the epicardial surface of either the lateral, postero-lateral or postero-basal aspect of the left ventricle may be considered abnormal and referable to infarction when,

(1) The time of onset to nadir of the Q wave exceeds 0.03 seconds, and the QR ratio exceeds 25 per cent,

(2) The Q wave is followed by an upstroke that is notched or coarsely slurred and consumes 0.05 seconds or more.

(b) <u>Differentiation of the normal and abnormal QR complexes in lead aVL in vertical, semi-vertical or intermediate positions of the heart.</u>

In the intermediate position of the heart the epicardial surface of the lateral wall of the left ventricle generally faces towards the left arm. The derivation of the potential variations of the left arm is comparable to that when the heart is horizontal or semi-horizontal. The diagnostic criteria,

therefore, are the same as those described above.

A vertical to semi-vertical position of the heart is generally accompanied by clockwise rotation about the longitudinal axis so that the potential variations of the anterior wall of the right ventricle or anterior terminus of the septum are transmitted to the left arm. Under these circumstances infarction of the lateral wall of the left ventricle is not detectable in lead aVL.

When vertical to semi-vertical position is accompanied by counter-clockwise rotation rather than the usual clockwise rotation about the longitudinal axis, the potential variations of the left ventricular cavity may be transmitted through the mitral orifice and left atrium to the left arm. As a consequence, lead aVL displays a deep and prolonged Q wave, usually followed by a late R wave, drived from activation of the postero-basal wall of the left ventricle. The QR or QS complex which occurs as a normal variant in lead aVL in a semi-vertical to vertical heart, rotated counter-clockwise on its longitudinal axis, may be identical with that which occurs as a manifestation of antero-lateral infarction in the intermediate position of the heart. Differentiation may some times be made through indirect evidence furnished by :-

(1) The QRS pattern in lead aVR.

(2) The direction and contour of the P wave and QRS complex in lead aVL, when the tracing is repeated in a different position and during deep respiration.

When the foregoing evidence is inconclusive, supplementary high praecordial and axillary leads are indicated.

When the rhythm is sinus, the direction and contour of the P wave in lead aVL is of considerable indirect aid in determining whether a QR or a QS complex is a manifestation of lateral-infarction, in an intermediate heart, or a normal variant associated with a vertical or semi-vertical position. The upright P wave, with gently sloping limbs, normally found in leads V5, V6 is due to the transmission of the potential variations of the lower part of the left atrium through the lateral wall of the left ventricle. The registration of an upright P wave in aVL, which is similar to that in leads V5 and V6, indicates that the potential variations of the left atrium are likewise transmitted through the lateral wall of the left ventricle to the left arm. This constitutes strong evidence, although indirect, that the predominant pathway for the transmission of the potential variation of the left ventricle to the left arm extends from the epicardial surface of the lateral wall, and not from the cavity through the mitral orifice. The registration of an inverted to diphasic P wave, and QR to QS complex in lead aVL indicates transmission of the potential variations of the superior or posterior walls of the left atrium directly to the left arm.

Posterior infarction.

As in the diagnosis of lateral myocardial infarctions the position of the heart is of prime importance in interrupting the

potential variations in lead aVF. Again the position of the heart may be classified into one of two groups,

(1) Horizontal or semi-horizontal,

(2) Intermediate, semi-vertical, or vertical.

Horizontal or semi-horizontal position of the heart.

In this position of the heart the potential variations in lead aVF are derived from the right side of the septum, and the epicardial surface of the posterior wall of the right ventricle, consequently it is impossible to diagnose posterior infarction in this position of the heart, unless the infarct has extended into the septum.

Intermediate, semi-vertical or vertical position of the heart.

Potential variations of the epicardial surface of the posterior wall of the left ventricle have a predominant effect upon the QRST pattern in lead aVF. The criteria for the diagnosis of a QR pattern in lead aVF are as follows :-

An abnormal QR pattern is differentiated from a normal QR pattern, in lead aVF, by the time of onset to the nadir of the Q wave, ratio of the Q wave to the R wave, and the contour of the ascending limb of the R wave. A QR complex with an amplitude of 0.5 millivolt or more, having a Q wave, whose duration from onset to nadir in 0.03 seconds or more, and whose ratio to the succeeding R wave is over 25 per cent, is considered diagnostic of infarction.

Borderline cases are met with and are considered diagnostic if they meet the following demands :-

(a) The time from the onset to the nadir of the Q wave is 0.04 seconds.

(b) The Q wave is coarsely slurred or notched.

(c) The tracing reveals RS-T deviation.

(d) The previous tracings, if available, are normal.

The above remarks are a summary of the diagnostic criteria for myocardial infarction in the three basic localisations :-

(a) Antero-septal.

(b) Lateral.

(c) Posterior.

Infarction may occur in the above localisations or in combinations of these. Thus infarction may be called :-

(a) Antero-septal.

(b) Lateral.

(c) Posterior.

(d) Antero-lateral.

(e) Postero-lateral, or

(f) Antero-posterior.

These remarks concern myocardial infarction but can also be applied to chronic coronary artery occlusion, with some modification, as discussed below :-

Chronic coronary occlusion.

The localisation of chronic coronary occlusion follows the same classification as that given for acute coronary occlusion. In the diagnosis of chronic coronary occlusion, one is more concerned with variations of T wave; whereas in acute coronary occlusion more importance is attached to changes in the QRS pattern, in chronic coronary occlusion more importance is attached to T wave changes. The typical findings, in chronic coronary occlusion are similar to those found in the experimental ischaemic zone, and in consequence, it is possible to determine the presence and site of chronic coronary occlusion, on the criteria listed under acute coronary occlusion. It should be pointed out, however, that difficulty may arise in the diagnosis of antero-septal coronary artery insufficiency, because the T wave in V1 and V2 leads may be inverted in normal individuals, and in consequence, in the antero-septal coronary artery insufficiency the T wave should be inverted in leads V1, V2, V3 and possibly in V4 also.

In a very large group of cases, however, as Wilson (4) points out complaints of breathlessness and other symptoms of myocardial insufficiency may be obtained but no typical history of angina or cardiac pain of effort. In these cases, provided they fall into the requisite age group (40 years onwards), arteriosclerosis of the coronary arteries is suspected either because of evidence of arteriosclerosis elsewhere, and the

absence of any other obvious cause, or because of the patient's age alone. These patients often display electrocardiographic evidence of myocardial disturbances, which are very probably of vascular origin. The electrocardiographic changes are often of slight extent, and are classified as "equivocal changes". The interpretation of these minor changes in the form of the electrocardiogram, either QRS complex or T waves, by themselves, is not sufficient proof of coronary disease, but when accompanied by a typical history of cardiac pain of effort or angina pectoris, are regarded as consistent with the diagnosis of coronary artery disease.

Atrioventricular block, bundle branch block, or intraventricular block, occurring in a patient, who gives a typical history of angina pectoris or cardiac pain of effort and who is above 40 years of age is, in my opinion, sufficient evidence for the diagnosis of coronary artery disease.

In the present investigation it was possible to localise the site of coronary artery insufficiency, by chest lead electrocardiography, in 77 cases. The results were as follows :-

1.	Antero-septal	:	17 cases.
2.	Antero-lateral	:	25 cases.
3.	Posterior	:	23 cases.
4.	Postero-lateral	:	4 cases.
5.	Antero-posterior	:	1 case.
6.	Lateral	:	7 cases.

Bundle branch block occurred in three cases; left bundle branch block in two cases, right bundle branch block in one case.

REFERENCES :

1. Pardee, H.E.B. : Arch. Int. Med. 26 : 244 : 1920.

2. Parkinson, T., and Bedford, D.E. :
   Heart, 14 : 195 : 1927 - 1929.

3. (a) Myers, G.B., Klein, H.A., and Stofer, B.E. :
   Amer. Heart J : 36 : 374 : 1948.

   (b) Myers, G.B., Klein, H.A., and Stofer, B.E. :
   Amer. Heart J : 36 : 535 : 1948.

   (c) Myers, G.B., Klein, H.A., and Hiratzka, B.E. :
   Amer. Heart J : 38 : 547 : 1949.

4. Wilson, F.N. : Diseases of the coronary arteries and cardiac pain. The MacMillan Company, 1936, p.281.

ELECTROCARDIOGRAPHY OF GALL BLADDER DISEASE.

The changes in the pre-operative electrocardiograms of 363 cases of gall bladder disease are summarised in the following tables :-

Rhythm.

Sinus tachycardia	= 58.	
Sinus bradycardia	= 5.	
Auricular fibrillation	= 3.	
Supra-ventricular extra systoles	= 11.	
Nodal extra systoles	= 2.	
Ventricular extra systoles	= 9.	'Pulsus bigeminus' in one case.
Potential heart block	= 2.	

P Wave.

Large, pointed in leads II, III = 5 cases.
(No other abnormality noted).

P-R interval.

Prolonged (above 0.22 seconds) = 2.

QRS complex.

Low voltage in lead	I = 26 :	Splintered in lead	I = 3
" " " "	II = 18 :	" " "	II = 10
" " " "	III = 73 :	" " "	III = 43

Q wave (exceeding 3mm).

Lead I	= 1.
" II	= 10.
" III	= 64.

S-T.

Elevated in Lead	I	=	1	:	Depressed in Lead	I	=	29.
" " "	II	=	1	:	" " "	II	=	33.
" " "	III	=	6	:	" " "	III	=	22.

T wave.

Low voltage in Lead	I	=	84	:	Diphasic in Lead	I	=	18.
" " " "	II	=	68	:	" " "	II	=	10.
" " " "	III	=	138	:	" " "	III	=	30.

Inverted in Lead	I	=	18.
" " "	II	=	13.
" " "	III	=	119.

Left axis deviation with inverted T in III = 82.

Diastolic hypertension occurred in 104 out of a total of 278 cases, in which blood pressure readings were taken.

The interpretation of these 363 electrocardiographs was as follows :-

Normal electrocardiogram	=	165	(51 per cent)
Coronary artery insufficiency	=	33	(9 " ")
Myocardial disease	=	64	(16 " ")
Left ventricular hypertrophy	=	20	(4 " ")
Left bundle branch block	=	2	(.5 " ")
Potential heart block	=	2	(.5 " ")
Suggestive of coronary artery insufficiency	=	39	(10 " ")
Suggestive of myocardial disease	=	4	(1 " ")

Equivocal changes = 34 (9 per cent)

The series of 100 chest leads was investigated with the following results :-

Normal electrocardiogram	=	59 per cent
Coronary artery insufficiency	=	18 " "
Suggestive of coronary artery insufficiency	=	8 " "
Left ventricular hypertrophy	=	6 " "
Equivocal changes	=	4 " "
Postural changes	=	3 " "
Left bundle branch block	=	1 " "
Auricular fibrillation	=	1 " "

The information obtained from chest lead electrocardiography is fuller and more exact, than that from the standard limb lead electrocardiography. When we compare the two series, we find that in chest lead electrocardiography.

1. The incidence of the coronary artery insufficiency is double.
2. The diagnosis of myocardial disease almost disappears.
3. The number of normal electrocardiograms increases.
4. The number of equivocal electrocardiograms is reduced.

A more complete picture of the difference in value of standard limb lead and chest lead electrocardiograms is obtained by comparing the diagnosis reached in 100 cases of gall bladder disease, in which both standard limb lead and chest lead electrocardiography was carried out. The diagnoses are tabulated below :-

Standard limb leads.

Normal	=	47 per cent
Suggestive of coronary artery disease	=	25 " "
Suggestive of myocardial disease	=	13 " "
Left ventricular hypertrophy	=	4 " "
Left bundle branch block	=	1 " "
Auricular fibrillation	=	1 " "
Equivocal	=	9 " "

Chest leads.

Normal	=	62 per cent
Coronary artery disease	=	18 " "
Suggestive of coronary artery disease	=	8 " "
Left ventricular hypertrophy	=	6 " "
Left bundle branch block	=	1 " "
Auricular fibrillation	=	1 " "
Equivocal	=	4 " "

It would seem that chest lead electrocardiography had helped towards making a more definite diagnosis in 43 cases. The greatest help was obtained in the investigation of

suspected coronary artery disease,when the presence of definite coronary artery disease was established in 18 cases out of 25 possibilities; nevertheless the total number of suspected cases with coronary artery disease remained essentially the same. In those cases labelled "Suggestive of myocardial disease", on the basis of low voltage QRS complex, and/or low voltage T waves, chest leads proved most useful in excluding any significant abnormality. Left ventricular hypertrophy, which is sometimes a difficult diagnosis to make from the standard limb leads,has confirmatory evidence in the chest leads to make the diagnosis more certain. The diagnosis of "Equivocal changes" was halved by the use of the chest lead electrocardiogram.

The electrocardiographic changes associated with acute cholecystitis and gall bladder colic seem to have received scant attention in the literature, in fact no reference can be found. In this investigation two cases showed electrocardiographic changes associated with acute cholecystitis and gall bladder colic respectively. The main features of the two cases are recorded below.

The first patient was a man, aged 64 years. Six weeks before admission to hospital he developed severe right subcostal pain, followed by vomiting and jaundice; the pain subsided in 48 hours. 12 hours before admission he had a similar attack, for which he was admitted to hospital (3.10.49).

Physical examination revealed him to be an elderly man, of rather heavy build. His sclerotics were jaundiced, and there was local tenderness in the right subcostal region. A distended gall bladder was palpable.

His pulse rate was 110 per minute and his blood pressure was 180/110. Heart sounds were soft, but pure. His urine contained bile.

On 4.10.49, before his symptoms had subsided his electrocardiogram (Fig. 16, Appendix 3) showed left axis deviation, with ST depression and an inverted T wave in lead I. Six days later, when he was symptom free, his electrocardiogram showed left axis deviation and an upright T wave in lead I; the unipolar limb leads, and chest leads were within normal limits.

About one week later, when he was convalescent, he developed severe praecordial pain, at rest in bed, associated with dyspnoea; these symptoms lasted for two days. His blood pressure did not change significantly but his electrocardiogram showed left axis deviation, with ST depression and diphasic T wave in lead I. The chest leads showed a large Q wave, S-T elevation and shouldering with T wave inversion in aVR, S-T depression with T wave inversion in aVL, absent R wave in V1-V4, and a large Q wave with S-T elevation and T wave inversion in V5. V6 showed similar but less marked changes than V5.

His symptoms and electrocardiographic signs were considered to be consistent with coronary occlusion. Two months later his electrocardiogram showed an upright T wave in lead I. In the chest leads the T wave was diphasic in V1 and V2, and inverted in V3, V4 and V5, confirming the above diagnosis.

The second case was a female, aged 45 years. The first electrocardiogram, taken on 1.4.40, during an attack of biliary colic, showed S-T depression in all the standard limb leads, together with a diphasic T wave in lead I, and inverted T wave in leads II and III. Four days later, when the colic had subsided, the S-T depression in all the leads had decreased, whilst the T waves were more positive.

On 26.1.50, the electrocardiogram, taken in a quiescent phase, had reverted to the type recorded during the attack of biliary colic.

These two patients showed similar S-T and T wave changes, during acute cholecystitis and gall bladder colic respectively. In the latter case the gall bladder colic produced electrocardiographic changes exactly the same, as developed naturally over the next ten years, i.e. it forecast the distribution of coronary artery sclerosis (electrocardiographically) ten years hence, or, at the time of onset, showed the distribution of latent coronary artery sclerosis.

The first case demonstrates the occurrence of acute

cholecystitis with electrocardiographic changes, followed by the development of coronary occlusion in the same patient.

The main findings of the investigation can be summarised as follows :-

1. Coronary artery disease forms the bulk of abnormal electrocardiograms in gall bladder disease. Out of 32 cases with abnormal electrocardiogram, i.e. excluding those with left ventricular hypertrophy, which resulted from hypertension, coronary disease (definite or suggestive) accounted for 26 cases. Even so, coronary artery disease might well account for the remaining abnormality - auricular fibrillation in one case, and "equivocal changes" in four others. Left bundle branch block occurred in a case, with hypertension, so that the latter condition probably accounted for this. In the 18 cases of coronary artery disease, the main sites were :-
   (a) Antero-septal in six cases.
   (b) Posterior in six cases.
   (c) Postero-lateral in four cases.
   (d) Antero-lateral in one case.
   (e) Antero-posterior in one case.

1. (contd.)

In the post mortem series, the incidence of coronary artery disease, in the gall bladder disease group, was 38 per cent. In the group of gall bladder disease cases, in this investigation, the incidence of coronary artery disease, diagnosed by electrocardiogram, was only 26 per cent, i.e. the electrocardiograph was only 70 per cent accurate.

2. The electrocardiographic diagnosis of left ventricular hypertrophy (six per cent) does not compare with that obtained clinically (37 per cent). Hypertension, however, may occur for some time without there being any detectable left ventricular enlargement except by post mortem examination.

3. There does not appear to be any characteristic or pathognomonic electrocardiographic change or changes found in gall bladder disease, although several people have noted changes in the electrocardiogram following operation.

4. Chest leads are an improvement of the standard limb leads in electrocardiographic diagnosis. The ways in which chest leads were helpful were as follows :-

4. (contd.)

(a) Equivocal changes in lead III were proved to be within normal limits - 12 cases.

(b) The diagnosis of coronary insufficiency could definitely be made in 16 cases - in four cases the standard limb leads were normal, but the chest leads revealed antero-septal coronary insufficiency.

In four cases posterior coronary insufficiency was diagnosed, when changes in the standard limb leads were equivocal; two cases were possible examples of ventricular hypertrophy (one left, one right), but the chest leads revealed coronary artery insufficiency. Lead III was equivocal in a further three cases, but chest leads confirmed coronary artery insufficiency to be present. In the remaining three cases chest leads confirmed the diagnosis of the standard limb leads but localised the lesion more accurately.

(c) Low voltage T waves occurred in four cases - three were shown to be due to coronary artery insufficiency, one to be within normal limits.

4. (contd.)

(d) Low voltage QRS complexes occurred in four cases and were shown to be within normal limits in the chest leads.

(e) In five cases the diagnosis left ventricular hypertrophy was made - in one case coronary artery insufficiency was a possible diagnosis from the standard limb leads. In the remaining four cases left axis deviation was present, but chest leads favoured left ventricular hypertrophy, as a diagnosis, rather than a horizontal position of the heart.

ELECTROCARDIOGRAPHY OF GALL BLADDER DISEASE

POST-OPERATIVE FOLLOW-UP.

Fitz-Hugh and Wolferth (1) described six cases with abnormal, pre-operative electrocardiograms (standard limb leads only). The first, one year before operation, had an inverted T wave in all leads. Six weeks after operation the electrocardiogram became normal. In the second, two days prior to operation, the T wave in lead I was flat, in leads II and III inverted. Three months after operation these abnormal findings had disappeared. In the third, one day before operation, the T wave in leads II and III was inverted. 18 days after operation, the electrocardiogram showed the beginning of a return towards normal; nine months after operation, the T waves were 'practically normal'. The remaining three cases had abnormal T waves, before operation, and there was a return towards normal, within a few weeks to several months, after surgical removal of gall stones. Boas and Levy (2), reported a case, in which flattened T waves became upright, after cholecystectomy. Weiss and Hamilton (3) reported 21 patients with cholelithiasis, four of whom had abnormal pre-operative electrocardiograms. Eight days after cholecystectomy, the electrocardiograms of three of these four cases, had returned to normal. One of the three cases, however, had hypertension so the authors claimed improvement in only two cases, as a result of gall bladder surgery. Both cases showed inverted T waves pre-operatively and upright ones

eight days later. Moschowitz (4) reported a case, in which the P-R interval was 0.30 seconds before operation, and 0.20 seconds after operation. Only two other cases with similar electrocardiographic findings have been reported, both by Willius and Fitzpatrick (5). Clark (6), described a case, in which the pre-operative electrocardiogram showed diphasic T waves in leads I and III, R-T elevation in lead I and, R-T depression in lead III. These changes disappeared following operation.

More recently Breitweiser (7) reviewed the pre- and post-operative electrocardiograms, over a six year period, in the University of Pennsylvania Hospital. 621 unselected gall bladder operations were performed in that hospital, but only 66 had had an electrocardiogram, within one year prior to operation, and of these 30 were normal. Of the remaining 36, with abnormal electrocardiograms, a follow-up was possible in 17. 10 cases of this group were claimed to show appreciable improvement in the post-operative electrocardiogram. In one case, however, the pre-operative electrocardiogram may have been due to a myocardial infarct, the healing of which caused a return of the electrocardiogram to normal. If we exclude this case, we find that half the cases showed post-operative electrocardiographic improvement, four cases showed no change, while three cases showed adverse electrocardiographic changes. Five cases of hypertension

were excluded from this list but were not considered to alter the improvement figure (50 per cent). She points out, however, that to a certain extent the 18 patients, which she reported, are a selected group, in that electrocardiograms were done only on those patients with known or suspected cardiac disease; therefore the results cannot be strictly applied to all gall bladder cases.

The main findings up to date, can be summarised as follows :-

1. Electrocardiographic changes may occur in gall bladder disease (54 per cent in one series). These changes are mainly flattening or inversion of the T wave in one or more leads, of the standard limb lead electrocardiogram.
2. The abnormal electrocardiograms often show improvement following gall bladder operation (50 per cent in one of the above series).
3. Occasionally electrocardiograms show changes indicative of deterioration following operation (16 per cent in one of the above series).

In the present investigation 49 patients had electrocardiographic investigations carried out for a period of six months after the operation. 45 of these had chest lead electrocardiography, the remaining had only standard limb lead electrocardiography. Two cases, which showed

electrocardiographic changes within a month of operation, died within the six months follow-up period, so that a final electrocardiogram was not obtained in these cases. The results can be summaried as follows :-

1. Number of cases showing no significant electrocardiographic changes post-operatively = 38.
2. Number of cases showing electrocardiographic changes post-operatively = 11.

The latter group was sub-divided as follows :-

(a) Number of cases showing improvement post-operatively, = 4.
(all these cases had electrocardiographic evidence of coronary artery insufficiency (one associated with hypertension) see Fig. 5 Appendix 3).

(b) Number of cases showing deterioration post-operatively = 2.
(see Fig. 9 and Fig. 11, Appendix 3).

(c) Number of cases showing temporary improvement = 3.
(One of these cases died at home, within the six months follow-up period, with a history very suggestive of coronary

(c) contd.

occlusion. The pre-operative electrocardiogram showed widespread coronary artery insufficiency. (See Fig. 6 Appendix 3). Another of these cases developed a cerebral haemorrhage, within a month of leaving hospital, and died from another cerebro-vascular incident, within the six months follow-up period (see Fig. 7, Appendix 3). The remaining case suffered from hypertension).

(d) Number of cases developing post-operative complications (pulmonary embolism) = 2.

The number of cases followed up is small, but it would appear from the results presented above, that electrocardiographic changes occur not infrequently, following gall bladder surgery.

The four cases showing improvement, which lasted for six months, all had cholecystostomies performed. The two cases, which showed deterioration, also had cholecystostomies performed. One of the cases, showing temporary improvement had a cholecystectomy, but she died within the six months follow-up period. The remaining two cases, showing temporary improvement had cholecystostomies. Of the two

cases of pulmonary embolism, one had a cholecystectomy, and the other had a cholecystostomy. The impression one gets from these results is, that the electrocardiogram response, post-operative, is not related to the type of surgery-cholecystostomy as opposed to cholecystectomy.

In the present series the effect of operative treatment of gall bladder disease, in the electrocardiogram, can be divided into five groups :-

1. No significant change post-operatively.
2. Improvement occurring within two/four weeks of operation, and maintained for at least six months.
3. Deterioration occurring after operation.
4. Improvement occurring within two/four weeks of operation but reverting to the original pre-operative electrocardiogram.
5. Temporary deterioration of the electrocardiogram due to post-operative complications, not necessarily associated with gall bladder surgery, e.g. pulmonary embolism.

Before discussing the reasons for these changes it would be interesting to note the electrocardiographic changes, in which the follow-up period lasted from eight/thirteen years.

It was possible to follow up 14 cases (Fig. 51-64, Appendix 3), 12 of whom had been subjected to operation. Three of these 12 cases showed electrocardiographic changes (standard limb leads only). One of these showed improvement, the remaining two showed deterioration. In the latter two cases, the patients were hypertensive, and one of them had developed diabetes mellitus in the follow-up period.

Of the two cases, not subjected to operation, one showed a temporary improvement of the electrocardiogram, after a period of rest and medical treatment in hospital, but when followed up a year later the electrocardiogram had reverted to its original form.

Having summarised the various types of electrocardiographic changes that may occur, after operative treatment of gall bladder disease, one must look for an explanation of these changes.

Group 1 above requires no further comment.

Group 2 will be discussed in detail below.

Group 3 appears to be accounted for by -

(a) Coronary occlusion, complicating operation, and possibly related to the trauma of operation decreasing the coronary blood flow.

(b) Hypertension, which in its natural course, irrespective of the presence of gall bladder disease, leads to coronary artery insufficiency.

Group 4 may be explained on bed rest, and restricted mode of life, and diet imposed on the patient following operation. After a while the advancement of the underlying disease process, either atherosclerosis or hypertension, causes a reduction in the coronary circulation, absolute or relative.

Group 5 requires no special comment because they result from complications which are common to operative procedures not necessarily related to the gall bladder.

The explanation of group (2) has aroused most interest and argument, but so far no complete explanation has been given.

Fitz-Hugh and Wolferth (1) list nine examples of T wave inversion which are capable of reversion to a normal type. They are found in the following conditions :-

1. During the recovery stage following exercise or myocardial anoxaemia.
2. During the recovery stage following the rapid ingestion of large amounts of cold water.
3. After withdrawal of drugs, which have produced changes in the T waves (digitalis or cinchona group).

4. Following restoration of normal thyroid or parathyroid function (after operation for hyperthyroidism, hyperparathyroidism or after treatment of myxoedema).
5. During the recovery stage of myocardial infarction.
6. During recovery from acute carditis (including pericarditis).
7. Following acute infections, such as pneumonia or influenza, which occasionally produce T wave changes, without other evidence of acute carditis.
8. Following the restoration of the heart from an abnormal to a normal position (termination of pregnancy, treatment of obesity).
9. Following the relief of anasarca, or large fluid collections in the chest.

These authors refuse to speculate as to the nature of the myocardial disturbances responsible for the electrocardiographic changes. They conclude, however, that not only may gall bladder disease injure the myocardium but that the process, to a certain extent, is reversible.

Clark (6), states that acute inflammatory conditions affecting the gall bladder create stimuli, which reflexly

act through autonomic pathways to restrict or in some other manner alter the coronary blood supply so that existing minor deficiencies in the coronary circulation become manifest. It seems probable that people with acute gall bladder disease, or acute duodenal lesions also, whose electrocardiograms show T wave changes as described above, do have minor alterations in their coronary circulation.

Moschowitz (4), in commenting on the electrocardiographic changes in gall bladder disease, pre- and post-operatively, says 'It is plausible to think that there is a latent myocardial dysfunction, due to coronary sclerosis, which renders the electrocardiographic curve more susceptible to changes consequent upon the trauma of the superimposed malady within the gall bladder'.

Breitweiser (7), in her paper summarised above, concludes that the cause of the abnormal T waves is not known, but states that, at times, they are part of a general picture, suggestive of myocardial damage, in which case the need for surgery must be weighed against the cardiac status.

It is obvious from the above excerpts, from the literature, that the explanations are along two main lines :-

1. That the T wave changes post-operatively are possibly due to myocardial damage, per se, which is reversible.

2. That the T wave changes post-operatively are possibly due to alterations in coronary blood flow, affecting the myocardium. This again is reversible.

In brief the reversible myocardial damage may result from :-

1. Toxic substances acting directly on the myocardium and presumably arising in the diseased gall bladder.
2. Reflex vaso-constriction of the coronary vessels, arising from the stimuli within the diseased gall bladder.

An attempt to elucidate these electrocardiographic changes in gall bladder disease experimentally was made by Hodge et al (8). This consisted of electrocardiographic studies of the effect of distension of the biliary tract in two groups of animals (dogs). The first group of animals, with normal hearts, served as a control; the second had experimentally produced lesions of the coronary arteries. In the control group of five dogs no significant alteration of the RS-T segment in the electrocardiogram was noted with distension of the biliary tract. In the group of five dogs in which there was interference with the coronary circulation by clamping of a coronary artery, there was alteration of the RS-T segment in four of the animals, during biliary distension. In only one animal, however, did the pattern

resemble the findings of coronary disease in man. The conclusion of the authors was that a general lowering of the blood pressure, and of viscero-cardiac reflexes, affecting the cardiac output, or the conducting system, may account for the electrocardiographic alterations in the animals with a pre-existing cardiac lesion. However, the injection of 1 mg. of atropine intravenously failed to prevent the changes in a single dog. Although it is well known that the electrocardiographic changes in the dog do not parallel those found in man, the above findings are interesting in that it seems necessary for a pre-existing coronary artery lesion to be present, before electrocardiographic changes can be induced by distending the gall bladder. The two main objections to this work, from the point of view of human beings with gall bladder disease are :-

1. Electrocardiographic changes occur in human beings with gall bladder disease without having a distended gall bladder, i.e. a much smaller stimulus seems to be sufficient in human beings.
2. The electrocardiographic changes in the dog did not resemble, except in one case, those found in human beings.

As recorded above attempts to substantiate the latter explanation have been made by experimental methods with not too convincing results. The author attempted to reproduce the experiments on dogs, on human beings (two cases). Three types of stimuli were applied to the gall bladder, each attempting to reproduce certain types of gall bladder disease :-

(a) Distending the gall bladder with saline : cf mucocele and empyema of gall bladder.

(b) Electrical stimulation of the mucous membrane of gall bladder : cf acute cholecystitis.

(c) Dilating the cystic duct with the tip of artery forceps : cf stone in cystic duct. Electrocardiograms (standard limb leads only) were taken.

(i) Prior to operation.

(ii) Whilst the patient was under the anaesthetic, immediately before operation.

(iii) After opening the abdomen, and during each of the above three procedures.

No significant electrocardiographic changes were noted in either case. It should be pointed out, however, that the two cases were normal individuals, without any clinical

or electrocardiographic evidence of coronary artery disease. It may be, as Moschowitz suggests, that a certain degree of 'latent coronary artery insufficiency' must be present before the above procedures produce T wave changes, i.e. the stimuli arising in diseased gall bladders (or those used experimentally) are insufficient to produce electrocardiographic changes in individuals with a normal coronary blood flow. These experiments consequently are being pursued, in an attempt to elucidate this problem.

As regards the first explanation offered above, it would appear to be impossible to prove that, in the intact living patient with gall bladder disease, there is direct myocardial damage, which becomes reversed, after operative treatment of the gall bladder.

An explanation of the electrocardiographic changes, following gall bladder surgery, however, if found, is not sufficient. It is desirable that a simple test be devised for selecting those cases, with abnormal pre-operative electrocardiograms, which will be restored to normal following surgery, from those cases, with abnormal pre-operative electrocardiograms, which will not be restored to normal following surgery, i.e. a means for screening those patients who have a 'reversible coronary insufficiency or myocardial change', from those with absolute coronary insufficiency or myocardial damage. This is also under investigation.

The conclusions are as follows :-

1. Electrocardiographic changes are not uncommon following gall bladder surgery (any attempt to describe how frequent they are is nullified by the small number of cases reported).
2. The electrocardiographic changes can be grouped into four types :-
   (a) Improvement, which is maintained.
   (b) Deterioration.
   (c) Temporary improvement.
   (d) Those changes associated with post-operative complications.
3. No satisfactory explanation for these changes has yet been found.

REFERENCES :

1. Fitz-Hugh, T. Jr., and Wolferth C.C. :
   Ann. Surg. 101 : 478 : 1935.
2. Boas, E.P., and Levy, H. : Amer. Heart J. 14 : 540 : 1937.
3. Weiss, M.M., and Hamilton, J.E. : Surgery 6 : 893 : 1939.
4. Moschowitz, E. : J. Mt. Sinai Hosp. 10 : 632 : 1943.
5. Willius, F.A., and Fitzpatrick, J. : J. Iowa State Med.
   Soc. 15 : 589 : 1925 (quoted by Moschowitz, E. :
   p. 633).
6. Clark, W.E. : Amer. Heart J. 29 : 631 : 1945.
7. Breitweiser, E.R. : Amer. J. Med. Sci. 213 : 598 : 1947.
8. Hodge, G.B., Messer, A.L., and Hill, H.C. :
   Arch. Surg. 55 : 710 : 1947.

THE RELATIONSHIP

BETWEEN

GALL BLADDER DISEASE

AND

CORONARY ARTERY DISEASE

DISCUSSION AND CONCLUSION.

In the preceding chapters single aspects of the problem, of a possible interrelationship between gall bladder disease, and coronary artery disease, have been dealt with, and conclusions have been drawn from results of particular investigations. It is now necessary to examine the results, as a whole, and decide what is known, what is in doubt, and what is not known, and further, to decide whether there are indications for further investigations.

The questions to which I sought an answer were :-

1. Is there any evidence of an association between gall bladder disease and coronary artery disease?
2. Is there any evidence of a common etiological factor or factors?
3. Does gall bladder disease cause, or intensify coronary artery disease, and does treatment of gall bladder disease cure, or improve coronary artery disease?
4. Does coronary artery disease cause, or intensify gall bladder disease?

Let us consider each of these questions in the light of my findings.

1. <u>Is there any evidence of an association between gall bladder disease and coronary artery disease?</u>

The evidence for an association between the two diseases

is contained in the chapter concerning the post mortem incidence of the two conditions. There it was shown :-

(a) The two diseases frequently co-existed.

(b) The association increases with advancing years.

(c) There was no significant difference in the incidence of gall bladder disease and coronary artery disease in the sexes.

These results were in accord with those of previous workers.

The results of the clinical investigation, however, showed that the association was not merely confined to gall bladder disease and coronary artery disease, but included hypertension and obesity. The problem of association, therefore, is not simply one of gall bladder disease, and coronary artery disease, but embraces gall bladder disease, coronary artery disease, hypertension, and obesity.

In both the post mortem and clinical investigations, the association between these four conditions increased with age, i.e., an 'ageing process' appeared to be a common factor, but it is felt that this is not necessarily the only one. One must, therefore, look for other, possible, common factors and these may be metabolic, dietary, infective, or endocrine.

2. Is there any evidence of common etiolotical factor or factors?

A definite answer cannot be given to this question because

the etiology of both diseases is not yet completely known. A common metabolic fault, viz. a disturbance of cholesterol metabolism, in the form of a hypercholesterolaemia, has been suggested. The results of the biochemical investigations were against this view :-

(a) Serum cholesterol levels, in coronary artery disease, were more frequently within the normal range than above it.

(b) The serum cholesterol levels, in gall bladder disease, were within normal limits.

(c) In patients with both gall bladder disease, and coronary artery disease, there was no evidence of hypercholesterolaemia being a frequent occurrence.

It is felt, however, that serum cholesterol levels alone are insufficient for determining the possible role of cholesterol, in the etiology of coronary artery disease, and gall bladder disease, especially when the biochemistry and physiology of cholesterol is still so imperfectly understood. Therefore, before rejecting a metabolic fault as a common etiological factor, further biochemical studies concerning lipid metabolism, as a whole, not merely cholesterol metabolism, are desirable.

3. Does gall bladder disease cause, or intensify coronary artery disease, and does treatment of gall bladder disease cure, or improve coronary disease?

It must be admitted straightaway that, in the light of our present knowledge, and the results of the present investigation, that no definite answer can be given to the first part of the question, viz., does gall bladder disease cause coronary artery disease?

In the clinical investigations, however, the post-operative follow-up, in the small group of 12 cases, over a long period (9-12 years) showed that, in 10 cases, coronary artery disease manifested itself clinically, after operation for gall bladder disease. This finding would suggest that gall bladder disease did not cause coronary artery disease, but no definite conclusion can be drawn from such a small series.

There is little doubt, from the electrocardiographic investigations, that gall bladder disease can intensify coronary artery disease, or rather, intensify the effects of coronary artery disease, as shown by the development of acute coronary artery insufficiency, in acute cholecystitis and gall bladder colic.

There are two possible explanations for this :-

(a) Reflex vaso-constriction of the coronary arteries.

(b) A disturbance in the splanchnic circulation, which produces a redistribution of blood such that coronary artery insufficiency becomes more obvious.

Both explanations postulate reflex changes, in one case supra- and, in the other, infra-diaphragmatic. There appears to be little doubt that nervous pathways for both do exist, but so far, no one has demonstrated that they function in human beings. It is highly probable, however, that both play a part in producing the acute coronary artery insufficiency, of acute cholecystitis, and gall bladder colic. Similar electrocardiographic changes, are found in acute pancreatitis, so that these electrocardiographic changes are found in "upper abdominal disease", rather than in gall bladder disease alone. Burton (1), suggests the possibility that repeated episodes of coronary artery spasm, in gall bladder disease,may result in structural changes, i.e. recurring functional changes can produce anatomical changes (a reversal of the more common form of pathological physiology). Such a theory is extremely difficult to prove or disprove, especially when coronary artery spasm, in gall bladder disease, although highly probable, has not yet been proved.

It is almost certain that treatment of gall bladder disease does not cure coronary artery disease, because coronary artery disease may progress, or even become manifest, as stated above, after surgical treatment of the gall bladder.

Electrocardiographic evidence suggests that treatment of gall bladder disease, in a small number of cases, can improve coronary artery disease or, rather, diminish the effects of coronary artery disease, as shown by the electrocardiographic improvement post-operatively. (This is discussed in detail in the chapter on "Electrocardiography of gall bladder disease - Post-Operative follow-up").

Regarding the improvement of the condition of the heart, in general, post-operatively, in some cases of gall bladder disease, several possibilities have been mentioned in the clinical chapter, viz :-

1. Removal of a septic focus.
2. Period of enforced bed rest following operation.
3. Restricted activity, after operation, usually for a period of several months.
4. Adherence to a stricter diet, with reduction in weight, post-operatively.

Some of the older physicians and surgeons were of the opinion, that gall bladder disease produced parenchymatous damage to the myocardium, a toxic myocarditis, and that

operative treatment allowed regression of these changes. To prove or disprove that such reversible damage occurs in a patient, who remains alive, is virtually impossible so that one cannot deny that such an association exists. The post-operative improvement in the electrocardiogram of some patients, particularly those, who require several months (6-9 months in some cases) to show the improvement, may be cited as evidence in favour of the occurrence of a degree of reversible parenchymatous damage to the heart. It is certainly difficult to explain the delayed improvement, in some cases, on the basis of the abolition of reflex vasoconstriction of the coronary arteries by operation.

4. Does coronary artery disease cause, or intensify gall bladder disease?

There is no evidence, at present, for believing that coronary artery disease causes gall bladder disease. It has been suggested that coronary artery disease, by enforcing a sedentary life, indirectly predisposes to biliary stasis, and the consequent formation of gall stones, but it is my impression that this factor is only of minor significance.

It must be concluded from this discussion, that an etiological relationship between gall bladder disease, and coronary artery disease had not been proved. It is possible, however, to draw certain conclusions :-

(a) Coronary artery disease and gall bladder disease co-exist frequently. The incidence of coronary artery disease, in patients with gall bladder disease, is more frequent than in a control group, and vice versa. An 'ageing process' is partly responsible for this.

(b) Myocardial insufficiency frequently occurs in gall bladder disease. The main causes of this are :-

1. Coronary artery disease.
2. Hypertension.
3. Obesity.

Gall bladder surgery not infrequently relieves the symptoms of myocardial insufficiency.

(c) Gall bladder disease, coronary artery disease, hypertension, and obesity frequently co-exist.

(d) Hypercholesterolaemia cannot be regarded as a common etiological factor in gall bladder disease and coronary artery disease. The serum cholesterol levels in gall bladder disease are within normal limits.

(e) There is no characteristic electrocardiograms in gall bladder disease.

The changes in the post-operative electrocardiogram, in gall bladder disease, can be divided into five groups, as

described above. No definite explanation for those showing improvement has been given so far. Acute coronary artery insufficiency occurs in gall bladder colic, and acute cholecystitis.

In conclusion, it is possible to suggest further investigation, or refinements of the present investigation, that could be done, in an attempt to elucidate the problem of the relationship of gall bladder disease and coronary artery disease.

These are :-

1. Pathological investigation :

   In order to find more absolute figures, than those obtained in this investigation -

   (a) The gall bladder would require to have a histological examination, in order to determine the presence, or absence of disease, i.e. microscopic rather than a macroscopic diagnosis.

   (b) Criteria for the diagnosis of early atherosclerosis must be established.

2. Clinical investigation :

   The ability to diagnose more accurately both gall bladder disease, and coronary artery disease is highly desirable, but the means, by which this can be achieved, are still obscure.

2. (contd.)

Advances in electrocardiography, and radiology might help.

3. Biochemical investigation :

More fundamental research into the biochemistry of cholesterol, and serum lipids, in general, is required. The estimation of serum lipids, in both coronary artery disease, and gall bladder disease might yield more information, than the estimation of serum cholesterol alone. Attempts to assess liver function, particularly in relation to lipid metabolism, would require more investigation.

4. Electrocardiography :

Experimental investigations, such as were carried out in two patients, mentioned in the chapter on the post-operative follow-up of gall bladder cases by electrocardiography, should be continued. Attempts should be made to try and assess, before operation, those cases, which will show improvement in the electrocardiogram following operation, and thus help in the selection of suitable cases for operation.

It may well be that future investigation will reveal that the concept of a relationship between gall bladder

disease and coronary artery disease require to be replaced by the broader conception of a relationship between 'hepatic disease' and 'heart disease'.

REFERENCE :

1. Burton, J.A.G. : Personal communication.

THE RELATIONSHIP

BETWEEN

GALL BLADDER DISEASE

AND

CORONARY ARTERY DISEASE

APPENDIX 1.

This volume contains the summaries of the case reports of patients, suffering from gall bladder disease. Those cases, which underwent operation are described first, (Case No. 1 - Case No. 67). The non-operated cases are described in (Case No. 68 - Case No. 108).

A.C., Female. Case No. 1.

Age :- 33 years. 1.10.43 - 25.4.49.

Present History : Recurring attacks of right subcostal pain with vomiting and jaundice of five years duration. No cardiovascular symptoms.

Past History : Appendicectomy in 1931.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 122/80. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder.

Operative findings : Chronic cholecystitis and gall stones. Cholecystostomy performed on 3.10.48.

Post-operative Course : Some flatulent dyspepsia. Occasional attacks of upper abdominal pain. No cardiovascular symptoms. Electrocardiogram showed no significant change.

Case No. 2.

J.C., Female.

Age :- 34 years. 21.2.49 - 12.11.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, and jaundice, of six months duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 126/80. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Non-functioning.

Biochemistry : Plasma Cholesterol = 189 mgm per 100 ml. (22.2.49).

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 23.2.49.

Post Operative Course : Flatulent dyspepsia much improved. No further attacks of right subcostal pain. No cardiovascular symptoms. Cardiovascular signs and electrocardiogram showed no significant change. On 11.4.49 Plasma Cholesterol = 191 mgm per 100 ml, on 12.7.49 = 222 mgm per 100 ml, and on 12.11.49 = 148 mgm per 100 ml.

Case No. 3.

M.K., Female.

Age :- 36 years. 31.5.49 - 2.2.50.

Present History : Flatulent dyspepsia, associated with recurring bouts of nausea, vomiting and right subcostal pain, of three years duration. Dyspnoea on exertion, headaches, and flushings of same duration.

Past History : Pregnancy terminated because of "Kidney Trouble" six years ago.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 220/120. Heart sounds of average quality. Short apical V.S. murmur.
Electrocardiogram : Antero-septal coronary artery insufficiency.

Gall Bladder : Right subcostal tenderness. Cholecystogram revealed a single calculus.

Biochemistry : Plasma Cholesterol = 334 mgm per 100 ml.
Free " = 23 per cent.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 1.6.49.

Post-Operative Course : Dyspepsia improved. Dyspnoea and headaches less severe. Electrocardiogram showed a return to normal by 31.1.50. B.P. = 220/116. On 2.2.50 Plasma Cholesterol = 286 mgm per 100 ml. (29 per cent free) on 2.2.50.

A.S., Female. Case No. 4.

Age :- 37 years. 8.3.49 - 5.4.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, nausea and vomiting of five years duration. Slight dyspnoea on exertion, and flushings of one year's duration.

Past History : Appendicectomy in 1942. Nephritis in 1942.

Family History : Negative.

General Examn. : Obese. Mucosae well coloured. Cyanosis of lips and cheeks.

Cardiovascular System : P.R. = 80 per min. B.P. = 170/104. Heart sounds pure and of good quality. Second basal sound is accentuated. Electrocardiogram : no significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 143 mgm per 100 ml.

Operative findings : Chronic cholecystitis. Cholecystostomy performed on 17.7.49.

Post-operative Course : Flatulent dyspepsia less. No further attacks of abdominal pain. No dyspnoea on exertion. Blood pressure unchanged (168/102) Electrocardiogram showed no significant alteration. On 12.7.49 Plasma cholesterol = 174 mgm per 100 ml, on 10.1.50 = 160 mgm per 100 ml.

C.S., Female. Case No. 5.

Age :- 39 years. 2.5.49 - 30.1.50.

Present History : Recurring attacks of right subcostal pain, and nausea, alternating with bouts of flatulence, during the past two years. Dyspnoea on exertion of same duration. Subject to bouts of paroxysmal tachycardia.

Past History : Femoral thrombosis with pulmonary embolism. (Post-partum) four years ago.

Family History : Negative.

General Examn. : Obese. Plethoric appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 112/70. Heart sounds of average quality. Blowing V.S. murmur at apex.
Electrocardiogram : Suggestive of myocardial insufficiency.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Single calculus present.

Operative findings : Chronic cholecystitis and gall stones. Cholecystostomy performed.

Post-operative Course : No improvement in dyspepsia. Dyspnoea on exertion and paroxysmal tachycardia were unchanged. B.P. rose to 130/90. Weight decreased by 3 stones after operation. Developed menopausal symptoms - flushings, headaches, palpitation and irregular menses.

M.C., Female. Case No. 6.

Age :- 40 years. 18.4.49 - 1.5.50.

Present History : Recurring attacks of right subcostal pain, nausea, and vomiting, of one year's duration. Dyspnoea on exertion, headaches, and occasional bouts of palpitation, of four years duration.

Past History : Gynaecological operations in 1929 and 1943.

Family History : Negative.

General Examn. : Small. Obese. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 250/120. Heart sounds of average quality. Aortic second sound accentuated.
Electrocardiogram : No significant abnormality.

Gall Bladder : Tenderness in right subcostal region.
Cholecystogram : Non-functioning organ (confirmed by repeat X-ray).

Biochemistry : Plasma cholesterol = 211 mgm per 100 ml.

Operative findings : Chronic cholecystitis and a single calculus. Cholecystostomy performed on 20.4.49.

Post-operative Course : No further attacks of upper abdominal pain. Dyspnoea on exertion and headaches more severe. Flushings very troublesome.
B.P. essentially unchanged.
Electrocardiogram : No significant change.
Plasma cholesterol = 234 mgm per 100 ml.

Case No. 7.

A.R., Female.

Age :- 40 years. 4.10.48 - 10.4.49.

Present History : Recurring attacks of upper abdominal pain, nausea, and vomiting, in the past year. Jaundice present on two occasions. Dyspnoea and praecordial pain, on exertion, of fifteen months duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Florid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 90 per min. B.P. = 110/70. Heart sounds soft. Short V.S. murmur at the base of the heart.
Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative.
Cholecystogram : Gall stones present.

Biochemistry : Plasma Cholesterol = 110 mgm per 100 ml.

Operation Notes : Chronic cholecystitis. Numerous gall stones. Cholecystostomy performed on 6.10.48.

Post-Operative Course : Developed pulmonary embolus four days after operation. Six months later still troubled with ready fatigue, dyspnoea, and

P.T.O.

Case No. 7.

Post-Operative Course (contd.) : praecordial discomfort on exertion; dyspepsia much improved. Menopausal symptoms present. On 12.4.49 Plasma Cholesterol = 182 mgm per 100 ml. For E.C.G. see Fig.

J.R., Female. Case No. 8.

Age :- 41 years. 20.11.48 - 11.7.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain and vomiting, of three months duration. No cardiovascular symptoms. Menopausal symptoms present over the past six months.

Past History : Left facial palsy in childhood, following a mastoidectomy.

Family History : Negative.

General Examn. : Stoutish build. Mucosae well coloured. Left facial palsy.

Cardiovascular System : P.R. = 80 per min. B.P. = 120/70. Heart sounds pure and of good quality. Electrocardiogram : Consistent with myocardial insufficiency.

Gall Bladder : Right subcostal tenderness. Straight X-ray of gall bladder showed gall stones.

Biochemistry : Plasma Cholesterol = 276 mgm per 100 ml.

Operative findings : Chronic cholecystitis and gall stones. Cholecystostomy performed on 22.11.48.

Post-operative Course : Flatulent dyspepsia much less severe. No further attacks of right subcostal pain. No cardiovascular symptoms. Menopausal symptoms less. Electrocardiogram normal. On 29.1.49 Plasma Cholesterol = 194 mgm per 100 ml., on 25.4.49 = 256 mgm per 100 ml., on 11.7.49 = 250 mgm per 100 ml.

Case No. 9.

M.T., Female.

Age :- 41 years. 26.1.49 - 17.1.50.

Present History : Flatulent dyspepsia, associated with attacks of epigastric pain, and vomiting, of three years duration. Jaundice present on one occasion. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 120/70. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Tender in right subcostal region. Straight X-Ray of abdomen showed gall stones to be present.

Biochemistry : Plasma Cholesterol = 191 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 29.1.49.

Post-Operative Course : No dyspepsia, provided patient adhered to her diet. No cardiovascular symptoms. Electrocardiogram showed no significant change. On 17.1.50 Plasma Cholesterol = 200 mgm per 100 ml.

J.G., Female. Case No. 10.

Age :- 43 years. 25.3.49 - 21.1.50.

Present History : Flatulent dyspepsia, associated with an aversion to greasy foods, and right subcostal discomfort of two years duration. Dyspnoea on exertion of same duration.

Past History : Jaundice in June, 1948. Appendicectomy in April, 1947. Oophorectomy in September 1939.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 126/80. Soft heart sounds. Blowing V.S. murmur at apex.

Electrocardiogram : Equivocal changes.

Gall Bladder : Clinical examination negative.

Biochemistry : Plasma Cholesterol = 191 mgm per 100 ml.

Operative Findings : Chronic cholecystitis and gall stones. Cholecystectomy performed on 30.3.40.

Post-operative Course : Three days after operation developed signs and symptoms of pulmonary embolism. Electrocardiogram seven days later showed changes consistent with pulmonary embolism. Right subcostal pain recurred. Dyspnoea on exertion remained unchanged. Plasma Cholesterol on 21.1.50 was 280 mgm per 100 ml. The electrocardiogram eventually returned to the pre-operative findings.

Case No. 11.

B.H., Female.

Age :- 43 years. 11.2.49 - 19.1.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, of three months duration. Dyspnoea on exertion and ready fatigue of six months duration.

Past History : Gynaecological operation in 1930.

Family History : Negative.

General Examn. : Slim build. Pallid skin and mucosae. (H.B. = 40 per cent, R.B.C. = 2,340,000, W.B.C. = 6,200).

Cardiovascular System : P.R. = 76 per min. B.P. = 116/80. Heart sounds of good quality. Short V.S. murmur at apex.
Electrocardiogram : Equivocal changes.

Gall Bladder : Tender in right subcostal region.
Cholecystogram : Non-functioning gall bladder.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 14.3.49.

Post-Operative Course : Flatulent dyspepsia much improved. No further attacks of right subcostal pain. Dyspnoea on exertion and ready fatigue unchanged. Blood count on 19.1.50 was H.B. = 42 per cent, R.B.C. = 2,440,000, W.B.C. = 6,000. Electrocardiogram showed no significant abnormality.

M.P., Female. Case No. 12.

Age :- 44 years. 31.10.49 - 20.5.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, nausea and vomiting of two years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Looks acutely ill. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 120/80. Heart sounds pure and of good quality. Electrocardiogram : Equivocal changes. X-ray of Chest : Inflammatory lesion at left base.

Gall Bladder : Right subcostal tenderness. Straight X-ray of abdomen showed gall stones.

Operative findings : Chronic cholecystitis and gall stones. Cholecystostomy performed on 5.11.49.

Post-operative Course : Flatulent dyspepsia and attacks of subcostal pain relieved. No significant changes in cardiovascular system. Electrocardiogram showed no essential change.

M.T., Female. Case No. 13.

Age :- 44 years. 27.8.44 - 18.12.48.

Present History : Severe pain inepigastrium and right subcostal region, associated with nausea, and vomiting, of three days duration. Dyspnoea on exertion of one year's duration.

Past History : Subject to attacks of bronchitis.

Family History : Negative.

General Examn. : Obese. Florid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 142/90. Heart sounds soft and distant. Blowing V.S. murmur at apex.
Electrocardiogram : Suggestive of anterior coronary artery insufficiency.

Gall Bladder : Tenderness and rigidity in right subcostal region.

Operative Findings : Chronic cholecystitis and gall stones. Cholecystostomy performed on 13.12.44.

Post-operative Course : General health improved but flatulent dyspepsia is still troublesome. Developed praecordial pain on exertion, bouts of paroxysmal tachycardia, and menopausal symptoms following operation. Electrocardiogram on 18.12.43 showed definite evidence of anterior coronary artery insufficiency, i.e. a deterioration from the pre-operative electrocardiogram.

A.C., Female. Case No. 14.

Age :- 45 years. 31.5.48 - 19.4.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, nausea and vomiting of four years duration. Dyspnoea and praecordial pain on exertion of the same duration.

Past History : Cardiac murmur noted in early childhood. No rheumatic history. Subject to bouts of bronchitis over many years.

Family History : Negative.

General Examn. : Small. Cyanosis of lips. Mucosae well coloured. No clubbing.

Cardiovascular System : P.R. = 88 per min. B.P. = 126/90. Heart sounds soft. Blowing V.S. murmur at base of heart.

Electrocardiogram : Coronary artery insufficiency.

X-ray of Chest : Consistent with inter-atrial septal defect.

Gall Bladder : Clinical examination negative.

Cholecystogram : Gall stones in a poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 222 mgm per 100 ml.

Operative findings : Empyema of gall bladder and gall stones. Cholecystostomy performed on 10.6.48.

Case No. 14.

Post-operative Course. (contd.) : Flatulent dyspepsia and right subcostal pain improved. Dyspnoea on exertion less severe. No significant change in the cardiovascular signs. The electrocardiogram showed improvement.

Case No. 15.

E.F., Female.

Age :- 47 years. 17.2.49 - 17.11.49.

Present History : Recurring attacks of right subcostal pain, nausea, and vomiting over the past ten years. No flatulent dyspepsia and no dyspnoea.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 160/100. Heart sounds of good quality and pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Tenderness and rigidity in right subcostal region. Cholecystogram revealed gall stones

Biochemistry : Plasma Cholesterol = 111 mgm per 100 ml. (21.2.49).

Operation Notes : Chronic cholecystitis and gall stones. Cholecystectomy performed on 23.2.49.

Post-Operative Course : No further attacks of pain. No dyspnoea on exertion. Blood pressure remained essentially unchanged, likewise electrocardiogram. On 7.3.49 Plasma Cholesterol = 125 mgm per 100 ml, on 11.7.49 = 148 mgm per 100 ml, on 19.11.49 = 118 mgm per 100 ml.

H.S., Female. Case No. 16.

Age :- 47 years. 9.1.49 - 17.1.50.

Present History : Flatulent dyspepsia, associated with recurring bouts of upper abdominal pain, and vomiting, of five years duration. Menopausal symptoms present.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 126/84. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Non-functioning gall bladder, with gall stones.

Operative Findings : Chronic cholecystitis and gall stones. Cholecystectomy performed on 14.4.49.

Post-operative Course : Flatulent dyspepsia less. Dyspnoea present before operation, disappeared after operation. Lost approximately two stones in weight. Menopausal symptoms more severe since operation (menses ceased). Blood pressure and electrocardiogram remained essentially unchanged.

Case No. 17.

E.G., Female.

Age :- 48 years. 14.7.49 - 20.7.49.

Present History : Recurring attacks of right subcostal pain, associated with jaundice, over the past two years. Dyspnoea on exertion, of many years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 128/74. Heart sounds are pure and of good quality. Electrocardiogram : Equivocal changes.

Gall Bladder : Clinical examination negative. Cholecystogram : Non-functioning gall bladder.

Operation Notes : Chronic cholecystitis with numerous gall stones. One stone in the common bile duct. Cholecystostomy performed on 18.7.49.

Post Operative Course : The patient died suddenly on 20.7.49 from a massive duodenal haemorrhage. (No post mortem examination carried out).

E.C., Female. Case No. 18.

Age :- 49 years. 2.2.49 - 19.11.49.

Present History : Flatulent dyspepsia with recurring attacks of right subcostal pain, and nausea of two years duration. Dyspnoea on exertion of six months duration.

Past History : Right subcostal pain with jaundice three years ago.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 74 per min. B.P. = 110/80. Heart sounds of good quality and pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Cystic mass palpable in right subcostal region. Cholecystogram : Non-functioning gall bladder with a single calculus.

Biochemistry : Plasma Cholesterol = 209 mgm per 100 ml.

Operative Findings : Mucocoele of gall bladder and gall stones. Cholecystostomy performed on 10.2.49.

Post-operative Course : General condition improved. Dyspepsia less but dyspnoea unchanged. Cardiovascular signs, and electrocardiogram showed no significant change. On 19.4.49 Plasma Cholesterol = 235 mgm per 100 ml.

J. McM., Female. Case No. 19.

Age :- 50 years. 14.10.45 - 15.10.48.

Present History : Recurring attacks of right subcostal pain and vomiting, of two years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Tendency to obesity. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 154/88. Heart sounds of average quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Right subcostal tenderness. Cholecystogram : Non-functioning gall bladder.

Operative Findings : Chronic cholecystitis. Empyema of gall bladder. Cholecystectomy performed on 1.11.45.

Post-operative Course : No further attacks of right subcostal pain. Menopausal symptoms troublesome. (Menses ceased after operation). Some dyspnoea on exertion. Cardiovascular signs, and electrocardiogram essentially unchanged.

Case No. 20.

J.Y., Female.

Age :- 50 years. 13.12.48 - 13.6.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of pain in the right subcostal region, nausea and vomiting, of eighteen months duration. Dyspnoea and left infra-mammory pain, on exertion, of same duration. Menopausal symptoms present.

Past History : Diabetes mellitus of two years duration; (requires 10 units P.2.1 daily).

Family History : Positive for hypertension.

General Examn. : Small. Obese. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 165/90. Heart sounds of average quality and pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning organ, containing stones.

Biochemistry : Plasma Cholesterol = 372 mgm per 100 ml. (15.12.48).

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 15.12.48.

Post-Operative Course : Flatulent dyspepsia improved. Dyspnoea on exertion more severe. Flushings troublesome.

P.T.O.

Case No. 20.

Post-Operative Course. (contd.) : Blood pressure on 13.6.49 was 160/112. Electrocardiogram showed no significant change. Plasma Cholesterol on 1.2.49 = 200 mgm per 100 ml, on 1.4.49 = 211 mgm per 100 ml, on 13.6.49 = 276 mgm per 100 ml.

Case No. 21.

M.R., Female.

Age :- 52 years. 3.1.49 - 26.7.49.

Present History : Recurring attacks of upper abdominal pain over the past twenty years. No cardio-vascular symptoms. Menopausal symptoms present.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Slightly overweight. Cyanosis of lips and cheeks.

Cardiovascular System : P.R. = 78 per min. B.P. = 178/90. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Tenderness in right subcostal region. Cholecystogram : Poorly functioning gall bladder with a single calculus.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy on 6.1.49.

Post-Operative Course : On the day following operation patient developed collapse of right lower lobe. Occasional bouts of upper abdominal pain. Complained of some dyspnoea on exertion. Blood pressure on 26.7.49 was 190/100. Electrocardiogram : Showed no significant alteration.

Case No. 22.

K.C., Female.

Age :- 53 years. 10.9.48 - 9.10.48.

Present History : Flatulent dyspepsia, associated with recurring attacks of epigastric pain, and vomiting, of five years duration. Dyspnoea and praecordial pain, on exertion, of same duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 136/90. Heart sounds soft but pure. Electrocardiogram : Consistent with a poor myocardium (suggestive of coronary artery insufficiency).

Gall Bladder : Tenderness in right subcostal region. Cholecystogram : Poorly functioning gall bladder with gall stones.

Biochemistry : Plasma Cholesterol = 236 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 15.9.48.

Post-Operative Course : The patient died on 9.10.48. Post Mortem examination revealed a suppurative peritonitis, and two chronic duodenal ulcers - recent haemorrhage from these had resulted in death. Coronary Artery disease (Atheroma) was present.

Case No. 23.

M.D., Female.

Age :- 53 years. 11.10.48 - 27.4.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of epigastric pain, nausea and vomiting, of ten months duration. No cardiovascular symptoms.

Past History : Artificial menopause in 1938.

Family History : Negative.

General Examn. : Average. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 72 per min. B.P. = 135/90. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Straight X-Ray of abdomen showed numerous calculi.

Biochemistry : Plasma Cholesterol = 235 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystitis and gall stones. Cholecystostomy performed on 13.10.48.

Post-Operative Course : Dyspeptic symptoms relieved. No cardiovascular symptoms but feels more nervous and irritable. No significant change in examination of cardiovascular system. Electrocardiogram showed no significant alteration. On 25.4.49 Plasma Cholesterol = 235 mgm per 100 ml.

Case No. 24.

I.P., Female.

Age :- 53 years. 3.3.49 - 14.4.49.

Present History : Flatulent dyspepsia, associated with attacks of right subcostal pain, nausea, and vomiting of five years duration. Dyspnoea on exertion of three years duration.

Past History : Menses ceased sixteen months ago.

Family History : Mother died from a "Heart attack" forty years ago. Father also - seventy-one years of age.

General Examn. : Obese. Healthy complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 182/102. Heart sounds of good quality and pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Tenderness and guarding in right subcostal region. Cholecystogram : Gall stones.

Biochemistry : Plasma Cholesterol = 272 mgm per 100 ml. (8.3.49).

Operation Notes : Chronic cholecystitis and gall stones. Cholecystectomy performed on

Post-Operative Course : Gained weight and dyspnoea increased in severity. After dieting weight decreased and dyspnoea lessened.

P.T.O.

Case No. 24.

Post-Operative Course (contd.) : Dyspepsia much improved. Blood pressure dropped to 118/78. Electrocardiogram showed no significant change. On 18.3.49 Plasma Cholesterol = 173 mgm per 100 ml, on 14.11.49 = 222 mgm per 100 ml.

Case No. 25.

C.B., Female.

Age :- 54 years. 10.1.49 - 11.7.49.

Present History : Flatulent dyspepsia, associated with recurring bouts of right subcostal pain, of two years duration. Dyspnoea on exertion of two years duration.

Past History : Menopause four years ago.

Family History : Negative.

General Examn. : Small. Obese. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 200/120. Heart sounds soft. Second aortic sound accentuated.

Electrocardiogram : Posterior coronary artery insufficiency.

X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Right subcostal discomfort.

Biochemistry : Plasma Cholesterol = 236 mgm per 100 ml.

Free " = 34 per cent.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 12.1.49.

Post-Operative Course : Developed post-operative phlebothrombosis. Flatulent dyspepsia disappeared. Dyspnoea decreased in severity. B.P. fell to 160/100 (11.7.49). Electrocardiogram showed a return to normal. Plasma Cholesterol (2.2.49) = 267 mgm per 100 ml; (11.7.49) = 533 mgm per 100 ml.

S.C., Female. Case No. 26.

Age :- 54 years. 1.10.49 - 3.11.50.

Present History : Flatulent dyspepsia, associated with recurring bouts of right subcostal pain, of five years duration. Dyspnoea on exertion, and ready fatigue, of the same duration approximately.

Past History : Puerperal fever.

Family History : Negative.

General Examn. : Average build. Jaundice of skin and sclerotics. Mucosae pale.
(Hb 46 = 62 per cent. R.B.C. = 4,360,000
W.B.C. = 4,200).

Cardiovascular System : P.R. = 76 per min. B.P. = 150/96.
Murmurs of mitral stenosis.

Gall Bladder : Right subcostal tenderness and guarding.
Cholecystogram : Poorly functioning gall bladder, containing numerous stones.

Biochemistry : Total plasma cholesterol = 235 mgm per cent.
Free plasma cholesterol = 70 mgm per cent.
Per cent free = 30.

Operative findings : Chronic cholecystitis, gall stones and chronic appendicitis. Cholecystectomy performed on 3.10.49.

Case No. 26.

Post-operative Course. : Dyspeptic symptoms relieved. Shortness of breath, and fatigue less severe.

On 31.11.50 Hb = 76 per cent.

R.B.C. = 4,470,000. W.B.C. = 5,600.

Heart murmurs unchanged. Electrocardiogram showed no significant alteration.

Plasma cholesterol on 10.1.50 =

258 mgm per 100 ml. Per cent free = 28.

Case No. 27.

M.S., Female.

Age :- 54 years. 7.2.49 - 7.8.49.

Present History : Flatulent dyspepsia, associated with attacks of right subcostal pain, of three years duration. Dyspnoea on exertion, and bouts of paroxysmal tachycardia, over the past three years.

Past History : Hypertension noted four years ago. Menses ceased four years ago.

Family History : Negative.

General Examn. : Small. Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 74 per min. B.P. = 178/108. Heart sounds of good quality. Blowing V.S. murmur at apex.
Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative.
Cholecystogram : Normally concentrating gall bladder with a single calculus.

Biochemistry : Plasma Cholesterol = 246 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and single calculus. Cholecystostomy performed on 8.2.49.

Post-Operative Course : General health much better. No further attacks of right subcostal pain, flatulence, nausea or vomiting.

P.T.O.

Case No. 27.

Post-Operative Course (contd.) : Dyspnoea less severe. Blood pressure on 7.8.49 was 150/90. Electrocardiogram showed no significant alteration. On 3.3.49 Plasma Cholesterol = 182 mgm per 100 ml, on 3.5.49 = 191 mgm per 100 ml, on 7.8.49 = 308 mgm per 100 ml.

Case No. 28.

A.T., Female.

Age :- 54 years. 1.10.49 - 3.10.49.

Present History	: Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, of ten years duration. No cardiovascular symptoms.
Past History	: Negative.
Family History	: Negative.
General Examn.	: Obese. Healthy appearance. Mucosae well coloured.
Cardiovascular System	: P.R. = 76 per min. B.P. = 124/84. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.
Gall Bladder	: Tenderness in right subcostal region. Cholecystogram : numerous gall stones. (Barium Meal and Test Meal normal).
Operative Finding	Chronic cholecystitis and gall stones. Cholecystectomy performed on 3.10.49.
Post-Operative Course	: Patient had severe bleeding during operation. In spite of blood transfusions she did not rally and died about seven hours after operation.

Case No. 29.

C.J., Female.

Age :- 55 years. 23.2.49 - 24.1.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, and vomiting, of one year's duration. No cardiovascular symptoms.

Past History : "Pernicious anaemia" of pregnancy twenty years ago. Menses ceased twelve years ago.

Family History : Negative.

General Examn. : Slim build. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 90 per min. B.P. = 170/96. Heart sounds of average quality and pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Non-functioning gall bladder.

Operation Notes : Empyema of gall bladder. Cholecystostomy performed on 14.3.49.

Post-Operative Course : General health improved. Flatulent dyspepsia much improved. No change in cardiovascular symptoms or signs. Electrocardiogram showed no significant alteration.

Case No. 30.

I. McC., Female.

Age :- 55 years. 12.4.48 - 2.11.48.

Present History : Flatulent dyspepsia, associated with recurring bouts of right subcostal discomfort, of six years duration. Dyspnoea on exertion of two years duration.

Past History : Menopause twelve years ago.

Family History : Negative.

General Examn. : Small. Average build. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 132/84. Heart sounds soft but pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Right subcostal tenderness and rigidity.

Biochemistry : Plasma Cholesterol = 143 mgm per 100 ml. Free " = 43 per cent.

Operation Notes : Chronic cholecystitis and pigment calculi. Cholecystostomy performed on 30.4.48.

Post-Operative Course : General condition and dyspepsia improved. Dyspnoea diminished. Electrocardiogram showed no significant change. Plasma Cholesterol (30.6.48) = 143 mgm per 100 ml.

Case No. 31.

M.R., Female.

Age :- 55 years. 1.3.48 - 12.3.48.

Present History : Flatulent dyspepsia and recurring attacks of right subcostal pain of three months duration. Dyspnoea on exertion, but no cardiac pain of effort, over the past ten years.

Past History : Subject to bronchitis over the past ten years.

Family History : Negative.

General Examn. : Small. Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 90 per min. B.P. = 130/80. Heart sounds soft but pure. Electrocardiogram : Suggestive of antero-septal coronary artery insufficiency.

Gall Bladder : Right subcostal tenderness and rigidity. Straight X-Ray of gall bladder revealed a laminated calculus.

Biochemistry : Plasma Cholesterol = 105 mgm per 100 ml.

Operation Notes : Chronic cholecystitis containing a single stone. Cholecystostomy performed on 10.3.48.

Post-Operative Course : The patient was unable to report because of dyspnoea on very slight exertion. She died two months after operation, from "Heart Disease".

M.R., Female. Case No. 32.

Age :- 56 years. 28.4.49 - 16.11.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, nausea, and vomiting of 10 years duration. Increasing dyspnoea on exertion.

Past History : Subject to attacks of bronchitis over the past 15 years.

Family History : Negative.

General Examn. : Average build. Slight cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 75 per min. B.P. = 150/195. Heart sounds soft and distant. Electrocardiogram : No significant abnormality.

Gall Bladder : Right subcostal tenderness and rigidity. Cholecystogram : Normal functioning gall bladder.

Operative Findings : Chronic cholecystitis and adhesions around gall bladder. Cholecystostomy, and division of adhesions, performed on 20.5.49.

Post-operative follow-up : Dyspeptic symptoms relieved. Dyspnoea on exertion less troublesome. Heart sounds of better quality. Blood pressure and electrocardiogram showed no significant alteration.

Case No. 33.

M.T., Female.

Age :- 56 years. 21.7.49 - 17.1.50.

Present History : Flatulent dyspepsia and abdominal distension, associated with recurring attacks of right subcostal pain, of three years duration. Dyspnoea on exertion of several years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Mucosae well coloured. Cyanosis of lips.

Cardiovascular System : P.R. = 86 per min. B.P. = 188/110. Heart sounds soft but pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 334 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 26.7.49.

Post-Operative Course : Dyspepsia much improved. Dyspnoea less severe but still present. Weight decreased by $1\frac{1}{2}$ stones in six months. B.P. unchanged. Electrocardiogram showed no significant alteration. Cholesterol on 17.1.50 was 297 mgm per 100 ml.

J.W., Female. Case No. 34.

Age :- 56 years. 7.9.48 - 7.9.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, and bilious vomiting, of three months duration. Praecordial pain on exertion of one year's duration.

Past History : Negative.

Family History : Negative.

General Examn. : Slightly overweight. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 160/106. Heart sounds are soft. Blowing V.S. murmur at apex.
Electrocardiogram : No significant abnormality.

Gall Bladder : Tender in right hypochondrium.
Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 142 mgm per 100 ml.

Operative Findings : Empyema of gall bladder. Cholecystostomy performed on 26.10.48.

Post-operative Course : Occasional attacks of upper abdominal pain and vomiting following dietary indiscretions. No cardiovascular symptoms. Cardiovascular signs and electrocardiogram essentially unchanged. On 7.7.49 Plasma Cholesterol = 334 mgm per 100 ml.

A.B., Female. Case No. 35.

Age :- 58 years. 19.5.49 - 30.1.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of upper abdominal pain, nausea, and vomiting, of thirty years duration. Jaundice present on several occasions. Slight dyspnoea on exertion of six years duration.

Past History : Menopause in 1943. Subject to bouts of paroxysmal tachycardia since.

Family History : Mother stated to have suffered from "Heart Disease".

General Examn. : Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 226/134. Heart sounds of average quality. Second basal sound accentuated.
Electrocardiogram : Equivocal changes.

Gall Bladder : Clinical examination negative.
Cholecystogram : Non-functioning gall bladder.

Operative Findings : Chronic cholecystitis. Chronic appendicitis. Cholecystectomy performed 23.5.49.

Post-operative Course : General condition improved. Flatulent dyspepsia less. Dyspnoea on exertion unchanged. No further attacks of paroxysmal tachycardia. Cardiovascular signs and electrocardiogram essentially unchanged.

Case No. 36.

E.H., Female.

Age :- 58 years. 21.1.43 - 26.4.48.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain and vomiting, of five years duration. Slight dyspnoea on exertion, of approximately same duration.

Past History : Duodenal ulcer for twenty-three years. Menses ceased in 1932.

General Examn. : Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 182/92. Heart sounds of good quality. Electrocardiogram : Equivocal changes.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder containing gall stones.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 28.9.47.

Post-Operative Course : Flatulent dyspepsia much improved. No further attacks of right subcostal pain. No cardiovascular symptoms. Cardiovascular signs and electrocardiogram essentially unchanged.

M.M., Female. Case No. 37.

Age :- 58 years. 5.3.49 - 14.11.49.

Present History : Flatulent dyspepsia, with recurring attacks of right subcostal pain, of five years duration. Jaundice present on one occasion. Dyspnoea on exertion of three years duration.

Past History : Menopause twelve years ago.

Family History : Father died from carcinoma of gall bladder.

General Examn. : Average build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 172/104. Heart sounds soft but pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Tenderness in right subcostal region.

Biochemistry : Plasma Cholesterol = 286 mgm per 100 ml.

Operative Findings : Chronic cholecystitis and gall stones. Cholecystectomy performed on 9.3.49.

Post-operative Course : General condition improved. Occasional flatulent dyspepsia and right subcostal pain. Dyspnoea persisted unchanged, likewise blood pressure; heart sounds were of better quality. Electrocardiogram showed no significant alteration.

Plasma Cholesterol, on 18.3.49 = 178 mgm per 100 ml, on 14.4.49 = 500 mgm per 100 ml.

Case No. 38.

E.D., Female.

Age :- 60 years. 2.1.49 - 8.7.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of upper abdominal pain, nausea, and vomiting of ten years duration. Dyspnoea and praecordial pain, on exertion, of same duration.

Past History : Acute cholecystitis twenty years ago.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 140/92. Soft short sounds. Short V.S. at apex. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 198 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 6.1.49.

Post-Operative Course : Occasional attacks of abdominal discomfort with nausea and vomiting. Cardiovascular symptoms, signs and electrocardiogram were essentially unchanged.

Plasma Cholesterol, on 7.3.49 = 200 mgm per 100 ml., on 8.7.49 = 308 mgm per 100 ml.

M.H., Female. Case No. 39.

Age :- 60 years. 5.1.49 - 25.7.49.

Present History : Recurring attacks of right subcostal and epigastric pain, and nausea, of nine months duration. Dyspnoea on exertion, and bouts of paroxysmal tachycardia of three years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Slimly built. Cyanosis of lips.

Cardiovascular System : P.R. = 86 per min. B.P. = 138/80. Heart sounds of average quality. Short V.S. at apex.

Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative.

Cholecystogram : Gall stones and a non-functioning gall bladder.

Biochemistry : Plasma Cholesterol = 266 mgm per 100 ml.

Operative Findings : Chronic cholecystitis and gall stones. Cholecystostomy performed on 7.1.49.

Post-operative Course : Dyspepsia persisted almost unchanged. Dyspnoea also persisted and lessened only temporarily. Electrocardiogram showed changes suggestive of a poor myocardium.

N. McG., Female. Case No. 40.

Age :- 60 years. 10.4.49 - 29.4.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, and vomiting, of many years duration. Severe attack of upper abdominal pain with vomiting on 14.9.49.

Past History : Hysterectomy in 1930.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 92 per min. B.P. = 118/80. Heart sounds soft and of poor quality. Electrocardiogram : Recent antero-septal infarction with extension into the lateral portion of apex of left ventricle.

Gall Bladder : Right subcostal tenderness and guarding.

Operative Findings : Chronic cholecystitis. Cholecystostomy performed on 19.9.49.

Post-operative Course : Apart from some praecordial discomfort the patient felt fairly well. She was unable to get out of bed, because of weakness, and when visited at her own home on 29.1.50 she had had a further severe attack of praecordial pain radiating into left arm,

Case No. 40.

Post-operative Course. (contd) : and collapse. She had been confined to bed since and had not been able to report to hospital. Post-operative electrocardiogram showed improvement.

Case No. 41.

J.R., Female.

Age :- 60 years. 29.4.49 - 18.1.50.

Present History : Attacks of right subcostal pain, nausea and vomiting, of eight years duration. Dyspnoea on exertion of seven years duration.

Past History : Appendicectomy 1941. Recurring attacks of bronchitis over many years.

Family History : Negative.

General Examn. : Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 132/84. Heart sounds of average quality. Short V.S. murmur at apex.
Electrocardiogram : No significant abnormality.

Gall Bladder : Tenderness and guarding in right subcostal region.

Operation Notes : Stone in common bile duct, chronic cholecystitis.

Post-Operative Course : Attacks of right subcostal pain have disappeared. Dyspnoea on exertion unchanged. Cardiovascular signs and E.C.G. essentially unchanged.

Case No. 42.

A.S., Female.

Age :- 61 years. 21.3.49 - 25.1.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, vomiting and jaundice over the past three years. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 174/122. Heart sounds of average quality. Split first sound at apex, accentuated second sound at base.
Electrocardiogram : Left ventricular strain.
X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Clinical examination negative. Straight X-Ray of gall bladder revealed numerous gall stones.

Biochemistry : Plasma Cholesterol = 160 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 22.3.49.

Post-Operative Notes : Flatulent dyspepsia less troublesome. Developed substernal discomfort, with excitement and exertion. On 25.1.50 B.P. = 212/130 Electrocardiogram showed more definite evidence of left ventricular strain.

E.B., Female. Case No. 43.

Age :- 65 years. 30.6.49 - 24.1.50.

Present History : Flatulent dyspepsia of five years duration. Severe right subcostal pain, nausea, and vomiting three weeks before admission. Increasing dyspnoea, on exertion, of ten years duration.

Past History : Known hypertensive of ten years duration.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 210/110. Soft heart sounds. Second aortic sound accentuated.

Electrocardiogram : Left bundle branch block.

Gall Bladder : Tenderness in right subcostal region.

Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 166 mgm per 100 ml.

Operative Findings : Empyema of gall bladder and gall stones. Cholecystostomy performed on 3.7.49.

Post-operative Course : Flatulent dyspepsia greatly improved. In November, 1949, she developed a cerebral

Case No. 43.

Post-operative Course. (contd) : haemorrhage with left hemiplegia and aphasia. When last seen on 24.1.50 she had been unable to get out of bed, was still aphasic, and had evidence of left hemiparesis. Electrocardiogram showed improvement.

Case No. 44.

J.C., Female.

Age :- 65 years.

31.5.48 - 25.4.49.

Present History : Flatulent dyspepsia, associated with bouts of nausea and vomiting, of nine months duration. Dyspnoea on exertion and ready fatigue, of same duration.

Past History : Treated for anaemia fourteen years ago.

Family History : Negative.

General Examn. : Tendency to obesity. Mucosae well coloured. Slight cyanosis of lips.

Cardiovascular System : P.R. = 76 per min. B.P. = 164/90. Heart sounds of average quality. Short apical V.S. murmur.

Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative.

Cholecystogram : Single laminated calculus.

Biochemistry : Plasma Cholesterol = 190 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and a single laminated calculus. Cholecystostomy performed on 2.6.48.

Post-Operative Course : Slight flatulent dyspepsia following operation. Cardiovascular symptoms unchanged. Blood pressure and electrocardiogram showed no significant alteration. On 25.4.49 Plasma Cholesterol = 250 mgm per 100 ml.

Case No. 45.

M.McD., Female.

Age :- 65 years. 26.5.49 - 14.1.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of upper abdominal pain, vomiting and jaundice, of five years duration. Dyspnoea on exertion of ten years duration.

Past History : Subject to attacks of bronchitis.

Family History : Son has haemolytic anaemia and gall bladder disease.

General Examn. : Average build. Pallid mucosae. Jaundice of skin and sclerotics.
(Hb = 50 per cent. RBC = 3,460,000
WBC = 8,200).

Cardiovascular System : P.R. = 88 per min. B.P. = 170/90.
Heart sounds soft. Short V.S. murmur at apex.
Electrocardiogram : No significant abnormality.

Gall Bladder : Tenderness in right subcostal region.
Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 148 mgm per 100 ml.

Operation Notes : Empyema of gall bladder with calculi.
Cholecystostomy performed on 20.7.49.

Post-Operative Course : General condition improved. Dyspepsia and dyspnoea on exertion less troublesome.
(Hb = 80 per cent RBC = 4,260,000
WBC = 7,000 14.1.50). Cardiovascular signs and E.C.G. unchanged. On 14.1.50 Plasma Cholesterol = 160 mgm per 100 ml.

A.G., Female. Case No. 46.

Age :- 67 years. 28.12.48 - 23.1.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, of five years duration. Jaundice present on one occasion. Shortness of breath and palpitation, on exertion, of five years duration.

Past History : Rheumatic fever in 1933.

Family History : Nil.

General Examn. : Small. Average build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 160/100. Heart sounds pure and of average quality. Electrocardiogram : Suggestive of early left ventricular hypertrophy.

Gall Bladder : Clinical examination negative. Straight X-ray of abdomen showed gall stones to be present.

Biochemistry : Plasma Cholesterol = 166 mgm per 100 ml.

Operative Findings : Chronic cholecystitis and gall stones. Cholecystostomy performed on 7.1.49.

Post-operative Course : Dyspepsia improved. Dyspnoea on exertion persisted and became associated with

Case No. 46.

Post-operative Course. (contd) : praecordial discomfort. The blood pressure was essentially unchanged (160/105). Electrocardiogram showed no significant change. On 22.1.50 Plasma Cholesterol = 381 mgm per 100 ml.

Case No. 47.

C.D., Female.

Age :- 70 years. 18.1.50 - 6.2.50.

Present History : Recurring attacks of epigastric pain, nausea, and vomiting over the past nine years. Jaundice has followed several of these attacks. Increasing dyspnoea on exertion of five years duration.

Past History : Chronic bronchitis of five years duration.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips. Mucosae well coloured. Obvious recent loss of weight.

Cardiovascular System : P.R. = 84 per min. B.P. = 118/70. Heart sounds 'pendulum-like'. Blowing V.S. murmur audible at the apex.
Electrocardiogram : Equivocal changes.

Gall Bladder : Right subcostal tenderness.
Cholecystogram not performed.

Biochemistry : Plasma Cholesterol = 226 mgm per 100 ml.

Operative findings. : Chronic cholecystitis. Dilated hepatic and common bile ducts. Cholecystectomy performed on 5.2.50.

Post Operative Course : Patient remained drowsy following the operation. She died on the following day 6.2.50.

P.T.O.

Case No. 47.

Post Mortem Findings : Fatty infiltration of myocardium particularly at the apex of the heart. Coronary vessels and aorta showed early atheromatous change. Otherwise heart was normal in size. Fatty infiltration of liver present.

Case No. 48.

A.F., Female.

Age :- 37 years. 9.11.43 - 18.1.50.

Present History : Recurring attacks of right subcostal pain, associated with nausea, flatulence, and vomiting, of six years duration. Dyspnoea, on exertion, of one year's duration.

Past History : Cholecystostomy in 1937. Pleurisy in 1930.

Family History : Mother died from coronary occlusion.

General Examn. : Obese. Nervous. Mucosae well coloured.

Cardiovascular System : No data available. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 200 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 21.4.43.

Post Operative Course : Still subject to attacks of right subcostal pain and vomiting. Menopausal symptoms now present. B.P. = 158/108. Heart sounds are soft but pure. Electrocardiogram shows no significant alteration. Plasma Cholesterol (on 18.1.50) = 220 mgm per 100 ml.

Case No. 49.

A.S., Female.

Age :- 38 years. 10.6.37 - 6.5.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, and vomiting, of six years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Obese. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 132/84. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder.

Operation Notes : Chronic cholecystitis. Cholecystostomy performed on 22.6.37.

Post Operative Course : Flatulent dyspepsia relieved. Developed diabetes mellitus two years ago. On 6.5.49 B.P. = 195/110. Heart sounds were of poor quality. Electrocardiogram showed changes consistent with myocardial insufficiency.

Plasma Cholesterol = 195 mgm per 100 ml.

Case No. 50.

M.O., Female.

Age :- 39 years. 3.8.39 - 25.1.50.

Present History	: Recurring attacks of right subcostal pain and vomiting of one year's duration. No cardiovascular symptoms.
Past History	: Negative.
Family History	: Negative.
General Examn.	: Obese. Healthy appearance. Mucosae well coloured.
Cardiovascular System	: No data available. Electrocardiogram : No significant abnormality.
Gall Bladder	: Right subcostal tenderness. Straight X-Ray of abdomen : Biliary calculi.
Biochemistry	: Plasma Cholesterol = 190 mgm per 100 ml.
Operation Notes	: Chronic cholecystitis with gall stones. Cholecystostomy performed on 16.8.39.
Post Operative Course	: General health good. No further attack of pain. No cardiovascular symptoms. Menses ceased five years ago. B.P. = 140/80 (on 25.1.50). Heart sounds of good quality. Electrocardiogram shows no significant abnormality. On 25.1.50 Plasma Cholesterol = 170 mgm per 100 ml.

Case No. 51.

C.M., Female.

Age :- 40 years. 1.5.37 - 4.4.49.

Present History : Recurring attacks of upper abdominal pain, flatulence, and vomiting of four weeks duration. No cardiovascular symptoms.

Past History : Right nephrectomy in 1928. Jaundice in 1902.

Family History : Negative.

General Examn. : Slim build. Sallow complexion. Mucosae well coloured.

Cardiovascular System : No data available.
Electrocardiogram : Equivocal changes.

Gall Bladder : Straight X-Ray of abdomen : Laminated calculus.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 11.5.37.

Post Operative Course : No further attacks of upper abdominal pain. Now complains of dyspnoea on exertion. Electrocardiogram on 4.4.49 showed no significant abnormality.

Case No. 52.

E.B., Female.

Age :- 41 years. 12.1.41 - 16.1.50.

Present History : Recurring bouts of nausea and vomiting of three years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : No data available.
Electrocardiogram : Lead III equivocal.

Gall Bladder : Clinical examination negative.
Cholecystogram : Non-functioning gall bladder.

Biochemistry : Plasma Cholesterol = 125 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 6.8.41.

Post Operative Course : Flatulent dyspepsia has recurred and is sometimes accompanied by upper abdominal pain. Jaundice occurred following an attack of abdominal pain three years ago. Menses ceased in January, 1949. Complains of dyspnoea on exertion, associated with a sense of constriction in her chest. B.P. = 168/92. Heart sounds average quality. Plasma Cholesterol (on 16.1.50) = 322 mgm per 100 ml. Electrocardiogram showed no significant change.

Case No. 53.

E.A., Female.

Age :- 42 years. 20.4.40 - 28.1.50.

Present History : Flatulent dyspepsia, associated with recurring bouts of upper abdominal pain, and vomiting, of four years duration. No cardiovascular symptoms.

Past History : Appendicectomy in 1923.

Family History : Father died from cerebral haemorrhage.

General Examn. : Small. Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : No data available.
Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative.
Cholecystogram : Non-functioning gall bladder

Biochemistry : Plasma Cholesterol = 266 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones.
Cholecystectomy performed on 30.4.40.

Post Operative Course : Flatulent dyspepsia still troublesome. Now complains of dyspnoea, with praecordial tightness on exertion. B.P. = 220/120. Heart sounds of good quality. Electrocardiogram showed no significant alternation. Plasma Cholesterol (on 28.1.50) = 262 mgm per 100 ml.

Case No. 54.

C.D., Female.

Age :- 45 years. 16.11.39 - 25.1.50.

Present History : Flatulent dyspepsia associated with recurring attacks of right subcostal pain and nausea of four years duration. Subject to bouts of paroxysmal tachycardia.

Past History : Menses ceased in January, 1944.
Appendicectomy in 1931.

Family History : Mother had gall bladder disease.

General Examn. : Average build. Fresh complexion. Mucosae well coloured.

Cardiovascular System : No data available.
Electrocardiogram : Left axis deviation.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Normal.
Test Meal : Normal curve.

Biochemistry : Plasma Cholesterol = 200 mgm per 100 ml.

Operation Notes : Chronic cholecystitis. Cholecystostomy performed on 21.11.39. Had a repeat cholecystostomy performed in January, 1944.

Post Operative Course : Flatulent dyspepsia is still very troublesome. Now complains of dyspnoea on slight exertion, and praecordial pain, which radiates into the left arm and is brought on by exertion.

P.T.O.

Case No. 54.

Post Operative Course (contd.) : Headaches are very troublesome. B.P. = 160/98. Plasma Cholesterol = 202 mgm per 100 ml. Electrocardiogram showed no significant change.

E.D., Female. Case No. 55.

Age :- 45 years. 22.1.38 - 17.1.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain and nausea, over the past fourteen years. No cardiovascular symptoms.

Past History : Appendicectomy in 1934.

Family History : Negative.

General Examn. : Small. Obese. Acne rosacea. Mucosae well coloured.

Cardiovascular System : Heart sounds of average quality (no further details obtainable).
Electrocardiogram : Left axis deviation.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Normal gall bladder.

Biochemistry : Plasma cholesterol = 250 mgm per 100 ml.

Operative Findings : Chronic cholecystitis. Cholecystostomy performed on 21.2.38.

Post-operative Course : Flatulent dyspepsia has been troublesome. Occasional right subcostal pain. During past three years has complained of dyspnoea on exertion and swelling of ankles. On 17.1.50 B.P. = 168/100. Electrocardiogram showed no significant alteration.
Plasma cholesterol = 258 mgm per 100 ml. (17.1.50).

Case No. 56.

J.M., Female.

Age :- 45 years. 27.4.39 - 17.1.50.

Present History : Severe epigastric pain, associated with flatulence and vomiting, nine weeks ago. Similar attack on 26.4.39. Dyspnoea on exertion of several years duration.

Past History : Erysipelas two months ago.

Family History : Negative.

General Examn. : Small. Very obese. Jaundice of skin and sclerotics.

Cardiovascular System : No data available.

Gall Bladder : Tenderness and rigidity over gall bladder. Cholecystogram : Non-functioning gall bladder.

Biochemistry : Plasma Cholesterol = 210 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy on 8.5.39.

Post Operative Course : Flatulent dyspepsia less severe. Still complains of dyspnoea on exertion, and is still very obese. B.P. = 224/142. Heart sounds of average quality. Blowing V.S. murmur at all areas. Electrocardiogram shows no significant change. Plasma Cholesterol (on 17.1.50) = 250 mgm per 100 ml.

Case No. 57.

J.M., Female.

Age :- 56 years. 1.10.42 - 8.7.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain and vomiting, of many years duration. Moderately severe dyspnoea on exertion, associated with bouts of paroxysmal tachycardia of three years duration.

Past History : Operation for gall stones in 1904.

Family History : Mother and three sisters had gall stones.

General Examn. : Obese. Florid complexion. Mucosae well coloured.

Cardiovascular System : No data available.
Electrocardiogram : Suggestive of myocardial disease.

Gall Bladder : Right subcostal tenderness. Straight X-Ray of abdomen revealed numerous biliary calculi.

Biochemistry : Plasma Cholesterol = 200 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 6.10.42.

Post Operative Course : General health improved. Flatulent dyspepsia, dyspnoea and bouts of paroxysmal tachycardia much improved.

P.T.O.

Case No. 57.

Post Operative Course (contd.) : Developed diabetes mellitus in 1949. Has lost five stones in weight in one year, (1948-49). B.P. = 180/102. Heart sounds of average quality.

Plasma Cholesterol (on 8.7.50) = 182 mgm per 100 ml.

Case No. 58.

A.M., Female.

Age :- 64 years. 4.6.37 - 26.4.48.

Present History : Recurring attacks of epigastric pain, nausea and vomiting over the past three years. Jaundice present on one occasion, during an attack. Dyspnoea on exertion of five years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : No data available.
Electrocardiogram : Left bundle branch block.

Gall Bladder : Right subcostal tenderness.
No cholecystogram done.

Operation Notes : Chronic cholecystitis. Cholecystostomy performed on 7.6.37.

Post Operative Course : Apart from an attack of severe right subcostal pain with vomiting two years ago, she has enjoyed good health. Complains of dyspnoea on exertion. B.P. = 180/90. Heart sounds of average quality. Electrocardiogram showed changes suggestive of myocardial insufficiency (no bundle branch block).

Case No. 59.

M.H., Female.

Age :- 65 years. 7.4.38 - 26.7.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of upper abdominal pain, and vomiting, of one year's duration. Praecordial tightness, on exertion, of same duration.

Past History : Hysterectomy for carcinoma of uterus in 1920.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 150/100. Heart sounds of average quality. Electrocardiogram : Lead III equivocal.

Gall Bladder : Slight right subcostal tenderness. Cholecystogram : Delayed emptying after a fatty meal.

Operation Notes : Hour-glass gall bladder with calculi. Cholecystostomy performed on 16.5.38.

Post Operative Course : Developed empyema of right chest. Now complains of dyspnoea on exertion, associated with praecordial pain. B.P. (on 26.7.49) = 190/110. Electrocardiogram showed evidence of left ventricular hypertrophy. Plasma Cholesterol (on 26.7.49) = 262 mgm per 100 ml.

Case No. 60.

R.M., Male.

Age :- 40 years. 24.5.48 - 26.8.48.

Present History : Flatulent dyspepsia, associated with recurring attacks of upper abdominal discomfort, nausea, and vomiting, of five months duration. No cardiovascular symptoms.

Past History : Subject to attacks of acute bronchitis.

Family History : Negative.

General Examn. : Small. Average build. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 122/84. Heart sounds of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder containing a single calculus.

Biochemistry : Plasma Cholesterol = 166 mgm per 100 ml.

Operation Notes : Chronic cholecystitis with a single calculus; and chronic appendicitis. Cholecystectomy and appendicectomy performed on 26.5.48.

Post Operative Course : Patient was progressing satisfactorily until 24.8.48. He was re-admitted complaining of colicky abdominal pain and vomiting.

P.T.O.

Case No. 60.

Post Operative Course : He died on the following day. Post mortem examination revealed an internal strangulated hernia due to adhesions. The coronary vessels were healthy.

C.C., Male. Case No. 61.

Age :- 42 years. 15.3.49 - 24.12.49.

Present History : Two attacks of severe epigastric pain, nausea and vomiting in the past four weeks. The first attack was associated with substernal pain, radiating into the left arm.

Past History : Appendicectomy 1937. Pleurisy 1934. Flatulent dyspepsia and increasing shortness of breath on exertion since 1941.

Family History : Negative.

General Examn. : Obese. Ruddy complexion. Dyspnoea on slight exertion.

Cardiovascular System : P.R. = 88 per min. B.P. = 140/96. Heart sounds soft but pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Right subcostal tenderness. Cholecystogram showed a poorly functioning gall bladder with numerous calculi.

Biochemistry : Plasma Cholesterol = 200 mgm per 100 ml.

Operative findings : Chronic cholecystitis and numerous gall stones. Cholecystostomy performed on 14.7.49.

Post-operative Course : Dyspepsia improved. Some dyspnoea on exertion. Cardiovascular signs and electrocardiogram unchanged.

Case No. 62.

R.G., Male.

Age :- 43 years. 1.2.49 - 1.8.49.

Present History : Flatulent dyspepsia associated with recurring attacks of right subcostal pain, nausea and vomiting, of five years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 152/114. Heart sounds pure and of average quality. Electrocardiogram : No significant abnormality

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder with stones.

Biochemistry : Plasma Cholesterol = 208 mgm per 100 ml. (1.2.49).

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 3.2.49.

Post-Operative Course : Flatulent dyspepsia improved, but now complains of recurring attacks of pain between shoulder blades. No dyspnoea. Blood pressure fell to 112/72 after operation. Electrocardiogram unchanged. On 22.3.49 Plasma Cholesterol = 210 mgm per 100 ml, on 1.8.49 = 250 mgm per 100 ml.

Case No. 63.

R.P., Male.

Age :- 47 years. 24.5.48 - 29.11.48.

Present History : Recurring bouts of right subcostal pain, and vomiting, of one year's duration. No cardiovascular symptoms.

Past History : Left orchidectomy fifteen years ago. Bilateral herniotomy twenty years ago.

Family History : Negative.

General Examn. : Small. Stout. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 158/106. Heart sounds average quality and pure. Electrocardiogram : Suggestive of posterior coronary artery insufficiency.

Gall Bladder : Clinical examination negative. Cholecystogram : Gall stones.

Biochemistry : Plasma Cholesterol = 133 mgm per 100 ml. Blood sugar curve revealed a renal glycosuria.

Operation Notes : Chronic cholecystitis. Gall stones. Cholecystostomy performed on 26.5.48.

Post Operative Course : Gall bladder symptoms disappeared. Blood pressure remained unchanged. Electrocardiogram showed improvement. Plasma Cholesterol 18.6.49 = 400 mgm per 100 ml.

Case No. 64.

R.B., Male.

Age :- 50 years. 10.11.48 - 13.12.49.

Present History : Flatulent dyspepsia, associated with right subcostal discomfort after meals, of two years duration. Recurring bouts of paroxysmal tachycardia, followed by praecordial pain, over the past six years.

Past History : Barium Meal in 1943 revealed a pre-pyloric ulcer.

Family History : Negative.

General Examn. : Small. Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 144/80. Heart sounds of good quality. Short V.S. murmur at all areas.
Electrocardiogram : No significant abnormality.

Gall Bladder : Right subcostal tenderness. Straight X-Ray of abdomen. Single gall stone calculus.

Operation Notes : Chronic cholecystitis and a single calculus. Cholecystostomy performed on 16.11.48.

Post Operative Course : Patient felt well for three months after operation. Then he had a recurrence of flatulent dyspepsia.

P.T.O.

Case No. 64.

Post Operative Course (contd.) : The bouts of paroxysmal tachycardia also recurred and he complained of headaches, giddiness and occasional 'black-outs'. There were no significant changes in blood pressure on electrocardiogram following operation.

Case No. 65.

R.L., Male.

Age :- 54 years. 5.4.48 - 21.12.48.

Present History : Flatulent dyspepsia, associated with recurring attacks of upper abdominal pain, nausea and vomiting, of ten years duration. No cardiovascular symptoms.

Past History : Appendicectomy in 1938. Duodenal ulcer since 1947.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 124/82. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder

Biochemistry : Plasma Cholesterol = 95 mgm per 100 ml.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy and gastro-enterostomy performed on 8.4.48.

Post-Operative Course : Flatulent dyspepsia improved. No further attacks of abdominal pain. No cardiovascular symptoms. Cardiovascular signs and E.C.G. are essentially unchanged. On 21.6.48 Plasma Cholesterol = 440 mgm per 100 ml.

Case No. 66.

D.B., Male.

Age :- 57 years. 13.2.50 - 13.8.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of epigastric pain and vomiting of twenty years duration. Dyspnoea and praecordial pain, on exertion, of three years duration.

Past History : Coronary occlusion in November, 1947, and February, 1949.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 120/80. Heart sounds tic-tac in quality. Electrocardiogram : Postero-lateral coronary artery insufficiency.

Gall Bladder : Clinical examination negative. Cholecystogram : Numerous gall stones.

Biochemistry : Plasma Cholesterol = 236 mgm per 100 ml.

Operation Findings : Chronic cholecystitis and gall stones. Cholecystostomy performed on 13.2.50.

Post-Operative Course : Flatulent dyspepsia improved. No change in cardiovascular symptoms, signs or electrocardiogram.

Case No. 67.

W.C., Male.

Age :- 68 years. 25.2.48 - 13.12.48.

Present History : Recurring attacks of right subcostal pain, associated with nausea and vomiting of five years duration. No cardiovascular symptoms.

Past History : Pneumonia thirty years ago.

Family History : Father died from hypertensive cerebro-vascular disease.

General Examn. : Average physique. Mucosae well coloured. Cyanosis of lips and cheeks.

Cardiovascular System : P.R. = 80 per min. B.P. = 150/90. Heart sounds soft but pure. Electrocardiogram : Left ventricular strain.

Gall Bladder : Tenderness and guarding in right subcostal region. Cholecystogram showed gall stones and a poorly functioning gall bladder.

Operation Notes : Chronic cholecystitis and gall stones. Cholecystostomy performed on 3.3.48.

Post-Operative Course : Flatulent dyspepsia and abdominal distension were troublesome after the operation. Later he developed increasing shortness of breath, cough, oedema of ankles, and hepatomegaly (congestive cardiac failure). Blood pressure was essentially unchanged. Electrocardiogram showed evidence of septal coronary artery insufficiency.

Case No. 68.

L.P., Female.

Age :- 27 years. 18.5.48 - 6.6.48.

Present History : Flatulent dyspepsia, associated with recurring attacks of pain between the scapulae, of four years duration. Slight dyspnoea on exertion of two years duration.

Past History : Pleurisy one year ago.

Family History : Positive for hypertension and "Heart Disease". An uncle had gall bladder disease.

General Examn. : Tall. Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 74 per min. B.P. = 122/76. Heart sounds of good quality. Blowing V.S. murmur audible at apex.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical examination negative.

Cholecystogram : Poorly functioning gall bladder, containing a single calculus. At operation chronic cholecystitis, and a single calculus was found.

Case No. 69.

M. McG., Female.

Age :- 32 years. 24.1.50 - 7.2.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of upper abdominal pain, and vomiting, of three years duration. No cardiovascular symptoms.

Past History : Pleurisy two years ago.

Family History : Negative.

General Examn. : Slim build. Pallid complexion. Mucosae well coloured. (Blood count normal).

Cardiovascular System : P.R. = 86 per min. B.P. = 132/80. Heart sounds of good quality and pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Normally functioning gall bladder, containing gall stones. (Confirmed at operation).

Biochemistry : Plasma Cholesterol = 148 mgm per 100 ml.

Case No. 70.

H.W., Female.

Age :- 38 years. 25.1.50 - 6.2.50.

Present History : Recurring attacks of upper abdominal pain over the past three years. No cardio-vascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Slim build. Pallid complexion. Mucosae well coloured.

P.R. = 86 per min. B.P. = 110/80.

Heart sounds pure and of good quality.

Electrocardiogram : No significant abnormality.

Gall Bladder : Tenderness in right subcostal region.

Cholecystogram : Non-functioning gall bladder.

On 3.2.50 operation confirmed a chronic cholecystitis.

Biochemistry : Plasma Cholesterol = 238 mgm per 100 ml.

Case No. 71.

A.O., Female.

Age :- 40 years. 13.1.48 - 18.1.49.

Present History : Recurring attacks of right subcostal pain, nausea and vomiting of six months duration. Some dyspnoea, on exertion, of two years duration.

Past History : Has been treated for pernivious anaemia for six years.

Family History : Negative.

General Examn. : Small. Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 132/82. Heart sounds pure and of good quality. Electrocardiogram : Equivocal changes.

Gall Bladder : Clinical examination negative. Straight X-Ray of gall bladder on 1.7.48 revealed two calculi. Repeat X-Ray on 1.10.48 showed two similar calculi but they appeared to be at lower end of common bile duct. Cholecystogram on 11.1.49 showed a non-functioning gall bladder without calculi. (The patient claims to have passed stones per rectum following a severe attack of right subcostal pain).

Biochemistry : Plasma Cholesterol = 167 mgm per 100 ml.
Free " = 25 per cent.

Case No. 72.

C.H., Female.

Age :- 41 years. 15.7.49 - 28.7.49.

Present History : Intermittent attacks of right subcostal pain in the past fourteen months. Increasing dyspnoea on exertion of the same duration. Menopausal symptoms present.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 128/84. Heart sounds of good quality. Blowing V.S. murmur at apex.
Electrocardiogram : No significant abnormality.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Normally functioning gall bladder. On 26.9.49 cholecystectomy was performed. At operation chronic cholecystitis with gall stones were present.

Biochemistry : Plasma Cholesterol = 400 mgm per 100 ml.

Case No. 73.

B.N., Female.

Age :- 42 years. 28.9.48 - 15.10.48.

Present History : Recurring attacks of right subcostal pain, nausea, vomiting, and jaundice, of two years duration. Menopausal symptoms present.

Past History : Appendicectomy in 1936.

Family History : Negative.

General Examn. : Obese. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 132/96. Heart sounds soft but pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Right subcostal tenderness. Cholecystogram showed three calculi in a non-functioning gall bladder.

Biochemistry : Plasma Cholesterol = 220 mgm per 100 ml.

Case No. 74.

M.K., Female.

Age :- 43 years. 10.12.49 - 31.12.49.

Present History : Flatulent dyspepsia, associated with recurring bouts of upper abdominal pain, nausea and vomiting of twelve years duration. Dyspnoea on exertion, praecordial discomfort, and bouts of paroxysmal tachycardia of six months duration. Menopausal symptoms present.

Past History : Negative.

Family History : Mother and father both had coronary artery disease.

General Examn. : Obese. Mucosae well coloured. Telangiectasis of feet.

Cardiovascular System : P.R. = 84 per min. B.P. = 124/70. Heart sounds of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Tenderness in right subcostal region. Cholecystogram, on two occasions, showed a non-functioning gall bladder. At operation an empyema of gall bladder was found.

Biochemistry : Plasma Cholesterol = 100 mgm per 100 ml.

Case No. 75.

M.S., Female.

Age :- 45 years. 1.2.50 - 26.3.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of upper abdominal pain, and vomiting, of four years duration. Slight dyspnoea on exertion of two years duration. Menopausal symptoms present.

Past History : Phlebitis of left leg 1946.

Family History : Negative.

General Examn. : Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 142/80. Heart sounds soft but pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Right subcostal tenderness and guarding. Cholecystogram showed a non-functioning gall bladder and ?calculus. (Operation confirmed chronic cholecystitis and gall stones).

Biochemistry : Plasma Cholesterol = 150 mgm per 100 ml.

Case No. 76.

H.W., Female.

Age :- 46 years. 8.5.50 - 20.5.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of pain between the shoulder blades, of one year's duration. Dyspnoea and praecordial tightness, on exertion, of same duration. Menopausal symptoms.

Past History : Pyelitis twenty years ago.

Family History : Negative. Post-puerperal thrombophlebitis on two occasions.

General Examn. : Stout build. Mucosae well coloured. Healthy appearance.

Cardiovascular System : P.R. = 86 per min. B.P. = 140/70. Heart sounds of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram, on two occasions, revealed a non-functioning gall bladder.

Biochemistry : Plasma Cholesterol = 192 mgm per 100 ml.

Case No. 77.

M.T., Female.

Age :- 47 years. 24.9.49 - 17.10.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, nausea and vomiting of three years duration. Dyspnoea on exertion of same duration. Menopausal symptoms present.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 74 per min. B.P. = 128/82. Heart sounds of good quality. Short V.S. murmur at apex.
Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative.
Cholecystogram : Poorly functioning gall bladder. Operation on 27.9.49 confirmed the presence of chronic cholecystitis. Chronic appendicitis was also found.

Case No. 78.

J.K., Female.

Age :- 48 years. 15.10.49 - 10.11.49.

Present History : Flatulent dyspepsia, associated with recurring bouts of right subcostal pain, and vomiting, of four years duration. Increasing shortness of breath, on exertion, of same duration.

Past History : Known hypertensive for eight years.

Family History : Mother died from cerebral haemorrhage.

General Examn. : Obese. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 220/140. Heart sounds of good quality. Second basal sound accentuated.
Electrocardiogram : Left ventricular strain.
X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Following an acute attack of right subcostal pain with vomiting, the patient was submitted to operation as a ? Empyema of gall bladder. At operation a cholesterolosis was found but the most striking feature was hepatic engorgement. Cholecystogram was normal.

Biochemistry : Plasma Cholesterol = 324 mgm per 100 ml.

Case No. 79.

I.G., Female.

Age :- 51 years. 7.8.48 - 10.8.48.

Present History : Colicky abdominal pain, with nausea and vomiting, over the past seven weeks. Increasing shortness of breath, on exertion, and swelling of the ankles, of two years duration.

Past History : Menses ceased in 1939. Severe attack of upper abdominal pain with jaundice twenty-one years ago. Flatulent dyspepsia has been troublesome since then.

Family History : Negative.

General Examn. : Very obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 186/124. Heart sounds are soft and distant. Electrocardiogram : Suggestive of posterior coronary artery insufficiency.

Gall Bladder : Tenderness and rigidity in right subcostal region. Cholecystogram revealed a non-functioning gall bladder. (Urine contained bile).

Biochemistry : Plasma Cholesterol = 89 mgm per 100 ml.
Free " = 53 per cent.

Case No. 80.

M.L., Female.

Age :- 53 years. 18.5.48 - 30.5.48.

Present History : Flatulent dyspepsia, associated with recurring bouts of right subcostal pain, nausea, and vomiting of three years duration. Praecordial pain on exertion of three years duration.

Past History : Menses ceased three years ago.

Family History : Negative.

General Examn. : Average build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 72 per min. B.P. = 192/104. Heart sounds of average quality. Second basal sound accentuated.
Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative.
Cholecystogram : Non-functioning gall bladder, containing a single calculus.

Biochemistry : Plasma Cholesterol = 108 mgm per 100 ml.
Free " = 24 per cent.

Case No. 81.

M.T., Female.

Age :- 53 years. 13.1.50 - 2.2.50.

Present History : Flatulent dyspepsia, associated with recurring attacks of upper abdominal pain, of six months duration. Slight dyspnoea on exertion of five years duration.

Past History : Menses ceased five years ago. Ten years ago had an attack of severe right subcostal pain followed by jaundice.

Family History : Negative.

General Examn. : Small. Obese. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 162/98. Heart sounds pure and of good quality. Electrocardiogram : Left ventricular hypertrophy and coronary artery insufficiency.

Gall Bladder : Right subcostal tenderness and rigidity. Cholecystogram : Biliary calculi. (Confirmed at operation).

Biochemistry : Plasma Cholesterol = 134 mgm per 100 ml.

Case No. 82.

E.A., Female.

Age :- 54 years. 30.12.47 - 10.2.48.

Present History : Flatulent dyspepsia, associated with recurring bouts of right subcostal pain, and vomiting, of five years duration. Increasing nervousness, dyspnoea on exertion, and palpitation, of three years duration.

Past History : Straight X-Ray of gall bladder four years ago revealed gall stones.

Family History : Positive for hypertension.

General Examn. : Slim build. Very nervous. Mucosae well coloured. Thyroid gland enlarged. Tremor of outstretched hands. No exophthalmos.

Cardiovascular System : P.R. = 110 per min. Auricular fibrillation present. B.P. = 170/110.
Electrocardiogram : Auricular fibrillation.
X-Ray of Chest : Generalised cardiac enlargement.

Gall Bladder : Right subcostal tenderness. Cholecystogram : Poorly functioning gall bladder with stones.

Biochemistry : Plasma Cholesterol = 114 mgm per 100 ml.
Basal Metabolic Rate = 90 per cent above standard.

Case No. 83.

J.H., Female.

Age :- 54 years. 25.6.48 - 14.9.48.

Present History : Flatulent dyspepsia, associated with attacks of right scapular pain, nausea and vomiting of ten years duration. Increasing nervousness, dyspnoea on exertion, and swelling of ankles of two years duration.

Past History : Right pleurisy in childhood.

Family History : Negative.

General Examn. : Slim build. Nervous. Enlargement of thyroid gland. Exophthalmo. Tremor of outstretched hands. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 140/70. Heart sounds soft. Short V.S. murmur at apex.

Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative.

Cholecystogram : Poorly functioning gall bladder containing numerous calculi.

Biochemistry : Plasma Cholesterol = 158 mgm per 100 ml.

Free " = 63 per cent.

Case No. 84.

J.T., Female.

Age :- 54 years. 15.12.48 - 27.12.48.

Present History : Flatulent dyspepsia, associated with recurring bouts of epigastric pain, nausea, and vomiting of three years duration. Shortness of breath on exertion of one year's duration.

Past History : Raynaud's Disease of many years duration.

Family History : Negative.

General Examn. : Small. Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 200/104. Heart sounds good quality. Short V.S. murmur at apex.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical examination negative. Straight X-Ray of gall bladder region revealed a gall bladder shadow. Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 216 mgm per 100 ml.

Free " = 34 per cent.

Case No. 85.

J.Y., Female.

Age :- 54 years. 14.4.48 - 18.7.48.

Present History : Recurrent attacks of severe epigastric pain, flatulence, nausea and vomiting of six months duration. Dyspnoea on exertion of three years duration.

Past History : Appendicectomy in 1946. Prior to operation she was subject to frequent bilious attacks. Menses ceased seven/ eight years ago.

Family History : Negative.

General Examn. : Tall. Obese. Mucous membranes are well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 166/104. Heart sounds pure and of good quality. Electrocardiogram : Left ventricular hypertrophy.

X- Ray of Chest : Slight generalised cardiac enlargement.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder (confirmed by repeat examination).

Case No. 86.

J. McK., Female.

Age :- 55 years. 10.2.48 - 3.3.48.

Present History : Flatulent dyspepsia, associated with recurring bouts of right subcostal pain, nausea, and vomiting of three years duration. Dyspnoea and substernal tightness, on exertion, of two years duration.

Past History : Appendicitis and peritonitis at eighteen years of age. Operation for severance of abdominal adhesions two years ago. At operation chronic cholecystitis, without stones, was noted.

Family History : Negative.

General Examn. : Average build. Plethoric facies. Slight oedema of feet and ankles.

Cardiovascular System : P.R. = 80 per min. B.P. = 180/110. Heart sounds pure and of average quality. Electrocardiogram : Very suggestive of posterior coronary artery insufficiency. X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder with delayed emptying after a fatty meal.

Biochemistry : Plasma Cholesterol = 267 mgm per 100 ml.
Free " = 21 per cent.

Case No. 87.

M.R., Female.

Age :- 56 years. 28.4.49 - 30.10.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, nausea and vomiting, of ten years duration. Increasing dyspnoea on exertion of five years duration.

Past History : Subject to attacks of bronchitis over the past fifteen years.

Family History : Negative.

General Examn. : Obese. Slight cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 75 per min. B.P. = 150/85. Heart sounds soft and distant. Electrocardiogram : Equivocal changes.

Gall Bladder : Right subcostal tenderness and rigidity. Cholecystogram : Normally functioning gall bladder.

Operation Findings : Chronic cholecystitis and adhesions around gall bladder. Cholecystostomy and division of adhesions performed on 20.5.49.

Case No. 88.

E.D., Female.

Age :- 57 years. 25.1.50 - 30.1.50.

Present History : Flatulent dyspepsia of many years duration. Severe epigastric pain and vomiting one week before admission. Dyspnoea on exertion, of five years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 155/100. Heart sounds of good quality and pure. Electrocardiogram : No significant abnormality. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical examination negative. Straight X-Ray of right subcostal region revealed a laminated calculus (chronic cholecystitis and gall stones found at operation).

Biochemistry : Plasma Cholesterol = 188 mgm per 100 ml.

Case No. 89.

S.D., Female.

Age :- 62 years. 9.9.48 - 19.9.48.

Present History : Recurring attacks of epigastric pain, nausea, and vomiting over the past fifteen years. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 158/98. Heart sounds of good quality. Blowing V.S. murmur at apex.
Electrocardiogram : No significant abnormality.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Poorly functioning gall bladder containing calculi.

Biochemistry : Plasma Cholesterol = 150 mgm per 100 ml.
Free " = 44.3 per cent.

Case No. 90.

A.S., Female.

Age :- 62 years. 9.6.49 - 12.7.49.

Present History : Flatulent dyspepsia, associated with intermittent fainting attacks, and giddiness, of two years duration.

Past History : Appendicectomy one year ago.

Family History : Negative.

General Examn. : Small. Obese. Sub-thyroid appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 210/118. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical examination negative. Cholecystogram : Normally functioning gall bladder containing three calculi.

Biochemistry : Plasma Cholesterol = 242 mgm per 100 ml. Free " = 25 per cent.

Case No. 91.

A.T., Female.

Age :- 62 years. 15.2.50 - 4.3.50.

Present History : Flatulent dyspepsia, associated with attacks of pain between the scapulae, of ten years duration. Left infra-mammary pain and dyspnoea, on exertion, of same duration.

Past History : Operation on right kidney in 1938 - ? Nephrectomy.

Family History : Negative.

General Examn. : Small. Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 204/110. Heart sounds soft. Blowing apical V.S. murmur. Second basal sounds accentuated. Electrocardiogram : Consistent with left ventricular hypertrophy.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder (confirmed by repeat X-Ray).

Case No. 92.

M.H., Female.

Age :- 64 years. 20.11.48 - 23.11.48.

Present History : Recurring attacks of right subcostal pain, nausea, and vomiting, of three/four years duration. Dyspnoea and substernal pain on exertion of five/six years duration.

Past History : Haematemesis one year ago.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 96 per min. B.P. = 150/110. Heart sounds of average quality. Second basal sound accentuated.
Electrocardiogram : Suggestive of left ventricular hypertrophy.

Gall Bladder : Tenderness in right subcostal region.
Cholecystogram : Non-functioning gall bladder (confirmed by repeat examination). (Urine contained urobilin).

Biochemistry : Plasma Cholesterol = 308 mgm per 100 ml.
Free " = 52 per cent.

Case No. 93.

A.W., Female.

Age :- 66 years. 28.2.49 - 7.3.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, nausea, and vomiting of five months duration. Dyspnoea and praecordial discomfort, on exertion, of three years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 66 per min. B.P. = 130/82. Heart sounds of average quality. Short V.S. murmur at apex.
Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative.
Cholecystogram : Poorly functioning gall bladder. (Confirmed by re-examination).

Biochemistry : Plasma Cholesterol = 250 mgm per 100 ml.

Case No. 94.

J.G., Female.

Age :- 68 years. 14.8.48 - 5.10.48.

Present History : Flatulent dyspepsia, associated with right subcostal discomfort, of nine years duration. Dyspnoea and substernal pain, on exertion, of approximately the same duration.

Past History : Bronchitis and asthma for forty years.

Family History : Negative.

General Examn. : Obese. Slight cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 220/110. Heart sounds of good quality. Second basal sound accentuated.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Right subcostal tenderness.

Cholecystogram : Gall stones present in a poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 124 mgm per 100 ml.

Free " = 26.5 per cent.

Case No. 95.

R.K., Female.

Age :- 69 years. 27.1.49 - 26.2.48.

Present History : Flatulent dyspepsia, associated with recurring bouts of upper abdominal pain, nausea and vomiting of four years duration. Dyspnoea and praecordial pain, on exertion, of five years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Slim build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 240/127. Heart sounds of average quality and pure. Second basal sound accentuated. Electrocardiogram : Left ventricular strain.

Gall Bladder : Slight tenderness in right subcostal region. Cholecystogram revealed a non-functioning gall bladder and a single calculus.

Case No. 96.

J.S., Female.

Age :- 69 years. 28.4.48 - 4.5.48.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, nausea, and vomiting of fifteen years duration. Dyspnoea on exertion of five years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Slight cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 145/90. Soft heart sounds. Blowing V.S. murmur at apex.

Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative.

Cholecystogram : Poorly functioning gall bladder, with a single calculus.

Biochemistry : Plasma Cholesterol = 166 mgm per 100 ml.

Free " = 24 per cent.

Other Investigations : Blood W.R. and Kahn : Positive.

Case No. 97.

L.P., Female.

Age :- 70 years. 31.12.49 - 8.2.50.

Present History : Flatulent dyspepsia, associated with upper abdominal discomfort, of six months duration. Increasing shortness of breath, on exertion, of two years duration.

Past History : Ovarian cyst removed in 1935.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 240/130. Soft heart sounds. Second basal sound accentuated.

Electrocardiogram : Equivocal changes.

Gall Bladder : Slight right subcostal tenderness.

Cholecystogram : Poorly functioning gall bladder with stones.

Biochemistry : Plasma Cholesterol = 194 mgm per 100 ml.

Case No. 98.

M.S., Female.

Age :- 74 years. 28.4.49 - 18.1.50.

Present History : Recurring attacks of central abdominal pain and vomiting of nine months duration. Dyspnoea on exertion of five years duration.

Past History : Chronic bronchitis of twenty years duration. Cerebral thrombosis.

Family History : Suggestive of hypertension.

General Examn. : Very obese. Orthopnoeic. Cyanosis of lips and cheeks.

Cardiovascular System : P.R. = 95 per min. B.P. = 170/120. Heart sounds are tic-tac in quality. Electrocardiogram : Left ventricular hypertrophy. X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Right subcostal tenderness and rigidity. Cholecystogram : Poorly functioning gall bladder with a calculus.

Biochemistry : Plasma Cholesterol = 218 mgm per 100 ml. Free " = 30 per cent.

Case No. 99.

I.C., Female.

Age :- 76 years. 20.4.48 - 2.5.48.

Present History : Flatulent dyspepsia and abdominal distension after meals, for the past ten years. Recurring bouts of nausea, and vomiting, in the past four months. Increasing dyspnoea, on exertion, over the past ten years. ? Coronary occlusion, ? gall bladder. Colic three months ago.

Past History : Recurring bronchitis for many years. An attack of right subcostal pain with jaundice five years ago.

Family History : Negative.

General Examn. : Elderly. Slim build. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 178/104. Heart sounds soft but pure. Electrocardiogram : Left axis deviation.

Gall Bladder : Eight years ago X-Ray of gall bladder region revealed calculi. Cholecystogram, on this occasion, showed the gall bladder to be non-functioning. Calculi present.

Biochemistry : Plasma Cholesterol = 143 mgm per 100 ml.
Free " = 42.6 per cent.

Case No. 100.

H. McC., Male.

Age :- 30 years. 20.10.47 - 23.1.50.

Present History : Recurring attacks of right subcostal pain, nausea, and vomiting, of three years duration. Praecordial pain on exertion, of one year's duration.

Past History : Negative.

Family History : Negative.

General Examn. : Tall. Muscular build. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 134/80. Heart sounds of good quality. Short V.S. murmur at apex.
Electrocardiogram : Equivocal changes.

Gall Bladder : Clinical examination negative.
Cholecystogram : Non-functioning gall bladder. (Confirmed by repeat examination).

Biochemistry : Plasma Cholesterol = 192 mgm per 100 ml.

Case No. 101.

D. McK., Male.

Age :- 40 years. 16.6.46 - 3.6.48.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal discomfort, and vomiting, since childhood. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Sallow complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 180/120. Heart sounds are pure and of good quality. Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical examination. Cholecystogram : Non-functioning gall bladder containing gall stones.

Biochemistry : Plasma Cholesterol = 133 mgm per 100 ml.

Free " = 14 per cent.

Case No. 102.

H.G., Male.

Age :- 52 years. 12.1.48 - 7.1.50.

Present History : Flatulent dyspepsia, associated with heart-burn, and recurring attacks of epigastric pain, readiating through between the scapulae, of many years duration. No cardiovascular symptoms.

Past History : In 1916 had severe right subcostal pain associated with jaundice. In 1946 had a perforated duodenal ulcer.

Family History : Negative.

General Examn. : Tall. Slim. Nervous. Mucous membranes well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 156/90.
Heart sounds good quality.
Electrocardiogram : Normal.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical examination negative. Straight X-Ray of abdomen revealed a single calculus. (Barium Meal revealed a scarring duodenal ulcer).

Biochemistry : Plasma Cholesterol = 204 mgm per 100 ml.

Case No. 103.

P. McP., Male.

Age :- 53 years. 1.8.47 - 2.4.48.

Present History : Flatulent dyspepsia, associated with recurring bouts of right subscapular pain, of one year's duration. Substernal pain, radiating up to the jaws, and brought on by exertion, of four years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 178/100. Heart sounds of good quality. Second basal sound accentuated.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Right subcostal fullness and tenderness.

Cholecystogram : Numerous gall stones.

Biochemistry : Plasma Cholesterol = 111 mgm per 100 ml.

Free " = 17.4 per cent.

Case No. 104.

J.A., Male.

Age :- 58 years. 10.2.48 - 7.1.50.

Present History : Flatulent dyspepsia, associated with occasional attacks of substernal pain, which radiates down the left arm, of eight years duration. Dyspnoea on exertion for many years duration.

Past History : Pneumonia sixteen years ago.

Family History : Negative.

General Examn. : Tall. Sallow complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 160/104.
Heart sounds soft and distant.
Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : No local tenderness.
Cholecystogram : Poorly functioning gall bladder, containing a single calculus. (Confirmed by a repeat examination).

Biochemistry : Plasma Cholesterol = 267 mgm per 100 ml.
Free " = 22 per cent.

Case No. 105.

H.C., Male.

Age :- 60 years. 7.12.49 - 19.12.49.

Present History : Flatulent dyspepsia, associated with aversion to greasy foods, of two years duration. Recurring attacks of praecordial tightness, radiating into the left arm, unrelated to exertion, or meals, over the same period of time.

Past History : Negative.

Family History : A brother of patient died from coronary occlusion.

General Examn. : Small. Average build. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 116/80. Heart sounds soft but pure. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder containing a single calculus.

Biochemistry : Plasma Cholesterol = 284 mgm per 100 ml.

Case No. 106.

W. McK., Male.

Age :- 61 years. 19.11.48 - 3.3.49.

Present History : Flatulent dyspepsia, associated with recurring bouts of vomiting, and giddiness, of two years duration. No cardiovascular symptoms.

Past History : Renal colic in 1935.

Family History : Negative.

General Examn. : Small. Slim build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 130/80. Heart sounds pure and of average quality. Electrocardiogram : No significant abnormality. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical examination negative. Cholecystogram : Non-functioning gall bladder. (confirmed by re-examination).

Biochemistry : Plasma Cholesterol on 16.12.48 = 210 mgm per 100 ml. On 4.3.49 = 167 mgm per 100 ml.

Case No. 107.

J.H., Male.

Age :- 64 years. 3.10.49 - 10.1.50.

Present History : Pain in right iliac fossa, with jaundice, six weeks before admission. Similar attack, but without jaundice, twelve hours before admission.

Past History : Known hypertensive for eight years.

Family History : Negative.

General Examn. : Tall. Obese. Cyanosis of lips. Jaundice of skin and sclerotics.

Cardiovascular System : P.R. = 90 per min. B.P. = 180/110. Heart sounds soft but pure. Electrocardiogram (4.10.49) : Anterior coronary artery insufficiency.

Gall Bladder : Tenderness and rigidity in right subcostal region. Cholecystogram showed a non-functioning gall bladder containing one calculus.

Progress : Six days after admission electrocardiogram returned to normal. Two weeks after admission, developed severe praecordial pain, with dyspnoea, lasting two days. Electrocardiogram showed antero-lateral coronary artery insufficiency. On 10.1.50 E.C.G. showed similar, but less severe changes, of antero-lateral coronary artery insufficiency.

Plasma Cholesterol = 168 mgm per 100 ml.

Case No. 108.

J. McD., Male.

Age :- 65 years. 4.11.48 - 14.11.48.

Present History : Intermittent attacks of upper abdominal pain, nausea, and vomiting over the past 25 years. No cardiovascular symptoms.

Past History : Chronic bronchitis for fifteen years.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 72 per min. B.P. = 126/68. Heart sounds soft but pure. Electrocardiogram : Posterior coronary artery insufficiency. X-Ray of Chest : Calcification of the aorta.

Gall Bladder : Clinical examination negative. Cholecystogram : Poorly functioning gall bladder containing a calculus.

Biochemistry : Plasma Cholesterol = 250 mgm per 100 ml. Free " = 13 per cent.

THE RELATIONSHIP

BETWEEN

GALL BLADDER DISEASE

AND

CORONARY ARTERY DISEASE

APPENDIX 2.

This volume contains the summaries of the case reports of patients suffering from coronary artery disease, (Case No. 109 - Case No. 208). The "equivocal cases" are summarised in (Case No. 209 - Case No. 250).

Case No. 109.

A.G., Female.

Age :- 39 years. 12.9.49 - 20.9.49.

Present History : Praecordial pain and dyspnoea, on exertion, of two years duration. No flatulent dyspepsia.

Past History : Scarlet fever at sixteen years of age.

Family History : Negative.

General Examn. : Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 210/140. Heart sounds of average quality. Second basal sound accentuated. Electrocardiogram : Coronary artery insufficiency and left ventricular hypertrophy.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 240 mgm per 100 ml.
Free " = 28 per cent.

M.K., Female. Case No. 110.

Age :- 40 years. 30.9.49 - 12.10.49.

Present History : Praecordial pain, of sudden onset, associated with flatulence six weeks ago. Cardiac pain of effort since. Menopausal symptoms present.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Florid complexion. Mucosae well coloured.

Cardiovascular System : B.P. = 136/90. Heart sounds are soft in quality.

Electrocardiogram : Suggestive of widespread coronary artery insufficiency.

X-ray of chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Test meal : Achlorhydria.

Biochemistry : Plasma cholesterol = 222 mgm per 100 ml.

Free cholesterol = 33 per cent.

Case No. 111.

J.A., Female.

Age :- 42 years. 12.9.49 - 16.9.49.

Present History : Substernal pain, radiating into both arms, on exertion, and accompanied by dyspnoea and flatulent dyspepsia, of six months duration.

Past History : Appendicectomy in 1927. Menses ceased in 1947.

Family History : Negative.

General Examn. : Stout. Florid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 196/116. Heart sounds of good quality. Second basal sound accentuated.

Electrocardiogram : Posterior coronary artery insufficiency.

X-Ray of Chest : Slight cardiac enlargement with prominence of left ventricle.

Gall Bladder : Some epigastric tenderness.

Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 208 mgm per 100 ml.

Free " = 27 per cent.

Case No. 112.

J.H., Female.

Age :- 42 years. 8.1.48 - 27.5.48.

Present History : Praecordial pain on exertion, associated with flatulent dyspepsia, of three months duration. Severe praecordial pain, of sudden onset, and associated with collapse, dyspnoea, and vomiting, three days ago.

Past History : Negative.

Family History : Negative.

General Examn. : Tall. Average build. Mucosae well coloured.

Cardiovascular System : P.R. = 72 per min. B.P. = 120/80.
Heart sounds 'pendulum-like'.
Electrocardiogram : Posterior coronary artery insufficiency (consistent with healing myocardial infarct).
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 117 mgm per 100 ml.
Free " = 23.9 per cent.

Case No. 113.

M.T., Female.

Age :- 42 years. 1.3.50 - 7.3.50.

Present History : Flatulent dyspepsia, associated with pain over the lower praecordium, of one year's duration. Bout of paroxysmal tachycardia one week ago.

Past History : Appendicectomy in 1946.

Family History : Negative.

General Examn. : Average height. Obese. Nervous. Mucous membranes well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 162/108. Heart sounds pure and of good quality. Electrocardiogram : Antero-septal coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination normal.

Biochemistry : Plasma Cholesterol = 306 mgm per 100 ml.

Case No. 114.

J.G., Female.

Age :- 43 years. 24.2.48 - 10.3.48.

Present History : Severe praecordial pain, radiating into both arms, five weeks ago. Similar attack four weeks ago. Duration of each attack was fifteen minutes. Cardiac pain of effort since first attack.

Past History : Similar attack of chest pain, as the above, but less severe, three years ago.

Family History : Father had coronary occlusion.

General Examn. : Tall. Florid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 142/110. Heart sounds of good quality. Second aortic sound is accentuated.

Electrocardiogram : Consistent with antero-septal infarction.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 200 mgm per 100 ml.

Free " = 28 per cent.

Case No. 115.

A.L., Female.

Age :- 46 years. 6.4.48 - 15.4.48.

Present History : Substernal pain, associated with collapse and dyspnoea, of sudden onset whilst at rest, and of twelve hours duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Slight cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 122/82. Heart sounds soft. Blowing V.S. audible all over the praecordium.

Electrocardiogram : Consistent with postero-lateral myocardial infarction.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Case No. 116.

M.M., Female.

Age :- 48 years. 19.10.49 - 24.10.49.

Present History : Substernal pain, on exertion, of several months duration. Recurring attacks of epigastric discomfort, and flatulent dyspepsia, of several years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 174/110. Heart sounds pure. Second basal sound accentuated.

Electrocardiogram : Suggestive of posterior coronary artery insufficiency.

X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Right subcostal tenderness.

Cholecystogram : Poorly functioning gall bladder.

Case No. 117.

A.M., Female.

Age :- 48 years. 22.3.50 - 30.3.50.

Present History : Upper abdominal pain, associated with nausea and vomiting, of two days duration. Flatulent dyspepsia, and dyspnoea on exertion, of several years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Pallid complexion. Cyanosis of lips. Mucous membranes well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 142/80. Heart sounds soft but pure.

Electrocardiogram : Lateral myocardial infarction.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 260 mgm per 100 ml.

Case No. 118.

A.T., Female.

Age :- 49 years. 16.2.48 - 9.9.48.

Present History : Severe praecordial pain, collapse and dyspnoea on 28.12.47. Pain in left shoulder on exertion since that time.

Past History : Sciatica in left leg of eleven years duration. Fracture of left clavicle in September, 1947.

Family History : Negative.

General Examn. : Slim. Wiry build. Flushed countenance. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 142/90. Heart sounds pure and of good quality. Electrocardiogram : Consistent with antero-lateral myocardial infarction.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 143 mgm per 100 ml.
Free " = 59 per cent.

Case No. 119.

M.B., Female.

Age :- 50 years. 10.11.48 - 13.11.48.

Present History : Flatulent dyspepsia associated with recurring bouts of vomiting and upper abdominal pain of twelve months duration. Substernal pain on exertion of same duration.

Past History : Phlebitis of left leg seven years ago.

Family History : Negative.

General Examn. : Tall. Slim build. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 160/90. Heart sounds of average quality and pure. Electrocardiogram : Consistent with antero-septal coronary artery insufficiency. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 250 mgm per 100 ml.
Free " = 14 per cent.

M.T., Female. Case No. 120.

Age :- 52 years. 26.4.48 - 6.5.48.

Present History : Increasing tiredness, listlessness, dyspnoea, associated with fainting attacks, over the past six months. No flatulent dyspepsia.

Past History : Menses ceased in 1945.

Family History : Negative.

General Examn. : Small. Sout. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 225/120.
Heart sounds of good quality.
Electrocardiogram : Posterior coronary artery insufficiency.
X-ray of chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

A.S., Female. Case No. 121.

Age :- 53 years. 21.7.49 - 7.8.49.

Present History : Recurring bouts of vague abdominal pain over the past twenty years. Praecordial discomfort on exertion of six years duration.

Past History : Appendicectomy twenty-four years ago. Barium meal, on three occasions, over the past twenty years, has been negative. Renal calculus twenty-eight years ago.

Family History : Patient's mother had gall stones.

General Examn. : Healthy appearance. Average nutrition. Mucosae well coloured.

Cardiovascular System : P.R. = 72 per min. B.P. = 130/74. Heart sounds are of average quality. Electrocardiogram : Suggestive of antero-lateral coronary artery insufficiency.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma cholesterol = 222 mgm per 100 ml. Free cholesterol = 25.8 per cent.

Other Investigations : Barium meal and enema negative.

Case No. 122.

C.A., Female.

Age :- 54 years. 28.4.48 - 4.5.48.

Present History : Praecordial pain on exertion, associated with slight flatulent dyspepsia of three years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 184/116. Heart sounds of average quality. Second basal sound accentuated.

Electrocardiogram : Antero-septal coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 138 mgm per 100 ml.

Free " = 30.4 per cent.

J.B., Female. Case No. 123.

Age :- 54 years. 16.8.49 - 21.8.49.

Present History : Substernal pain, on exertion, associated with increasing listlessness, and breathlessness, of fifteen months duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 140/80. Heart sounds soft and pure. Triple rhythm audible at the apex.

Electrocardiogram : Posterior coronary artery insufficiency.

X-ray of chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

Case No. 124.

R.F., Female.

Age :- 54 years. 15.2.50 - 21.2.50.

Present History : Dyspnoea on exertion, associated with substernal discomfort radiating into the left arm, of one year's duration.

Past History : Three attacks of haematemesis and melaena in the past eighteen years.

Family History : Negative.

General Examn. : Small. Average build. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 165/105. Heart sounds pure and of good quality. Electrocardiogram : Antero-lateral coronary artery insufficiency.

Gall Bladder : Epigastric and right subcostal tenderness. Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 202 mgm per 100 ml.

Case No. 125.

A.R., Female.

Age :- 54 years. 12.2.48 - 24.3.48.

Present History : Praecordial pain, radiating into both arms, and brought on by exertion, excitement or meals, of one year's duration. Flatulent dyspepsia of several years duration.

Past History : In January, 1941, collapsed with severe praecordial pain. Had a similar attack in February, 1941.

Family History : Negative.

General Examn. : Average build. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 180/102. Heart sounds are of average quality. Long blowing murmur at apex.

Electrocardiogram : Consistent with previous antero-septal infarction. Left ventricular hypertrophy.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 266 mgm per 100 ml.

J.R., Female. Case No. 126.

Age :- 56 years. 26.3.49 - 3.4.49.

Present History : Praecordial tightness, on exertion, of one year's duration, associated with flatulent dyspepsia and occasional attacks of right subcostal pain.

Past History : Negative.

Family History : Suggestive of coronary artery disease.

General Examn. : Stocky build. Sallow complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 236/124. Heart sounds average quality. Second basal sound accentuated.
Electrocardiogram : Suggestive of anterior coronary artery insufficiency.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Normal.

Biochemistry : Plasma cholesterol = 358 mgm per 100 ml.
Free cholesterol = 36 per cent.

Case No. 127.

Mrs. W., Female.

Age :- 56 years. 6.12.49 - 16.12.49.

Present History : Severe praecordial pain and tightness, of sudden onset, six months ago. Duration of the attack twelve hours. Recurring flatulent dyspepsia, associated with heart-burn and abdominal distension, of fifteen years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Heavy build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 165/98. Heart sounds are 'pendulum-like'. Electrocardiogram : Antero-septal coronary artery insufficiency. X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Right subcostal tenderness. Cholecystogram : Poorly functioning gall bladder containing numerous stones.

Biochemistry : Plasma Cholesterol = 286 mgm per 100 ml.

H. McE., Female. Case No. 128.

Age :- 57 years. 10.12.48 - 17.12.48.

Present History : Praecordial pain, radiating down the left arm and induced by exertion, of two years duration. Flatulent dyspepsia and increasing dyspnoea, on exertion, of one year's duration.

Past History : Menses ceased three years ago. Appendicectomy in 1910.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips. Mucous membranes well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 122/78. Heart sounds are soft but pure.
Electrocardiogram : Suggestive of coronary artery insufficiency.
X-ray of chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Case No. 129.

M.M., Female.

Age :- 57 years. 10.5.49 - 27.5.49.

Present History : Increasing shortness of breath, and praecordial discomfort on exertion, of three years duration. Flatulent dyspepsia, associated with recurring bouts of right subcostal pain and vomiting, over the past fifteen years.

Past History : Since 1944 has been given "Liver Injections" for anaemia.

Family History : Negative.

General Examn. : Obese. Mucosae well coloured. Oedema of feet and ankles.

Cardiovascular System : P.R. = 82 per min. B.P. = 178/110. Heart sounds of average quality. Rough V.S. murmur at apex.
Electrocardiogram : Left ventricular hypertrophy and coronary artery insufficiency (Antero-septal).

Gall Bladder : Clinical examination negative.
Cholecystogram : Poorly functioning gall bladder containing gall stones.

Case No. 130.

E.H., Female.

Age :- 58 years. 24.2.50 - 2.3.50.

Present History : Left infra-mammary pain, associated with dyspnoea and praecordial tightness, of sudden onset, eight days before admission.

Past History : Thyrotoxicosis since 1910. Operation for papillomata of bladder in 1949.

Family History : Negative.

General Examn. : Elderly. Nervous. Dyspnoeic at rest. Cyanosis of lips. Exophthalmos present. Enlargement of thyroid gland.

Cardiovascular System : P.R. = 100 per min. B.P. = 100/60. Heart sounds tic-tac in quality.

Gall Bladder : Clinical examination negative.

Post Mortem Diagnosis : Recent myocardial infarction. Coronary atheroma. Gall Bladder normal.

Case No. 131.

Mrs. McA., Female.

Age :- 58 years. 19.10.49 - 21.10.49.

Present History : Praecordial pain, radiating into the left arm on exertion, of eighteen months duration. Sudden substernal pain, whilst at rest, associated with collapse and dyspnoea two months ago.

Past History : Flatulent dyspepsia of many years duration.

Family History : Negative.

General Examn. : Average build. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 132/90. Heart sounds soft. Short V.S. murmur at mitral area.

Electrocardiogram : Lateral coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Tenderness in right subcostal region.

Cholecystogram : Showed a non-functioning gall bladder with calculi.

Biochemistry : Plasma Cholesterol = 374 mgm per 100 ml.

Free " = 31 per cent.

Case No. 132.

J.M., Female.

Age :- 59 years. 16.4.48 - 26.4.48.

Present History : Praecordial pain, associated with a choking sensation and dyspnoea, while at rest, five weeks ago. Praecordial pain on exertion, with flatulent dyspepsia, since that date.

Past History : In October, 1947, had a similar but more severe attack, diagnosed as coronary occlusion (no electrocardiogram).

Family History : Negative.

General Examn. : Small. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 152/90.
Heart sounds soft and toneless.
Electrocardiogram : Consistent with previous posterior infarct.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 160 mgm per 100 ml.
Free " = 19.1 per cent.

Case No. 133.

M.B., Female.

Age :- 60 years. 18.3.48 - 5.4.48.

Present History : Increasing dyspnoea on exertion, nervousness and palpitation of three years duration.

Past History : Menses ceased in 1927.

Family History : Negative.

General Examn. : Slim build. Nervous. Mucosae well coloured.

Cardiovascular System : P.R. = 72 per min. B.P. = 165/100.
Heart sounds of average intensity.
Electrocardiogram : Antero-lateral coronary artery insufficiency.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 133 mgm per 100 ml.
(Basal Metabolic Rate = plus 41 per cent.).

Case No. 134.

A. O'M., Female.

Age :- 60 years.

27.7.49 - 29.7.49.

Present History : Cardiac pain of effort of two years duration. Recurring bouts of right subcostal pain, nausea and vomiting of same duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips. Slight oedema of ankles.

Cardiovascular System : P.R. = 78 per min. B.P. = 164/85.
Heart sounds soft but pure.
Electrocardiogram : Equivocal changes.
X-Ray of Chest : Shows cardiac enlargement.

Gall Bladder : No right subcostal tenderness.
Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 246 mgm per 100 ml.
Free " = 24 per cent.

Case No. 135.

M.B., Female.

Age :- 61 years. 10.2.50 - 19.2.50.

Present History : Substernal pain radiating into the left arm, on exertion, of one year's duration. Severe substernal pain with vomiting ten weeks ago. Duration twenty-four hours.

Past History : Flatulent dyspepsia with upper abdominal distension and pain, of five years duration. Right mastectomy twenty-one years ago.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 180/90. Heart sounds 'pendulum-like' but pure. Electrocardiogram : Anterior coronary artery insufficiency. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness. Cholecystogram : Normal. Calcified cyst of liver noted. (Barium Meal : Negative).

Case No. 136.

A. McA., Female.

Age :- 61 years. 26.12.47 - 12.2.48.

Present History : Praecordial pain, radiating up into the neck, on exertion, of three years duration. Severe praecordial pain, associated with collapse, dyspnoea and vomiting of sudden onset on 26.12.47.

Past History : Flatulent dyspepsia of many years duration.

Family History : Mother died from coronary artery disease.

General Examn. : Small. Obese. Florid complexion.

System Heart sounds are of average quality and pure.

Electrocardiogram : Consistent with posterior myocardial infarction.

X-Ray of Chest : Enlarged left ventricle.

Gall Bladder : Clinical and radiological examination negative.

Case No. 137.

M.P., Female.

Age :- 61 years. 3.6.49 - 14.7.49.

Present History : Praecordial tightness, on exertion, of two weeks duration. Gripping pain across upper chest, associated with a feeling of weight in the arms, ten days ago.

Past History : Flatulent dyspepsia for many years.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 136/98. Accentuated first heart sound at the apex. Second sound almost inaudible.
Electrocardiogram : Antero-lateral coronary artery insufficiency.
X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Non-functioning gall bladder, with translucent calculi.

Biochemistry : Plasma Cholesterol = 308 mgm per 100 ml.
Free " = 28 per cent (on 7.6.49).
Plasma " = 222 mgm per 100 ml.
Free " = 33 per cent (on 2.7.49).

Case No. 138.

E.G., Female.

Age :- 62 years. 16.1.50 - 20.1.50.

Present History : Praecordial discomfort, associated with dyspnoea on exertion, of ten months duration. Intermittent attacks of epigastric pain and flatulent dyspepsia of several years duration.

Past History : Known to have hypertension for many years.

Family History : Negative.

General Examn. : Small. Obese. Cyanosis of lips and cheeks. Mucous membranes well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 190/102. Soft heart sounds. Soft systolic murmur audible all over the praecordium.

Electrocardiogram : Suggestive of posterior coronary artery insufficiency.

X-Ray of Chest : Generalised cardiac enlargement.

Gall Bladder : Right subcostal tenderness.

Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 222 mgm per 100 ml.

Case No. 139.

A. McC., Female.

Age :- 62 years. 29.6.49 - 12.8.49.

Present History : Praecordial pain, of a cramping character, brought on by exertion, and accompanied by severe flatulent dyspepsia, of five years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Florid complexion. Mucosae well coloured.

Cardiovascular System : B.P. = 132/98. Heart sounds are of average quality. Second basal sound accentuated.

Electrocardiogram : Antero-lateral coronary artery insufficiency.

X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 267 mgm per 100 ml.

Free " = 21.9 per cent.

Case No. 140.

A. McG., Female.

Age :- 63 years. 31.12.48 - 21.4.49.

Present History : Dyspnoea on exertion, associated with a sensation of choking, of four months duration. Praecordial pain, at rest, radiating into the left arm, one day before admission to hospital. Flatulent dyspepsia of ten years duration.

Past History : Nephrectomy (right) at thirty years of age.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips and cheeks. Mucous membranes are well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 120/80. Heart sounds of average quality and pure. Electrocardiogram : Antero-lateral coronary artery insufficiency.

X-Ray of Chest : Tortuous calcified aorta.

Gall Bladder : No right subcostal tenderness or rigidity. Straight X-Ray of gall bladder : single gall bladder calculus.

Biochemistry : Plasma Cholesterol = 174 mgm per 100 ml.

Case No. 141.

J.S., Female.

Age :- 63 years. 27.7.48 - 13.8.48.

Present History : Right subcostal pain, on exertion, of one year's duration. Severe epigastric pain, radiating up into both arms, seven weeks ago. Flatulent dyspepsia for many years.

Past History : Typhoid fever in 1916. Epistaxis, due to hypertension, in 1947.

Family History : Negative.

General Examn. : Elderly woman. Obese. Sallow complexion. Mucous membranes well coloured.

Cardiovascular System : P.R. = 72 per min. B.P. = 150/90. (During an attack of praecordial pain, blood pressure has been recorded as high as 220/140).
Heart sounds are soft and distant.
Electrocardiogram : Antero-septal coronary artery insufficiency.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 150 mgm per 100 ml.

Case No, 142.

A. McI., Female.

Age :- 65 years.

3.6.49 - 11.8.49.
28.7.49 - 16.8.49.

Present History : Substernal pain on exertion, of six months duration. Crushing substernal pain, collapse and vomiting, on 3.6.49.

Past History : Rheumatic fever in 1910. Pleurisy in 1935. and 1942. Herpes Zoster in 1943.

Family History : Negative.

General Examn. : Small, slim build. Dyspnoeic at rest. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 120/84. Loud first apical sound and split second sound, followed by a rumbling diastolic murmur.

Electrocardiogram : Anterior coronary artery insufficiency.

Gall Bladder : Slight right subcostal tenderness. Cholecystogram normal.

Biochemistry : Plasma Cholesterol = 342 mgm per 100 ml.

Case No. 143.

M. McR., Female.

Age :- 65 years. 3.7.49 - 18.7.49.

Present History : Severe substernal pain on exertion of three weeks duration. Severe substernal pain, radiating into the left arm, three days before admission.

Past History : Attack of substernal pain, dyspnoea and collapse three years ago. (Two months in bed).

Family History : Negative.

General Examn. : Average build. Orthopnoeic. Pale mucous membranes. Oedema of legs and lumbo-sacral region. (Hb = 60 per cent : RBC = 2,360,000 : WBC = 4,200).

Cardiovascular System : P.R. = 92 per min. B.P. = 100/72. Heart sounds are soft but pure.
Electrocardiogram : Posterior myocardial infarction.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical examination negative.

Biochemistry : Plasma Cholesterol = 222 mgm per 100 ml.

Post Mortem Diagnosis : Posterior myocardial infarct. Chronic interstitial nephritis. Gall bladder normal.

Case No. 144.

M.F., Female.

Age :- 66 years. 16.11.48 - 22.12.48.

Present History : Praecordial pain, radiating in to the left arm, brought on by exertion, and associated with slight flatulent dyspepsia. Duration two years.

Past History : Typhoid fever in 1893. Rheumatic fever in 1902. Puerperal fever in 1908. Appendicectomy in 1937. Mastoidectomy in 1934. Right mastectomy in 1938.

Family History : Father died from coronary artery disease.

General Examn. : Elderly. Obese. Pasty complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 140/80. Soft heart sounds. Short V.S. murmur at apex.

Electrocardiogram : Antero-lateral coronary artery insufficiency.

X-Ray of Chest : Calcification of the aortic arch.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 222 mgm per cent.

Free " = 52 per cent.

Case No. 145.

J.W., Female.

Age :- 66 years. 26.1.49 - 29.1.49.

Present History : Sudden epigastric pain associated with dyspnoea and vomiting three weeks ago. Flatulent dyspepsia of many years duration.

Past History : Known hypertensive since March, 1948.

Family History : Negative.

General Examn. : Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 220/110. Heart sounds soft. Blowing V.S. murmur at base of heart.
Electrocardiogram : Posterior coronary artery insufficiency.

Gall Bladder : Tenderness in right subcostal region.
Chole cystogram : Calculus present in gall bladder.

Case No. 146.

R.T., Female.

Age :- 68 years. 30.4.48 - 26.5.48.

Present History : Dyspnoea on exertion, associated with substernal discomfort, of five years duration. Recurring attacks of right subcostal pain and vomiting in the past two years.

Past History : History suggestive of coronary occlusion, five months ago.

Family History : Negative.

General Examn. : Average build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 170/104. Soft heart sounds. Short V.S. murmur at the apex.

Electrocardiogram : Left ventricular hypertrophy and coronary artery insufficiency.

Gall Bladder : Clinical examination negative.

Cholecystogram : Primary gall bladder shadow; poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 166 mgm per 100 ml.

Free " = 30 per cent.

Case No. 147.

E.D., Female.

Age :- 71 years. 13.10.49 - 3.11.49.

Present History : Flatulent dyspepsia associated with pain between scapulae and nausea of four years duration. Dyspnoea on exertion associated with substernal pain of same duration.

Past History : Negative.

Family History : Mother died from "Heart attack", aged 65 years.

General Examn. : Average nutrition. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 142/60. Heart sounds soft. Electrocardiogram : Coronary artery insufficiency.

Gall Bladder : Normal at operation. (Chronic appendicitis present).

Biochemistry : Plasma Cholesterol = 254 mgm per 100 ml. Free " = 23 per cent.

Case No. 148.

J.F., Female.

Age :- 76 years. 14.4.49 - 21.4.49.

Present History : Severe praecordial and substernal pain, whilst hurrying, six weeks ago. Duration thirty minutes. Similar attack two weeks later.

Past History : Gastric ulcer in 1896. Bronchial asthma since 1909. Recurring attacks of diarrhoea with blood in stools since 1909. Pneumonia on two occasions. Frequent attacks of bronchitis.

Family History : Suggestive of coronary artery disease.

General Examn. : Elderly woman. Average build. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 150/80. Heart sounds soft and pure.

Electrocardiogram : Antero-lateral coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 138 mgm per 100 ml.

Free " = 68 per cent.

R.R., Male. Case No. 149.

Age :- 36 years. 30.6.48 - 15.7.48.

Present History : Recurring attacks of praecordial pain, brought on by exertion, and associated with dyspnoea and severe flatulent dyspepsia, of two years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Powerful build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 130/80. Heart sounds are of good quality. Electrocardiogram : Anterior coronary artery insufficiency. X-ray of chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma cholesterol = 154 mgm per 100 ml. Free cholesterol = 20 per cent.

J.A., Male. Case No. 150.

Age :- 38 years. 24.2.48 - 6.3.48.

Present History : Recurring headaches and giddiness associated with praecordial discomfort on exertion of two years duration. No flatulent dyspepsia.

Past History : Negative.

Family History : Father died suddenly from "Heart trouble".

General Examn. : Tall. Powerful build. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 194/140.
Heart sounds are soft.
Electrocardiogram : Suggestive of antero-lateral coronary artery insufficiency.
X-ray of chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma cholesterol = 363 mgm per 100 ml.

Case No. 151.

G.C., Male.

Age :- 39 years. 3.1.48 - 23.2.48.

Present History : Dull heavy pain on left side of chest, lasting continuously for three days, four months ago. Flatulent dyspepsia of four months duration.

Past History : Bouts of dizziness two years ago.

Family History : Negative.

General Examn. : Tall. Good physique. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 130/90. Heart sounds are soft but pure.

Electrocardiogram : Suggestive of postero lateral coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 95 mgm per 100 ml.

G.B., Male. Case No. 152.

Age :- 42 years. 10.3.50 - 11.5.50.

Present History : Substernal pain, of sudden onset, associated with collapse and vomiting, of six hours duration.
No history of flatulent dyspepsia.

Past History : Intermittent claudication, since 1949.

Family History : Negative.

General Examn. : Average build. Slight cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 100/85.
Triple thythm audible at apex.
X-ray of chest : Normal cardiac outline.
Electrocardiogram : Antero-lateral myocardial infarction.

Gall Bladder : Clinical and radiological examination negative.

Case No. 153.

A.D., Male.

Age :- 42 years. 16.4.48 - 18.4.48.

Present History : Right subcostal pain, radiating to right shoulder and arm, of three weeks duration. It is brought on by exertion, relieved by rest, and is accompanied by flatulence.

Past History : Pneumonia and pleurisy in 1933. Scarlet fever with nephritis in 1923.

Family History : Negative.

General Examn. : Small. Obese. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 152/102. Heart sounds are soft but pure. Electrocardiogram : Posterior coronary artery insufficiency. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 200 mgm per cent. Free " = 32 per cent.

D.H., Male. Case No. 154.

Age :- 42 years. 20.10.48 - 17.1.49.

Present History : Severe upper abdominal pain, radiating up over the praecordium, associated with dyspnoea and vomiting in September, 1948.

Past History : Negative.

Family History : Negative.

General Examn. : Slim. Wiry build. Grey haired. Slight cyanosis of lips and cheeks.

Cardiovascular System : P.R. = 78 per min. B.P. = 126/80.
Heart sounds of average quality but pure.
Electrocardiogram : Posterior coronary artery insufficiency.
X-ray of chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma cholesterol = 211 mgm per 100 ml.
Free cholesterol = 35 per cent.

Case No. 155.

T.W., Male.

Age :- 43 years. 12.2.48 - 1.3.48.

Present History : Severe praecordial pain with collapse in May, 1946. Had similar attack in January, 1947.

Past History : Flatulent dyspepsia of eight years duration.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 170/100. Heart sounds pure and of average quality. Electrocardiogram : Consistent with left ventricular hypertrophy and previous antero-septal infarction.

X-Ray of Chest : Slight prominence of left ventricle.

Gall Bladder : Right subcostal tenderness. Radiologically there was delayed emptying after a fatty meal.

Biochemistry : Plasma Cholesterol = 340 mgm per 100 ml.

Free " = 23 per cent.

Case No. 156.

H.C., Male.

Age :- 44 years. 29.3.50 - 18.7.49.

Present History : Severe upper abdominal pain, spreading up over the praecordium, nine weeks ago. Duration three hours. No flatulent dyspepsia.

Past History : Mucous colitis of ten years duration.

Family History : Negative.

General Examn. : Average build. Nervous. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 156/110. Heart sounds soft but pure.

Electrocardiogram : Consistent with antero lateral myocardial infarction.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 160 mgm per 100 ml.

Case No. 157.

J.E., Male.

Age :- 44 years. 10.2.48 - 26.2.48.

Present History : Severe gripping praecordial pain of sudden onset whilst walking three months ago. It was associated with dyspnoea and nausea. (Duration one hour). Cardiac pain of effort since then.

Past History : 1946 - X-Ray of gall bladder (because of flatulent dyspepsia) normal.

Family History : Negative.

General Examn. : Tall. Healthy appearance. Mucous membranes well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 150/100. Heart sounds are pure and of good quality. Electrocardiogram : Consistent with a healing antero-lateral infarction. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 322 mgm per 100 ml.
Free " = 16 per cent.

Case No. 158.

G.F., Male.

Age :- 44 years. 14.4.48 - 20.4.48.

Present History : Praecordial pain, following meals and on exertion of six months duration. Flatulent dyspepsia, associated with occasional right subcostal discomfort, of three years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Slight cyanosis of lips and ears. Mucosae well coloured.

Cardiovascular System : P.R. = 74 per min. B.P. = 128/84. Heart sounds pure and of good quality. Electrocardiogram : Very suggestive of coronary artery insufficiency.

Gall Bladder : Clinical and radiological examination negative.

Test Meal : Normal.

Biochemistry : Plasma Cholesterol = 166 mgm per 100 ml.

Free " = 33.1 per cent.

Case No. 159.

C.W., Male.

Age :- 44 years. 11.12.48 - 13.1.49.

Present History : Recurring attacks of praecordial pain associated with collapse, of three years duration.

Past History : Amoebic dysentery in 1928.

Family History : Mother died from heart trouble, aged 72 years.

General Examn. : Stocky build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 146/84. Heart sounds are pure and of good quality. Electrocardiogram : Posterior coronary artery insufficiency. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness. Cholecystogram : Normal. Test Meal : Hyperchlorhydria. (Barium Meal : Normal).

Biochemistry : Plasma Cholesterol = 160 mgm per 100 ml. Free " = 21 per cent.

Case No. 160.

J.A., Male.

Age :- 45 years. 1.2.50 - 5.2.50.

Present History : Substernal pain, dyspnoea, and collapse of sudden onset, four weeks ago.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Plethoric appearance. Slight cyanosis of lips and cheeks.

Cardiovascular System : P.R. = 78 per min. B.P. = 210/140. Heart sounds of good quality. Second aortic sound accentuated.
Electrocardiogram : Suggestive of left ventricular hypertrophy and lateral coronary insufficiency.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 240 mgm per 100 ml.

J.C., Male. Case No. 161.

Age :- 45 years. 12.7.51 - 22.7.51.

Present History : Sudden constricting pain, across front of chest, radiating into both arms, of 36 hours duration. No history of flatulent dyspepsia.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Cyanosis of lips and cheeks. Jaundice of sclerotics. Oedema of ankles.

Cardiovascular System : P.R. = 92 per min. B.P. = 96/76. Cardiac dullness increased to the left. Heart sounds tic-tac in quality. Electrocardiogram : Posterior myocardial infarction.

Gall Bladder : Clinical examination obscured by presence of hepatomegaly (due to congestive cardiac failure).

Post Mortem : Infarct of posterior wall of left ventricle. Gall bladder normal.

W.D., Male. Case No. 162.

Age :- 45 years. 3.5.48 - 18.5.48.

Present History : Lack of energy and recurring bouts of breathlessness of three months duration. No flatulent dyspepsia.

Past History : ? Acute nephritis in 1943.

Family History : Negative.

General Examn. : Well nourished. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 182/118. Heart sounds of good quality. Electrocardiogram : Anterior coronary artery insufficiency. X-ray of chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination normal.

Biochemistry : Plasma cholesterol = 182 mgm per 100 ml. Free cholesterol = 19.8 per cent.

Case No. 163.

A.G., Male.

Age :- 45 years. 12.10.49 - 16.10.49.

Present History : Severe praecordial pain, of sudden onset, ten weeks ago. Pain in left shoulder, on exertion, since that date.

Past History : Pneumonia in 1931.

Family History : A brother died suddenly ten weeks ago from "Heart Disease". History of "Heart Trouble" in family.

General Examn. : Small. Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 182/80. Loud first sound at apex. Blowing V.S. murmur at apex.

Electrocardiogram : Anterior coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination normal.

Biochemistry : Plasma Cholesterol = 216 mgm per 100 ml.

A.P., Male. Case No. 164.

Age :- 45 years. 29.12.45 - 5.3.48.

Present History : Recurring attacks of epigastric pain, spreading up into the chest and down both arms of three-four years duration. Each attack lasts about 20 minutes, and is brought on by exertion. Slight flatulent dyspepsia.

Past History : Negative.

Family History : Negative.

General Examn. : Tall. Greyish-cyanotic complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 160/100. Heart sounds are soft but pure. Electrocardiogram : Antero-lateral coronary artery insufficiency. X-ray of chest : Normal cardiac outline.

Gall Bladder : Clinical examination negative. Cholecystogram : Non-functioning gall bladder and a single gall stone.

Biochemistry : Plasma cholesterol = 200 mgm per 100 ml. Free cholesterol = 60 per cent.

Case No. 165.

J.C., Male.

Age :- 46 years. 30.11.49 - 9.12.49.

Present History : Cardiac pain of effort of nine weeks duration. Severe substernal pain lasting several days six weeks ago. Epigastric pain, heartburn and flatulent dyspepsia of several years duration.

Past History : Pneumonia and pleurisy in 1929.

Family History : Negative.

General Examn. : Small. Average build. Pallid complexion but mucosae well coloured. Cyanosis of lips and cheeks.

Cardiovascular System : P.R. = 84 per min. B.P. = 130/70. Heart sounds are tic-tac in quality. Soft systolic murmur at all areas.

Electrocardiogram : Posterior coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination normal. (Barium meal : Duodenal ulcer).

Biochemistry : Plasma Cholesterol = 174 mgm per 100 ml.

Case No. 166.

J.F., Male.

Age :- 46 years. 24.1.48 - 1.5.48.

Present History : Pain in left forearm on exertion of eighteen months duration. Severe praecordial pain, whilst walking, on 19.1.48 and again four days later. Duration five minutes.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Obese. Cyanosis of lips and cheeks Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 120/82. Heart sounds soft but pure.

Electrocardiogram : Consistent with postero-lateral myocardial infarction.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 211 mgm per 100 ml.

Free " = 12 per cent.

Case No. 167.

G.C., Male.

Age :- 47 years. 30.11.49 - 2.12.49.

Present History : Severe substernal pain, radiating into the left arm, of sudden onset three weeks ago. Cardiac pain of effort since.

Past History : Negative.

Family History : Negative.

General Examn. : Tendency to obesity. Colour good. Mucosae well coloured.

Cardiovascular System : P.R. = 72 per min. B.P. = 126/90. Heart sounds are soft. Short, soft apical systolic murmur.

Electrocardiogram : Lateral coronary artery insufficiency.

X-Ray of Chest : Normal cardiac contour.

Gall Bladder : Clinical examination negative. Cholecystogram revealed a poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 250 mgm per 100 ml.

Free " = 22 per cent.

Case No. 168.

J.T., Male.

Age :- 47 years. 25.1.50 - 28.1.50.

Present History : Dyspnoea on exertion, associated with gripping praecordial pain which radiates into the left arm, and flatulent dyspepsia of two years duration.

Past History : Left pleural effusion in childhood.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured. No cyanosis or oedema.

Cardiovascular System : P.R. = 86 per min. B.P. = 140/90. Heart sounds are pure and of good quality. Electrocardiogram : Suggestive of coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 302 mgm per 100 ml.

Case No. 169.

D.C., Male.

Age :- 49 years. 6.2.50 - 10.2.50.

Present History : Praecordial pain, radiating into the left axilla, and brought on by exertion, of five years duration. Flatulent dyspepsia of three years duration.

Past History : Scarlet fever in childhood.

Family History : Negative.

General Examn. : Average build. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 136/100. Heart sounds are pure and of good quality. Electrocardiogram : Lateral coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 229 mgm per 100 ml.

Free " = 41 per cent.

Case No. 170.

N.C., Male.

Age :- 49 years. 8.10.48 - 26.11.48.

Present History : Left scapular pain on exertion of five months duration. Stabbing pain in epigastrium, radiating to the right shoulder, of sudden onset six days before admission.

Past History : In 1942 collapsed at work with severe epigastric pain. In 1937 right mastoidectomy.

Family History : Negative.

General Examn. : Average build. Slight cyanosis of lips and cheeks. Right facial paresis

Cardiovascular System : P.R. = 80 per min. B.P. = 120/84. Heart sounds are soft. Pericardial friction audible for almost four weeks.

Electrocardiogram : Anterior myocardial infarction.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 143 mgm per 100 ml.

Case No.171.

T.C., Male.

Age :- 49 years. 13.2.48 - 17.2.48.

Present History : Praecordial pain on exertion, associated with increasing shortness of breath on exertion, palpitation, and flatulent dyspepsia, of two years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average physique. Florid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 160/90. Heart sounds are soft but pure. Electrocardiogram : Consistent with antero-septal infarction. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination (twice) negative.

Case No. 172.

A.D., Male.

Age :- 49 years. 9.1.50 - 13.4.50.

Present History : Severe substernal tightness, associated with pain in both forearms on 6.10.49. Collapse, with vomiting, on 7.10.49. No flatulent dyspepsia.

Past History : Negative.

Family History : Negative.

General Examn. : Tall. Powerful build. Nervous. Mucosae well coloured.

Cardiovascular System : P.R. = 90 per min. B.P. = 128/84. Heart sounds pure but tic-tac in quality. Electrocardiogram : Consistent with antero-lateral myocardial infarction. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 200 mgm per 100 ml.

Case No. 173.

A.F., Male.

Age :- 49 years. 21.9.49 - 30.9.49.

Present History : Praecordial tightness, on exertion, of two years duration. Severe praecordial pain, associated with loss of consciousness, lasting ten minutes, fourteen weeks ago.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips. Mucosae well coloured. Readily made dyspnoeic.

Cardiovascular System : P.R. = 84 per min. B.P. = 120/100. Heart sounds soft; gallop rhythm audible at apex.

Electrocardiogram : Antero-lateral coronary artery insufficiency.

X-Ray of Chest : Generalised cardiac enlargement.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 248 mgm per 100 ml.

Free " = 31 per cent.

Case No. 174.

A.G., Male.

Age :- 49 years. 3.3.50 - 6.3.50.

Present History : Intermittent attacks of substernal pain, not specially related to exertion or meals, associated with severe flatulent dyspepsia, of two years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Greyish cyanotic complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 140/100. Heart sounds are soft and toneless. Electrocardiogram : Suggestive of postero-lateral coronary artery insufficiency. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 360 mgm per 100 ml.

Case No. 175.

A.T., Male.

Age :- 49 years. 16.2.48 - 6.9.48.

Present History : Severe substernal pain, of sudden onset, and of twelve hours duration, two months ago. Pain in left shoulder on exertion of one month's duration.

Past History : Flatulent dyspepsia with heartburn of many years duration.

Family History : Negative.

General Examn. : Slim, wiry build. Grey haired. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 142/90. Heart sounds pure and of good quality. Electrocardiogram : Consistent with previous antero-septal infarction, with extension into the lateral wall of left ventricle. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Case No. 176.

H.W., Male.

Age :- 49 years. 24.2.48 - 29.2.48.

Present History : Severe praecordial pain brought on by exertion seven weeks ago. Praecordial pain and tightness, of less severity, since that date.

Past History : Pneumonia 1942.

Family History : Negative.

General Examn. : Average height and build. Fresh complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 142/80. Heart sounds of average quality. Short blowing apical systolic murmur.
Electrocardiogram : Consistent with antero-septal coronary artery insufficiency.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 143 mgm per 100 ml.
Free " = 42 per cent.

A.F., Male. Case No. 177.

Age :- 50 years. 15.11.49 - 26.11.49.

Present History : Recurring attacks of praecordial pain especially when fatigued, associated with flatulent dyspepsia of six months duration.

Past History : Negative.

Family History : Negative.

General Examn. : Tall. Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 160/100. Heart sounds soft and toneless.

Electrocardiogram : Very suggestive of anterior coronary artery insufficiency.

X-ray of chest : Showed a normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma cholesterol = 250 mgm per 100 ml.

Free cholesterol = 33 per cent.

Case No. 178.

W.M., Male.

Age :- 50 years. 9.3.48 - 21.3.48.

Present History : Praecordial discomfort on exertion, associated with dyspnoea and slight flatulent dyspepsia of one year's duration.

Past History : Negative.

Family History : Positive for hypertension.

General Examn. : Tall. Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 190/140. Heart sounds soft and toneless. Second basal sound accentuated.

Electrocardiogram : Anterior coronary artery insufficiency.

X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 154 mgm per 100 ml.

Free " = 47.7. per cent.

Case No. 179.

A. McW., Male.

Age :- 50 years. 12.1.49 - 19.1.49.

Present History : Epigastric pain on exertion, associated with slight flatulent dyspepsia, of one year's duration.

Past History : Appendicectomy in 1948 because of long standing dyspepsia, characterised mainly by heartburn after meals; no flatulence.

Family History : Negative.

General Examn. : Wiry build. Greyish complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 160/98. Soft heart sounds. Long blowing systolic murmur at apex.

Electrocardiogram : Posterior coronary artery insufficiency.

X-Ray of Chest : Generalised cardiac enlargement, but particularly left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

Test Meal : Achlorhydria.

Biochemistry : Plasma Cholesterol = 191 mgm per 100 ml.

Free " = 40 per cent.

Case No. 180.

E.M., Male.

Age :- 51 years. 7.12.49 - 12.12.49.

Present History : Nausea and vomiting followed by praecordial pain, passing into the left arm, five weeks ago. Cardiac pain of effort since. Slight flatulent dyspepsia.

Past History : ? Gastric ulcer in 1939.

Family History : Negative.

General Examn. : Small. Slim build. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 132/80. Soft heart sounds. Short blowing V.S. at apex.

Electrocardiogram : Posterior myocardial infarction.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination normal.

Biochemistry : Plasma Cholesterol = 312 mgm per 100 ml.

Case No. 181.

J.A., Male.

Age :- 52 years. 16.12.50 - 20.12.50.

Present History : Severe substernal pain, associated with a feeling of faintness and vomiting, of three hours duration on 16.10.50. No flatulent dyspepsia.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 134/72. Heart sounds of average quality. Short V.S. murmur at apex. Electrocardiogram : Consistent with posterior myocardial infarction. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 150 mgm per 100 ml.

M.B., Male. Case No. 182.

Age :- 52 years. 7.1.48 - 29.9.48.

Present History : Had typical coronary occlusion (with electrocardiographic evidence) on 6.3.46, and again on 30.9.47.

Past History : Severe bout of vomiting in May, 1947, associated with upper abdominal pain.
Cholecystogram : poorly functioning gall bladder.
Barium meal : negative.

Family History : Negative.

General Examn. : Slightly obese. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 124/80.
Heart sounds of average quality and pure.
Electrocardiogram : Consistent with previous antero-lateral myocardial infarction.
X-ray of chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness and guarding.
Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma cholesterol = 275 mgm per 100 ml.

D.D., Male. Case No. 183.

Age :- 52 years. 20.1.50 - 27.3.50.

Present History : Severe pain across the upper back, associated with dyspnoea, of sudden onset, four months ago. (Duration of pain two hours). Dyspnoea has persisted and oedema of ankles has appeared in past two weeks. No flatulent dyspepsia.

Past History : Bilateral pneumonia in 1940.

Family History : Negative.

General Examn. : Acutely ill. Orthopnoeic. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 100/60. Heart sounds of poor quality.

Electrocardiogram : Antero-posterior coronary artery insufficiency.

X-ray of chest : generalised cardiac enlargement.

Gall Bladder : Clinical examination negative.

Biochemistry : Plasma cholesterol (on successive days) = 246 mgm per 100 ml, 276 mgm per 100 ml, 286 mgm per 100 ml.

Post Mortem Examination : Atheroma of coronary vessels. Recent myocardial infarct. Gall bladder normal.

Case No. 184.

W. McD., Male.

Age :- 52 years. 9.3.50 - 15.3.50.

Present History : Substernal pain on exertion, associated with flatulent dyspepsia of three years duration.

Past History : Cystoscopic examination in 1926 - ? Bladder stone.

Family History : Negative.

General Examn. : Stocky build. Florid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 150/82. Heart sounds are 'pendulum-like'. Electrocardiogram : Equivocal change. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 152 mgm per 100 ml.

Case No. 185.

D. McI., Male.

Age :- 52 years. 10.9.48 - 7.10.48.

Present History : Praecordial pain, radiating into the left arm, and brought on by exertion, of six months duration. Severe flatulent dyspepsia of one year's duration.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Slim build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 162/94. Heart sounds of good quality. Short V.S. murmur at apex.

Electrocardiogram : Equivocal changes.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 268 mgm per 100 ml.

Free " = 50 per cent.

Case No. 186.

P.S., Male.

Age :- 52 years. 29.1.48 - 10.2.48.

Present History : Praecordial pain on exertion of seven months duration. Severe flatulent dyspepsia of many years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Tall. Powerful build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 168/92. Heart sounds are pure and of average quality. Electrocardiogram : Lateral coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 180 mgm per 100 ml.

Free " = 25 per cent.

Case No. 187.

G.F., Male.

Age :- 53 years.

6.2.48 - 9.4.48.

Present History : Sudden praecordial pain, associated with collapse, dyspnoea and nausea five weeks ago. Duration of pain was 12 hours.

Past History : Flatulent dyspepsia associated with right subcostal discomfort intermittently over the past 20 years.

Family History : Negative.

General Examn. : Average build. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 116/70. Heart sounds are soft and pure.
Electrocardiogram : Consistent with healing antero-septal infarction.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical examination negative.
Cholecystogram : Delayed emptying of gall bladder after a fatty meal.

Biochemistry : Plasma Cholesterol = 140 mgm per 100 ml.
Free " = 22 per cent.

Case No. 188.

W.F., Male.

Age :- 54 years.

27.2.48 - 10.3.48.

Present History : Sudden praecordial pain, associated with a feeling of weakness, one year ago. Substernal pain on exertion, together with severe flatulent dyspepsia since. Praecordial pain and vomiting of sudden onset three months ago. (Duration seven hours).

Past History : Found to have hypertension in 1937. Barium meal in 1939 - Negative.

Family History : Negative.

General Examn. : Small. Slim build. Grey cyanotic complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 135/92. Soft heart sounds. Short, blowing, apical, systolic murmur.

Electrocardiogram : Antero-lateral coronary artery insufficiency.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 160 mgm per 100 ml.

Free " = 59 per cent.

Case No. 189.

J. McQ., Male.

Age :- 54 years. 27.9.49 - 26.1.50.

Present History : Praecordial pain of sudden onset, associated with nausea, vomiting and flatulence, ten days ago.

Past History : ? Coronary occlusion in 1940. Gastro-enterostomy in 1947. Occasional praecordial pain on exertion during the past nine years.

Family History : Negative.

General Examn. : Slim build with evidence of recent loss of weight. Mucosae well coloured. Early clubbing of fingers.

Cardiovascular System : P.R. = 80 per min. B.P. = 140/85.
Heart sounds are soft but pure.
Electrocardiogram : Anterior coronary artery insufficiency.
X-Ray of Chest : Slight prominence of left ventricle.

Gall Bladder : Clinical and radiological examination normal.
(Barium Meal : Duodenal ulcer).

Biochemistry : Plasma Cholesterol = 222 mgm per 100 ml.

Case No. 190.

T. McG., Male.

Age :- 55 years. 11.1.50 - 30.1.50.

Present History : Substernal pain on exertion, of three months duration. Severe, gripping praecordial pain, radiating down both arms, of twelve hours duration, two months ago. Slight flatulent dyspepsia.

Past History : Quinsy throat in 1922 and 1937.

Family History : Negative.

General Examn. : Average build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 136/80. Heart sounds pure and of average quality. Electrocardiogram : Antero-lateral coronary artery insufficiency. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 286 mgm per 100 ml. Free " = 14 per cent.

J.B., Male. Case No. 191.

Age :- 56 years. 28.4.51 - 18.6.51.

Present History : Severe praecordial pain, radiating into both arms, one week prior to admission to hospital. Duration of pain was five minutes. Flatulent dyspepsia, associated with upper abdominal discomfort, and aversion to greasy foods, of many years duration.

Past History : Intermittent claudication of legs, of three years duration.
Appendicectomy in 1935.

Family History : Negative.

General Examn. : Average build. Plethoric facies. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 115/80.
Cardiac dullness increased to left.
Soft heart sounds. Split first sound at apex.
Electrocardiogram : Antero-lateral myocardial infarction.

Gall Bladder : Tenderness in right subcostal region.
Cholecystogram : Poorly functioning gall bladder with calculi.

Biochemistry : Fasting blood sugar = 190 mg per cent.

Case No. 192.

D.H., Male.

Age :- 56 years.

28.1.48 - 26.2.48.

Present History : Increasing shortness of breath on exertion over the past two-three years. Praecordial tightness on exertion of five weeks duration.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 178/100. Loud first apical sound. Second basal sound is accentuated. A blowing V.S. murmur audible at the base.

Electrocardiogram : Left bundle branch block.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 185 mgm per 100 ml.

Free " = 31 per cent.

Case No. 193.

J.C., Male.

Age :- 57 years. 17.10.49 - 28.11.49.

Present History : Increasing dyspnoea on exertion, associated with ready fatigue, and praecordial discomfort, on exertion, of two years duration.

Past History : Appendix abscess in September, 1948. Gall stones noted during operation.

Family History : Negative.

General Examn. : Obese. Slight cyanosis of lips and cheeks. Mucous membranes well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 140/80. Soft heart sounds. Blowing apical systolic murmur.

Electrocardiogram : Suggestive of lateral coronary artery insufficiency.

X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Right subcostal tenderness.

Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 204 mgm per 100 ml.

Case No. 194.

J.F., Male.

Age :- 57 years. 16.11.49 - 20.11.49.

Present History : Praecordial tightness on exertion of one year's duration. Praecordial pain, radiating to both shoulders, of several hours duration, six weeks beforehand. Flatulent dyspepsia of several years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Average build. Healthy appearance. Mucosae well coloured. No cyanosis of oedema.

Cardiovascular System : P.R. = 86 per min. B.P. = 120/70. Soft heart sounds. Blowing apical systolic murmur.

Electrocardiogram : Equivocal changes.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical examination negative. Equivocal radiological changes.

Biochemistry : Plasma Cholesterol = 191 mgm per 100 ml.

Free " = 21 per cent.

Case No. 195.

A.H., Male.

Age :- 57 years.

22.8.49 - 7.12.49.

Present History : Pain in epigastrium and lower praecordium, associated with nausea, of sudden onset three weeks ago. Cardiac pain of effort since.

Past History : Typhoid fever in 1929.

Family History : Negative.

General Examn. : Average height and build. Mucosae well coloured. No cyanosis.

Cardiovascular System : P.R. = 78 per min. B.P. = 130/80. Heart sounds are tic-tac in quality.

Electrocardiogram : Anterior coronary artery insufficiency.

X-Ray of Chest : Cardiac outline normal.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 224 mgm per 100 ml.

Case No. 196.

J. McM., Male.

Age :- 57 years. 18.3.49 - 30.4.49.

Present History : Substernal pain, radiating up into neck and both arms, associated with collapse, and dyspnoea, one week ago.

Past History : Dyspnoea on exertion, associated with occasional "black-outs", of ten years duration.

Family History : Suggestive of hypertension and cardiovascular disease.

General Examn. : Obese. Florid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 108/70.
Cardiac sounds are soft but pure.
Electrocardiogram (serial) : Anterior myocardial infarction.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 334 mgm per 100 ml.
Free " = 32 per cent.

Case No. 197.

A.B., Male.

Age :- 58 years. 9.6.49 - 14.7.49.

Present History : Frequent attacks of substernal pain, brought on by exertion, of one year's duration.
Flatulent dyspepsia of two years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Mucosae well coloured. Cyanosis of lips.

Cardiovascular System : P.R. = 74 per min. B.P. = 140/80.
Heart sounds are soft but pure.
Electrocardiogram : Posterior coronary artery insufficiency.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 242 mgm per 100 ml.
Free " = 38 per cent.

J.D., Male. Case No. 198.

Age :- 58 years. 13.4.51 - 6.6.51.

Present History : Pain along the lateral aspect of left arm, and between the scapulae, of sudden onset, associated with collapse and vomiting, on 13.4.51. Duration two hours. No history of flatulent dyspepsia.

Past History : Pleurisy and pneumonia in 1944. Erysipelas in 1938.

Family History : Negative.

General Examn. : Average build. Dyspnoeic at rest. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 106 per min. B.P. = 165/85. Heart sounds of tic-tac quality. Electrocardiogram : Antero-septal myocardial infarction.

Gall Bladder : Clinical and radiological examination negative.

J.G., Male. Case No. 199.

Age :- 58 years. 20.7.51 - 20.7.51.

Present History : Severe, gripping, substernal pain, radiating down both arms, of sudden onset, associated with collapse and vomiting. Duration of pain four hours. Flatulent dyspepsia of three years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Pallid complextion. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 110/70. Cardiac dullness normal. Split first sound at apex. Electrocardiogram : Consistent with recent anterior myocardial infarct.

Gall Bladder : Tenderness in right subcostal region.

Post Mortem : 1. Anterior myocardial infarct.
2. Chronic cholecystitis.

Case No. 200.

A. McC., Male.

Age :- 58 years. 12.1.48 - 16.1.48.

Present History : Crushing pain across front of chest nine years ago, followed by praecordial tightness on exertion, excitement or after heavy meals. Flatulent dyspepsia of six years duration.

Past History : Diphtheria on two occasions 1914, 1932.

Family History : Negative.

General Examn. : Small. Wiry build. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 140/80. Heart sounds are soft and toneless but pure.
Electrocardiogram : Consistent with posterior myocardial infarction.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Increased resistance and tenderness to palpation in the right subcostal region.
Cholecystogram : Poorly functioning gall bladder.

Biochemistry : Plasma Cholesterol = 160 mgm per 100 ml.

Case No. 201.

R.L., Male.

Age :- 59 years.

5.10.49 - 21.11.49.

Present History : Substernal pain of sudden onset six weeks ago, followed by dyspnoea on exertion, weakness and flatulent dyspepsia.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Sun-tanned complexion. Mucosae well coloured. Cyanosis of lips.

Cardiovascular System : P.R. = 74 per min. B.P. = 110/80. Heart sounds are soft. Basal systolic bruit.

Electrocardiogram : Antero-septal infarction.

X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 223 mgm per 100 ml.

Case No. 202.

A.H., Male.

Age :- 60 years.

21.2.48 - 14.3.48.

Present History : Substernal pain, associated with flatulent dyspepsia, of sudden onset, four months ago.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 160/80.
Heart sounds are soft but pure.
Electrocardiogram : Consistent with antero-septal infarction extending into the lateral wall of left ventricle.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 64 mgm per 100 ml.
Cree " = 54 per cent.

Case No. 203.

E.B., Male.

Age :- 60 years.

13.9.48 - 9.12.48.

Present History : Cardiac pain of effort, associated with dyspnoea on exertion of three years duration. Severe substernal pain and dyspnoea at rest, on night before admission.

Past History : Injury to back in 1943. Flatulent dyspepsia for many years.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips and cheeks. Becomes dyspnoeic after slight movement.

Cardiovascular System : P.R. = 88 per min. B.P. = 160/110. Heart sounds are soft but distant. Electrocardiogram : Posterior coronary artery insufficiency. X-Ray of Chest : Slight cardiac enlargement.

Gall Bladder : Right subcostal tenderness. Cholecystogram : Poorly functioning gall bladder with translucent calculi.

Biochemistry : Plasma Cholesterol = 242 mgm per 100 ml.

Case No. 204.

R.I., Male.

Age :- 61 years. 17.3.48 - 7.4.48.

Present History : Gripping praecordial pain, associated with collapse and dyspnoea eight weeks ago. Praecordial pain on exertion since that date.

Past History : Negative.

Family History : Negative.

General Examn. : Heavy build. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 150/100. Heart sounds pure and of good quality. Electrocardiogram : Consistent with antero-lateral infarction. X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 90 mgm per 100 ml. Free " = 30 per cent.

Case No. 205.

J.P., Male.

Age :- 62 years. 4.8.49 - 12.8.49.

Present History : Praecordial pain on exertion of nine months duration. Stabbing praecordial pain of two hours duration and of sudden onset thirteen weeks ago. Slight flatulent dyspepsia.

Past History : Acute orchitis in 1947. Appendicectomy in 1909.

Family History : Negative.

General Examn. : Elderly, frail man. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 130/80. Heart sounds soft. Blowing apical systolic murmur.

Electrocardiogram : Left bundle branch block.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 222 mgm per 100 ml.

Free " = 45 per cent.

Case No. 206.

C.C., Male.

Age :- 63 years. 6.12.48 - 12.12.48.

Present History : Severe substernal pain, associated with collapse, of three hours duration, eleven years ago. Frequent attacks of a similar nature since 1942. Flatulent dyspepsia associated with recurring bouts of right subcostal discomfort of two years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Elderly. Obese. Mucosae well coloured. Cyanosis of lips and cheeks.

Cardiovascular System : P.R. = 78 per min. B.P. = 140/88. Heart sounds are tic-tac in quality.

Electrocardiogram : Antero-lateral coronary artery insufficiency.

X-Ray of Chest : Normal cardiac contour.

Gall Bladder : Clinical and radiological examination negative.

Case No. 207.

A.H., Male.

Age :- 64 years. 25.5.49 - 9.6.49.

Present History : Sudden praecordial pain, radiating down left arm, associated with collapse and dyspnoea two months ago.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Average build. Mucosae well coloured.

Cardiovascular System : P.R. = 90 per min. B.P. = 170/110. Heart sounds are pure and of average quality.

Electrocardiogram : Posterior myocardial infarct.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Case No. 208.

W. McC., Male.

Age :- 65 years. 12.12.50 - 29.12.50.

Present History : Praecordial discomfort, on exertion of eleven months duration. Right subcostal pain, associated with nausea, vomiting and jaundice in September, 1950. No flatulent dyspepsia.

Past History :Negative.

Family History : Negative.

General Examn. : Tall. Slim build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 160/90. Heart sounds soft and distant.

Electrocardiogram : Antero-lateral coronary artery insufficiency. Right bundle branch block.

X-Ray of Chest : Prominence of left ventricle.

Gall Bladder : Right subcostal tenderness.

Cholecystogram : Non-functioning gall bladder.

Biochemistry : Plasma Cholesterol = 210 mgm per 100 ml.

R. McI., Male. Case No. 209.

Age :- 40 years. 5.5.48 - 7.5.48.

Present History : Praecordial pain, dyspnoea and collapse of sudden onset nine weeks ago. No flatulent dyspepsia.

Past History : Negative.

Family History : Negative.

General Examn. : Good physique. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 72 per min. B.P. = 150/100. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality. X-ray of chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma cholesterol = 133 mgm per 100 ml. Free " = 27 per cent.

Case No. 210.

J.S., Male.

Age :- 65 years. 11.7.49 - 22.7.49.

Present History : Severe praecordial pain, collapse and dyspnoea, of several hours duration, five months ago.

Past History : ? Coronary occlusion ten years ago. History of cardiac pain of effort, associated with slight flatulent dyspepsia since.

Family History : Negative.

General Examn. : Elderly. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 130/82. Heart sounds of average quality. Electrocardiogram : Equivocal changes. X-Ray of Chest : Left ventricular enlargement and arteriosclerotic configuration of the aortic arch.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 256 mgm per 100 ml. Free " = 24 per cent.

Case No. 211.

M.O., Female.

Age :- 53 years. 24.1.46 - 28.1.46.

Present History : Flatulent dyspepsia, associated with recurring bouts of epigastric pain, nausea and vomiting, of twelve years duration. Dyspnoea on exertion of five years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 150/100. Heart sounds of good quality. 2nd basal sound accentuated.
Electrocardiogram : Equivocal changes.
X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 247 mgm per 100 ml.
Free " = 10 per cent.

Case No. 212.

I.S., Female.

Age :- 34 years. 2.4.49 - 11.4.49.

Present History : Flatulent dyspepsia, associated with recurring bouts of epigastric pain and vomiting of three years duration. No cardiovascular symptoms.

Past History : Appendicectomy in 1932. Duodenal ulcer in 1946.

Family History : Negative.

General Examn. : Slim build. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 128/88. Heart sounds of good quality and pure. Electrocardiogram : No significant abnormality. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness and guarding. Cholecystogram : Normal. Test meal : Achlorhydria. (Barium meal : Negative).

Biochemistry : Plasma Cholesterol = 264 mgm per 100 ml. Free " = 30 per cent.

Case No. 213.

R.S., Male.

Age :- 58 years.

21.5.49 - 31.5.49.

Present History : Flatulent dyspepsia, associated with recurring bouts of upper abdominal pain and distension, of three months duration. No cardiovascular symptoms.

Past History : Right herniorrhaphy in 1941.

Family History : Negative.

General Examn. : Small. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 74 per min. B.P. = 180/118.
Heart sounds of average quality. 2nd basal sound accentuated.
Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Normal.
(Barium meal : Negative).

Biochemistry : Plasma Cholesterol = 245 mgm per 100 ml.
Free " = 14 per cent.

Case No. 214.

E.T., Female.

Age :- 23 years.

4.6.43 - 16.6.48.

Present History : Recurring attacks of upper abdominal pain, associated with nausea and vomiting, of four years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Slim build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 128/64.
Heart sounds pure and of good quality.
Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Tenderness in right subcostal region.
Cholecystogram : Normal.
Test meal : Achlorhydria.

Biochemistry : Plasma Cholesterol = 218 mgm per 100 ml.
Free " = 10 per cent.

Case No. 215.

S.W., Male.

Age :- 45 years.

30.3.48 - 1.4.48.

Present History : Flatulent dyspepsia, associated with upper abdominal discomfort and occasional bouts of vomiting, of three years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Tall. Muscular build. Fresh complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 138/82. Heart sounds of good quality. Short V.S. murmur audible at all areas.

Electrocardiogram : Equivocal changes.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Test meal : Achlorhydria.

Biochemistry : Plasma Cholesterol = 128 mgm per 100 ml.

Case No. 216.

D.L., Male.

Age :- 44 years.

6.5.48 - 20.5.48.

Present History : Flatulent dyspepsia, associated with substernal pain after meals, of six months duration. No other cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Tendency to obesity. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 74 per min. B.P. = 130/86. Heart sounds of average quality. Short V.S. murmur at apex.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness.

Cholecystogram : Poorly functioning gall bladder.

Repeat cholecystogram : Normally functioning gall bladder.

Test meal : Achlorhydria.

Biochemistry : Plasma Cholesterol = 189 mgm per 100 ml.

Free " = 26 per cent.

Case No. 217.

A.R., Male.

Age :- 52 years.

28.9.49 - 5.10.49.

Present History : Flatulent dyspepsia, associated with upper abdominal discomfort, of five years duration. Ready fatigue and dyspnoea on exertion of same duration.

Past History : Appendicectomy in 1928. Gastro-enterostomy in 1932.

Family History : Negative.

General Examn. : Small. Slim build. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 120/80.
Heart sounds soft but pure.
Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 286 mgm per 100 ml.
Free " = 29 per cent.

Case No. 218.

J.B., Female.

Age :- 45 years. 7.6.48 - 27.6.48.

Present History : Recurring attacks of pain between the scapulae, associated with nausea and vomiting, of ten years duration. No cardiovascular symptoms.

Past History : Sciatica in 1945.

Family History : Father died from hypertensive cerebrovascular disease.

General Examn. : Small. Slim build. Pallid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 170/90. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 200 mgm per 100 ml. Free " = 14 per cent.

Case No. 219.

W.G., Male.

Age :- 50 years.

23.2.49 - 4.3.49.

Present History : Flatulent dyspepsia, associated with bouts of vomiting, of ten years duration. No cardiovascular symptoms.

Past History : Malaria in 1942.

Family History : Negative.

General Examn. : Small. Slim build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 130/80.
Heart sounds pure and of good quality.
Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness.
Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 195 mgm per 100 ml.
Free " = 43 per cent.

Case No. 220.

I.G., Male.

Age :- 44 years.

23.1.47 - 28.1.48.

Present History : Praecordial discomfort, associated with Flatulent dyspepsia, of three weeks duration. These symptoms are unrelated to meals or exercise.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Slim build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 140/82. Heart sounds of good quality. Short blowing V.S. murmur at all areas.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative. (Cholecystogram one year ago was also negative).

Biochemistry : Plasma Cholesterol = 458 mgm per 100 ml.

Free " = 4 per cent.

Case No. 221.

S.C., Female.

Age :- 46 years.

14.9.49 - 21.9.49.

Present History : Flatulent dyspepsia and aversion to greasy foods of six months duration. Severe pain in right subcostal region twelve hours before admission to hospital. Dyspnoea on exertion of twenty years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 120/70. Heart sounds pure and of average quality. Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Tenderness in right subcostal region. Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 250 mgm per 100 ml.

Free " = 24 per cent.

Case No. 222.

C.S., Female.

Age :- 51 years. 7.10.49 - 12.10.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, nausea and vomiting, of twelve years duration. Menopausal symptoms present.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Obese. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 162/90. Heart sounds of good quality. Short V.S. murmur at the Apex.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness.

Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 340 mgm per 100 ml.

Free " = 26 per cent.

Case No. 223.

M.B., Female.

Age :- 43 years. 8.3.48 - 10.3.48.

Present History : Flatulent dyspepsia, associated with upper abdominal discomfort and distension, of three months duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Average physique. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 142/86. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical and radiological examination negative.
(Barium meal : Negative).

Biochemistry : Plasma Cholesterol = 160 mgm per 100 ml.
Free " = 27 per cent.

Case No. 224.

N.S., Male.

Age :- 31 years. 7.1.49 - 2.4.49.

Present History : Flatulent dyspepsia, associated with right subcostal discomfort, after meals, of two years duration. No cardiovascular symptoms.

Past History : Appendicectomy in 1930. Infective hepatitis in 1941.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 86 per min. B.P. = 120/84. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical and radiological examination negative.
(Barium meal : Negative).

Biochemistry : Plasma Cholesterol = 236 mgm per 100 ml.
Free " = 28 per cent.

Case No. 225.

H. McR., Female.

Age :- 51 years. 22.4.48 - 15.12.48.

Present History : Flatulent dyspepsia associated with praecordial discomfort after meals of three years duration. Dyspnoea on exertion, palpitation and flushings of one year's duration.

Past History : Menses ceased one year ago.

Family History : Negative.

General Examn. : Obese. Florid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 186/102. Heart sounds soft and distant. Second basal sound relatively accentuated.
Electrocardiogram : Suggestive of left ventricular hypertrophy.
X-Ray of Chest : Prominent left ventricle.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 174 mgm per 100 ml.
Free " = 34 per cent.

Case No. 226.

J.C., Female.

Age :- 62 years. 12.4.49 - 8.6.49.

Present History : Recurring attacks of right subcostal pain, associated with nausea and vomiting, over the past nine weeks. No cardiovascular symptoms.

Past History : Appendicectomy in 1929.

Family History : Negative.

General Examn. : Slim build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 160/90.
Heart sounds soft but pure.
Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 240 mgm per 100 ml.

Case No. 227.

J.G., Female.

Age :- 37 years. 1.4.48 - 22.4.48.

Present History : Flatulent dyspepsia, associated with upper abdominal pain after meals, of nine months duration. No cardiovascular symptoms.

Past History : Goitre in 1934. Menses ceased in 1947.

Family History : Negative.

General Examn. : Average build. Nervous. Thyroid enlargement. Tremor of outstretched hands. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 120/80. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 172 mgm per 100 ml.

Case No. 228.

F.W., Male.

Age :- 44 years. 24.11.49 - 28.11.49.

Present History : Recurring attacks of epigastric discomfort and praecordial tightness, associated with feeling of faintness and nausea, of five years duration. Dyspnoea on exertion of the same duration.

Past History : Negative.

Family History : Negative.

General Examn. : Wiry build. Sallow complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 142/82. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormal ity.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

(Barium meal : Normal).

Biochemistry : Plasma Cholesterol = 186 mgm per 100 ml.

Free " = 27 per cent.

Case No. 229.

M.R., Female.

Age :- 32 years. 26.4.48 - 27.4.48.

Present History : Recurring attacks of right subcostal pain, nausea and vomiting of four years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Obese. Slight cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 146/94. Heart sounds of average quality. Blowing V.S. murmur at Apex.
Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical and radiological examination negative.
(Barium meal : Negative).

Biochemistry : Plasma Cholesterol = 175 mgm per 100 ml.

Case No. 230.

J.G., Female.

Age :- 59 years. 10.11.49 - 14.11.49.

Present History : Recurring attacks of right subcostal pain, nausea and vomiting of six years duration. Increasing dyspnoea on exertion of three months duration.

Past History : Haemoptysis in 1945.

Family History : Negative.

General Examn. : Obese. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 74 per min. B.P. = 180/100. Heart sounds soft. Short V.S. murmur at apex.

Electrocardiogram : No significant abnormality.

Gall Bladder : Tenderness in right subcostal region.

Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 191 mgm per 100 ml.

Free " = 34 per cent.

Case No. 231.

J.G., Male.

Age :- 56 years.

10.11.49 - 14.11.49.

Present History : Flatulent dyspepsia, associated with recurring attacks of pain between the scapulae, of five years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Tall. Good physique. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 150/90. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness.

Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 358 mgm per 100 ml.

Free " = 36 per cent.

Case No. 232.

B.G., Female.

Age :- 46 years. 28.11.49 - 29.12.49.

Present History : Flatulent dyspepsia and heartburn, following meals, of six weeks duration. Recurring attacks of substernal pain, related to meals, of two months duration.

Past History : Appendicectomy in 1937.
Phlebitis in 1947.

Family History : Negative.

General Examn. : Strong build. Pallid complexion.
Mucosae well coloured.

Cardiovascular System : P.R. = 90 per min. B.P. = 190/94.
Heart sounds good quality. Second basal sound accentuated.
Electrocardiogram : Suggestive of left ventricular hypertrophy.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.
(Barium meal : Negative).

Biochemistry : Plasma Cholesterol = 148 mgm per 100 ml.
Free " = 21 per cent.

Case No. 233.

J.R., Male.

Age :- 55 years. 21.2.48 - 1.3.48.

Present History : Flatulent dyspepsia, associated with recurring bouts of nausea and vomiting, of one year's duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Suggestive of coronary artery disease. (Father died suddenly from "Heart disease").

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 110/70. Heart sounds of good quality. Short blowing V.S. murmur at base of heart. Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness. Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 221 mgm per 100 ml.
Free " = 15 per cent.

Case No. 234.

J.K., Female.

Age :- 33 years. 13.9.48 - 29.9.48.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain and nausea, of three years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Slim build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 118/76. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 143 mgm per 100 ml.

D. McI., Male. Case No. 235.

Age :- 52 years. 10. 9.48 - 7.10.48.

Present History : Praecordial pain, radiating into the left arm, and brought on by exertion, of six months duration. Severe flatulent dyspepsia of one year's duration.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Slim build. Cyanosis of lips. Mucosae well coloured.

Cardiovascular System : P.R. = 80 per min. B.P. = 162/94.
Heart sounds of good quality.
Short V.S. murmur at apex.
Electrocardiogram : No significant abnormality.
X-Ray of chest : A normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma cholesterol = 268 mgm per 100 ml.
Per cent free = 50.

Case No. 236.

M.J., Female.

Age :- 56 years. 15.3.48 - 26.3.48.

Present History : Praecordial pain, on exertion, of three years duration. No flatulent dyspepsia.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Obese. Subthyroid appearance. Xanthomatous nodules on elbows, knees, and buttocks. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 220/110. Heart sounds of good quality. Second basal sound accentuated.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 181 mgm per 100 ml.

Case No. 237.

A.S., Male.

Age :- 48 years. 6.4.48 - 22.4.48.

Present History : Praecordial pain and dyspnoea of six hours duration, whilst resting, seven weeks ago. Pain in left chest of sudden onset, followed by haemoptysis, two weeks ago.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 160/90. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline. Lung fields clear.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 143 mgm per 100 ml.

Case No. 238.

D.F., Male.

Age :- 57 years. 25.2.48 - 8.3.48.

Present History : Praecordial pain on exertion, associated with dyspnoea and flatulent dyspepsia, of nine months duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Healthy appearance. Slight cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 78 per min. B.P. = 160/100. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.
X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 250 mgm per 100 ml.

Case No. 239.

J.B., Male.

Age :- 45 years. 9.11.49 - 25.11.49.

Present History : Praecordial pain of sudden onset following a heavy meal, and of five minutes duration, three weeks ago. Praecordial pain on exertion since.

Past History : Flatulent dyspepsia of many years duration.

Family History : Negative.

General Examn. : Small. Average build. Mucosae well coloured.

Cardiovascular System : P.R. = 70 per min. B.P. = 152/86.
Heart sounds pure and of good quality.
Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 258 mgm per 100 ml.
Free " = 25 per cent.

Case No. 240.

G.W., Male.

Age :- 50 years. 26.2.48 - 1.5.48.

Present History : Severe substernal pain and dyspnoea, coming on while at rest, in January, 1948. Praecordial tightness on exertion since that date. No flatulent dyspepsia.

Past History : Negative.

Family History : Suggestive of coronary artery disease.

General Examn. : Tall. Heavy build. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 150/98. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality. X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 315 mgm per 100 ml. Free " = 13 per cent.

Case No. 241.

J.R., Male.

Age :- 58 years. 6.3.48 - 14.3.48.

Present History : Praecordial pain on exertion, associated with dyspnoea and flatulent dyspepsia, of two years duration.

Past History : Duodenal ulcer with recurring bouts of haematemesis and melaena since 1918.

Family History : Negative.

General Examn. : Tall. Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 200/120. Heart sounds are soft. Blowing V.S. murmur at apex. Second basal sound accentuated.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 154 mgm per 100 ml.

Free " = 22 per cent.

Case No. 242.

R.F., Female.

Age :- 58 years. 14.1.48 - 16.1.48.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, and vomiting, of one year's duration. Substernal pain on exertion of six months duration.

Past History : Attack of substernal pain nine months ago, diagnosed as "Coronary Spasm".

Family History : Suggestive of Coronary artery disease.

General Examn. : Obese. Cyanosis of lips and cheeks. Mucosae well coloured.

Cardiovascular System : P.R. = 84 per min. B.P. = 230/100. Heart sounds of good quality. Second basal sound accentuated.
Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 289 mgm per 100 ml.

Case No. 243.

P. McI., Male.

Age :- 51 years. 6.8.47 - 7.11.47.

Present History : Flatulent dyspepsia, associated with recurring bouts of right subcostal pain and heartburn, of thirty years duration. Gripping praecordial pain on exertion of six months duration.

Past History : Negative.

Family History : Negative.

General Examn. : Average build. Weatherbeaten complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 122/78. Heart sounds soft. Short V.S. murmur at apex.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 167 mgm per 100 ml.

Case No. 244.

J.S., Female.

Age :- 62 years. 9.6.49 - 26.7.49.

Present History : Flatulent dyspepsia, associated with recurring bouts of faintness, nausea and vomiting, of two years duration. Dyspnoea on exertion, swelling of ankles and headaches of same duration.

Past History : Appendicectomy in 1947.

Family History : Negative.

General Examn. : Small. Obese. Subthyroid appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 210/118. Heart sounds soft. Short apical V.S. murmur. Second basal sound accentuated.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Left ventricular enlargement.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 242 mgm per 100 ml.

Free " = 25 per cent.

Case No. 245.

R. McG., Female.

Age :- 43 years. 10. 4.48 - 22.4.48.

Present History : Flatulent dyspepsia, associated with recurring attacks of right subcostal pain, of one year's duration. Praecordial pain on exertion of nine months duration. Menopausal symptoms present.

Past History : Negative.

Family History : Negative.

General Examn. : Stout. Florid complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 88 per min. B.P. = 180/100. Heart sounds of good quality. Second basal sound accentuated.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Tenderness in right subcostal region.

Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 128 mgm per 100 ml.

Free " = 25 per cent.

Case No. 246.

S.N., Male.

Age :- 34 years. 10. 5.48 - 20. 5.48.

Present History : Praecordial discomfort, not related to exertion, but accompanied by dyspnoea and flatulence of four years duration.

Past History : Negative.

Family History : Negative.

General Examn. : Slim build. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 130/80. Heart sounds of good quality. Short V.S. murmur at apex.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Right subcostal tenderness.

Cholecystogram : Normal.

Biochemistry : Plasma Cholesterol = 91 mgm per 100 ml.

Free " = 25 per cent.

Case No. 247.

A.R., Male.

Age :- 63 years. 16.4.48 - 25.4.48.

Present History : Flatulent dyspepsia, associated with right subcostal discomfort, and vomiting, of six weeks duration. Increasing dyspnoea on exertion, associated with substernal pain, of five years duration.

Past History : Bilateral pneumonia in 1928. Trench fever during 1914-18 war.

Family History : Negative.

General Examn. : Stocky build. Fresh complexion. Mucosae well coloured.

Cardiovascular System : P.R. = 64 per min. B.P. = 136/82. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical and radiological examination negative.

Biochemistry : Plasma Cholesterol = 160 mgm per 100 ml.
Free " = 36 per cent.

Case No. 248.

W.S., Male.

Age :- 46 years. 13.1.49 - 19.1.49.

Present History : Flatulent dyspepsia associated with upper abdominal pain and distension after meals of thirty years duration. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Tall. Slim build. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 110/70.
Heart sounds pure and of good quality.
Electrocardiogram : No significant abnormality.
X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Epigastric tenderness.
Cholecystogram : Normal.
(Barium meal : gastric ulcer).

Biochemistry : Plasma Cholesterol = 308 mgm per 100 ml.
Free " = 28 per cent.

Case No. 249.

G.C., Male.

Age :- 52 years. 29.4.48 - 9.5.48.

Present History : Praecordial pain, associated with a feeling of heaviness, when fatigued, of six weeks duration. No flatulent dyspepsia.

Past History : Appendicectomy in 1923.

Family History : Negative.

General Examn. : Small. Tendency to obesity. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 82 per min. B.P. = 126/84. Heart sounds pure and of good quality.

Electrocardiogram : No significant abnormality.

X-Ray of Chest : Normal cardiac outline.

Gall Bladder : Clinical and radiological examination negative.

(Barium meal : Duodenal ulcer).

Biochemistry : Plasma Cholesterol = 266 mgm per 100 ml.

Free " = 30 per cent.

Case No. 250.

H.B., Male.

Age :- 45 years. 7.2.50 - 14.2.50.

Present History : Recurring attacks of upper abdominal discomfort, associated with flatulence, nausea and vomiting, over the past four years. No cardiovascular symptoms.

Past History : Negative.

Family History : Negative.

General Examn. : Small. Tendency to obesity. Healthy appearance. Mucosae well coloured.

Cardiovascular System : P.R. = 76 per min. B.P. = 128/74. Heart sounds pure and of good quality. Electrocardiogram : No significant abnormality.

Gall Bladder : Clinical and radiological examination negative.
(Barium meal : Showed changes consistent with a duodenitis : no ulcer crater seen).

Biochemistry : Plasma Cholesterol = 330 mgm per 100 ml.

THE RELATIONSHIP

BETWEEN

GALL BLADDER DISEASE

AND

CORONARY ARTERY DISEASE

APPENDIX 3.

This volume contains the pre- and post-operative electrocardiograms, of gall bladder disease,
Fig. 1 - Fig. 63.
Fig. 64 - Fig. 70 are examples of the electrocardiograms of coronary artery disease.

Fig. 1. Case No. 3. : The pre-operative electrocardiogram, taken on 31.5.49, shows low voltage, upright QRS complexes in the standard limb leads, with low voltage upright T waves in leads I, II, and isoelectric T wave in lead III. The T wave is isoelectric in aVF, inverted in V1 and V2, diphasic in V3, V4, and V5, and low voltage upright in V6.

The post-operative electrocardiograms, taken on 19.7.49 and 31.1.50, show an increase in the voltage of the T waves, in the standard limb leads. The T waves in aVF and V2 - V6 show a great increase in amplitude.

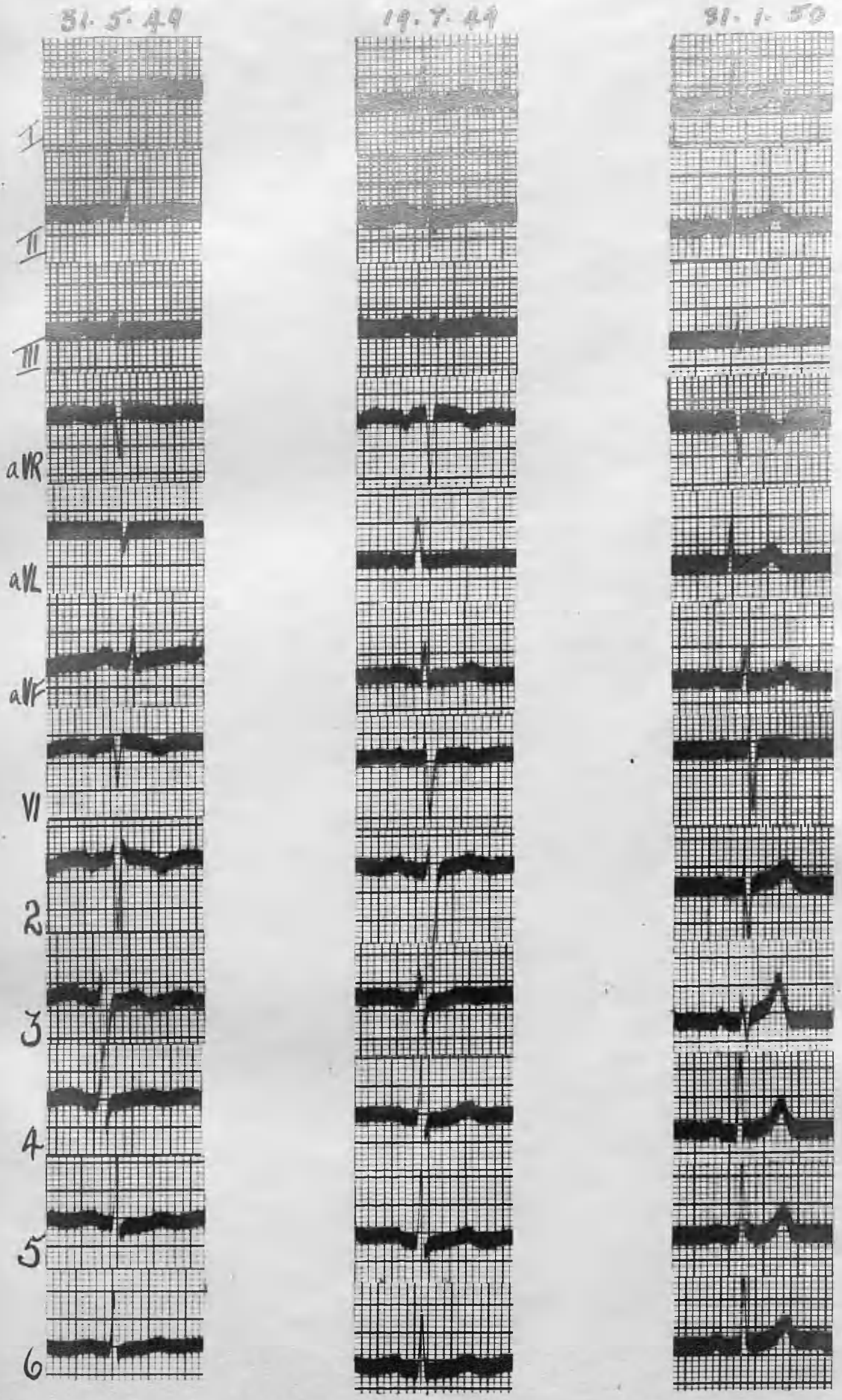

FIG. 1.

Fig. 2. Case No. 8. : The pre-operative electrocardiogram, taken on 23.11.48, shows an isoelectric T wave in lead II, a QR complex with inverted T wave in lead II, low voltage inverted T wave in aVF, and low voltage upright T waves in V4, V5, V6. The pos-operative electrocardiograms, taken on 3.2.49 and 11.7.49, show an increase in amplitude, greater on 11.7.49 than on 3.2.49, in the T waves in leads I, II and V2-6. The T wave in lead III has become isoelectric, and in lead aVF upright.

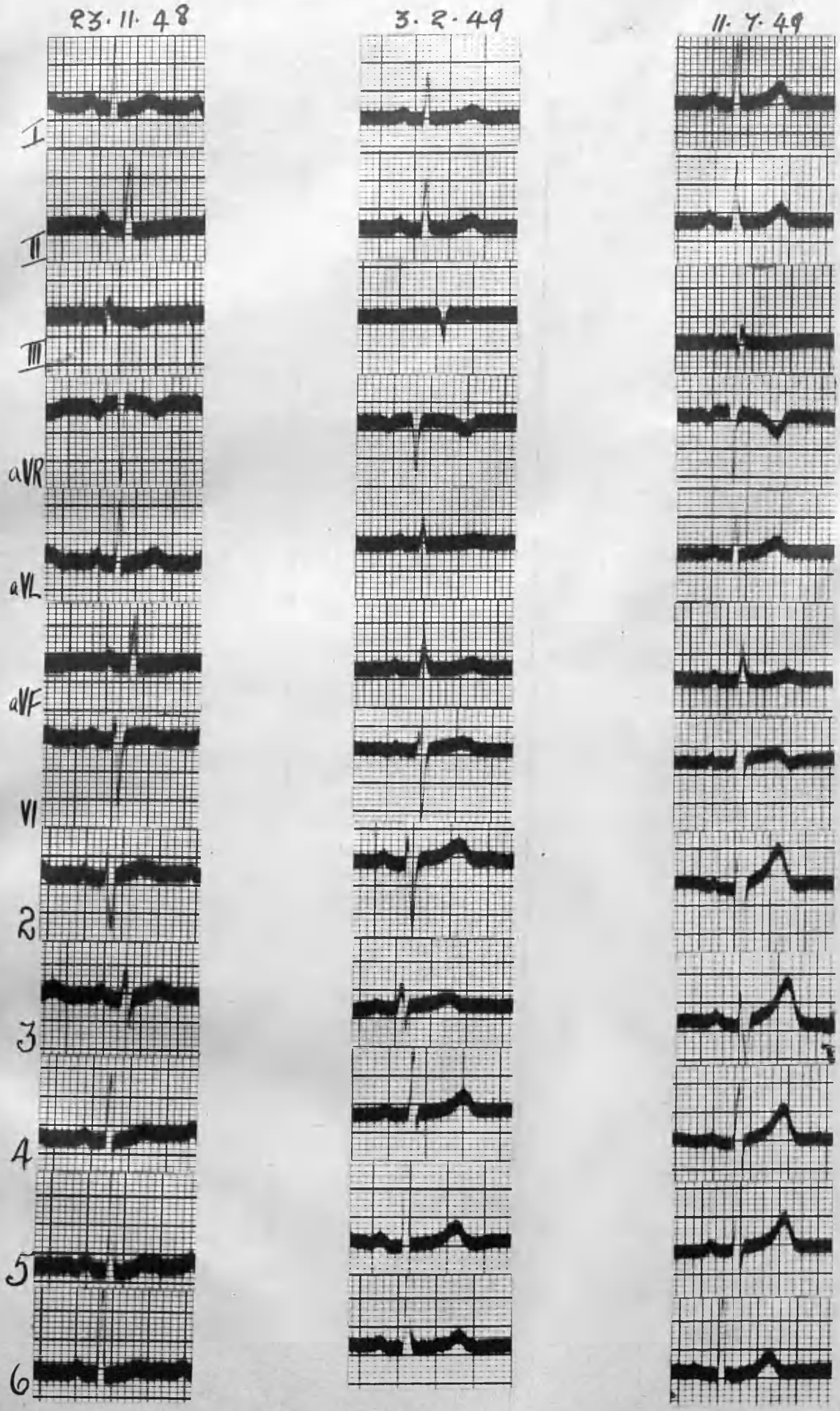

FIG. 2.

Fig. 3. Case No.11. : The pre-operative electrocardiogram, taken on 11.2.49, shows a low voltage, splintered R wave, and isoelectric T wave in aVF.

The post-operative electrocardiogram, taken on 30.3.49, shows in increase in voltage, a diminution in the splintering of the R wave, and an upright T wave in aVF.

The electrocardiogram, taken on 19.1.50, is similar to that of 30.3.49, except that T in lead III has become isoelectric in addition.

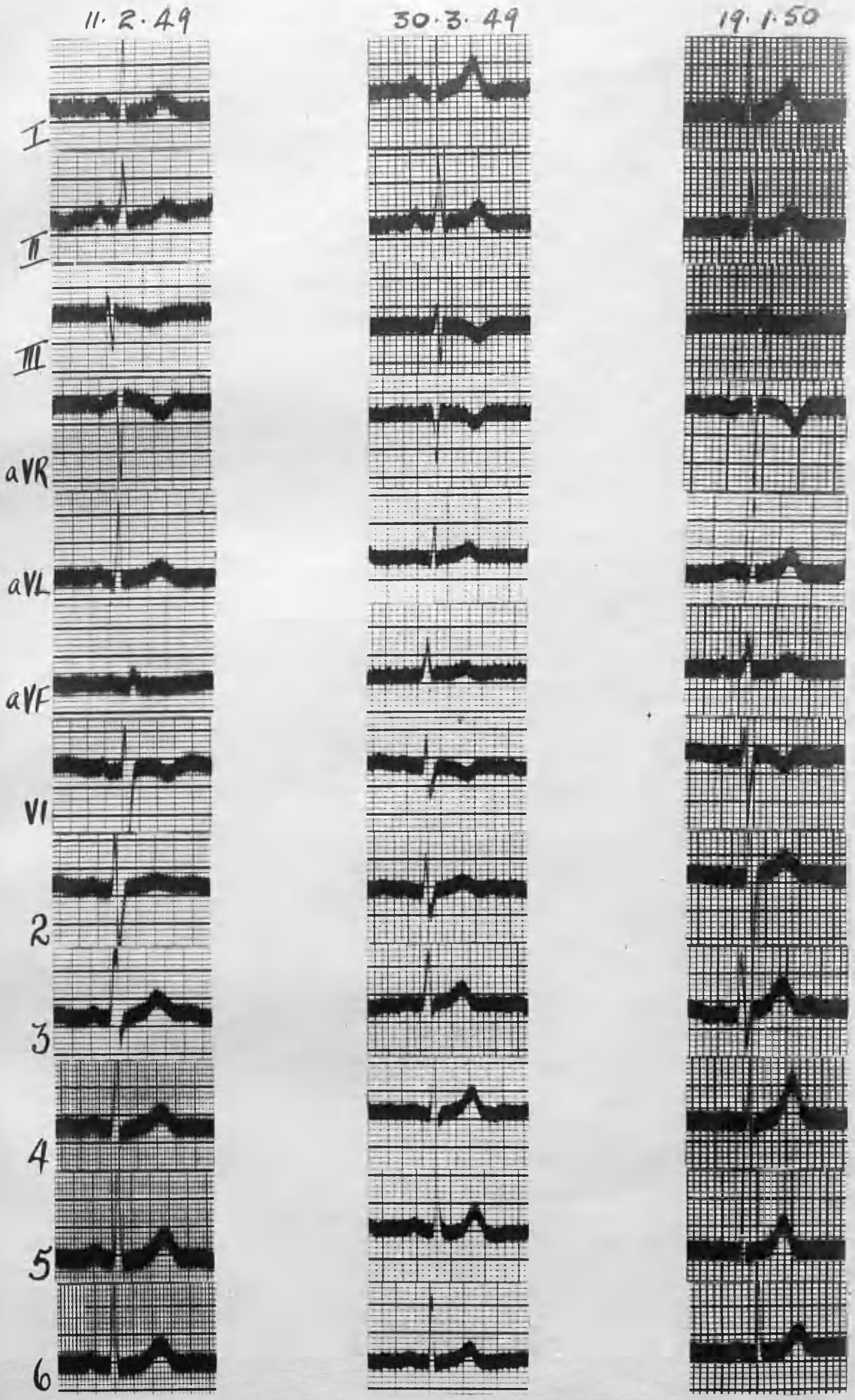

FIG. 3.

Fig. 4. : The pre-operative electrocardiogram, taken on 1.6.48, shows right axis deviation with diphasic T waves in leads I, II and aVF, and inverted T waves in leads V3-6.

Case No.14. The post-operative electrocardiograms, taken on 19.4.49 and 22.6.49, show right axis deviation with upright T waves in leads II, III, aVF, V4-6, in spite of the fact that the chest electrocardiograms have not been placed exactly in the same position as in the pre-operative electrocardiogram.

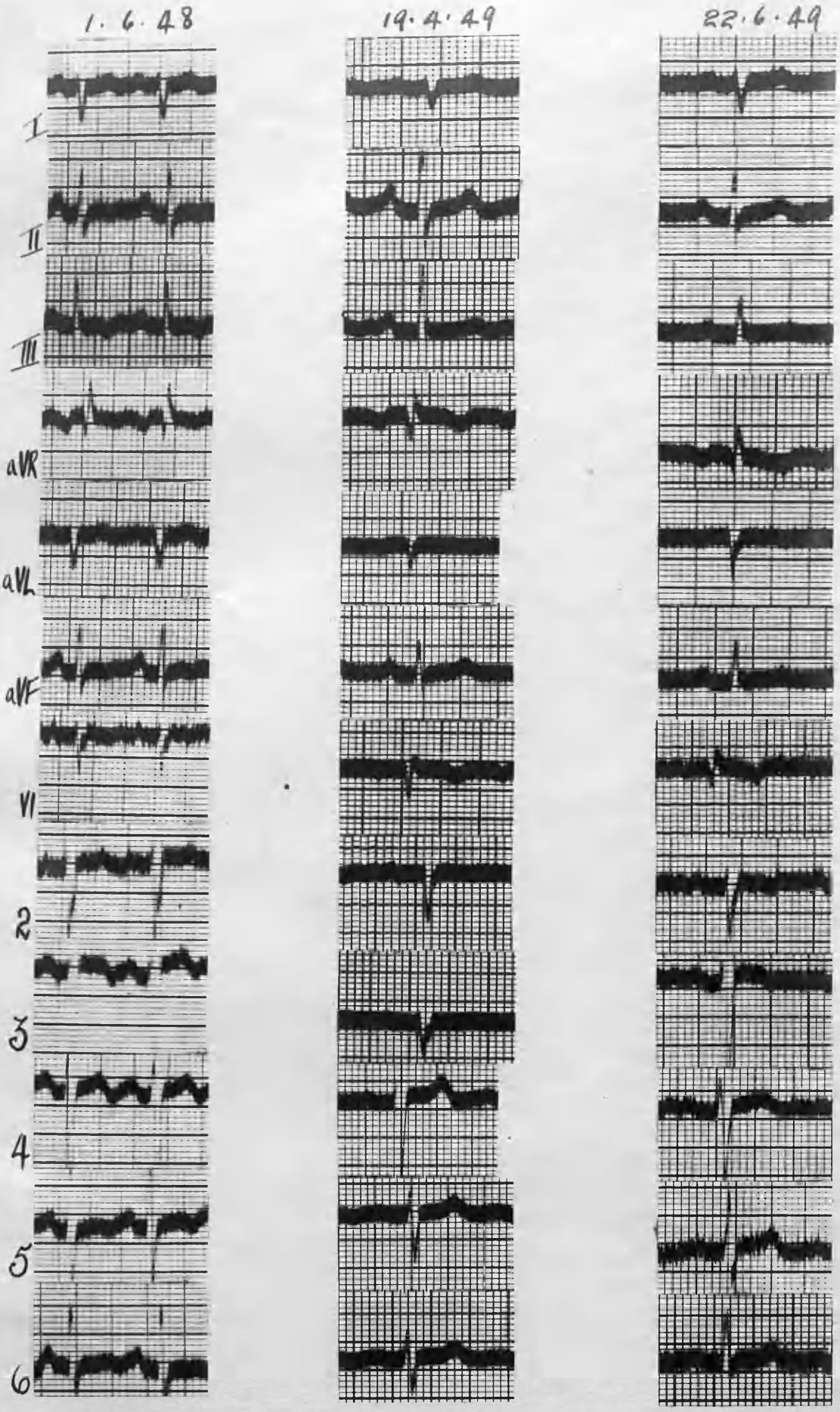

FIG. 4.

Fig. 5. : The pre-operative electrocardiogram,
Case No. 42. taken on 21.3.49 shows changes consistent with left ventricular hypertrophy.

The post-operative electrocardiogram, taken on 5.4.49, shows improvement, in that the T waves in leads I, V4, V5, and V6 are less deeply inverted.

The electrocardiogram, taken on 25.1.50, shows a return to the pre-operative electrocardiogram of 21.3.49.

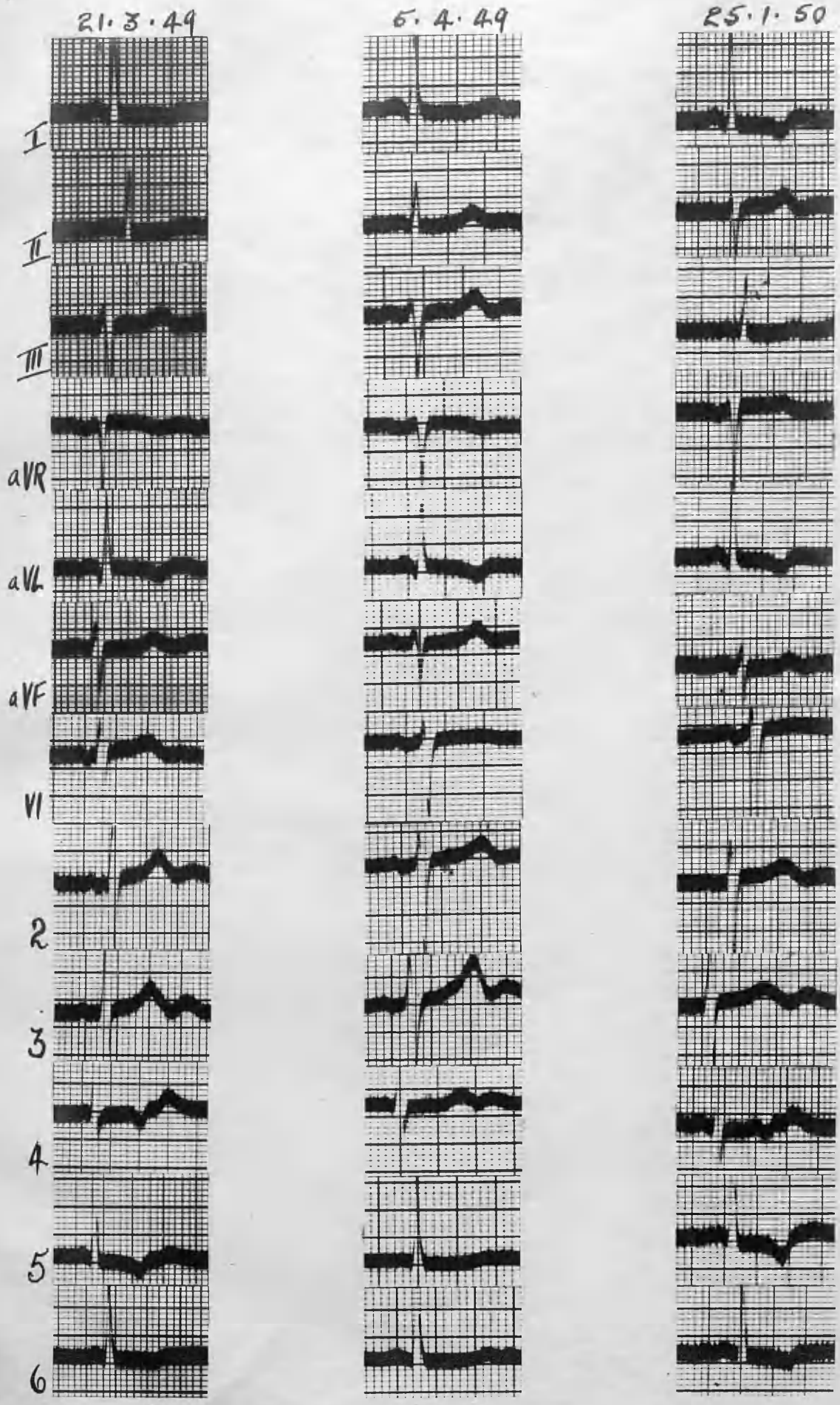

FIG. 5.

Fig. 6. Case No.40. : The pre-operative electrocardiogram, taken on 16.4.49, shows an inverted T wave in lead I, ST elevation in VI-4, with T wave inversion in aVL, VI-6.

The post-operative electrocardiogram, taken on 29.4.49, shows an isoelectric T wave in lead I and aVL, and low voltage, upright T waves in VI-6.

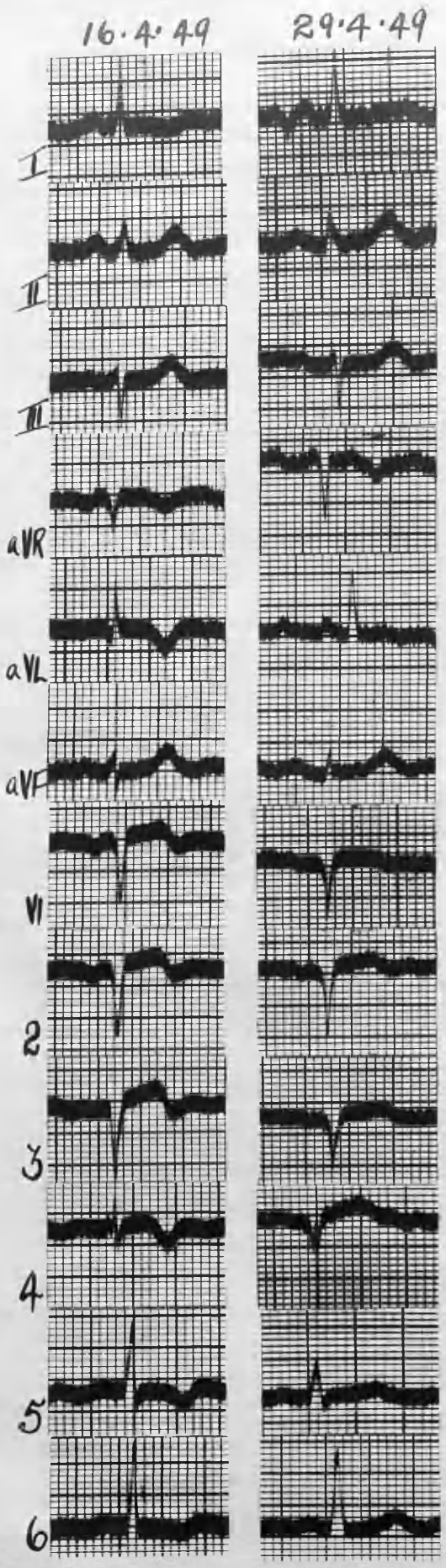

FIG. 6.

Fig. 7. Case No. 43. : The pre-operative electrocardiogram, taken on 2.7.49, shows left bundle branch block. The post-operative electrocardiogram, taken on 19.7.49, shows no significant change in the pattern of QRS-T complexes in any of the leads, but the duration of the QRS complex has, in many leads, become reduced from 0.16 seconds to 0.12 seconds, i.e. the degree of bundle branch block has decreased.

Fig. 8. Case No. 32. : The pre-operative electrocardiogram, taken on 28.4.49 is within normal limits.

The post-operative electrocardiogram, taken on 16.11.49 shows no significant change.

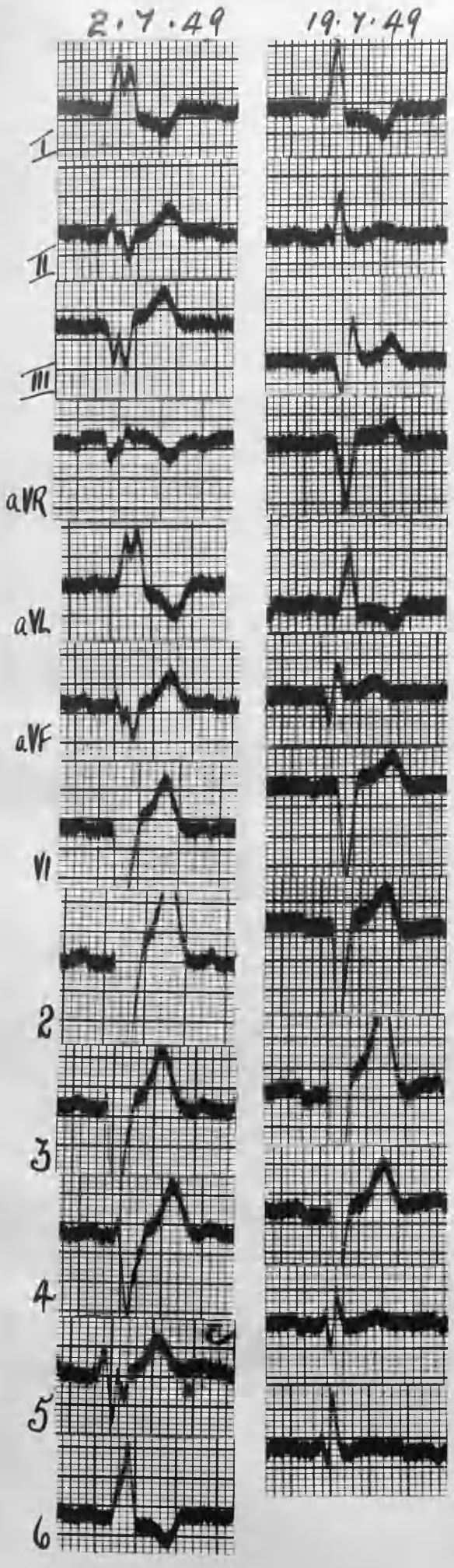
2·7·49
19·7·49
I
II
III
aVR
aVL
aVF
VI
2
3
4
5
6

FIG. 7.

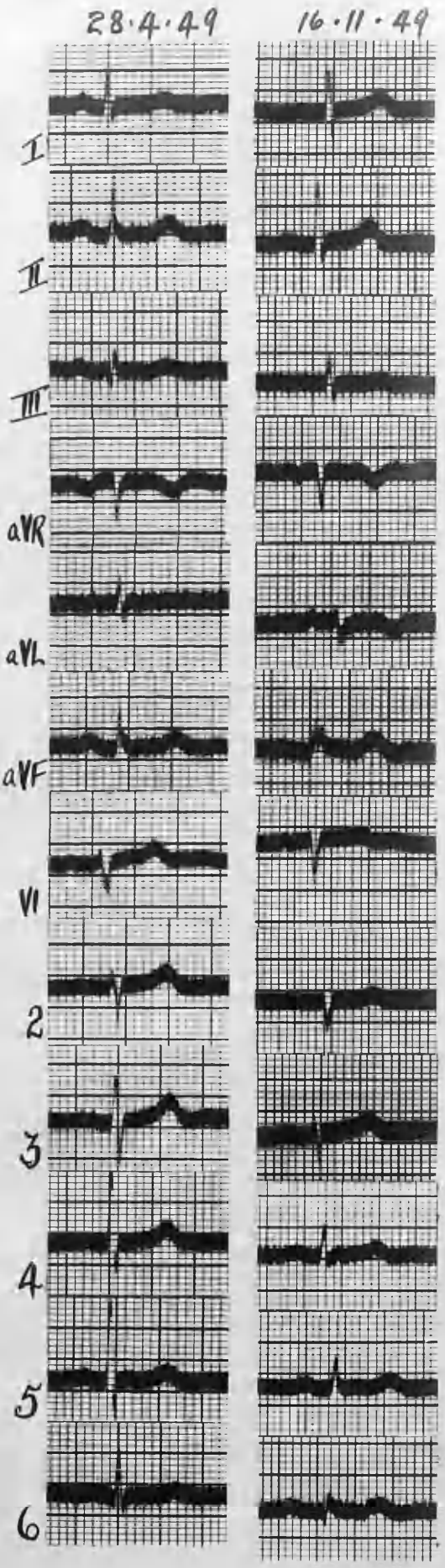
28·4·49
16·11·49
I
II
III
aVR
aVL
aVF
VI
2
3
4
5
6

FIG. 8.

Fig. 9. : The pre-operative electrocardiogram, taken on 25.2.48, shows left axis deviation with an inverted T wave in lead I. The post-operative electrocardiogram, taken on 17.3.48, shows no significant change, but the electrocardiogram taken on 17.4.48, shows the development of a Q wave with ST elevation and T wave inversion in V3, and inversion of the T wave in V4. On 13.12.48 the T wave in V4 and V5 is inverted, and in V6 diphasic.

Case No. 67.

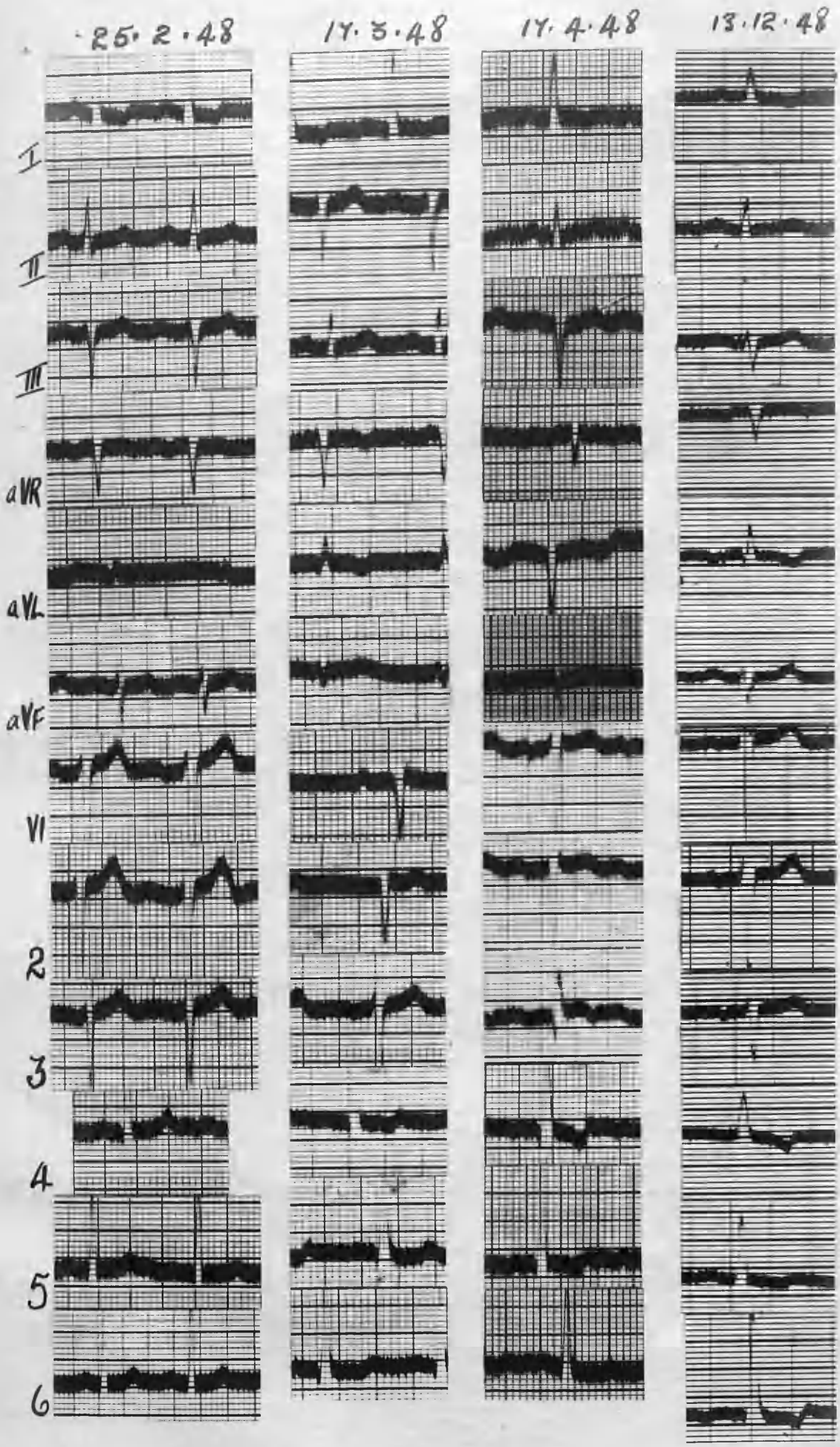

FIG. 9.

Fig. 10. Case No. 64. : The post-operative electrocardiogram, which was taken on 13.12.49, shows no significant change from the pre-operative electrocardiogram, taken on 10.11.48. They are both within normal limits.

Fig. 11. Case No. 13. : The pre-operative electrocardiogram, taken on 28.4.44 shows an isoelectric T wave in lead I. The post-operative electrocardiogram, taken on 13.12.48 shows an inverted T wave in lead I.

Fig. 12. Case No. 36. : The pre-operative electrocardiograms, taken on 21.1.43 and 18.10.47 show a change in the position of the heart as revealed by a comparison of lead III.

The post-operative electrocardiogram taken on 26.4.48, shows no significant change from the pre-operative electrocardiogram taken on 18.10.47. They are all within normal limits.

Fig. 13. Case No. 19. : The post-operative electrocardiogram, taken on 15.10.48 shows no significant change from the pre-operative electrocardiogram, taken on 14.10.45. They show no significant abnormality.

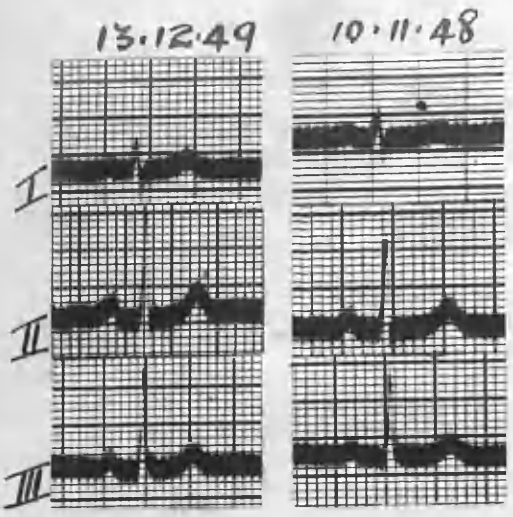

FIG. 10

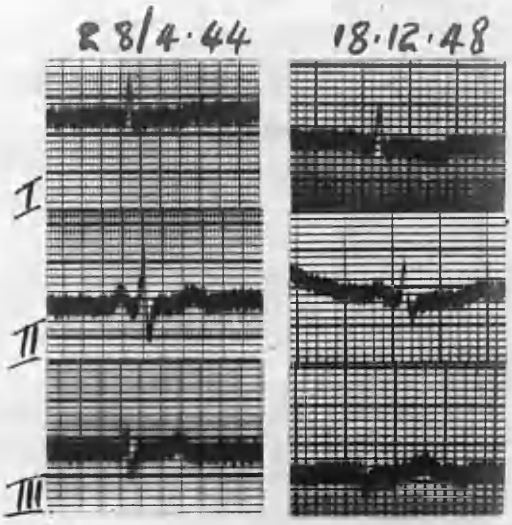

FIG. 11.

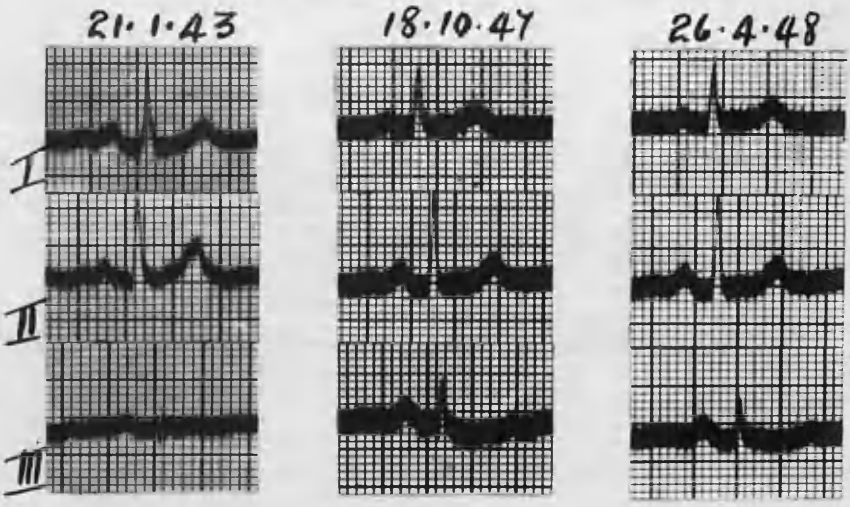

FIG. 12.

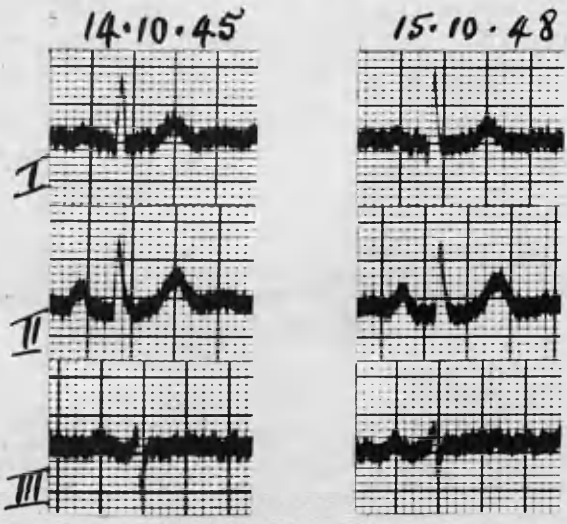

FIG. 13.

Fig. 14. Case No. 7. : The pre-operative electrocardiogram, taken on 6.10.48, is within normal limits. The post-operative electrocardiograms, standard limb leads only, taken on 8.10.48 and 10.10.48, show changes consistent with pulmonary embolism - ST elevation leads II and III and T wave inversion in II, III. Further post-operative electrocardiogram, taken on 7.12.48 and 12.4.49, show a return to the normal pre-operative electrocardiogram of 6.10.48.

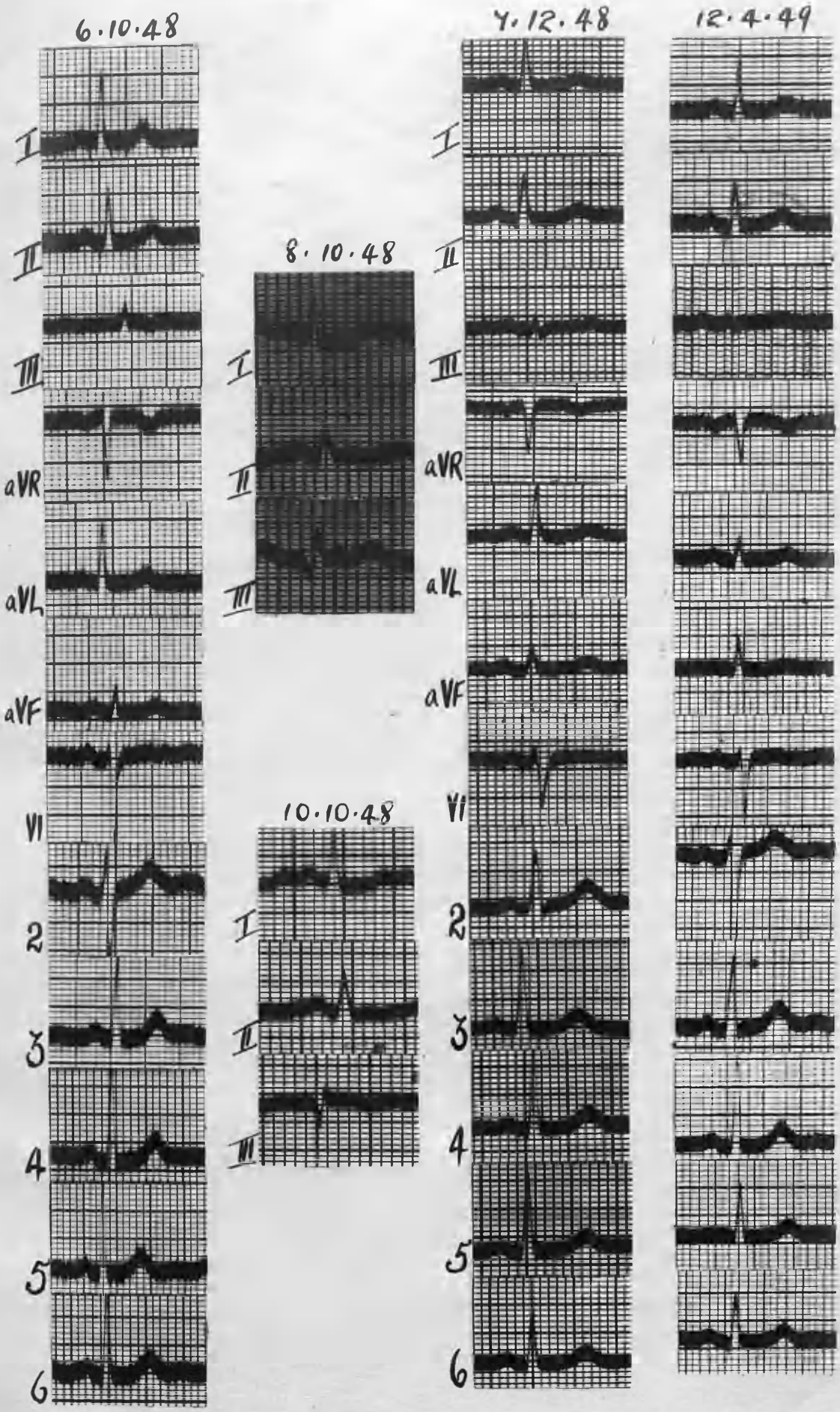
6.10.48
I
II
III
aVR
aVL
aVF
VI
2
3
4
5
6
8.10.48
I
II
III
10.10.48
I
II
III
4.12.48
I
II
III
aVR
aVL
aVF
VI
2
3
4
5
6
12.4.49

FIG. 14.

Fig. 15. : The pre-operative electrocardiogram,
Case No. 10. taken on 25.3.49, shows an inverted
T wave in VI and diphasic T wave in
V2 and V3.
The post-operative electrocardiogram,
taken on 9.4.49, following the
development of a pulmonary embolism,
shows inverted T waves in VI-4.
The electrocardiogram taken on
21.1.50, shows a return to the pre-
operative electrocardiogram of
25.3.49.
Note that the standard limb leads show
no significant change throughout.

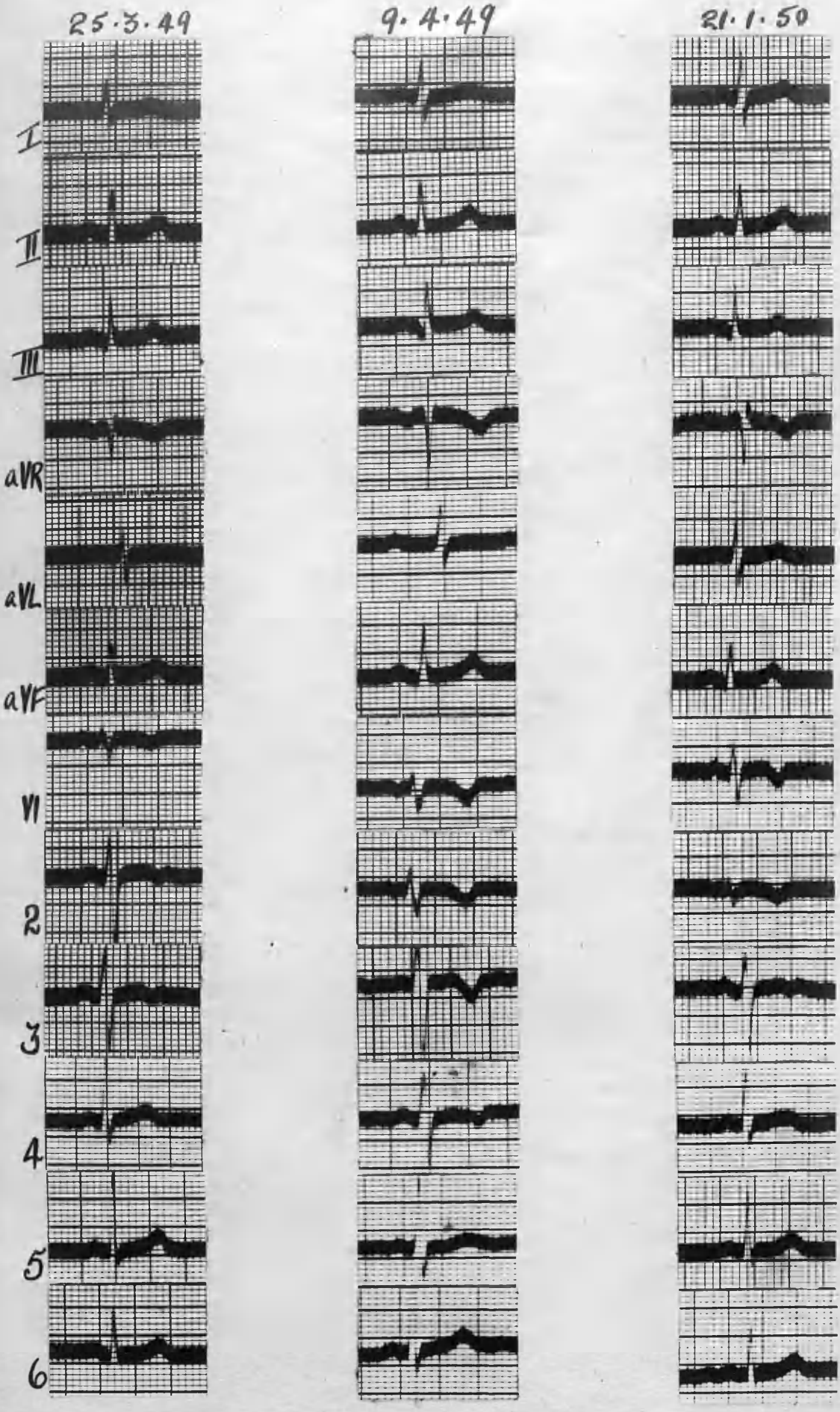

FIG. 15.

Fig. 16. : The first electrocardiogram, taken on
Case No. 47. 4.10.49, during an attack of biliary colic, shows left axis deviation with ST depression and diphasic T wave in Lead I. The electrocardiogram taken on 10.10.49, after the attack of biliary colic had subsided, shows T in lead I upright.

On 1.11.49 the patient had a severe attack of chest pain, diagnosed clinically as coronary occlusion. The electrocardiograms taken on 1.11.49 and 10.1.50 supported this diagnosis.

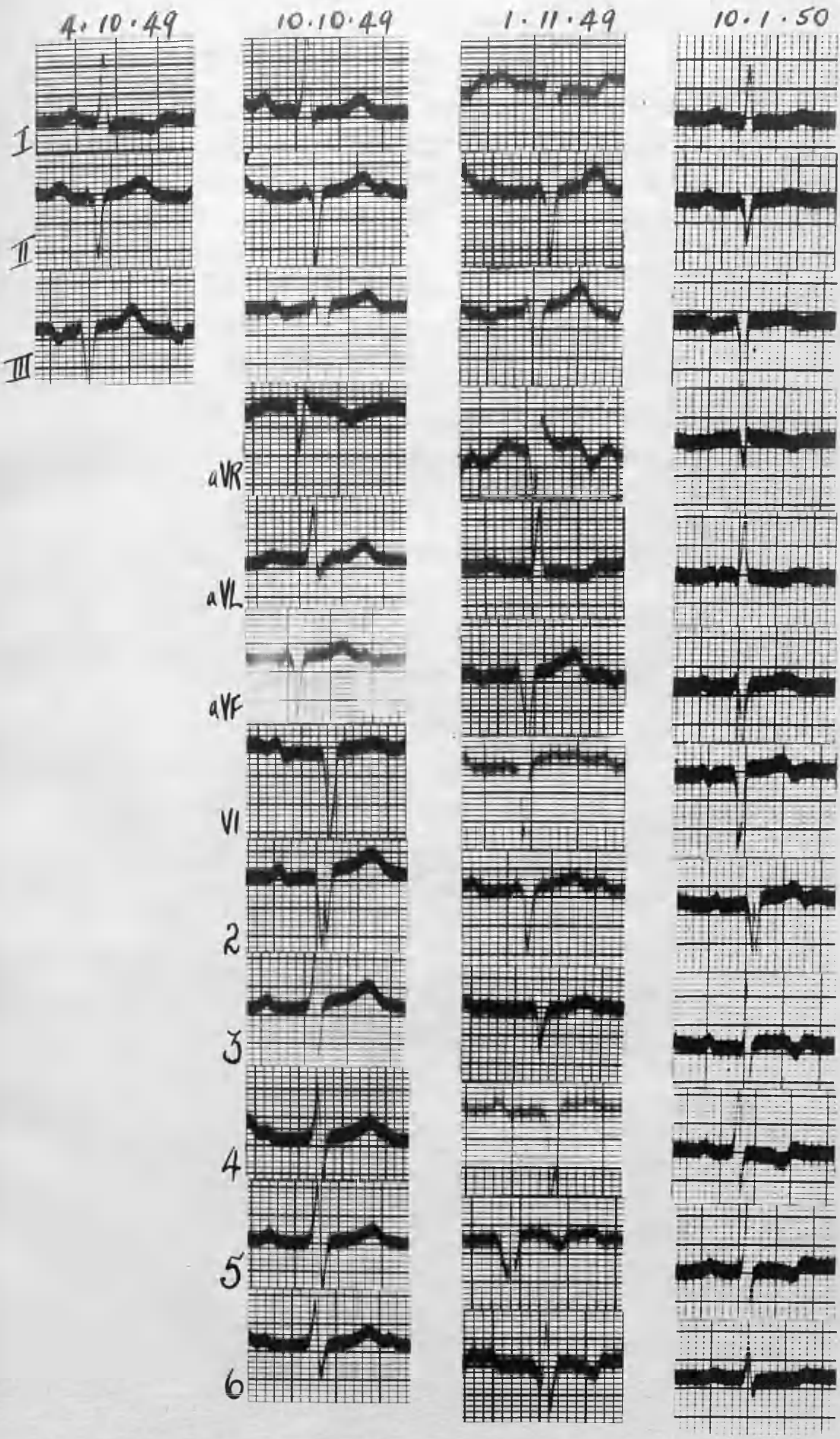

FIG. 16.

Fig. 17. : The first pre-operative electrocardiogram was taken on 5.10.43.

Case No. 1. The second pre-operative electrocardiogram, taken on 9.2.49, shows no significant change.

The post-operative electrocardiograms, taken on 10.3.49 and 25.4.49, show no significant change from the pre-operative electrocardiograms.

All the electrocardiograms are within normal limits.

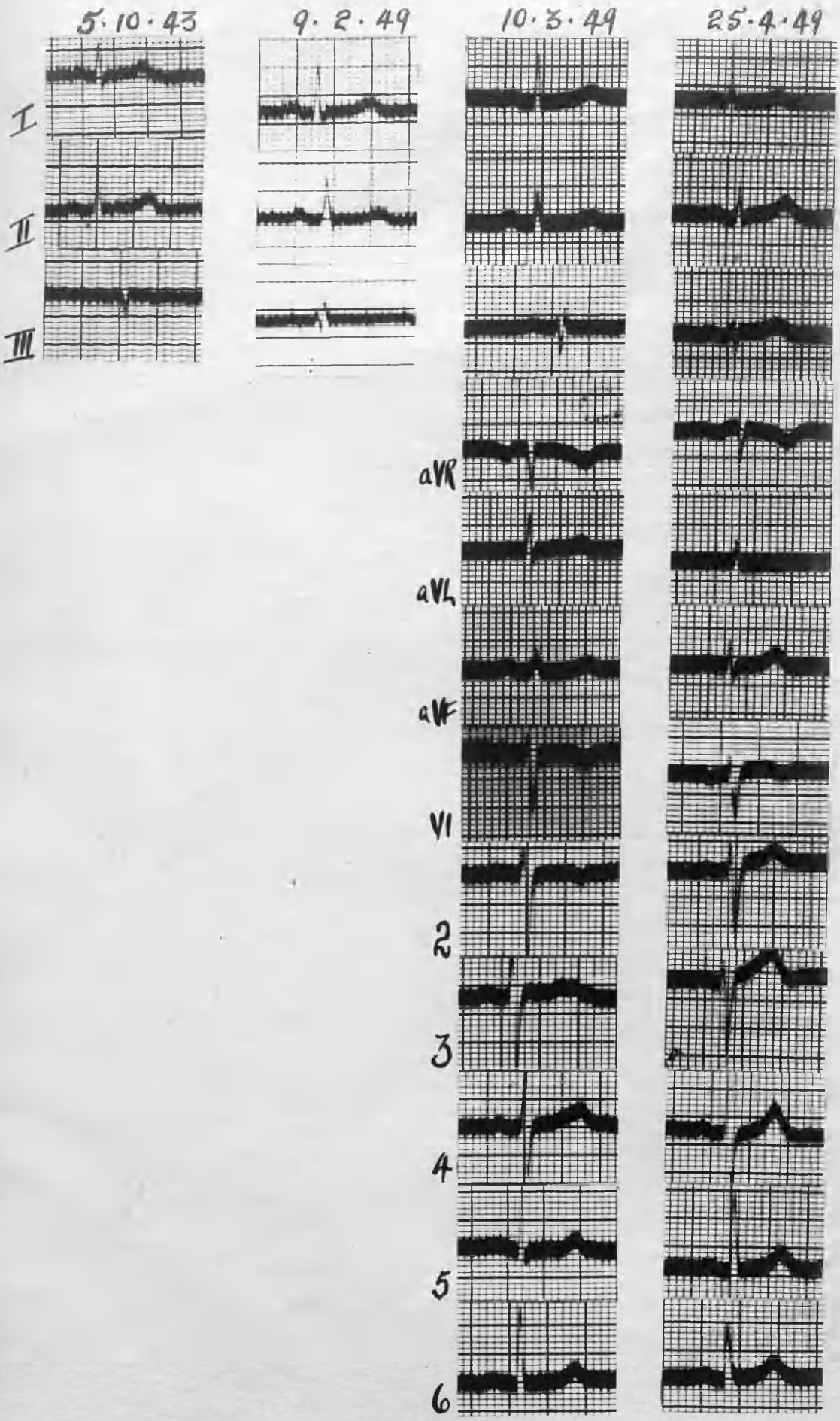

FIG: 17.

Fig. 18. : The pre-operative electrocardiogram,
Case No. 2. taken on 22.2.49, is within normal limits.

The post-operative electrocardiograms, taken on 12.5.49 and 7.11.49, show no significant change.

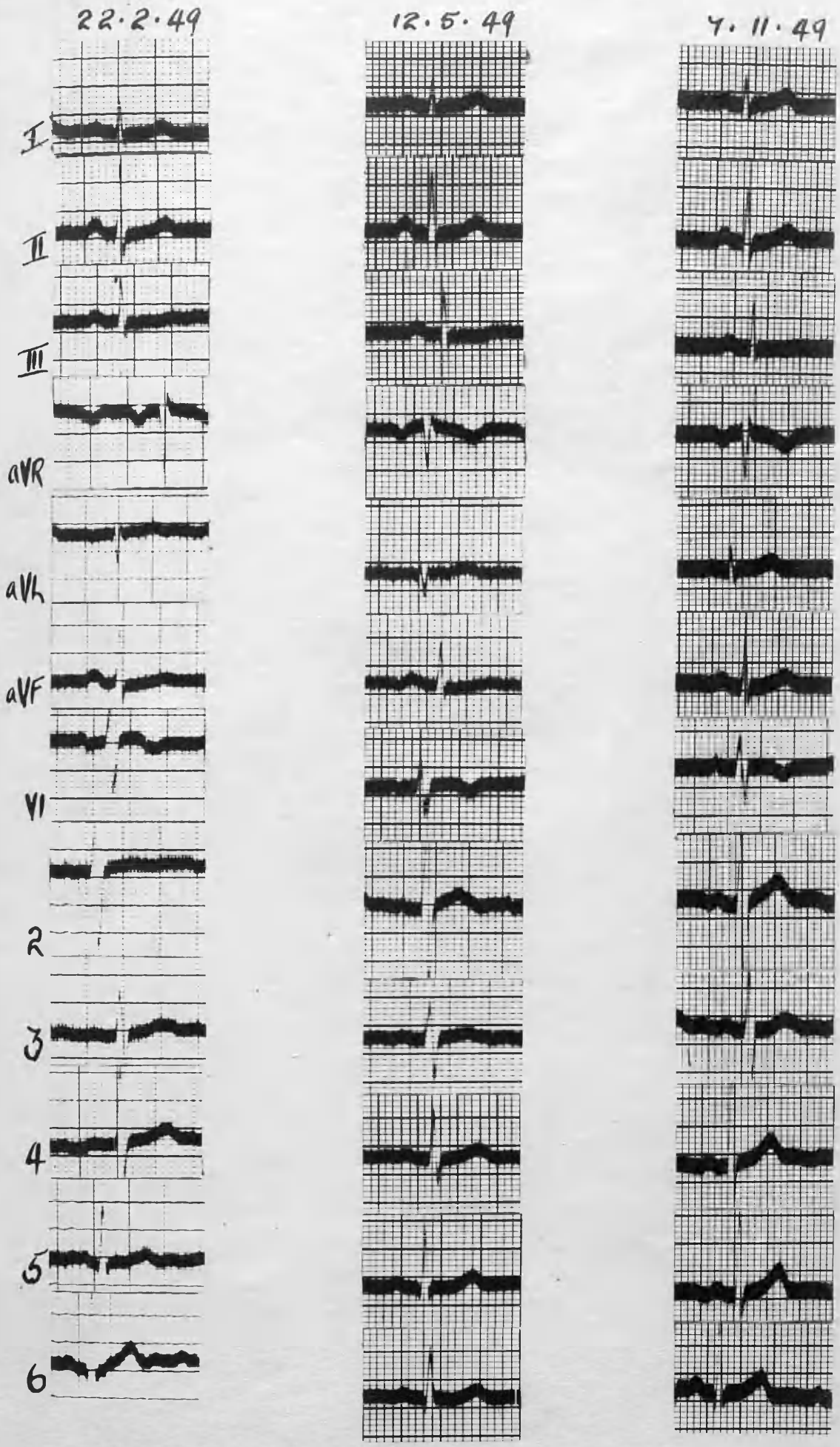

FIG. 18.

Fig. 19. : The pre-operative electrocardiogram,
Case No. 4. taken on 8.3.49, is within normal limits.

The post-operative electrocardiograms, taken on 5.4.49 and 10.1.50, show no significant change.

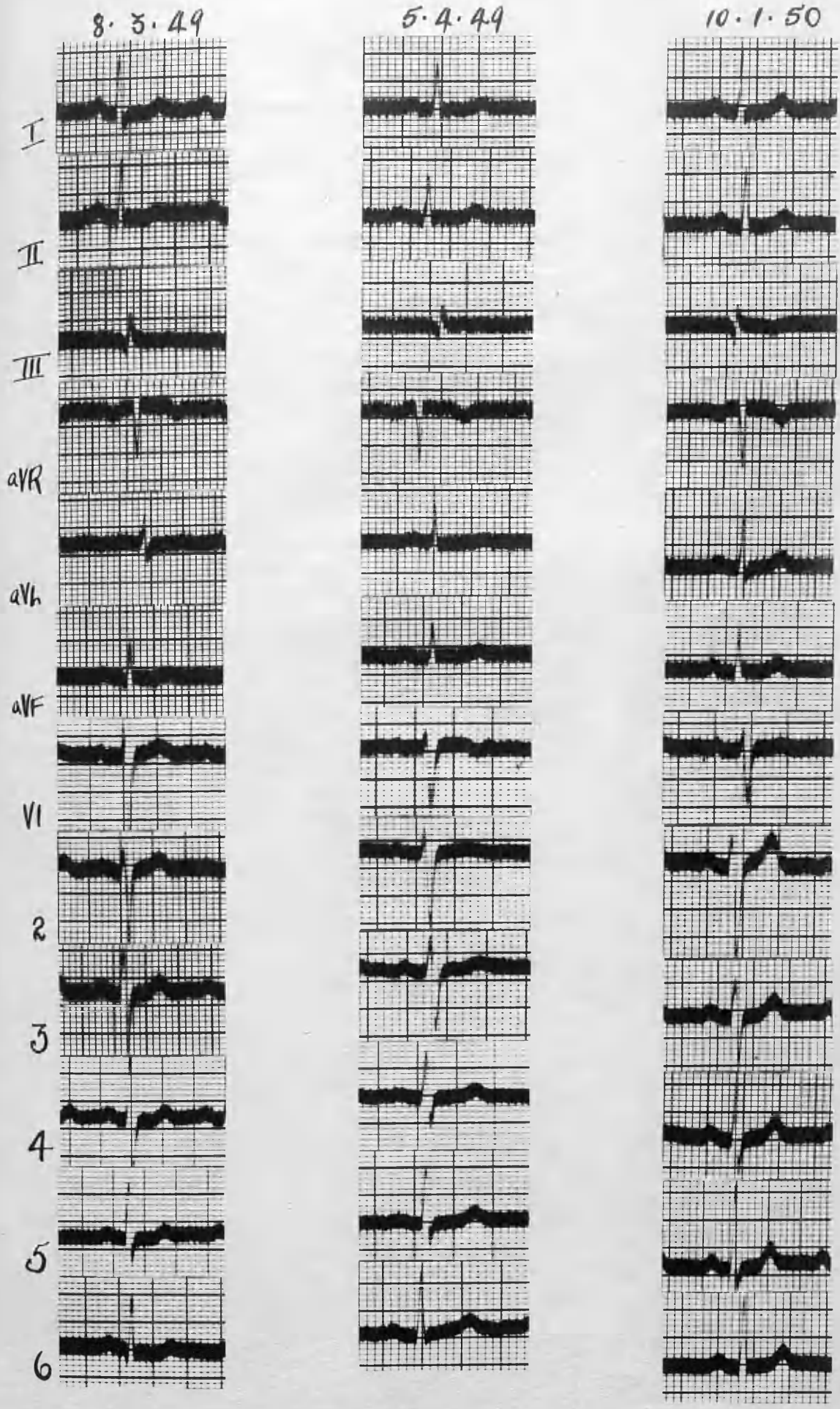

FIG. 19.

Fig. 20. Case No. 5. : The pre-operative electrocardiogram, taken on 2.5.49, shows "equivocal changes".

The post-operative electrocardiograms, taken on 16.5.49 and 30.1.50, show no significant change.

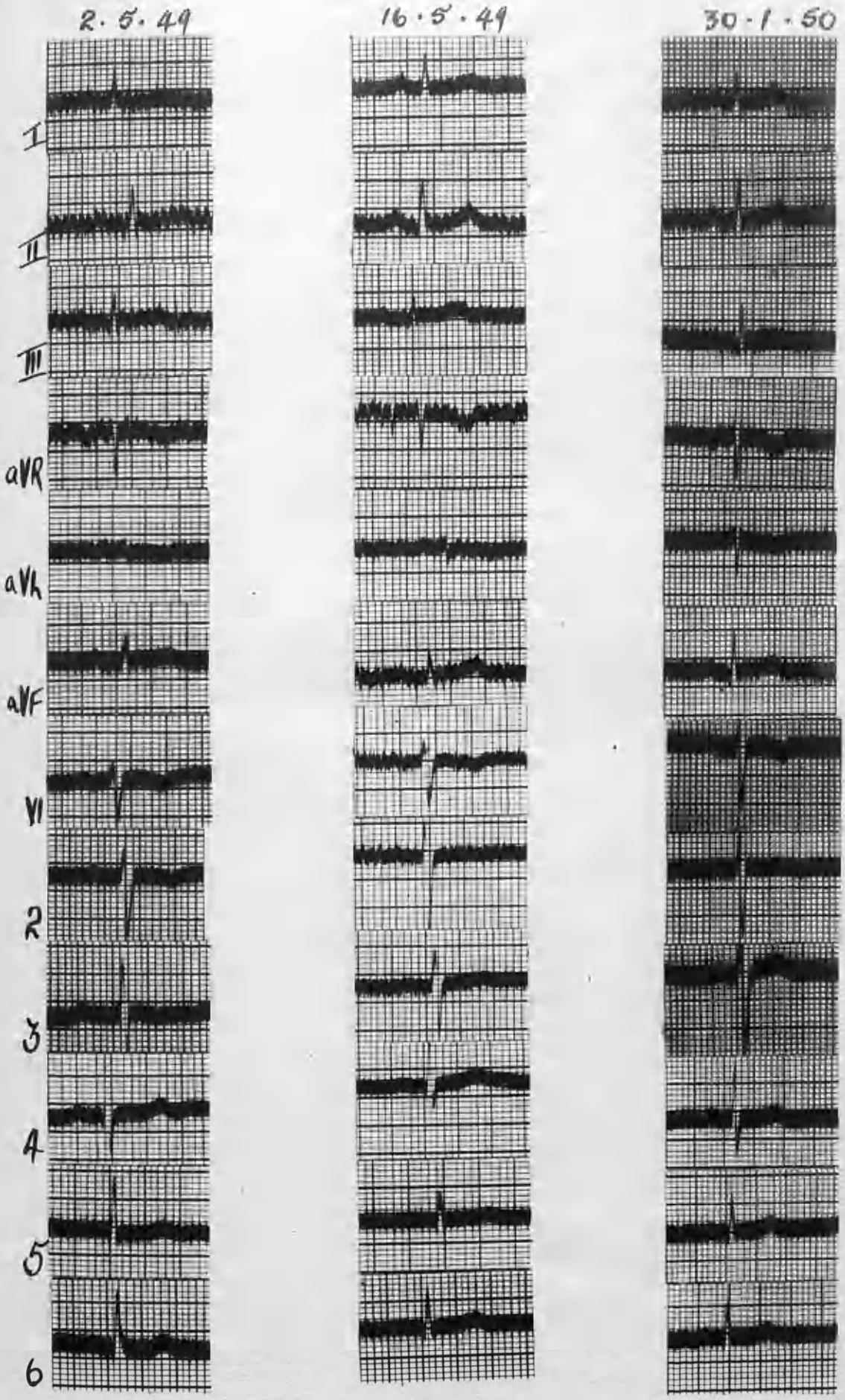

FIG.20.

Fig. 21. Case No. 6. : The pre-operative electrocardiogram, taken on 19.4.49, is within normal limits. The post-operative electrocardiograms, taken on 29.4.49 and 1.5.50, show no significant change.

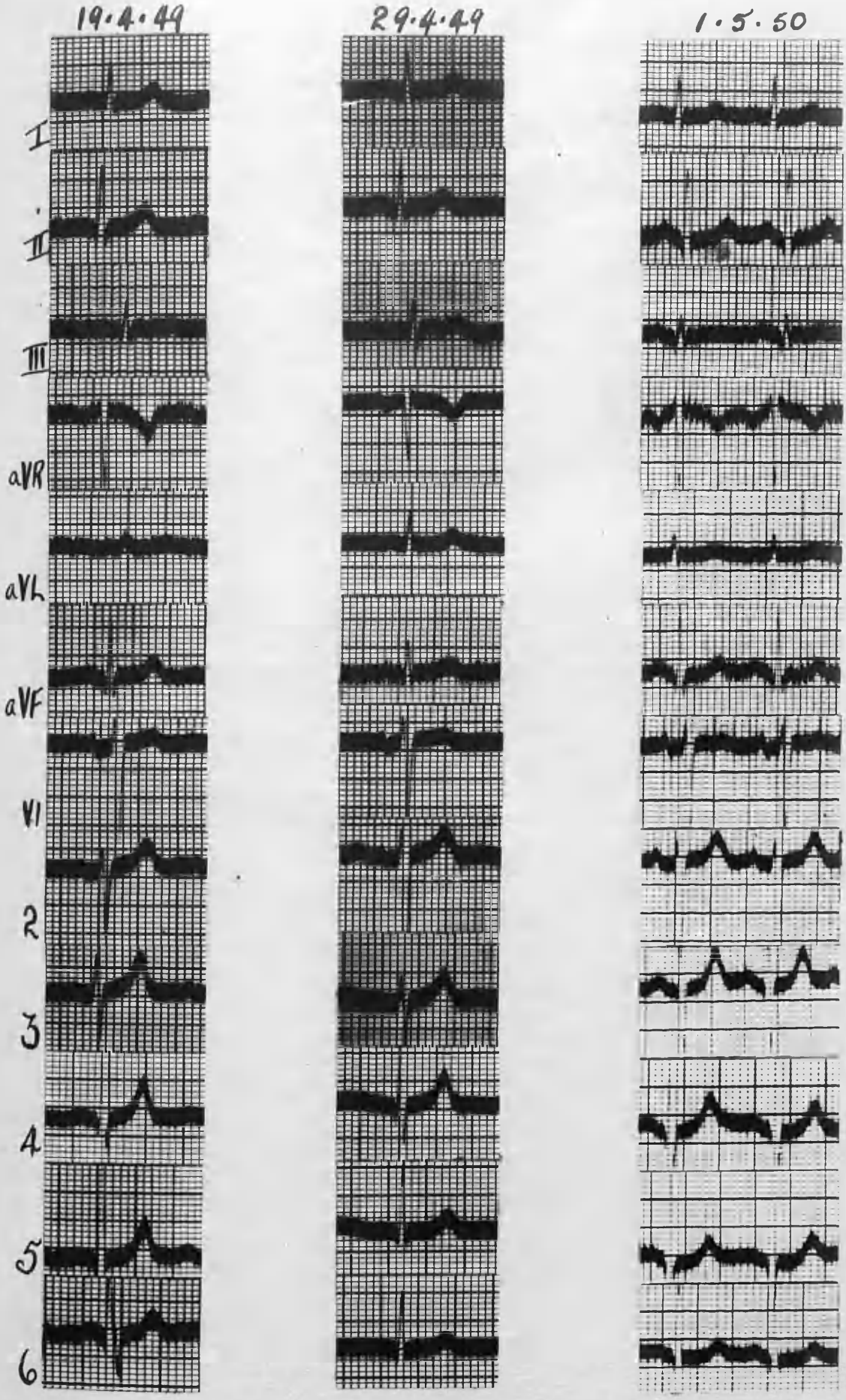

FIG. 21.

Fig. 22. Case No. 9. : The pre-operative electrocardiogram, taken on 28.1.49, is within normal limits.

The post-operative electrocardiograms, taken on 2.5.49 and 17.1.50, show no significant alteration, although there has been a change in the electrical axis of the heart (compare leads aVL and aVF).

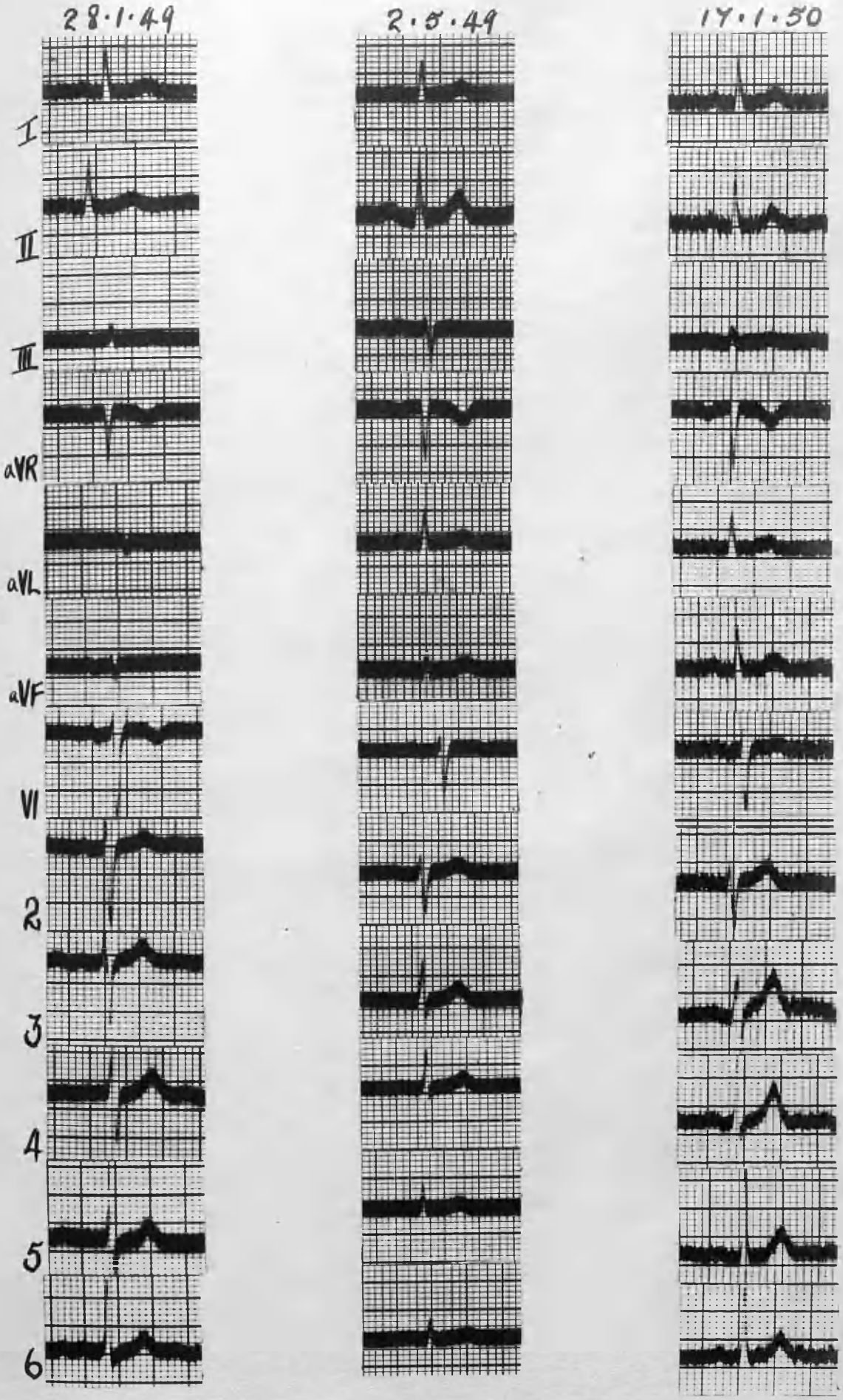

FIG. 22.

Fig. 23. Case No. 12. : The pre-operative electrocardiogram, taken on 4.11.49, shows splintering of R in lead I, QS in aVR, and R in aVL. The post-operative electrocardiogram, taken on 20.5.50, shows no significant change.

Fig. 24. Case No. 46. : The pre-operative electrocardiogram, taken on 6.1.49, shows changes suggestive of early left ventricular hypertrophy. The post-operative electrocardiogram, taken on 23.1.50, shows no significant change, although there has been a change in the electrical axis of the heart.

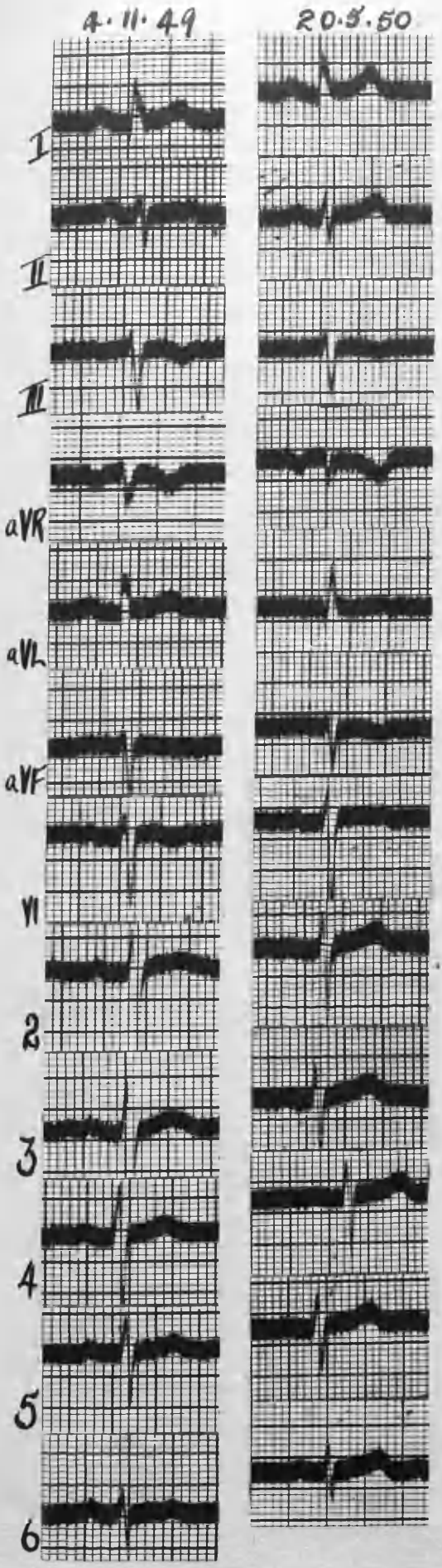
4·11·49
20·3·50
I
II
III
aVR
aVL
aVF
VI
2
3
4
5
6

FIG. 23

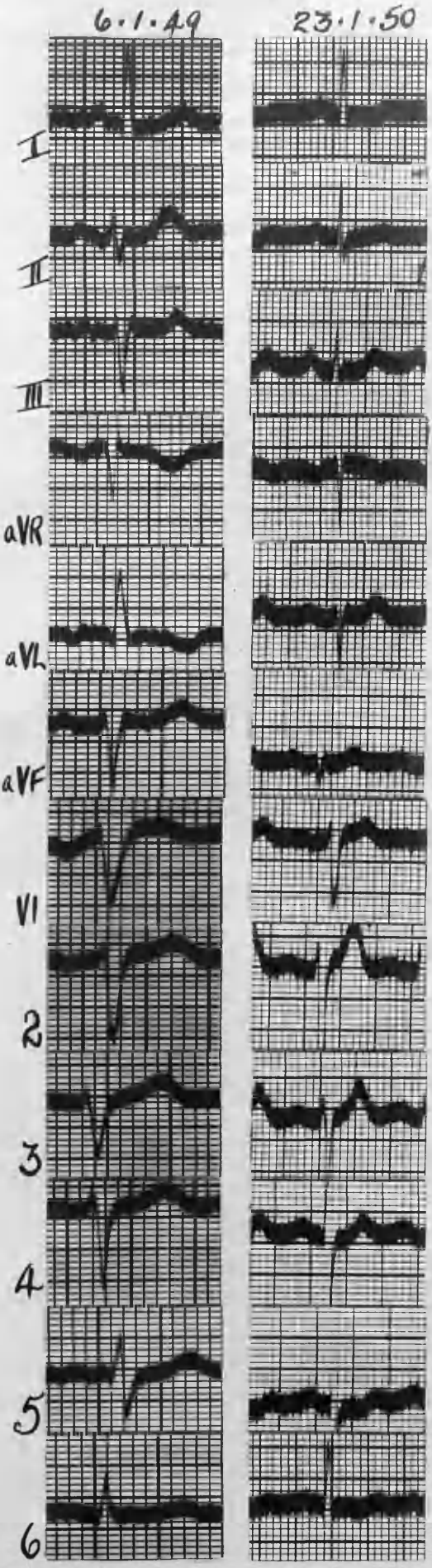
6·1·49
23·1·50
I
II
III
aVR
aVL
aVF
VI
2
3
4
5
6

FIG. 24.

Fig. 25. : The pre-operative electrocardiogram, taken on 19.2.49, was within normal limits. The post-operative electrocardiograms, taken on 8.3.49 and 17.11.49, show no significant change.

Case No. 15.

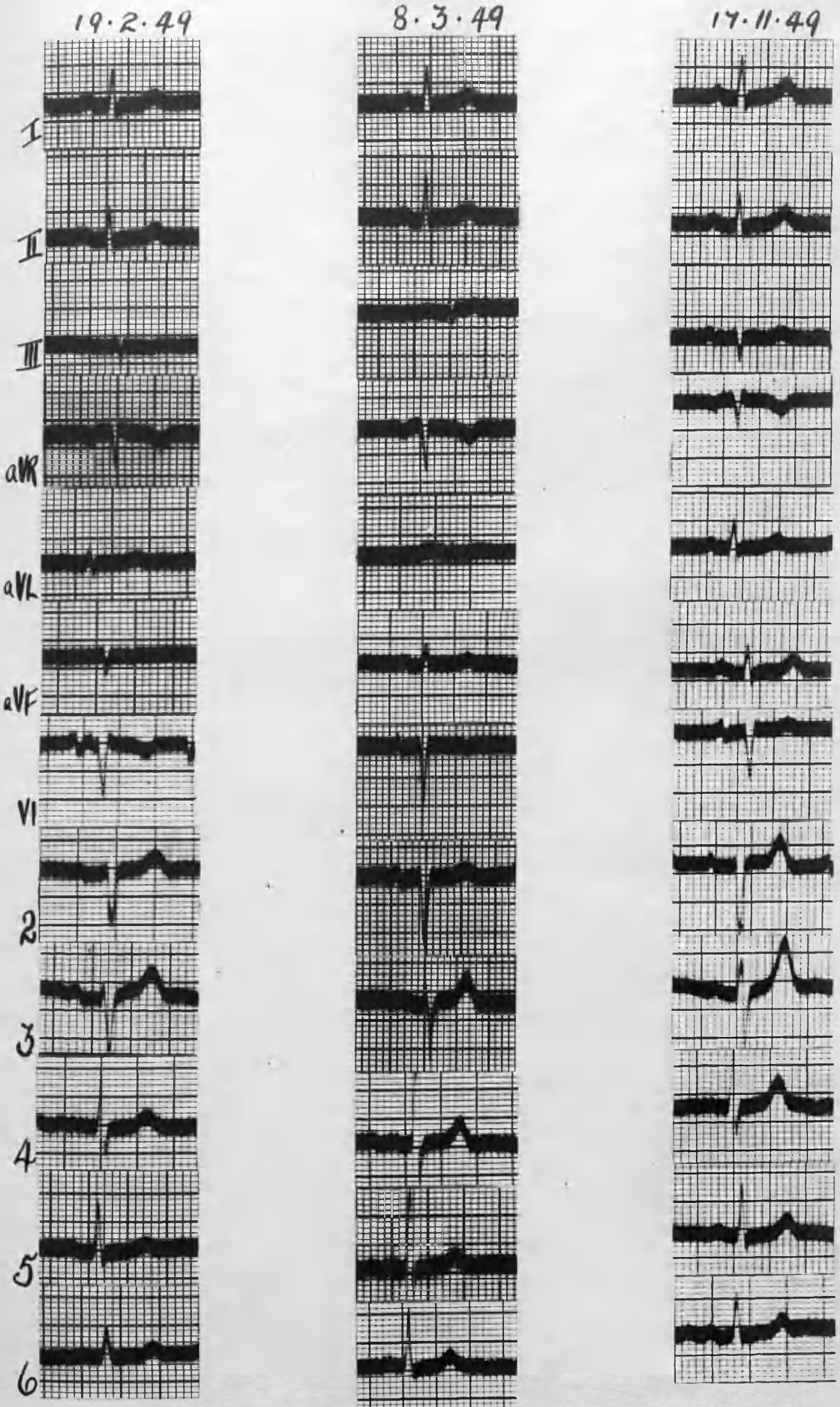

FIG. 25.

Fig. 26. Case No.18. : The pre-operative electrocardiogram, taken on 4.2.49, is within normal limits. The post-operative electrocardiograms, taken on 23.2.49 and 19.11.49, show no significant change.

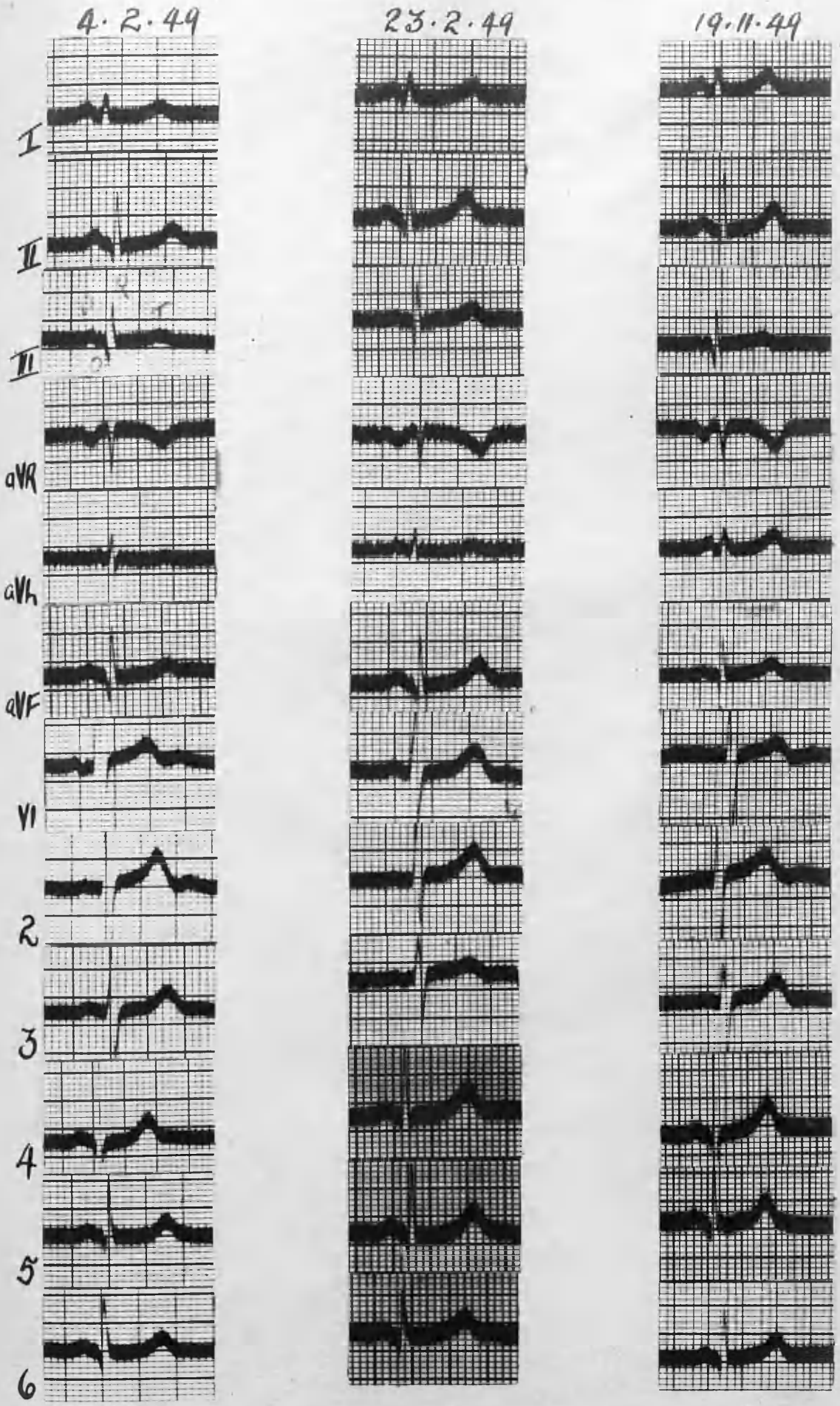

FIG. 26.

Fig. 27, Case No. 24. : The pre-operative electrocardiogram, taken on 14.12.48 is within normal limits.

The post-operative electrocardiograms, taken on 1.2.49 and 13.6.49, show no significant change.

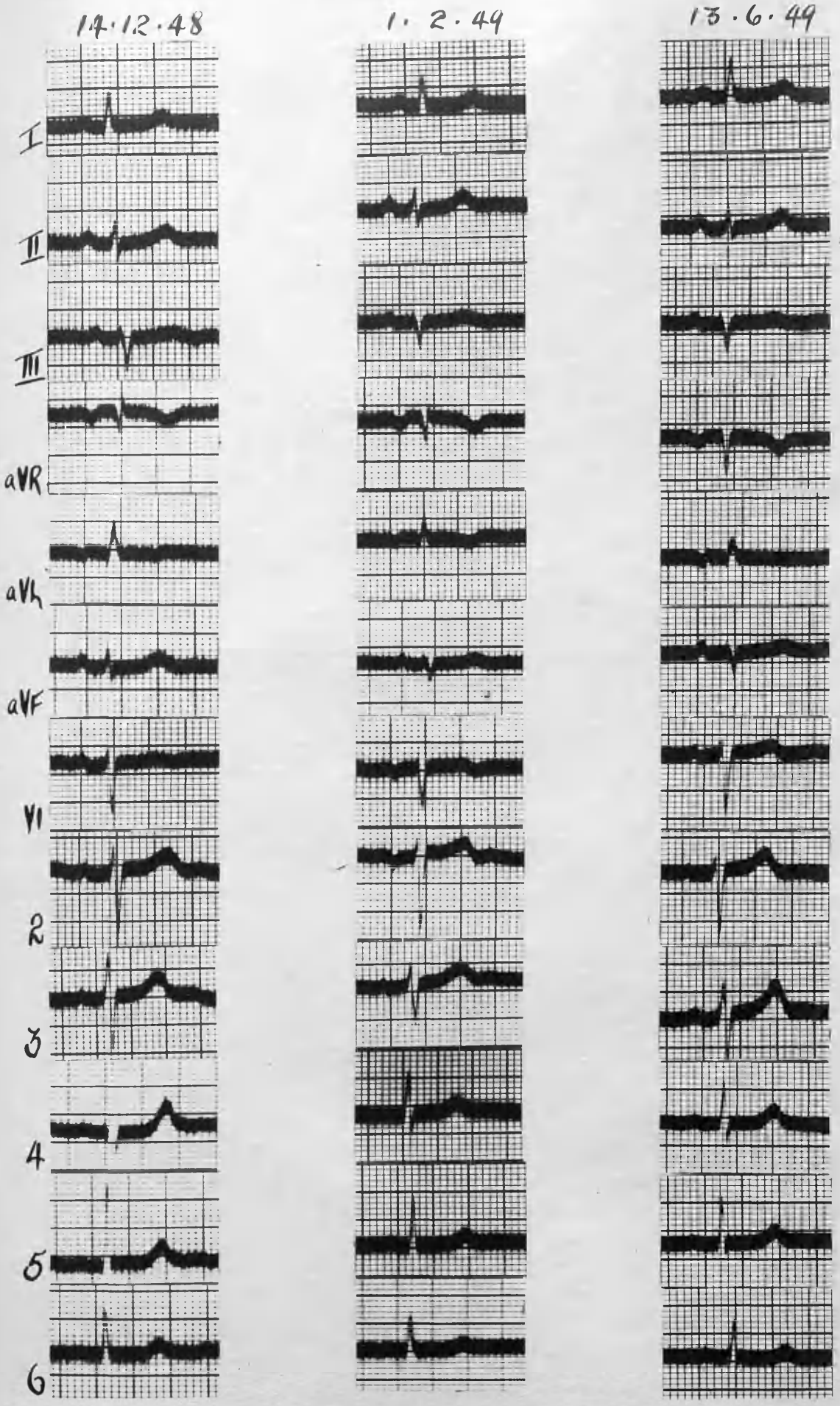

FIG.27.

Fig. 28. : The pre-operative electrocardiogram,
Case No. 21. taken on 9.1.49, is within normal limits.

The post-operative electrocardiograms, taken on 20.1.49 and 8.7.49, show no significant change.

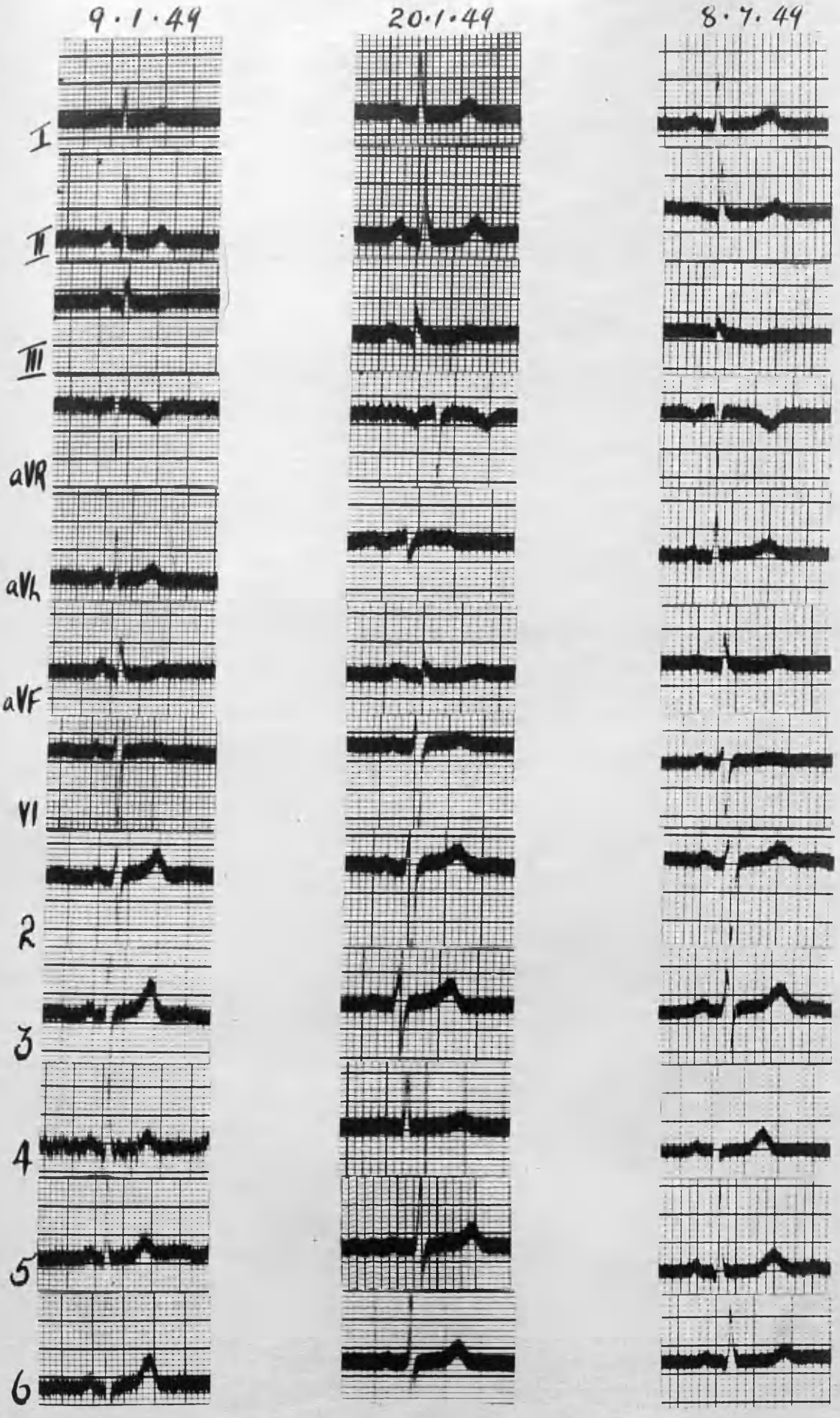

FIG. 28

Fig. 29. Case No. 23. : The pre-operative electrocardiogram, taken on 12.10.48, is within normal limits.

The post-operative electrocardiogram, taken on 27.4.49 shows no significant change.

Fig. 30. Case No. 30. : The pre-operative electrocardiogram, taken on 13.4.48, is within normal limits.

The post-operative electrocardiogram, taken on 30.4.49, shows no significant change.

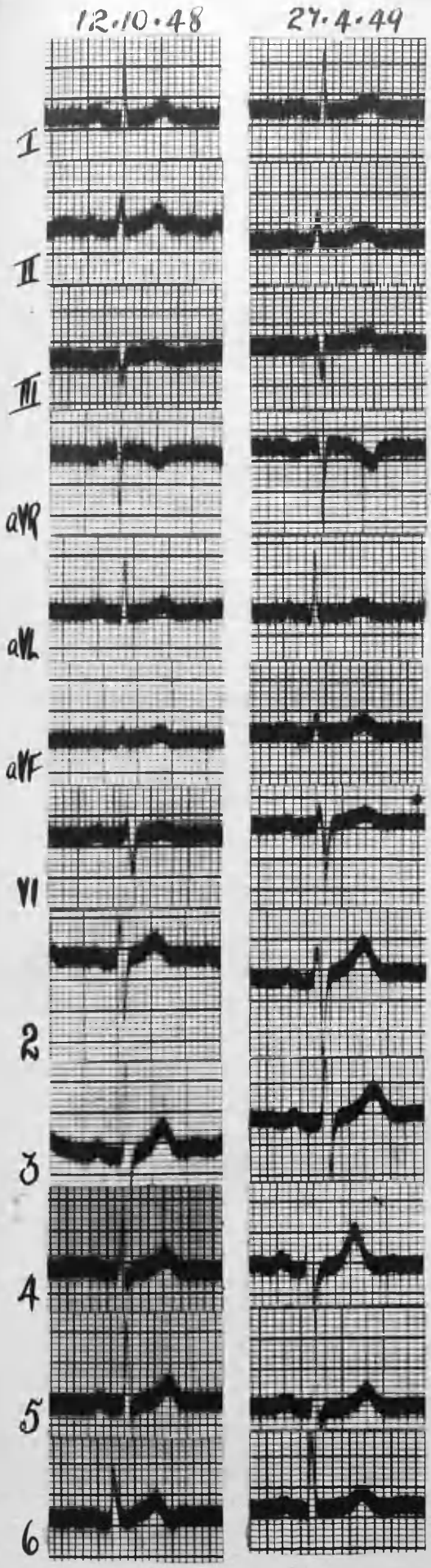
12.10.48
27.4.49
I
II
III
aVR
aVL
aVF
V1
2
3
4
5
6

Fig. 29.

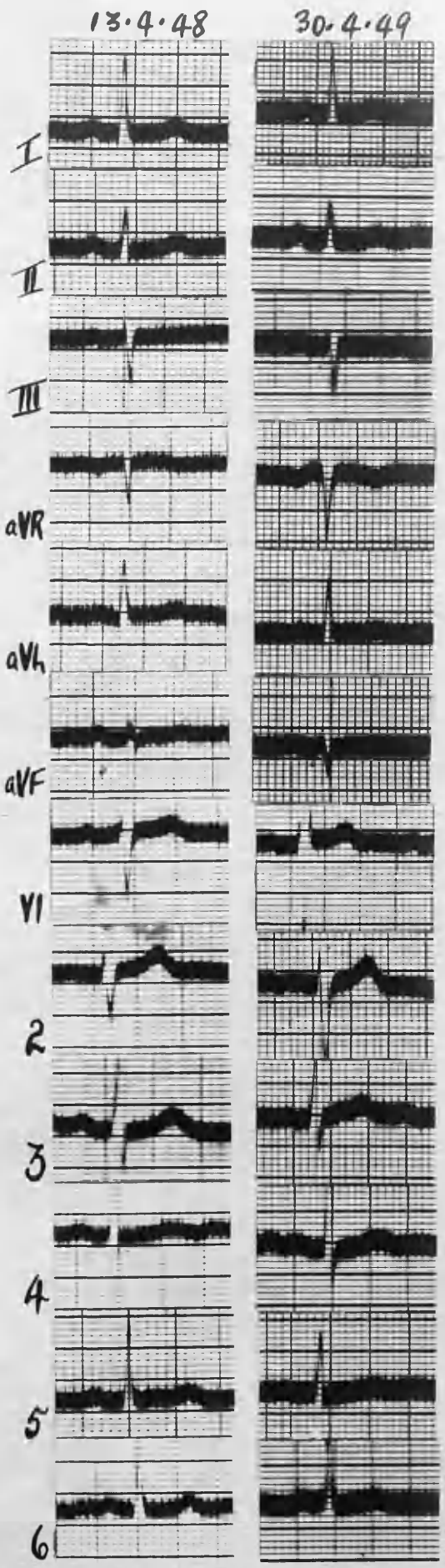
13.4.48
30.4.49
I
II
III
aVR
aVL
aVF
V1
2
3
4
5
6

Fig. 30.

Fig. 31. Case No. 24. : The pre-operative electrocardiogram, taken on 5.3.49, is within normal limits.

The post-operative electrocardiograms, taken on 19.3.49 and 14.11.49, show no significant change.

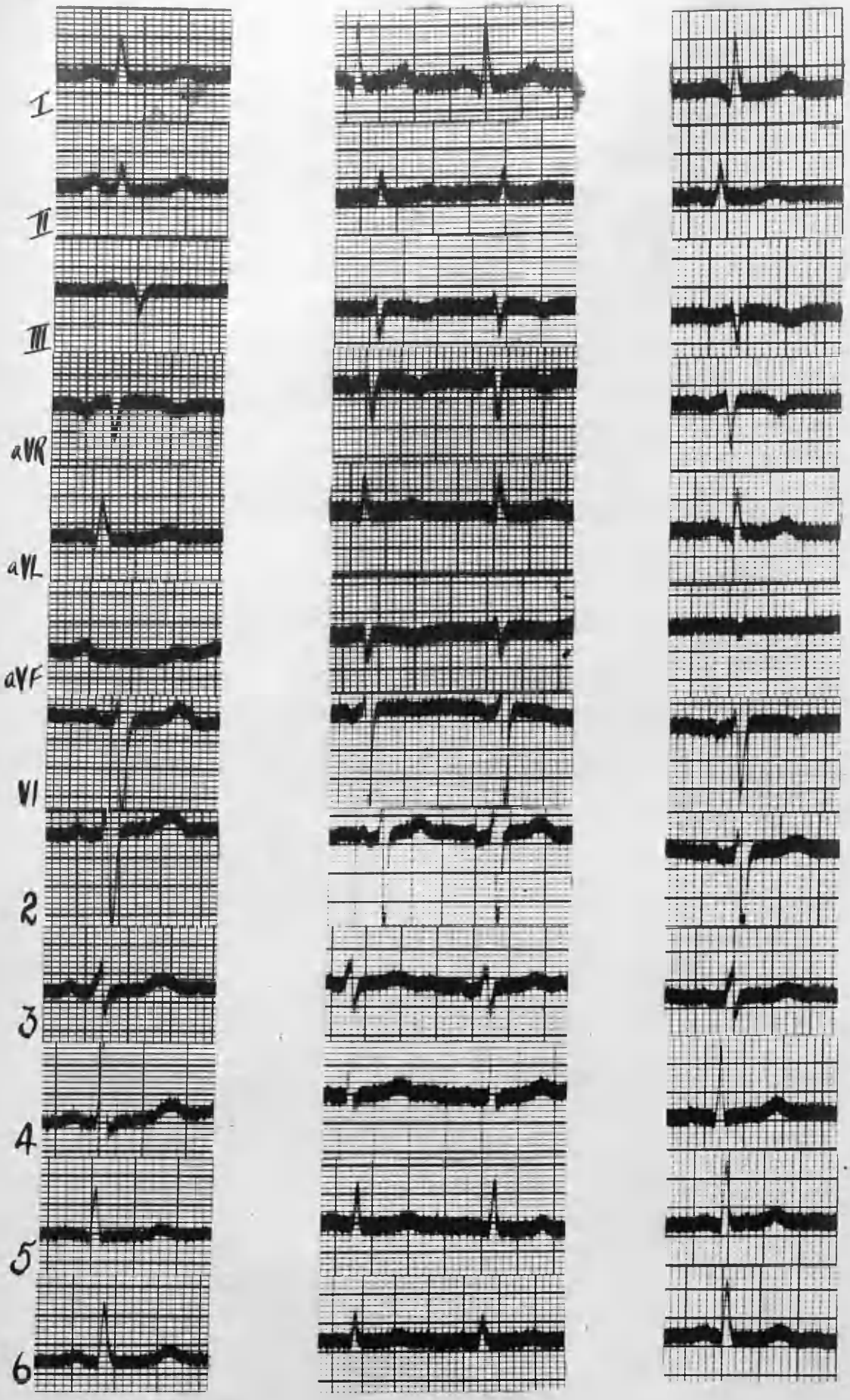

FIG. 31.

Fig. 32. : The pre-operative electrocardiogram,
Case No. 25. taken on 18.1.49, shows a Q wave and an inverted T wave in lead III, and aVF.

The post-operative electrocardiogram, taken on 1.2.49, shows an upright T wave in lead III and aVF, but an inverted T wave in VI, and diphasic T wave in lead V2. By 11.7.49 the standard limb leads had reverted to their pre-operative pattern, but the unipolar limb leads showed a change of electrical axis of the heart.

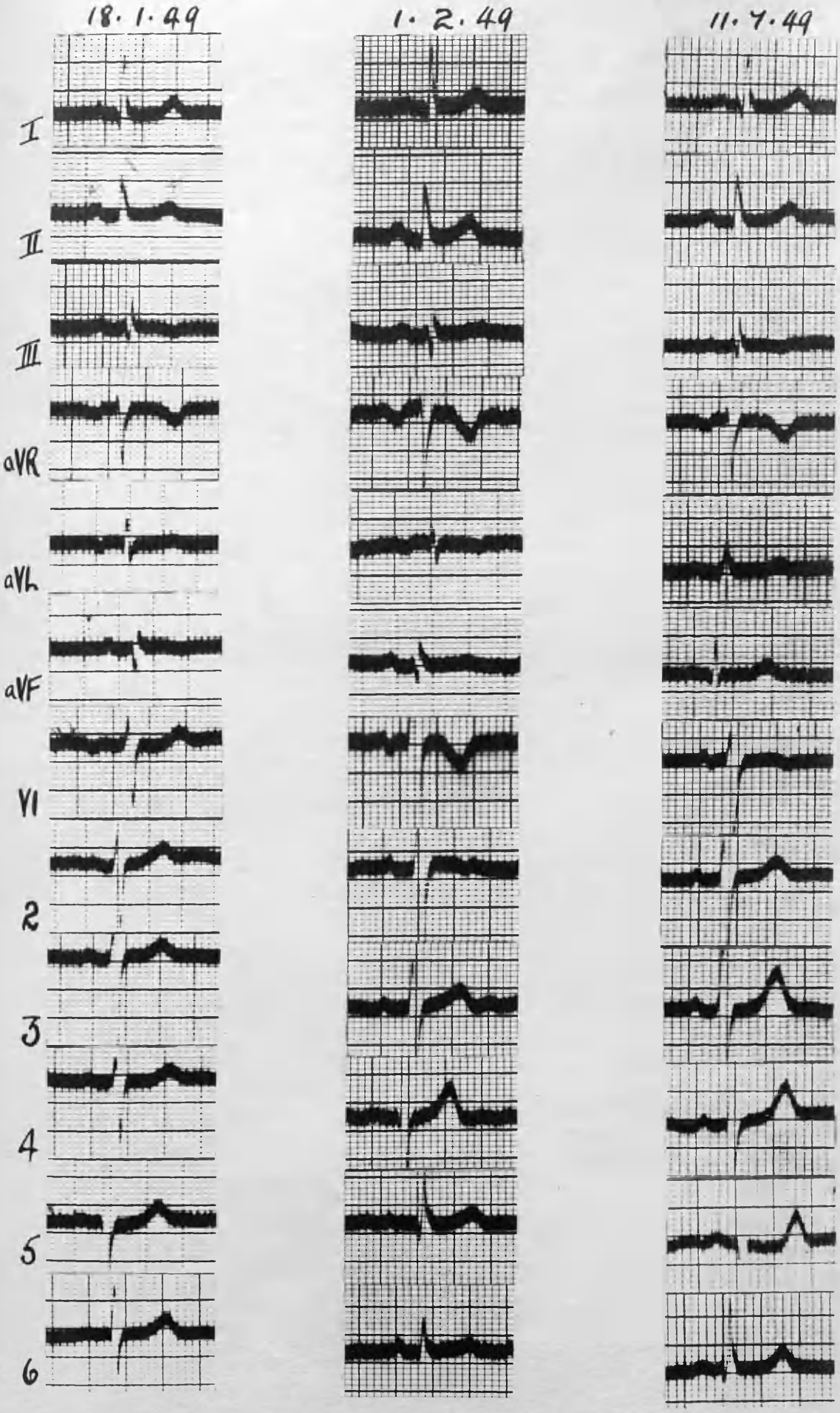

FIG. 32.

Fig. 33. : The pre-operative electrocardiogram,
Case No. 26. taken on 1.10.49, is within normal limits.

The post-operative electrocardiograms, taken on 21.10.49 and 10.1.50, show no significant change.

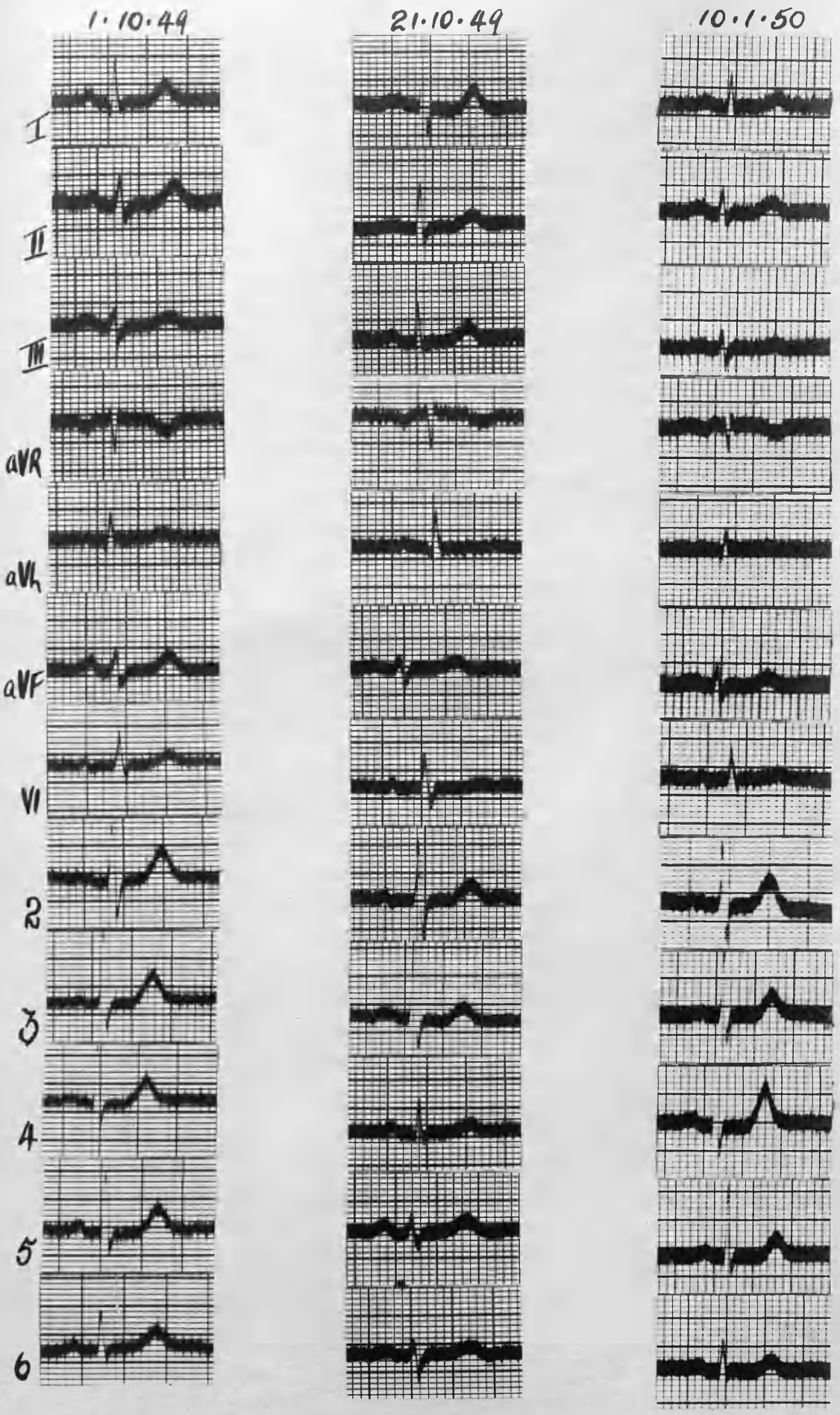

FIG. 33.

Fig. 34. : The pre-operative electrocardiogram,
Case No. 27. taken on 7.2.49, is within normal limits.

The post-operative electrocardiograms, taken on 3.3.49 and 10.8.49, show no significant change.

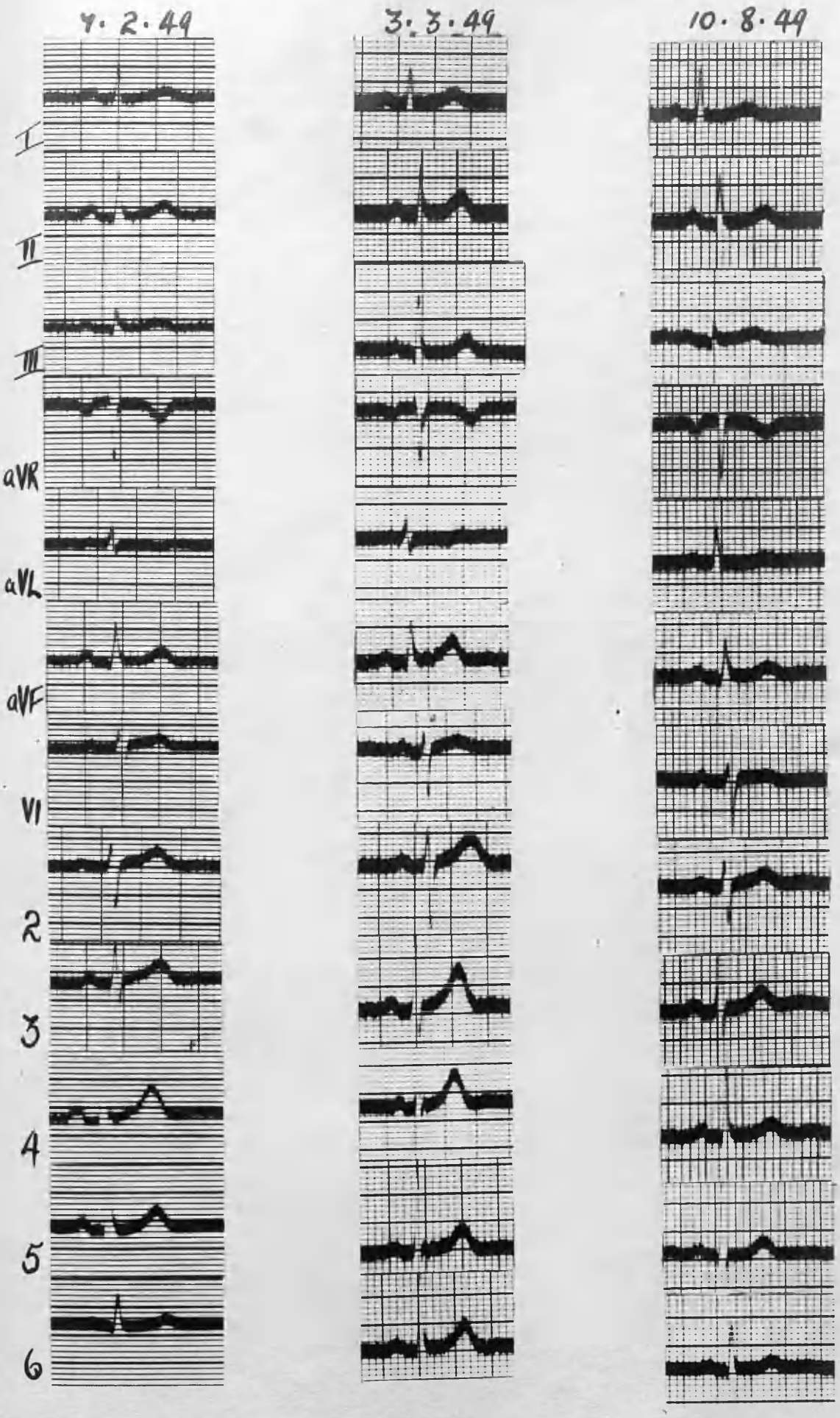

FIG.34.

Fig. 35. : The pre-operative electrocardiogram, taken on 27.2.49, is within normal limits. The post-operative electrocardiograms, taken on 31.3.49 and 24.1.50, show no significant change.

Case No. 29.

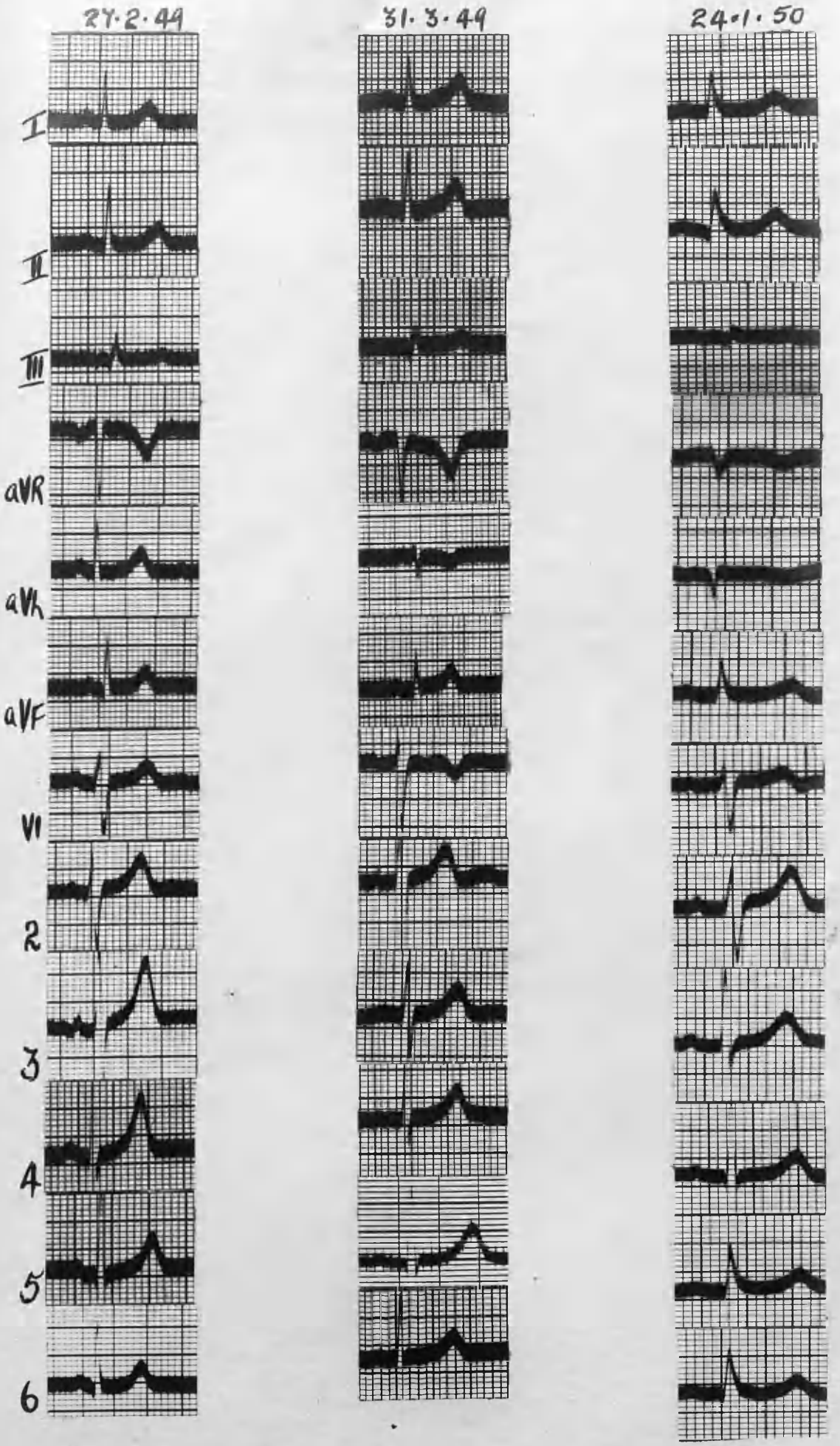

Fig. 35.

Fig. 36. Case No. 33. : The pre-operative electrocardiogram, taken on 23.7.49, is within normal limits.

The post-operative electrocardiogram, taken on 17.1.50, shows no significant change.

Fig. 37. Case No. 16. : The pre-operative electrocardiogram, taken on 9.1.49, is within normal limits.

The post-operative electrocardiogram, taken on 17.1.50, shows no significant change.

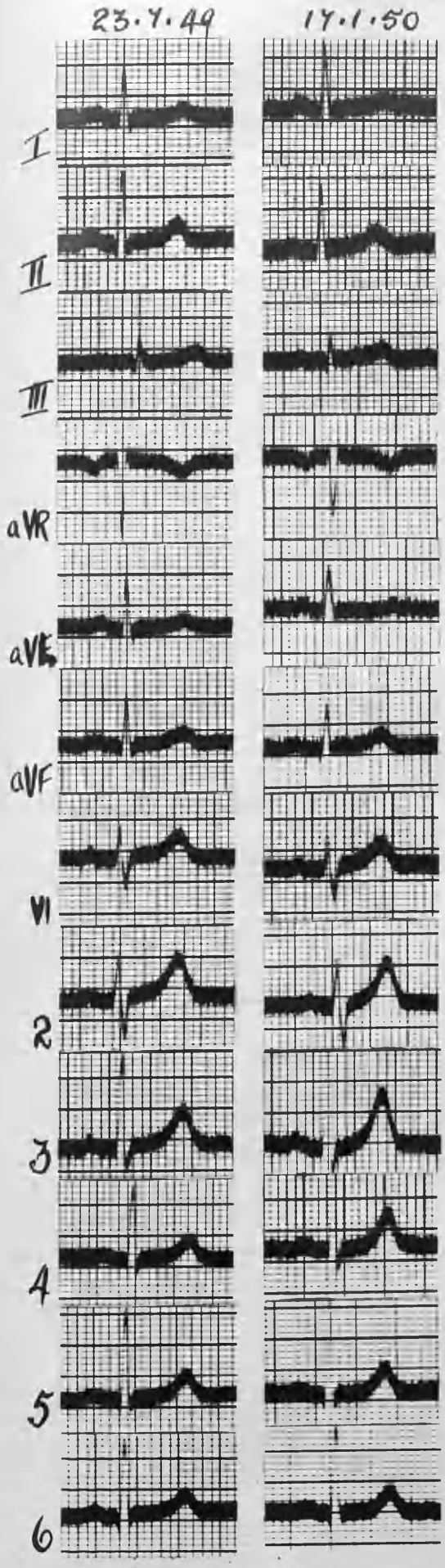
23.7.49
17.1.50
I
II
III
aVR
aVL
aVF
VI
2
3
4
5
6

FIG. 36.

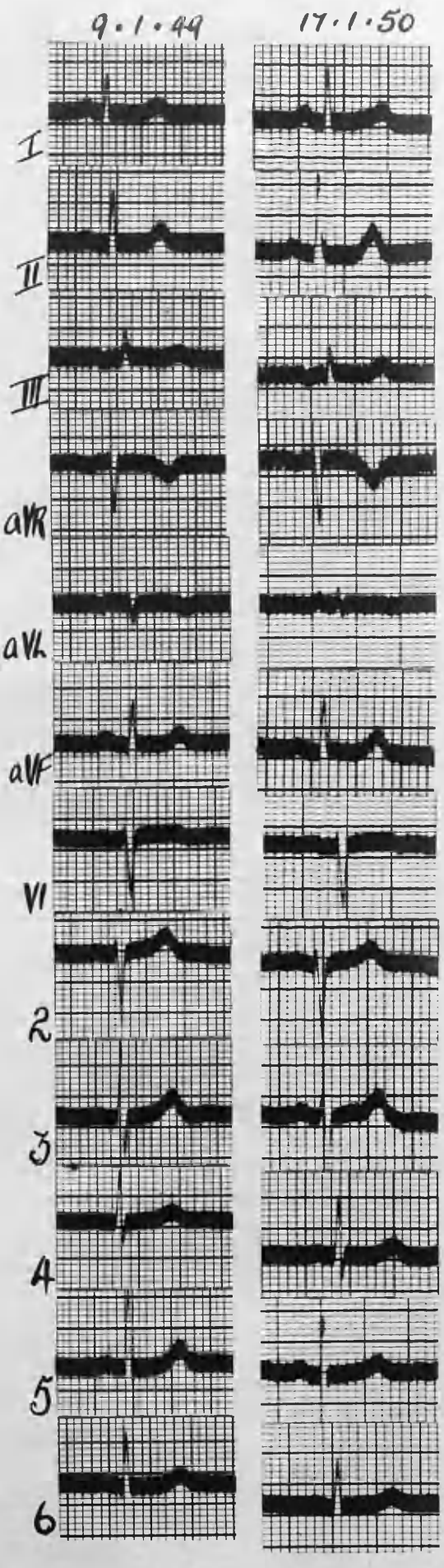
9.1.49
17.1.50
I
II
III
aVR
aVL
aVF
VI
2
3
4
5
6

FIG. 37.

Fig. 38. Case No. 34. : The pre-operative electrocardiogram, taken on 21.10.48, is within normal limits.

The post-operative electrocardiograms, taken on 7.7.49 and 7.9.49, show no significant change.

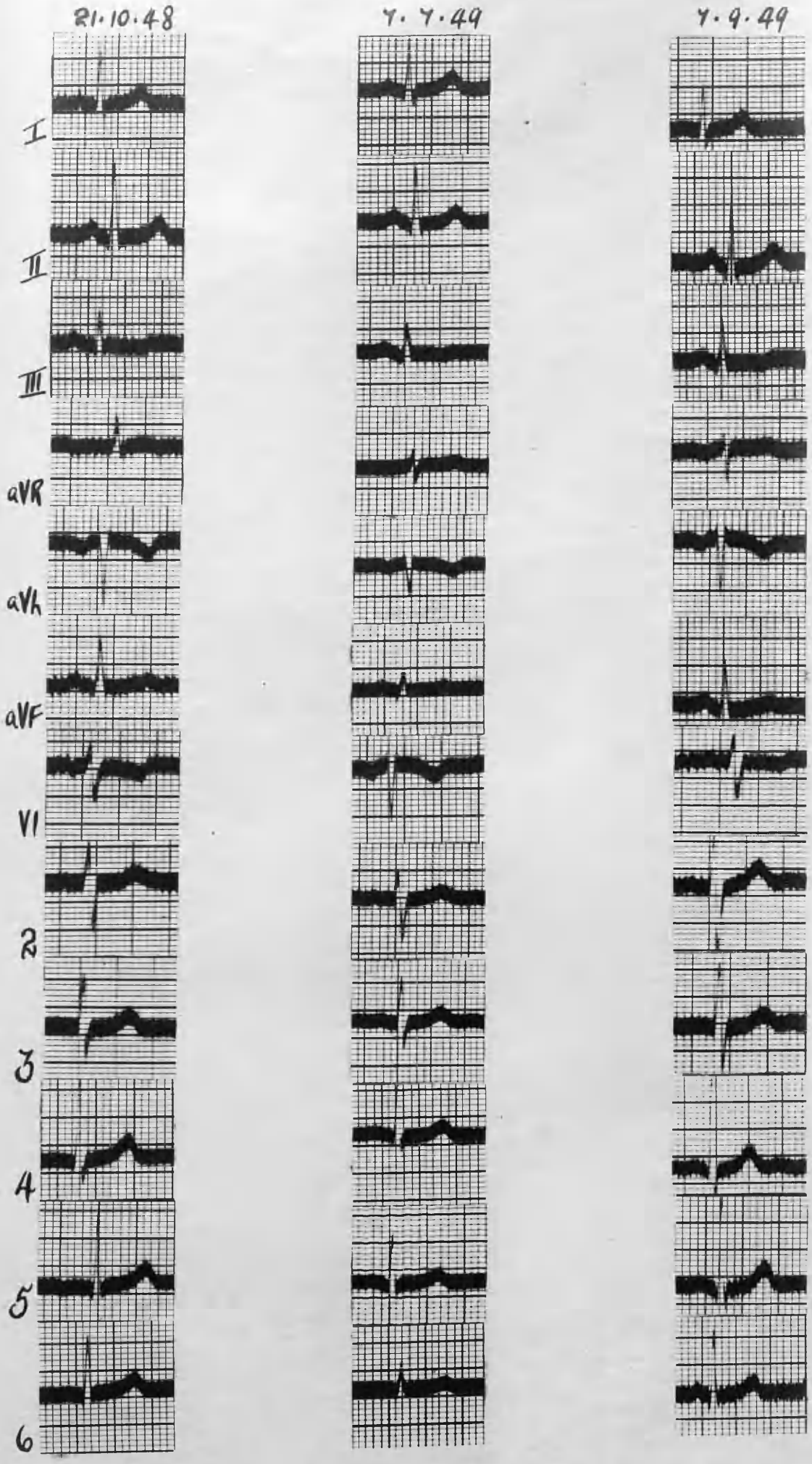

FIG.38.

Fig. 39. : The pre-operative electrocardiogram,
Case No. 37. taken on 5.3.49, is within normal limits.

The post-operative electrocardiograms, taken on 19.3.49 and 14.11.49, show no significant change.

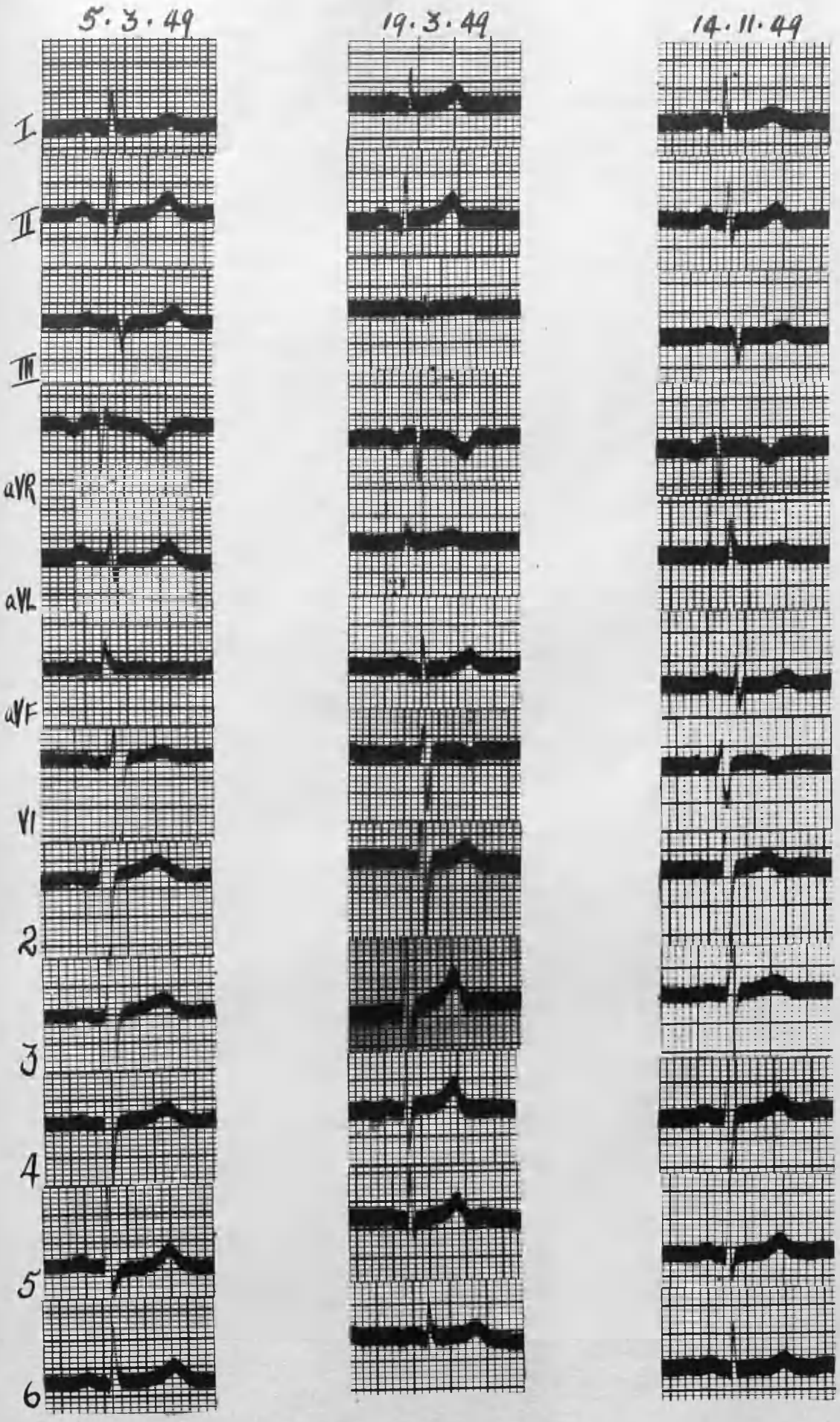

FIG. 39.

Fig. 40. : The pre-operative electrocardiogram,
Case No. 38. taken on 4.1.49, is within normal limits. The post-operative electrocardiogram, taken on 28.2.49 and 8.7.49, show no significant change.

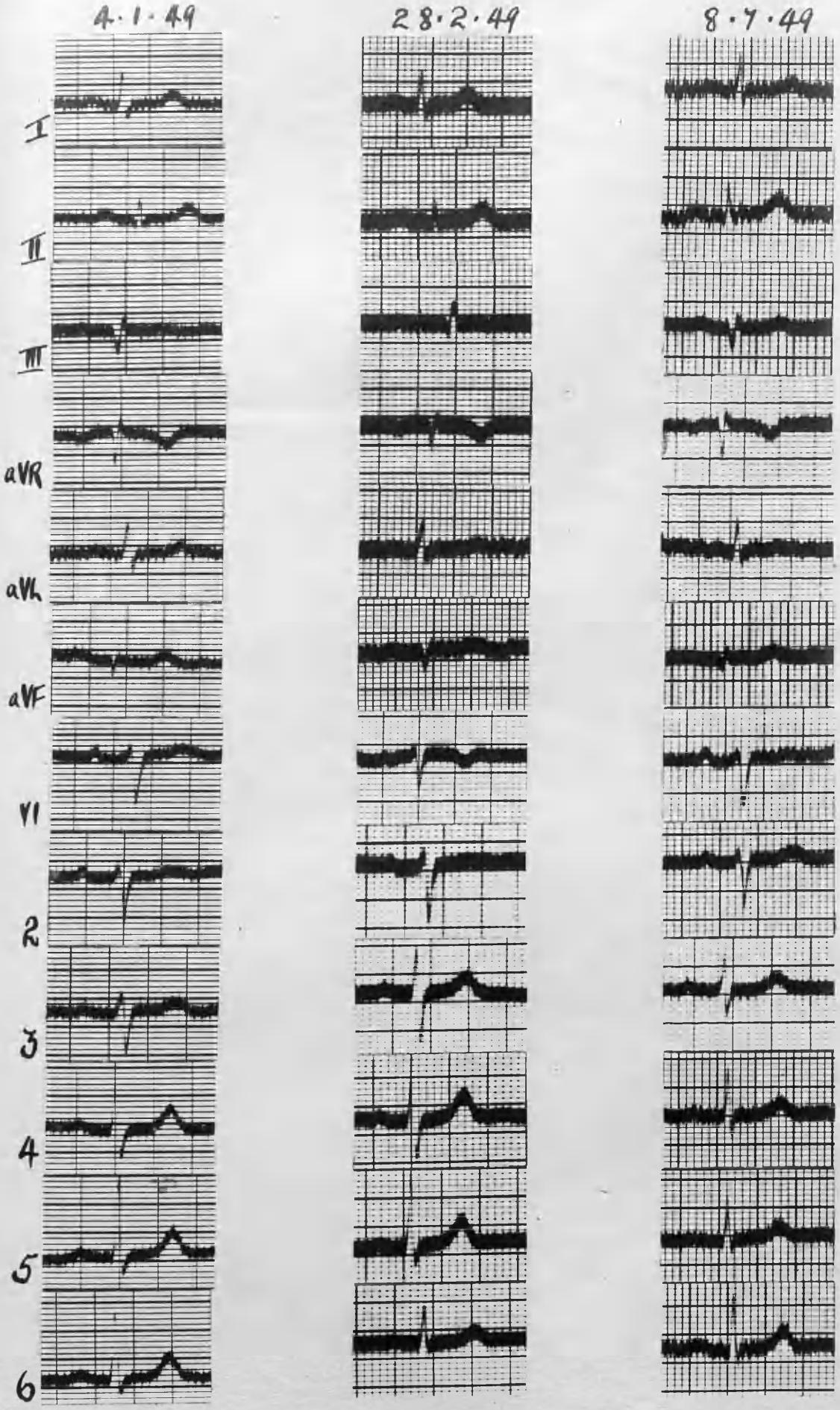

FIG. 40.

Fig. 41. : The pre-operative electrocardiogram,
Case No. 39. taken on 7.1.49, is within normal limits.

The post-operative electrocardiograms, taken on 12.4.49 and 25.7.49, show no significant change.

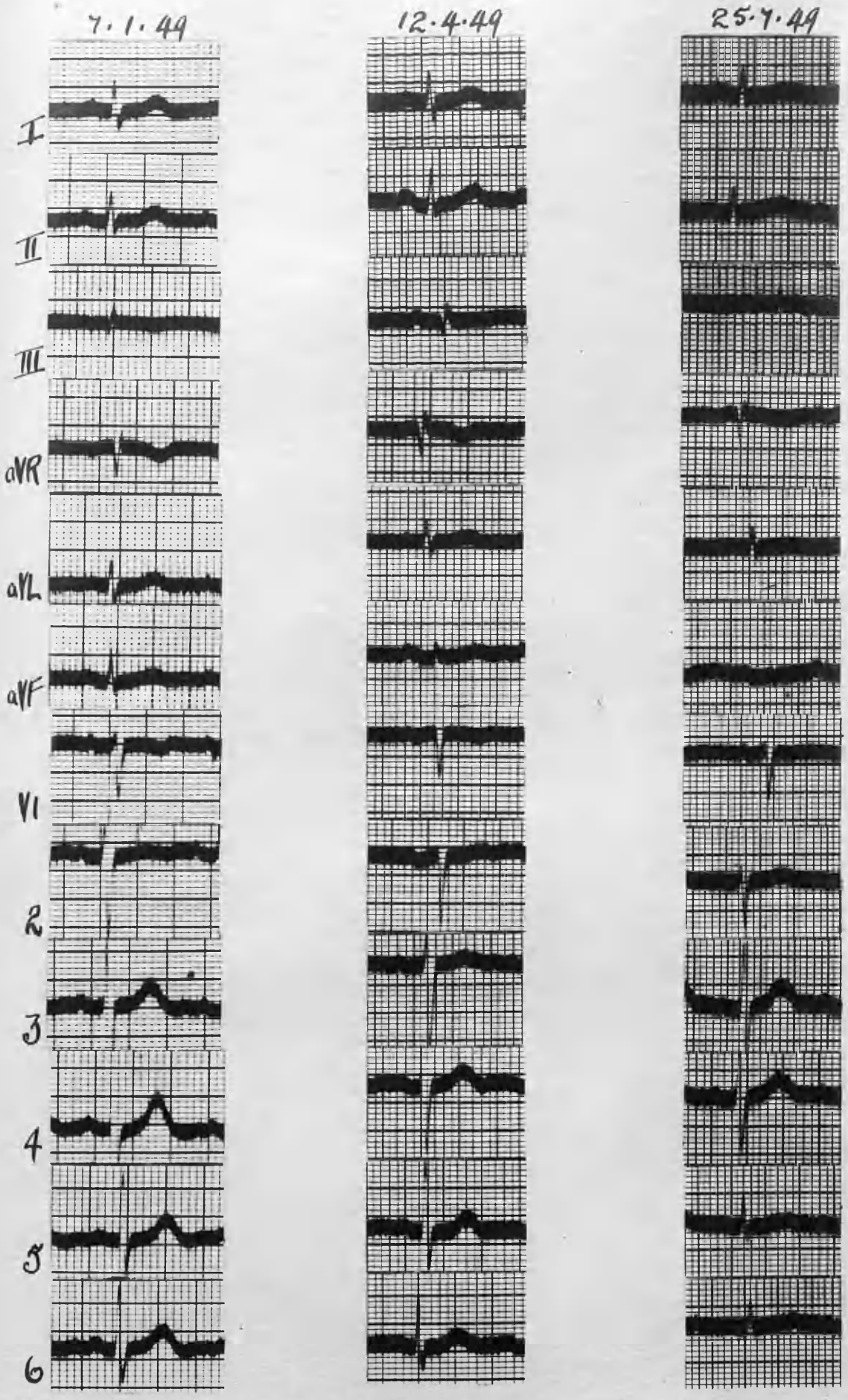

FIG. 41.

Fig. 42. Case No. 41. : The pre-operative electrocardiogram, taken on 2.5.49, is within normal limits.
The post-operative electrocardiogram, taken on 18.1.50, shows no significant change.

Fig. 43. Case No. 45. : The pre-operative electrocardiogram, taken on 19.7.49, is within normal limits.
The post-operative electrocardiogram, taken on 14.1.50, shows no significant change.

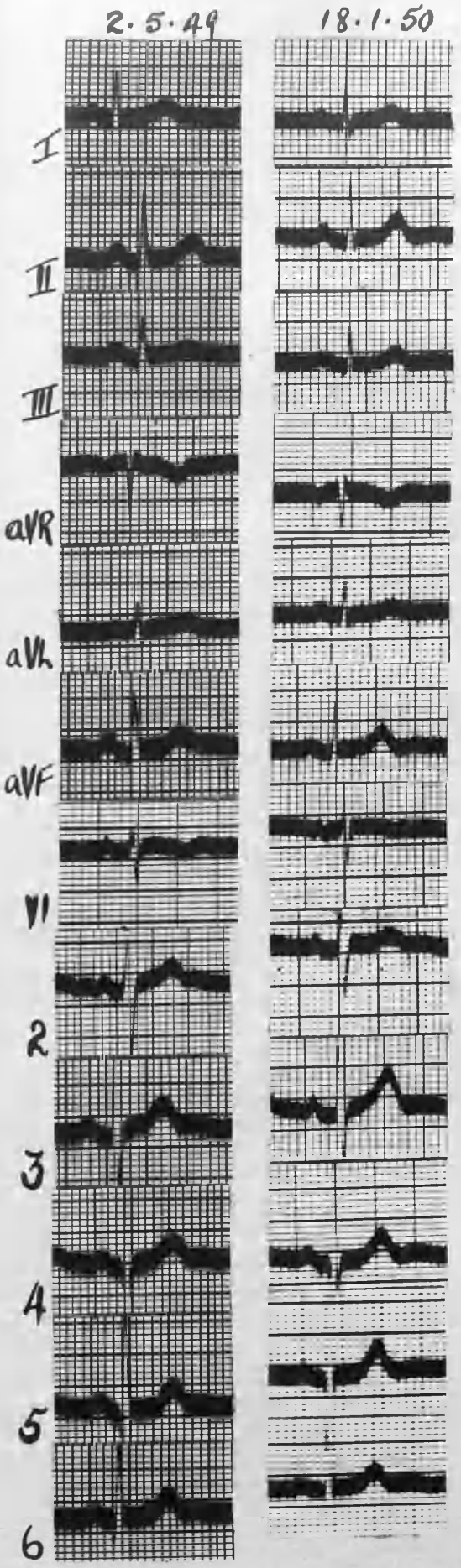
2·5·49
18·1·50
I
II
III
aVR
aVL
aVF
V1
2
3
4
5
6

FIG.42.

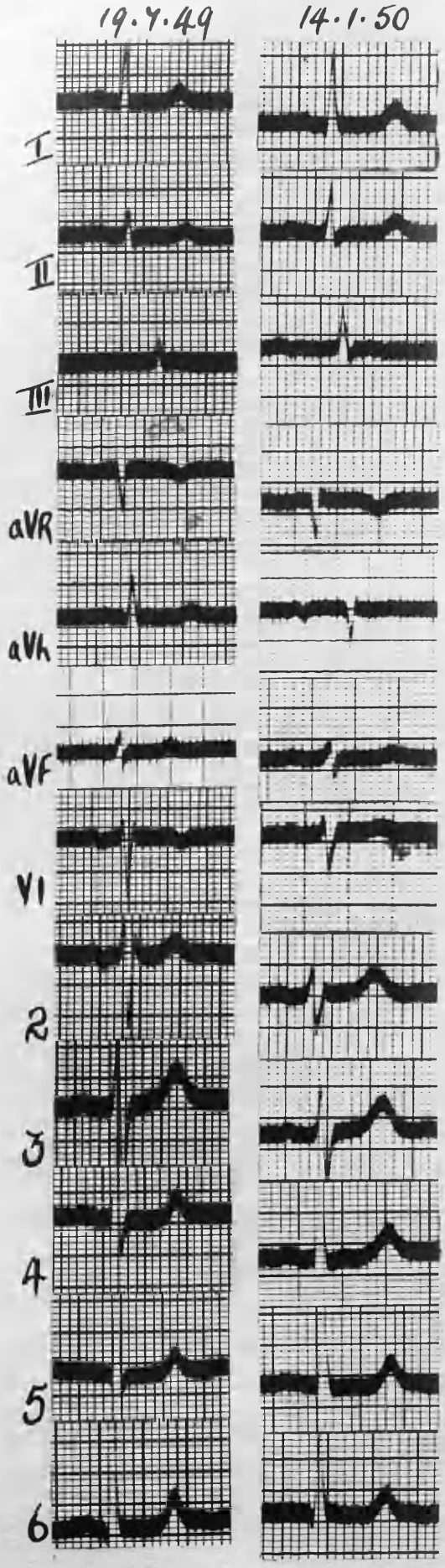
19·7·49
14·1·50
I
II
III
aVR
aVL
aVF
V1
2
3
4
5
6

FIG.43.

Fig. 44. : The pre-operative electrocardiogram,
Case No. 44. taken on 1.6.48, is within normal limits.

The post-operative electrocardiogram, taken on 3.2.49, shows no significant change.

Fig. 45. : The pre-operative electrocardiogram,
Case No. 35. taken on 20.5.49, shows low voltage QRS complexes in the standard limb leads, unipolar limb leads, and in VI - V3.

The post-operative electrocardiogram, taken on 30.1.50, shows no significant change.

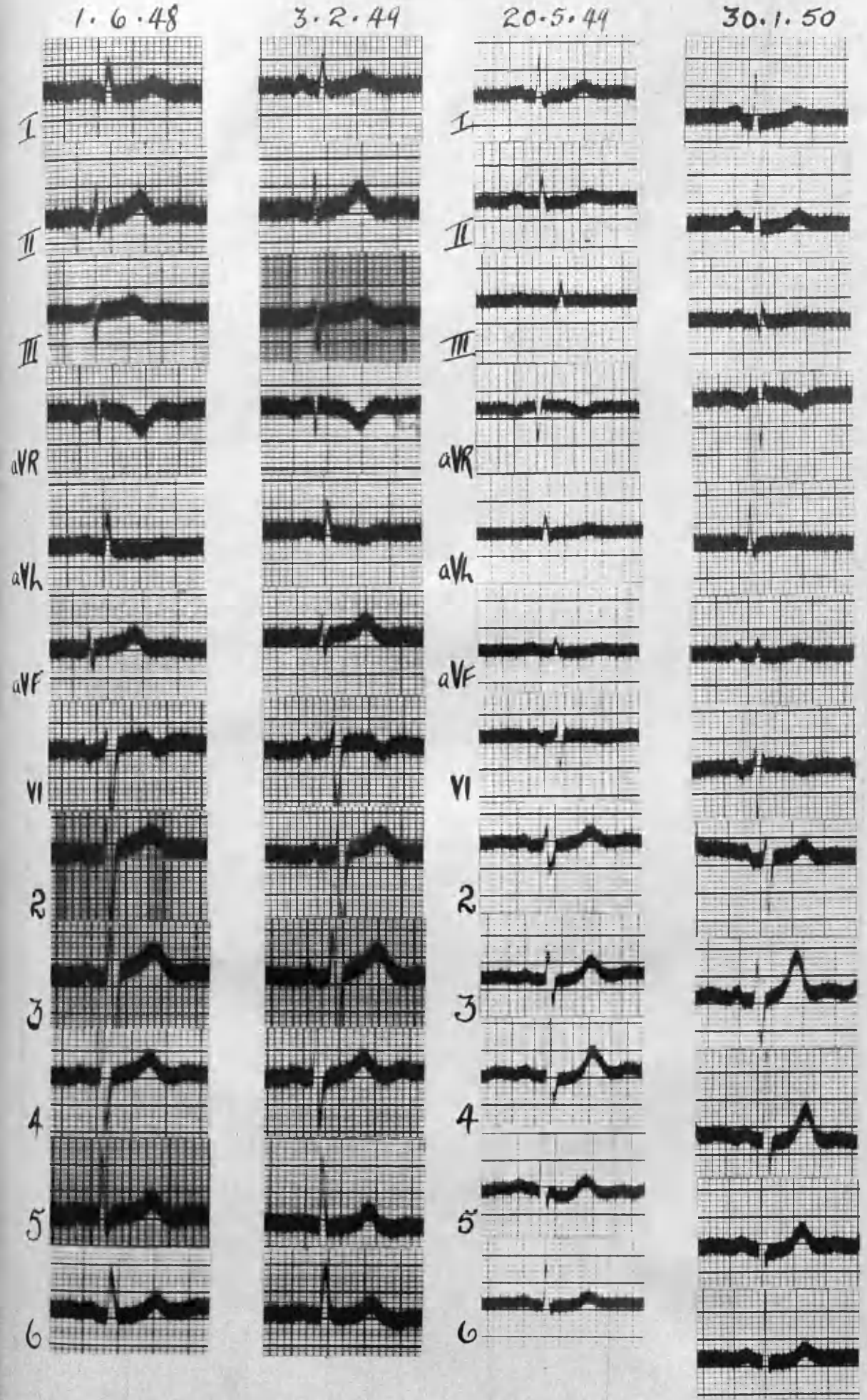

FIG. 44.

FIG. 45.

Fig. 46. : The first electrocardiogram, taken on 15.3.49 one day after an attack of biliary colic, shows an inverted P wave in lead III.

Case No. 61.

The second electrocardiogram, taken on 1.6.49, during a quiescent period, shows an upright P wave in lead III.

The two chest lead electrocardiograms, taken pre-operatively on 21.6.49 and 7.9.49 are within normal limits.

The post-operative electrocardiogram, taken on 23.12.49 show no significant change.

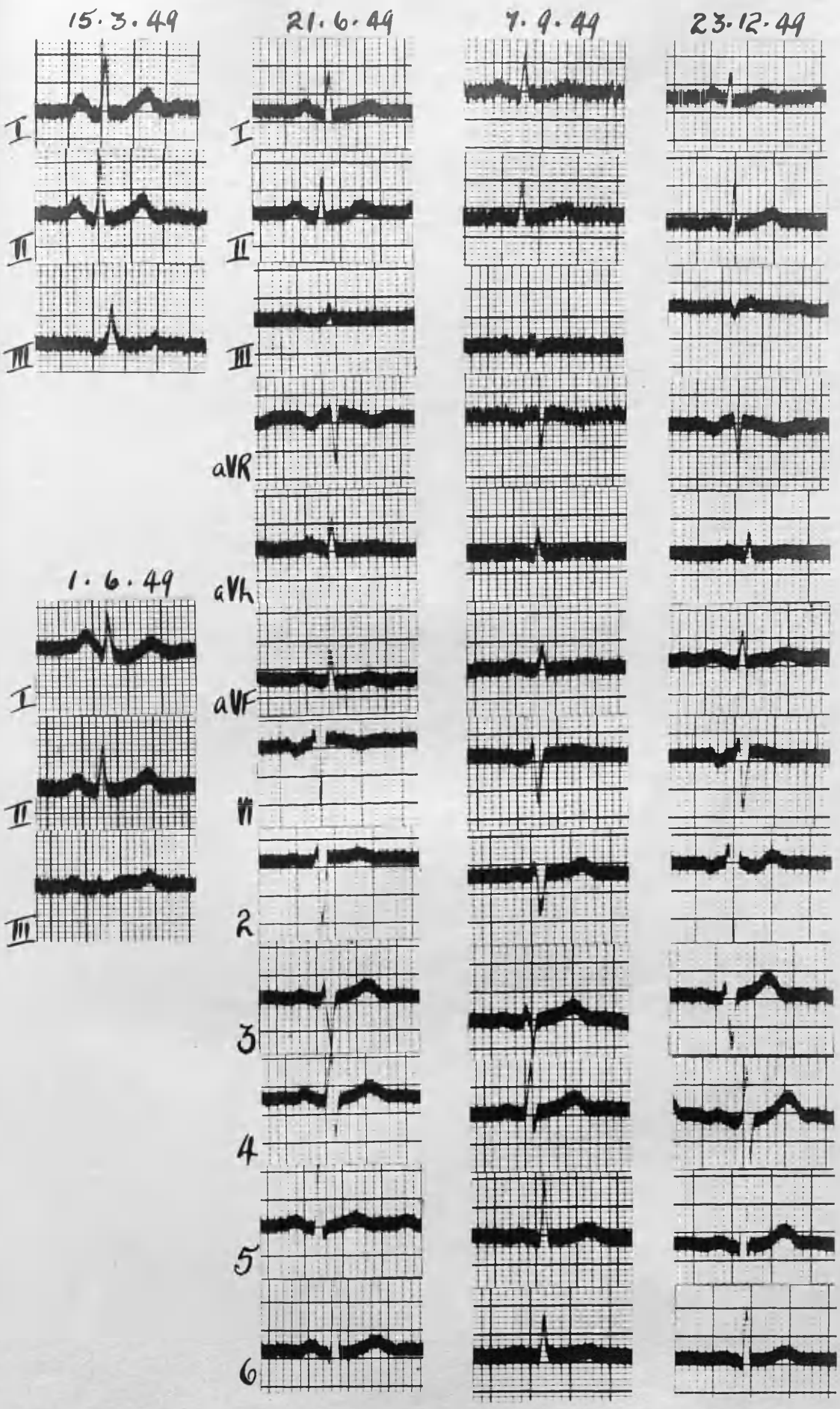

FIG. 46.

Fig. 47. : The pre-operative electrocardiogram, taken on 1.2.49, shows a slight degree of splintering of R in lead II, S in lead III, and R and S in aVF. The post-operative electrocardiograms, taken on 22.3.49 and 1.8.49, show no significant change, in view of the change of electrical axis of the heart.

Case No. 62.

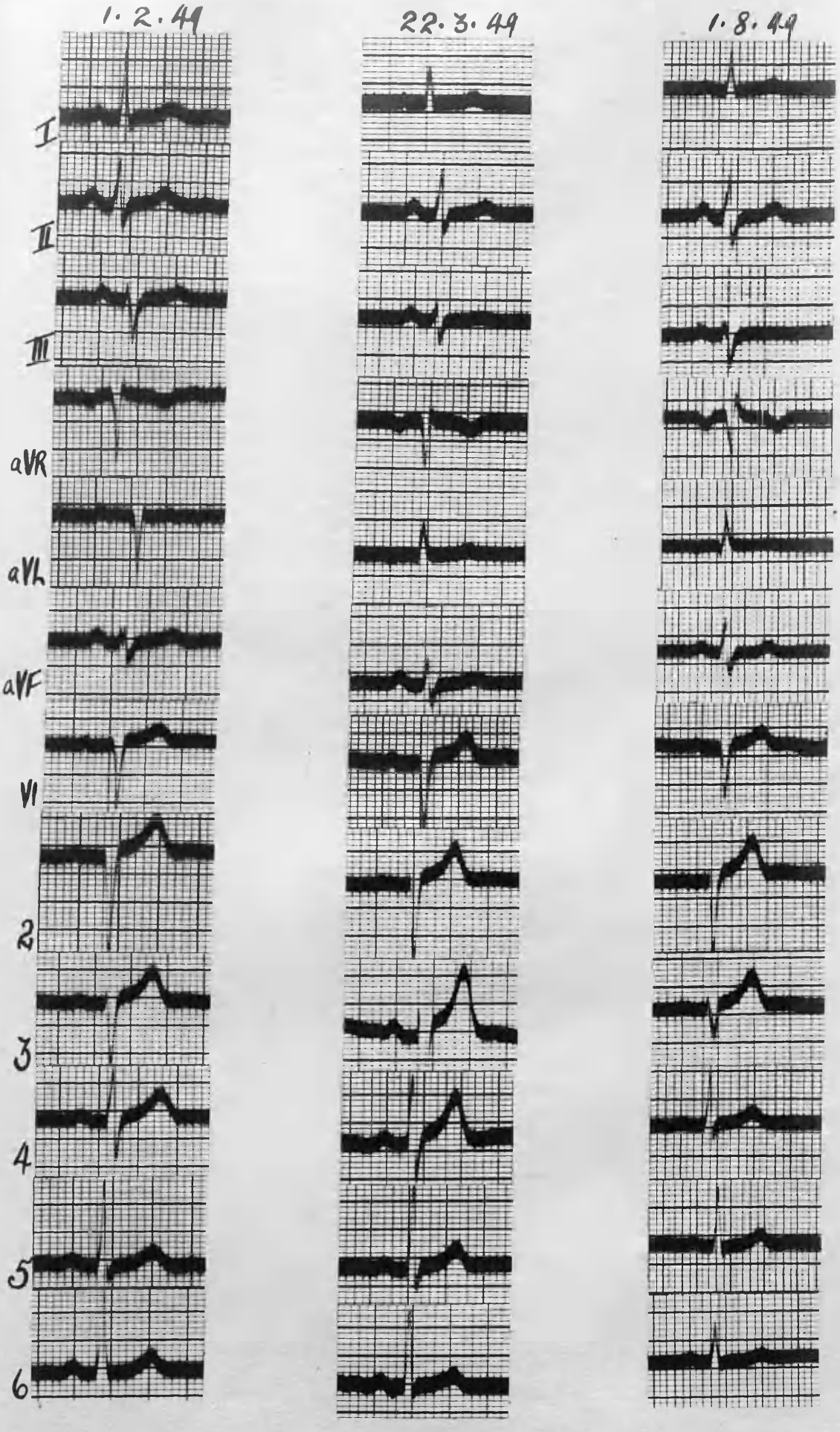

FIG. 47.

Fig. 48. : The pre-operative electrocardiogram,
Case No. 63. taken on 27.5.48, shows an inverted T wave in lead III, and QS deflection with inverted T wave in aVF.

The post-operative electrocardiograms taken on 17.6.48 and 21.11.48 show the T wave in leads II and III to be upright, but there has been a change in the electrical axis of the heart as shown by leads aVL and aVF.

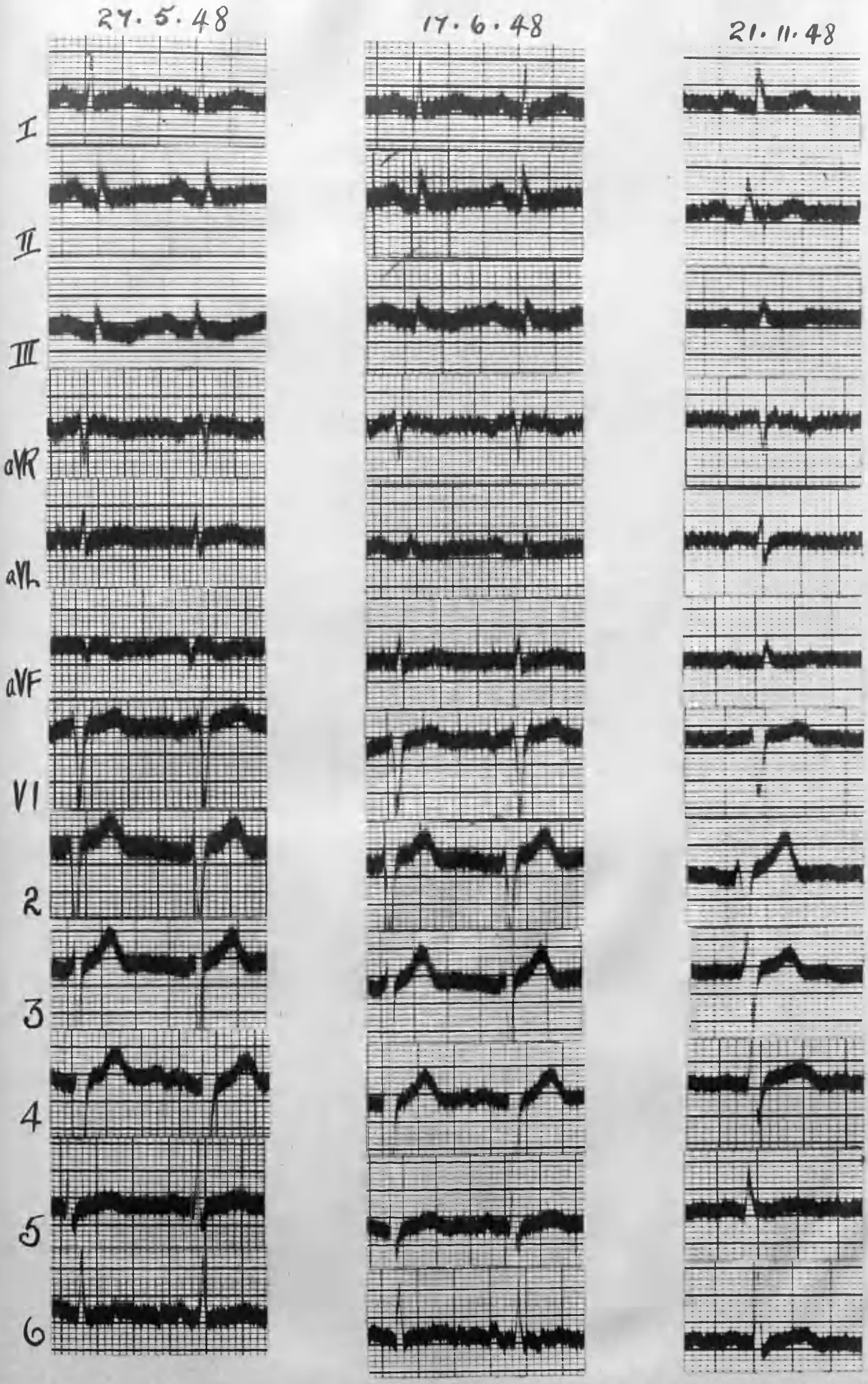

FIG. 48.

Fig. 49. : The pre-operative electrocardiogram,
Case No. 65. taken on 7.4.48, shows no significant abnormality.

The post-operative electrocardiograms, taken on 19.4.48 and 21.12.48, show no significant change.

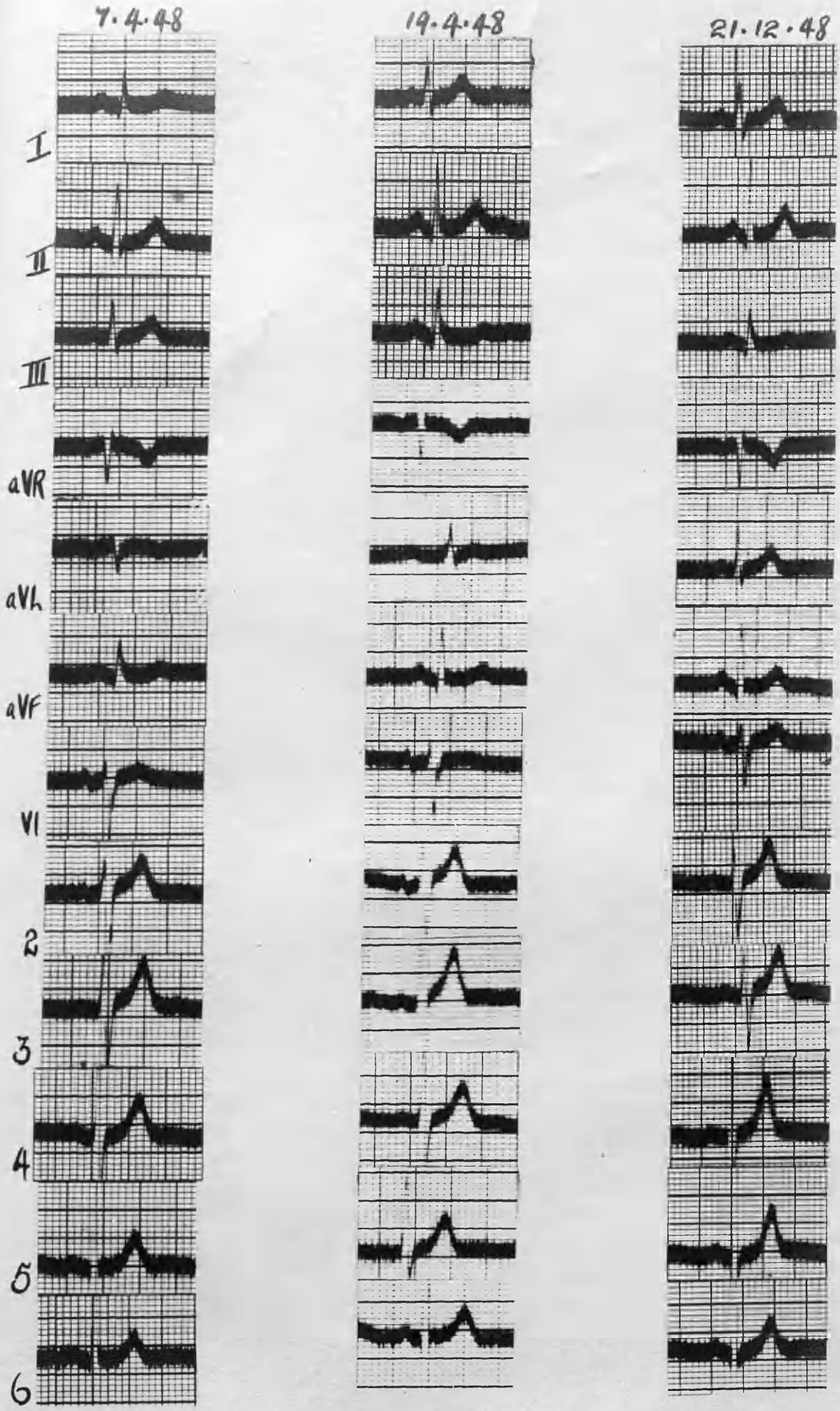

FIG. 49.

Fig. 50. : The pre-operative electrocardiogram,
Case No. 66. taken on 5.3.50, shows changes in keeping with lateral coronary artery insufficiency.

The post-operative electrocardiograms, taken on 6.2.50 and 4.6.50, do not show any significant alteration.

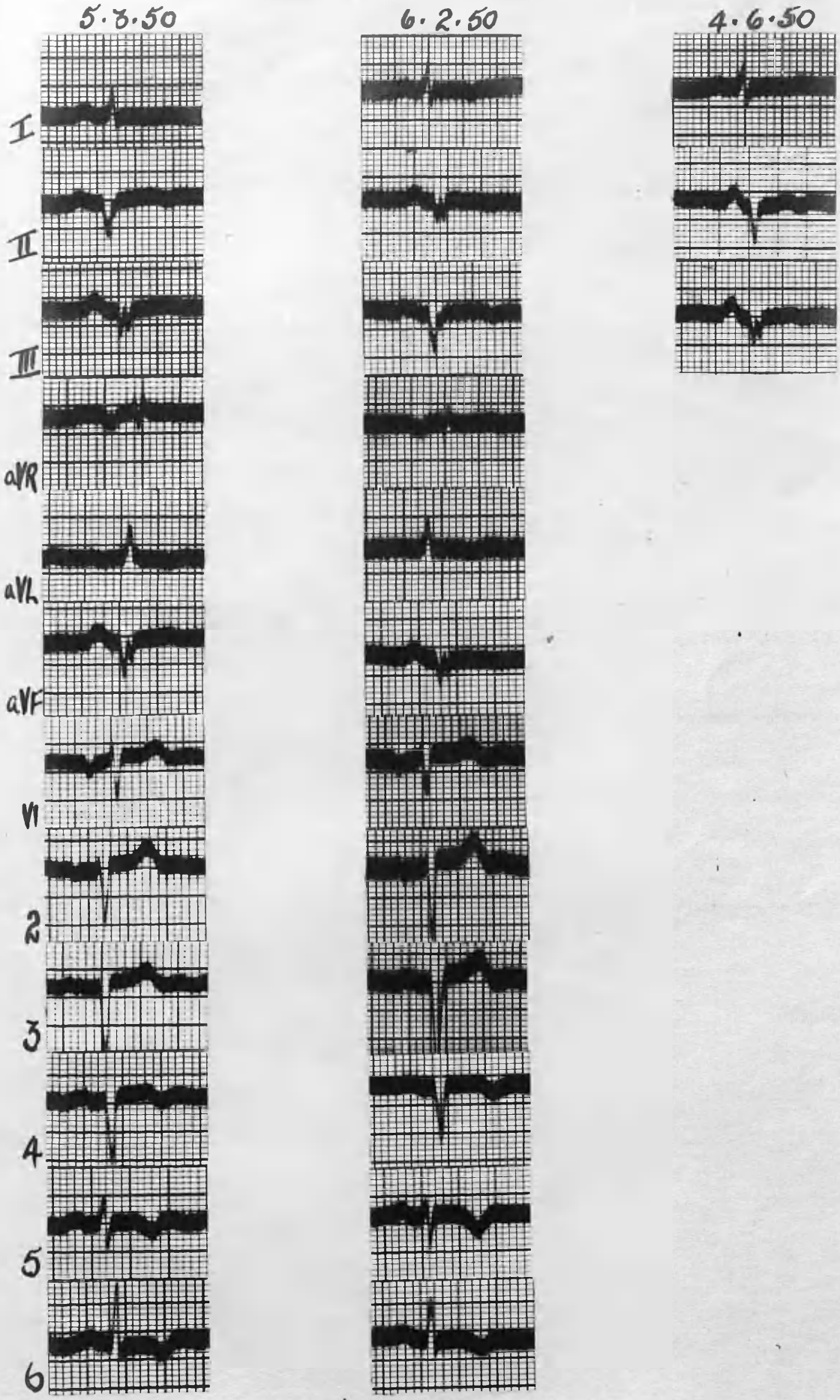

FIG. 50.

Fig. 51. : The post-operative electrocardiogram
Case No. 48. taken on 19.1.50 shows no significant change from the pre-operative electrocardiogram taken on 20.4.42.

Fig. 52. : The post-operative electrocardio-
Case No. 55. gram, taken on 17.1.50, shows no significant change from the pre-operative electrocardiogram taken on 22.1.38.

Fig. 53. : The electrocardiogram taken on
Case No. - 25.10.39, shows slight splintering of the R wave in leads II and III. The electrocardiogram taken on 13.1.50, shows no significant change.

Fig. 54. : The post-operative electrocardiogram
Case No. 50. taken on 17.1.50, shows no significant alteration from the pre-operative electrocardiogram, taken on 29.4.39, allowance being made for the change in the electrical axis.

Fig. 55. : The post-operative electrocardiogram,
Case No. 53. taken on 28.1.50, shows no significant change from the pre-operative electrocardiogram taken on 2.3.40.

Fig. 56. : The pre-operative electrocardiogram,
Case No. 52. : taken on 18.1.41, shows a deeply inverted T wave in lead III. The post-operative electrocardiogram, taken on 16.1.50 shows an almost isoelectric T wave in lead III.

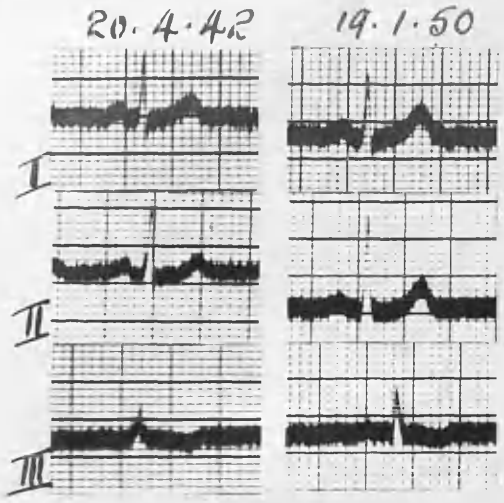

FIG.51

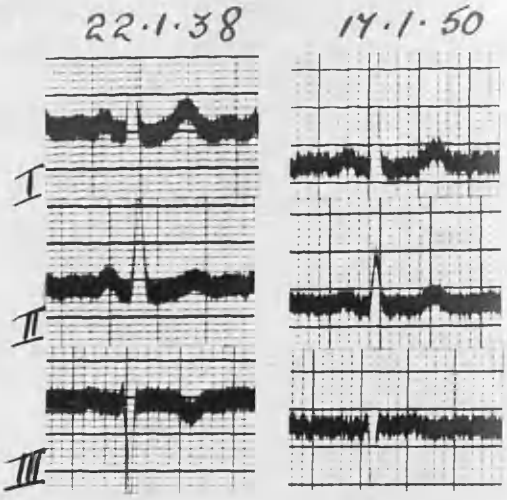

FIG.52.

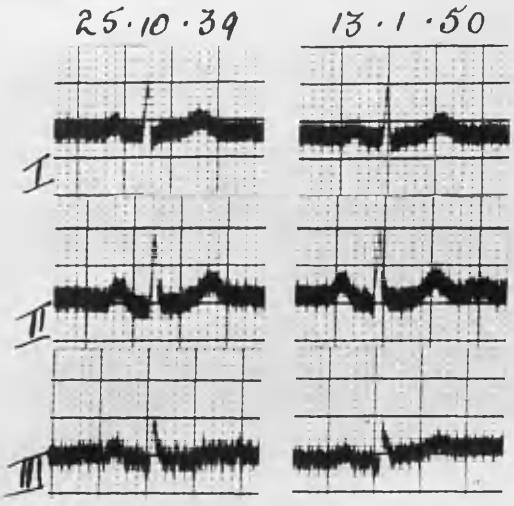

FIG.53

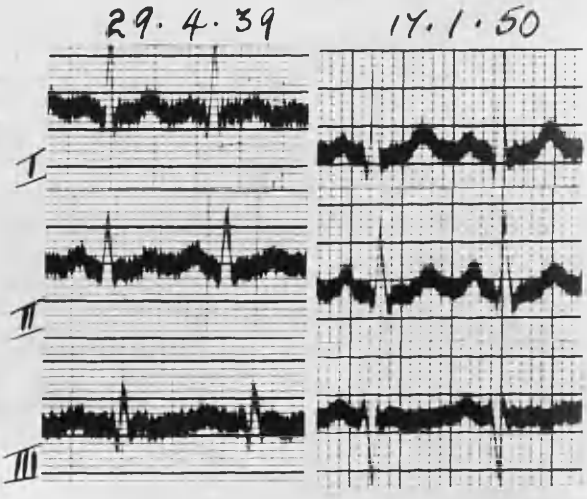

FIG.54.

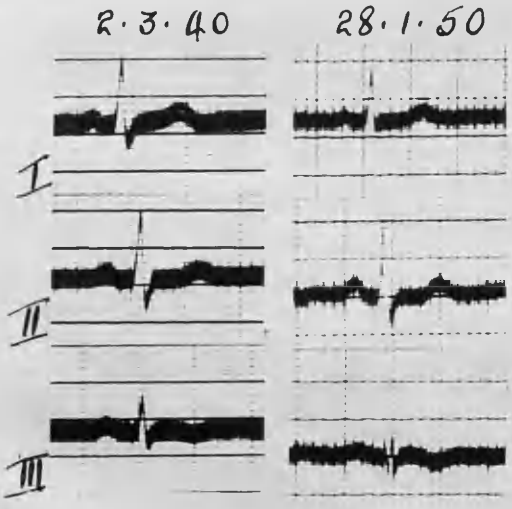

FIG.55

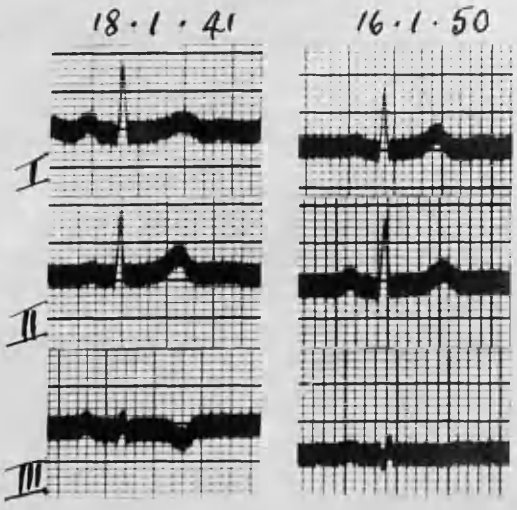

FIG.56.

Fig. 57. : The pre-operative electrocardiogram,
Case No. 58. taken on 5.6.37, shows an incomplete bundle branch block pattern.
The post-operative electrocardiogram, taken on 26.4.48, shows a complete disappearance of the bundle branch block pattern.

Fig. 58. : The pre-operative electrocardiogram
Case No. 56. taken on 3.5.37, shows an inverted T wave in lead III and diphasic T wave in lead II.
The post-operative electrocardiogram, taken on 4.4.49, shows an upright T wave in all leads.

Fig. 59. : The post-operative electrocardiogram,
Case No. 49. taken on 6.5.49, shows no significant change from the pre-operative electrocardiogram taken on 12.6.37.

Fig. 60. : The pre-operative electrocardiogram,
Case No. 59. taken on 9.4.38, shows left axis deviation with an inverted T wave in lead III.
The post-operative electrocardiogram, taken on 26.7.49, shows left axis deviation with an inverted T wave in lead I.

Fig. 61. : The post-operative electrocardiogram,
Case No. 50. taken on 25.1.50, shows no significant change from the post-operative electrocardiogram taken on 4.8.39.

Fig. 62. : The pre-operative electrocardiogram,
Case No. 57. taken on 3.10.42, shows upright T waves in all leads.
The post-operative electrocardiogram, taken on 8.7.50, shows a diphasic (- +) T wave in lead I.

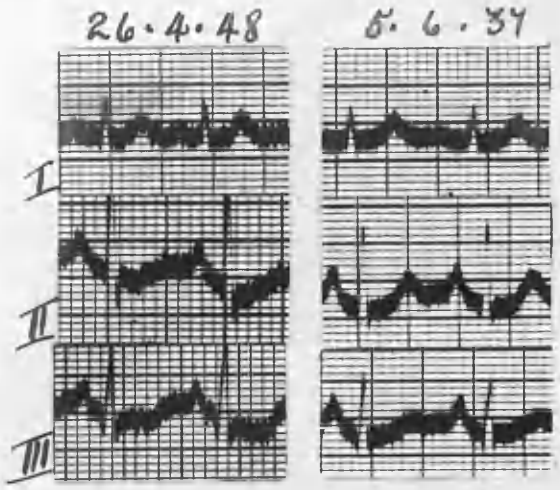

FIG.57

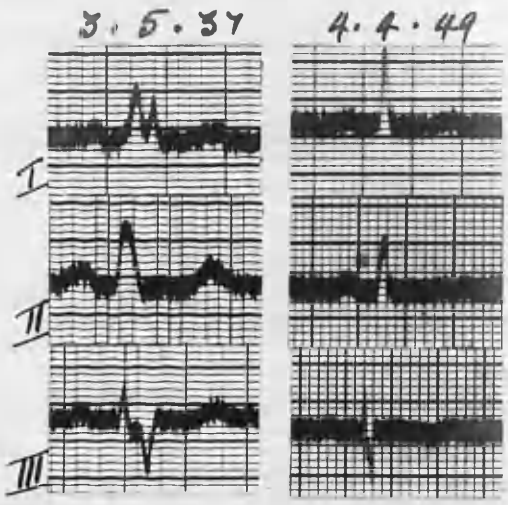

FIG.58

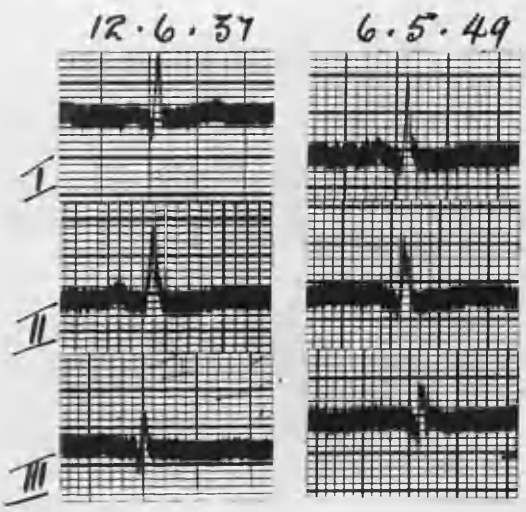

FIG.59.

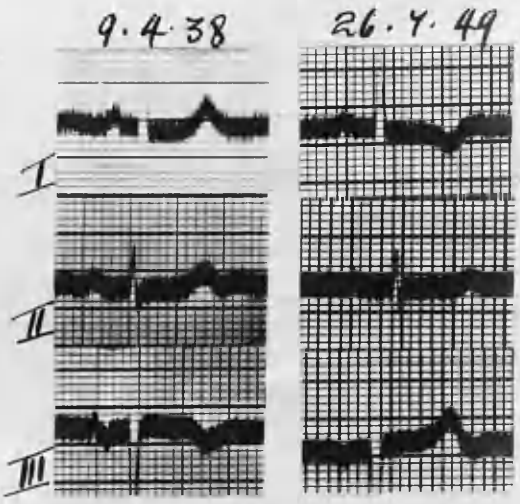

FIG.60.

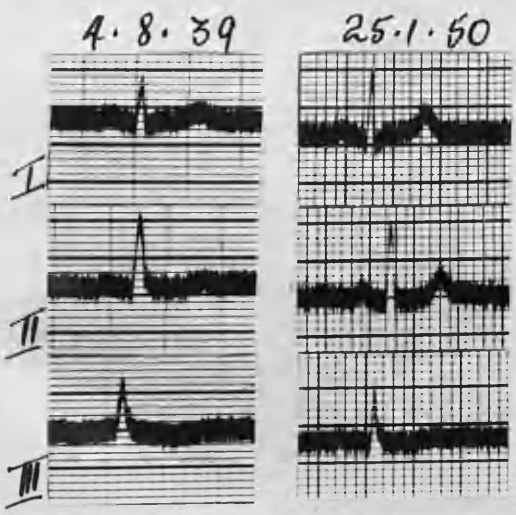

FIG.61.

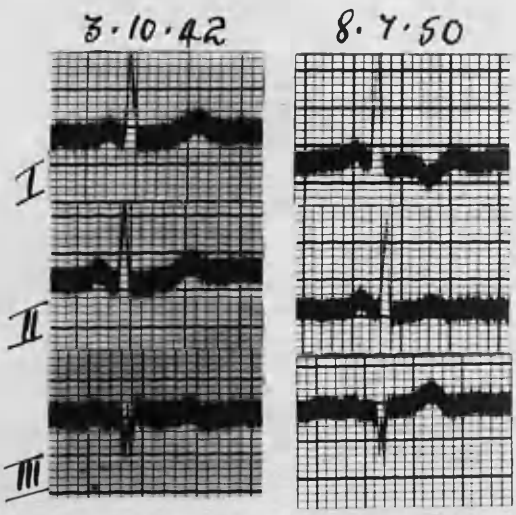

FIG.62.

Fig. 63. : The pre-operative electrocardiogram,
Case No. 54. taken on 4.11.39, shows left axis devisation with an isoelectric T wave in lead III.
The post-operative electrocardiogram, taken on 1.2.44 and 26.1.50 shows no significant change. (This patient had a cholecystostomy performed on two occasions - see case report).

Fig. 64. : The first electrocardiogram, taken
Case No. - on 1.4.40, during an attack of biliary colic, shows ST depression in all the standard limb leads together with a diphasic T wave in lead I and inverted T wave in leads II and III.
Four days later, when the biliary colic had subsided the ST depression in leads had decreased, whilst the T waves in all leads were more upright.
On 26.1.50, almost ten years later, the electrocardiogram taken in a quiescent phase, had reverted to the type recorded during an attack of biliary colic.

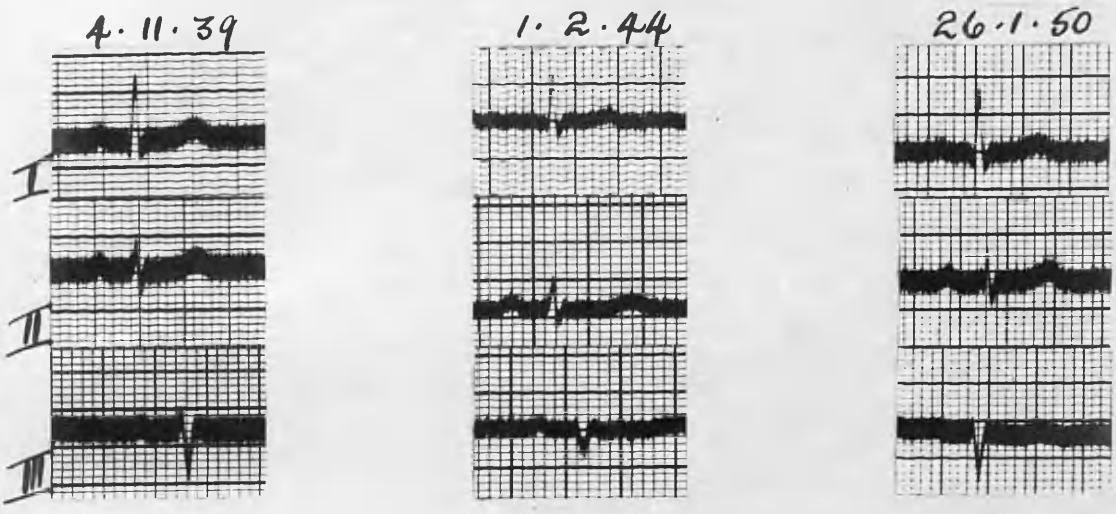

FIG. 63.

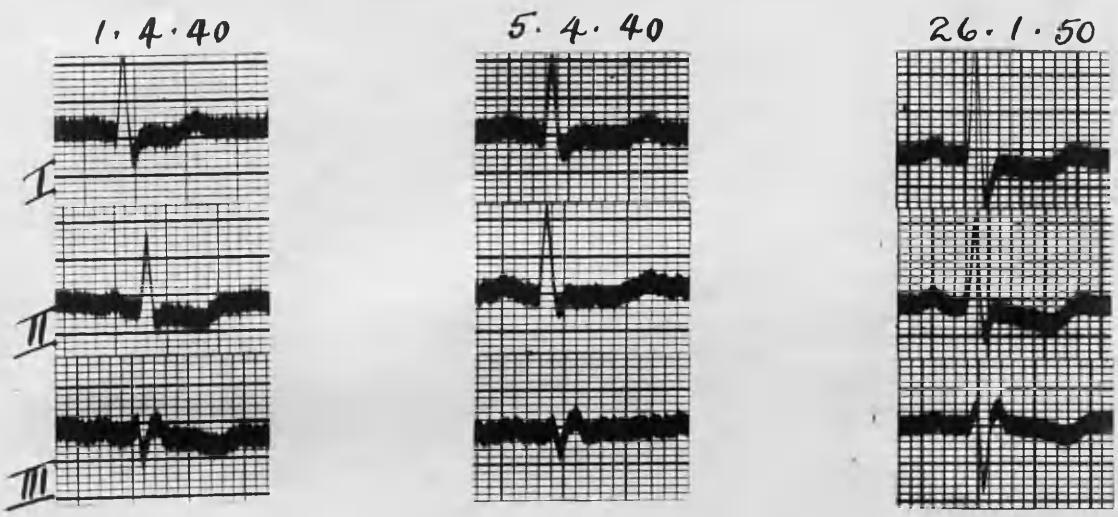

FIG. 64.

Fig. 65. : Antero-septal coronary artery insufficiency. Note the diphasic T wave in V2, the inverted T waves in V3, V4 and the low voltage upright T in lead I.

Case No. -

Fig. 66. : Posterior coronary artery insufficiency. Note the inverted T waves in leads I, II and aVF.

Case No. -

Fig. 67. : Lateral coronary artery insufficiency. Note the inverted T waves in lead I and aVL.

Case No. -

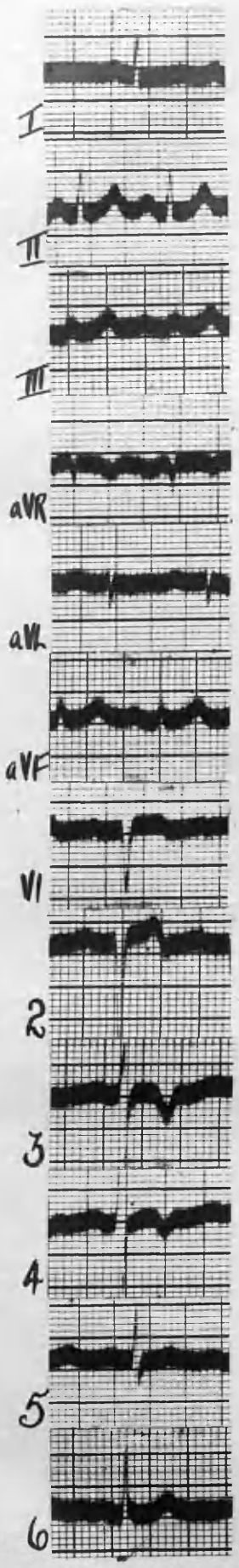

FIG. 65

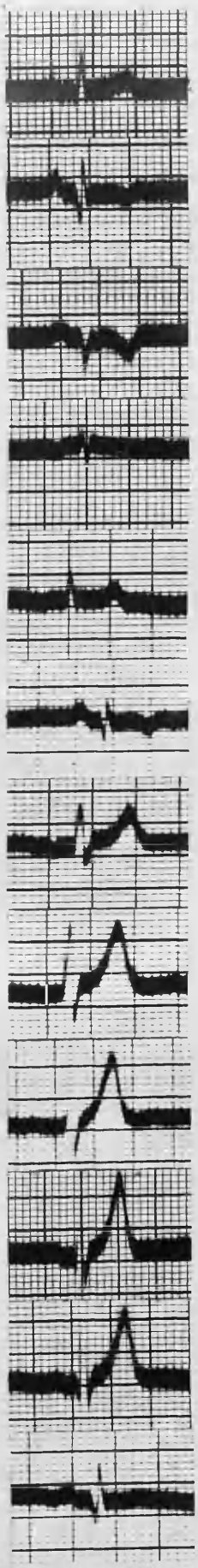

FIG. 66.

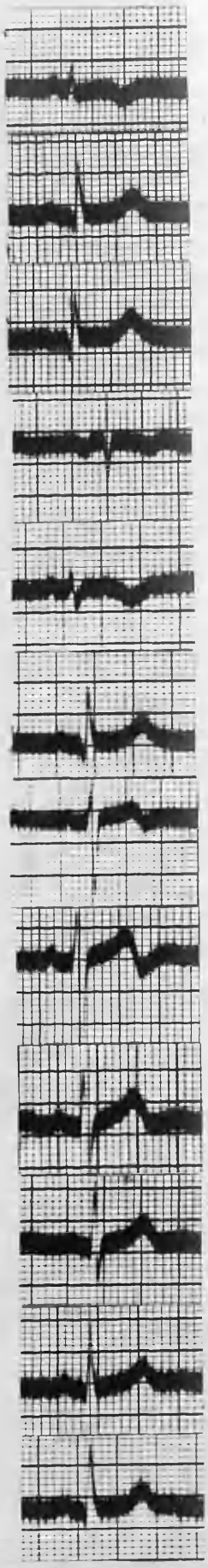

FIG. 67.

Fig. 68. : Antero-lateral coronary artery insufficiency. Note the inverted T wave in lead I, aVL, V3, V4, V5 and V6.

Case No. -

Fig. 69. : Postero-lateral coronary artery insufficiency. Note the inverted T waves in leads II, III, aVF, V5 and V6.

Case No. -

Fig. 70. : Antero-posterior coronary artery insufficiency. Note the inverted T waves in leads I, II, III, aVF, and V1-V6.

Case No. -

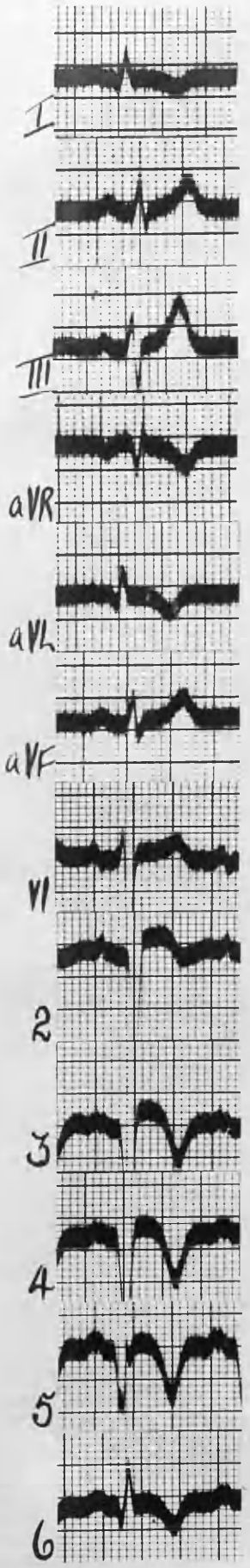

FIG. 68.

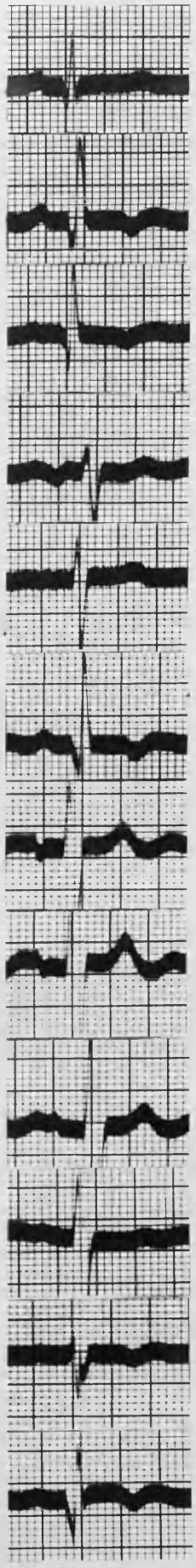

FIG. 69.

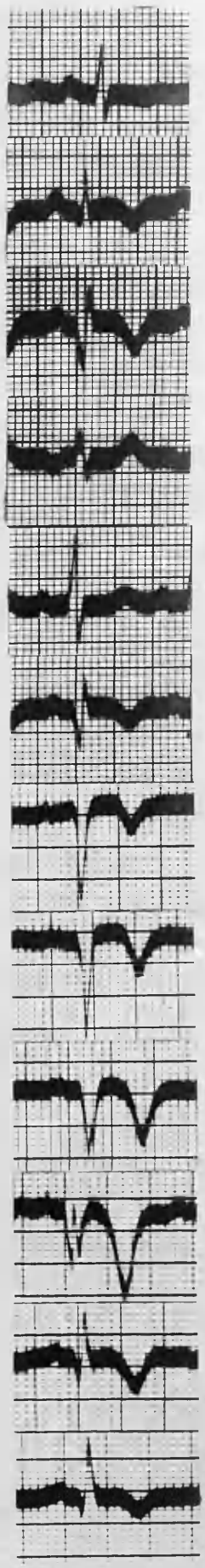

FIG. 70.