A clinical study of acute coronary artery occlusion; with a review of the factors controlling the coronary circulation, and their alterations subsequent to myocardial infarction.

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I N T R O D U C T I O N.

In this thesis a clinical study has been made of a small series of fifteen cases of acute coronary occlusion. Some of the cases have been confirmed by electrocardiographic records or pathological examination; facilities for the former were not frequently available. The diagnosis of a typical case of coronary thrombosis can usually be made easily from the clinical condition.

A study is made of the etiology of the condition and the effect of the infarction on the working of the heart. The problem of the development of the collateral circulation is also examined. There is no detailed examination of these points in the literature.

Some clinical aspects have been considered in detail, especially the action of drugs on the coronary circulation.

It is proposed first to present the case records of the fifteen patients.

The historical aspect of the subject is ably dealt with by Levine (1) in his monograph. It has long been recognised that sudden obstruction of a coronary vessel could cause sudden death. Herrick (2,3) seems to have been the first to distinguish the typical symptom complex of myocardial infarction from the different forms of angina pectoris. Little has been added to our clinical knowledge since Herrick's paper, but the literature on other aspects of the disease, especially those concerned with the use of the electrocardiogram in diagnosis, has grown enormously. Smith(4) investigated in 1918 the effects of experimental coronary ligation. Pardee (5) described the typical electrocardiographic curve which bears his name in 1920. Parkinson and Bedford (6) in 1928

described the evolution in the serial electrocardiogram of the R S -T changes. Barnes and Whitten (7,8) in 1929 attempted to show that the site of the infarction could be deduced from the electrocardiographic changes in the R S - T segment. Wilson (9) and his associates have recently described changes in the Q wave which may have a localizing value.

Coronary thrombosis is now recognised frequently; whether or not it is on the increase it is difficult to say. The literature on the subject is mainly confined to British and American writers; continental writers have contributed little of importance; their papers consist mainly of case reports.

CASE NO. 1. MR. CLARK. MANUAL WORKER. AGED 68 YEARS.

This patient was first seen in May 1935. He complained of breathlessness of three months' duration. There was nothing of importance in his previous history or in his family history. He was a rather stout, overweight, florid man. It was noticed that the heart's action was irregular and it was evident that at that time the auricles were fibrillating. The blood pressure was 175/110 mm. Hg. There was clinically no cardiac enlargement and no evidence of valvular disease. He was considered a case of auricular fibrillation associated with fibrosis of the myocardium and hypertension. He was given digitalis but he only took the medicine for a fortnight and he was not seen until the acute attack which came on a month later. He had no effort angina.

In June 1935 this patient suddenly became acutely ill with pain over the praecordium, which radiated upwards towards the left shoulder but not to the left arm. When first seen he was rolling about in bed holding the front of the chest with his hands, and complaining incessantly of the pain, which he described as tearing in character and associated with a sense of constriction. He was very pale, the lips and the ears were cyanosed, and his face was covered with cold perspiration. There was no vomiting.

The pulse rate was completely irregular at 76 beats per minute and apparently the rhythm was no different from what it had been before the attack. There was no thickening of the radial vessels. The temperature was 98 deg. F. The systolic blood pressure was 84 mm.Hg; the diastolic pressure could not be determined.

CASE NO. 1. (Continued)

EXAMINATION OF THE HEART. The apex beat was in the sixth interspace, in the mammary line and was 8'6 cms from the left edge of the sternum, and the breadth of the heart in the fourth interspace was 10 cms. These measurements did not differ much from those made before the attack. The heart's action was irregular and the sounds were very muffled. A month before the attack they had been heard quite easily but now they were only audible at a small area near the apex beat.

RESPIRATORY SYSTEM. The respiratory rate was 24 per minute, the respirations were shallow in character; there was no pain on breathing. Except for some harshness of the breath sounds at the left base, auscultation of the lungs revealed no abnormality.

ABDOMINAL EXAMINATION. The liver was enlarged so that its lower edge was a fingersbreadth below the right costal margin; the remainder of the abdominal examination was negative.

The urine was tested the following day and showed no abnormality.

PROGRESS OF THE CASE.

The patient was treated on the usual lines. Omnopon gr$\frac{1}{2}$ was given twice in the first six hours. After twelve hours he began to rally and the pain was greatly alleviated forty-eight hours after the onset of the illness, although a sense of discomfort persisted. On the second day the temperature rose to 100 deg.F. His blood pressure on the third day was 90/71 mm.Hg. He was now fairly comfortable although the heart sounds were very distant. The pulse rate was still 76 beats per minute, and it was still completely irregular. He showed a tendency to move too freely

CASE NO. 1. (Continued)

in bed and he was warned against this. On the sixth day he was left unattended for a short period; during this time he noticed his pipe lying on a table near by; he turned round in bed, sat up and stretched out his hand. He immediately had an acute seizure of pain in the chest; he collapsed, became very pale, and the pulse became imperceptible at the wrist while the heart sounds became inaudible on auscultation. The patient gradually became comatose and died three hours after the second attack of pain.

CASE NO. 2. MR. STOBBS. AGED 78 YEARS. HOUSEFACTOR.

In January 1932 this patient took suddenly ill with acute pain in the chest. This was diagnosed at that time as an attack of coronary thrombosis; and this was later confirmed by an electrocardiogram. He made a good recovery and was able to attend his work although his exercise tolerance was greatly reduced. He had no effort angina after the attack of thrombosis but suffered from indigestion.

He was a tall stout man whose blood pressure in December 1933 was 140/90 mm.Hg. The heart sounds at this time were very weak but no clinical enlargement of the heart could be made out.

In January 1934 he was suddenly wakened from his sleep by a severe pain in the chest which radiated down the inner aspect of the left arm. When seen he was very pale and collapsed. There was a little dyspnoea and a little cyanosis of the lips and ears, but the main picture was that of great prostration. There was no vomiting. The pulse was regular and the rate was 76 per minute. It was very feeble at the wrist. There was no apparent thickening of the radial vessels. The respirations were 24 per minute and the temperature was 97'6 deg. F. The blood pressure was 100/70 mm.Hg.

CARDIOVASCULAR SYSTEM.

The apex beat was impalpable. The breadth of the heart in the fourth interspace was 10'8 cms. The heart sounds were very distant. No murmurs were detected. The urine was normal.

The patient was given several administrations of

CASE NO. 2. (Continued).

Morphine and omnopon and Ephedrine Hydrochloride gr¼ t.i.d. The pain began slowly to subside but it persisted in a modified form until the fifth day. The patient was extremely prostrated and was unable to turn in bed; on the second day the temperature rose to 101'4 deg. F. and varied between this level and 98'6 deg.F. on the fifth day. The blood pressure on the fifth day was 110/75 mm.Hg. The heart rate remained steady between 72 and 88 beats per minute. The heart sounds were still muffled.

On the tenth day the blood pressure was 108/76 mm.Hg. He was still very weak.

On the eleventh day while moving his head to drink from a feeding cup he fell backwards and died immediately.

This patient survived a first attack for two years and had enjoyed a fair degree of health. The pain in this case was not of such great severity as in some other cases but the extreme weakness was a marked feature. The drop in the systolic blood pressure from 140 mm.Hg. to 100 mm.Hg. was not great but on the tenth day the systolic pressure was still falling. No doubt the dyspepsia from which he suffered after the first attack was cardiac in origin; the indigestion often came on at bed-time and had no relationship to the taking of food. There was no flat-ulence.

He died on the eleventh day, the day on which death is common in myocardial infarction. The movement which preceded the fatal collapse was very small.

CASE NO. 3. MR. STIRLING. AGED 72. RETIRED LABOURER.

This patient had complained of breathlessness for three months before the attack but he had no medical examination before the onset of the present illness.

This patient, who lived alone, took ill one night at 3 a.m. with severe pain in the chest which wakened him from sleep. He managed to rouse a neighbour but he collapsed immediately afterwards and had to be assisted into bed. He was small and rather stout. When seen thirty minutes after the onset of the attack he was obviously critically ill. He was very pale, the pallor being widespread over the abdomen and the lower limbs. He was covered with perspiration; the lips, ears, and finger nails had a cyanotic tinge. There was coldness of the extremities. There was a marked degree of dyspnoea; this did not seem however to aggravate the pain in the chest. The patient was very restless, and complained continually of a tearing sensation behind the sternum. He had vomited once at the onset of the attack. Temperature was 97'4 deg.F. the respirations were 24 per minute; only the systolic blood pressure (90 mm.Hg.) could be recorded. The pulse was regular but only faintly perceptible at the wrist. There was no thickening of the radial artery. The pulse rate was 78 beats per minute.

CARDIOVASCULAR SYSTEM.

The apex beat was impalpable. The breadth of the heart in the fourth interspace was 11'2 cms. The heart sounds were inaudible. There was nothing abnormal on auscultation of the lungs. The urine was not examined.

CASE NO. 3. (Continued)

Morphine gr½ was administered; this made the patient less restless, but Cheyne-Stokes breathing eventually set in and the patient died two and a half hours after the onset of the attack.

This was a typical case of coronary occlusion in a patient who gave little previous history of a cardiac complaint. The degree of shock was very great. The blood pressure recordings were difficult to take owing to the feebleness of the heart's action, and the restless condition of the patient.

The complete inaudibilty of the heart sounds was very striking.

CASE NO. 4. MRS. STEELE. AGED 70. HOUSEWIFE.

This patient was seen first during April 1936. She had been quite healthy until three months previously when she began to feel easily tired on exertion.

She was a stout florid woman.

On examination at this time it was found that the pulse rate was regular at 72 beats per minute. There was thickening of the radial vessels. There was enlargement of the heart, especially towards the right side, the right border being 2 cms to the right of the sternal border. The apex beat was in the fifth interspace lateral to the midclavicular line and 8'2 cms from the left sternal border. The heart measured 14'4 cms in the fourth interspace. The heart sounds were pure. The 2nd aortic was emphatic. The first sound at the apex was of very poor tone. The blood pressure was 200/150 mm.Hg.

The urine was normal.

Nothing abnormal was made out in the respiratory system.

The Wassermann reaction was negative.

Two days from the date of this examination the patient took suddenly ill. She had been confined to bed since the date of the previous examination. She was lying in bed awake about 10 p.m. when suddenly she was seized with acute pain, radiating up to the left shoulder but not down the arm.

The patient was collapsed; her face was pale, covered with cold sweat and her lips showed cyanosis. She had marked dyspnoea; the breathing was rapid (32 per minute) and of a shallow

CASE NO.4. (Continued)

irregular type. She had no vomiting. Temperature was 98 deg.F. The pulse rate was 42 per minute and very feeble. The rate of the heart and the apex beat was the same.

The heart's action was regular. The apex beat was impalpable. The heart sounds were pure but very muffled. There was some difficulty in estimating the size of the heart and the blood pressure owing to the collapsed and restless state of the patient but the size of the heart did not apparently differ from that recorded before the attack. The systolic blood pressure was about 78mm.Hg. No diastolic recordings were obtained.

No abnormality in the respiratory system could be detected.

The usual measures to counteract shock were taken. Atropine gr 1/50 and mm5 of adrenalin Hydrochloride solution (1'1000) were administered hypodermically. Owing to the irregularity of the respirations Morphine was at first with-held. The pulse rate remained regular at 42 beats per minute. As the patient was in great pain Morphine gr$\frac{1}{4}$ was administered after half an hour. The patient gradually became comatose; coldness appeared in the extremities and the pulse gradually became weaker although the bradycardia persisted until just before death. She died two hours after the onset of the acute attack.

There are several interesting points about this case. The patient was apparently in good health until two days before the coronary thrombosis set in. It is worthy of note that she had been confined to bed before the attack; this had been done as a

therapeutic measure to see what effect rest would have on her high blood pressure.

The slow pulse after the attack is also noteworthy; in the light of Schwartz's (11) series of cases the amount of adrenalin administered was too small. An impression was gained that the administration of morphine in this case adversely affected the patient.

CASE NO. 5. MR. J. CHRISTIE. AGED 69. RETIRED BANK MANAGER.

In 1934 this patient had an attack of glaucoma in the left eye. The eye was ultimately removed. At this time he had no cardiac symptoms but his blood vessels were thickened, and the blood pressure was 200/144 mm.Hg. He had some enlargement of the left side of the heart, the apex beat being in the sixth interspace, 11 cms from the left sternal border. There was a faint systolic murmur over the aortic area; the second aortic sound was emphatic with a ringing quality. This patient was of thin build; at rest there was a little cyanosis of the lips. For three weeks before the attack he had pain in the chest on exertion which he put down to digestive disturbances.

In May 1936 at 4 a.m. the patient was awakened from sleep by severe pain in the chest which caused him to roll about in bed. The pain was situated behind the lower edge of the sternum, and radiated down the inner border of the left arm. He had one attack of vomiting.

When seen three hours after the onset of the attack he was lying in bed in a state of collapse; he was perspiring freely; the face was pale and the lips cyanotic. There was little dyspnoea. No pulse was perceptible at the wrist although the thickened vessel wall was easily felt. Temperature was 97'4 deg.F. Respirations were 22 per minute. The blood pressure was 95/72mm.Hg.

The apex beat was impalpable; the size of the heart had not altered since the previous examination. The heart rate on auscultation was 78 beats per minute. It was regular.

CASE NO. 5. (Continued)

The sounds were very faint; the emphatic second aortic sound had disappeared.

The urine was normal. The lungs appeared to be normal also.

The pain lasted for forty eight hours; on the second day friction appeared over the region of the apex beat and persisted for a week. The blood pressure on the fifth day was 120/93 mm.Hg. The temperature rose to 100'2 deg.F. on the third day and remained elevated until the tenth day, the highest temperature recorded being 100'8 deg.F. on the 8th day.

Blood pressure on the tenth day was 138/99 mm.Hg.

In the third week the blood pressure rose to 160/130 mm.Hg.

Towards the end of June 1936 he took suddenly ill one night. He had felt well before going to bed but during the night he was suddenly wakened from sleep by a coughing spasm, associated with a sense of suffocation. Dyspnoea was a very marked feature. He began to perspire freely; soon a very profuse frothy blood stained sputum appeared. The temperature was 98'0 deg.F. the pulse rate 68 per minute. The lungs were full of moist sounds. He was propped up, given ¼gr morphine and 1/50 gr Atropine sulphate. In three hours he dozed off and in the morning he felt much better. In twenty four hours all the adventitious sounds had disappeared from the lungs.

For two days afterwards there was an occasional irregularity of the pulse due to extra systoles.

CASE NO. 5. (Continued)

The patient was able to get up by July 1936; he had lost all his former vigour and energy but he had no dyspnoea or angina of effort. The blood pressure four and a half months after the attack was 170/130 mm.Hg.

The patient removed to the South of England as it was thought that the climate there would be beneficial. He remained in good health until his death on 10th December 1936.

No details of this are known, but he collapsed suddenly.

This patient had extensive arterial changes. The attack of pulmonary oedema came on without any obvious cause, and although the patient looked very ill during the attack it did not seem to prolong the convalescence. The way in which the crepitations cleared out of the chest after the height of the attack was passed was very remarkable.

CASE NO. 6. WALTER O'NEIL. AGED 64. RAILWAY EMPLOYEE.

This patient was known to suffer from an advanced degree of arterio-sclerosis. The radial arteries were thickened and the retinal arteries were tortuous. The blood pressure was 180/140 mm.Hg. He had however no symptoms of any cardiac trouble; no breathlessness; and no effort angina. His previous history showed nothing of importance.

The patient took suddenly ill on 2nd July 1935 at 10 p.m. while in bed. He complained of great pain, radiating from the sternum down the inner aspect of the left arm. He had vomited once.

The patient was a tall thin man. When seen on this day, he was very pale and collapsed. He was very restless and was covered with perspiration. There was cyanosis of the lips and the lobes of the ears. There was no cough. The pulse rate was regular at 110 per minute but of very poor volume. The respirations were 22 per minute; the temperature was 97'8 deg.F. The blood pressure was 120/95 mm.Hg.

The apex beat was felt very faintly in the fifth interspace. The heart measured 11'2 cms in the 4th interspace. The heart sounds were very far off and muffled. No cardiac murmurs were detected.

The remainder of the examination was negative. The patient was treated by the administration of Morphine gr$\frac{1}{2}$ and measures were taken to counteract the shock.

On the second day the temperature rose to 100 deg.F. and for three days varied between 99 deg.F. and 101 deg.F.

CASE NO. 6. (Continued)

reaching normal on the fourth day. The acute pain began to pass off in twenty-four hours, and had disappeared by the third day although at this period his left shoulder began to feel uncomfort--able. The pulse rate gradually dropped and reached 78 per minute on the sixth day. The blood pressure on the sixth day was 135/100 mm.Hg. The white cell count on the tenth day was 10,400 per cm. The heart sounds gradually improved in tone. In three weeks time the blood pressure was 142/100 mm.Hg. There was a faint systolic murmur at the aortic area.

The patient was confined to bed for six weeks. About the sixth or tenth day of the illness the patient began to complain of persistent severe pain in the left shoulder and this pain persisted for many months afterwards, and indeed a year later it was still present. It was obvious that he had a marked limitation of abduction of the left shoulder joint; he was at first unable to use this limb for dressing himself although a year later he had so far recovered as to be able to raise his arm vertically above his head. The pain seemed to be seated over two main regions. (1) at the lower border of the deltoid on the outer side of the arm. (2) in the region of the bicipital groove. It was rather difficult to say what was the cause of the limitation of the abduction but it seemed to be due to some degree of contracture of the deltoid; probably also there were some intra-articular adhesions in the shoulder joint. The shoulder joint complication was dismissed as probably rheumatic in origin until the occurrence of a similar case (No.10)focussed attention on this

CASE NO. 6. (Continued)

condition. None of the larger series of Levine, or Parkinson and Bedford mention it. However recently Edeiken and Wolferth have described similar cases.

The patient made a good recovery; he is able to get about very slowly although he is unfit for work. He has no effort angina.

An electrocardiogram taken at Hospital was said to confirm the diagnosis.

CASE NO. 7. MR. T. JOHNSTONE. AGED 36. LABOURER.

This case was seen in hospital in 1929. The patient was admitted to the surgical wards as an acute abdominal case; owing to the difficulty in the diagnosis a consultation was held with a member of the medical staff.

The patient had been in good health until the morning of his illness. On that day about half an hour after breakfast he was seized with acute abdominal pain. He fell to the floor but did not faint. He vomited three times in the first hour. The patient was sent to hospital as an acute abdominal emergency.

He was seen about three hours after admission to hospital and about four hours after the onset of the attack.

He was a tall muscular man. When seen he was pale, collapsed and very restless. The pain seemed to be very severe, and was situated entirely in the epigastrium. There was no radiation to the arms. There was little dyspnoea, and little cyanosis. The temperature was 97'8 deg.F. The respiratory rate was 24 per minute. The pulse was of poor volume but regular. The rate was 106 per minute. There was no thickening of the radial artery. The blood pressure was 110/70 mm.Hg.

DIGESTIVE SYSTEM

The abdomen was examined first. There was marked rigidity of the muscles in the epigastric region. However the rigidity was localized to this area and was absent in the lower abdominal areas. There was no hyperaesthesia over the epigastric area and no tenderness on deep palpation. There were no signs of

fluid in the abdomen, no hepatic enlargement and no distention.

CARDIOVASCULAR SYSTEM.

The apex beat was impalpable. The breadth of the heart in the fourth interspace was 10'8 cms. The heart sounds were very faint at the apex and inaudible over the base of the heart. There were no murmurs.

RESPIRATORY SYSTEM.

There were many crepitations at the left base and here the air entry was impaired. Nothing else abnormal was made out in the respiratory system. The urine was normal. The blood Wassermann reaction was reported to be positive.

The patient was given four administrations of Morphine gr$\frac{1}{2}$ hypodermically at four hourly intervals. He still was restless and complained of great pain. He gradually became comatose and died the following morning.

At post-mortem examination the size of the heart was within normal limits (exact weight was not recorded) A large haemorrhagic infarction occupied all of the anterior surface of the left ventricle, except for a small portion at the apex and base. The septum was not involved. No perforation of the infarction was present and no fluid was found in the pericardial cavity.

The coronary arteries showed no arterio-sclerosis. The left anterior descending branch was obstructed by a thrombus distal to the origin of this vessel from the left coronary artery.

CASE NO. 7. (Continued)

The aorta showed marked lesions of syphilitic aortitis; the vegetations covered the first two inches of the aorta but the aortic cusps did not seem to be implicated. The coronary orifices were not occluded by the aortic disease, but their ostia were rather irregular and deformed. The other organs were normal.

This was the only known syphilitic case in the series, and he was also the youngest patient.

The main difficulty was in the diagnosis; several observers considered the possibility of a perforated gastric or duodenal ulcer while others considered that a diagnosis of Pneumonia might be justified.

The case resembles very closely these described by Levine and Tranter (10) and it is easy to see how a laparotomy could be performed under the impression that an acute abdominal condition was present. This actually happened in one of the cases reported by Levine and Tranter.

CASE NO. 8. J. T. AGED 70. RETIRED LABOURER.

There is no clinical history of this case but the account of his previous health has been obtained from his relatives and the family practitioner.

This patient had been in good health up till three months before his death. At this time he began to feel breathless on exertion. He had no angina pectoris. His doctor found that he had high blood pressure and advanced arterio-sclerosis. The urine examined two months before his death showed no abnormality. The patient left his home at 9-30 p.m. to go for his habitual evening walk. The actual details of his death are unknown but he was found unconscious on the roadway at 10 p.m. and he was dead by the time he was admitted to hospital.

The post-mortem findings were as follows;-

The body was that of a stout thickset man below medium height. On opening the pericardium a large haemorrhagic infarction was seen on the anterior wall of the left ventricle. It involved the base of the ventricle but not the apex. The heart itself was not enlarged although the myocardium of both ventricles showed patchy fibrosis. The inter-ventricular septum was normal. There were no appearances of perforation of the infarction. The heart valves were normal.

There was a remarkable degree of sclerosis of the coronary vessels; on cutting across the vessels the walls split into solid longitudinal strands. A thrombus was present at the junction of the anterior descending branch and the left coronary artery. It apparently blocked both vessels.

CASE NO. 8. (Continued)

Marked arterio-sclerotic changes were present in the cerebral and renal vessels. The kidneys themselves showed granular changes. The other organs were normal.

This case is noteworthy because of the few premonitory symptoms present although extensive arterial changes were found at post-mortem. The degree of sclerosis of the coronary vessels was so extreme that it was remarkable that they were still able to perform their function. From the condition of their walls it must be concluded that long before the fatal thrombosis the vessels had merely been channels for the blood and that they had lost all power of altering their calibre in response to external stimuli.

In these cases one wonders what exactly was the cause which precipitated the infarction. He must have been in danger of this catastrophe for a long time. Perhaps he had walked a little further than usual and thus upset the precarious balance of the coronary circulation; or perhaps some extra cardiac reflex, digestive in origin, had been the immediate cause of the thrombosis.

CASE NO. 9. ROBERT MUIRHEAD. AGED 46. LABOURER.

This patient took ill on 2nd April 1935 with severe pain in the chest. There was nothing of importance in his family history. He was a chronic alcholic case. He had no angina previous to the attack in April 1935 but he said that he had been getting breathless for four months previously and had began to tire easily at his work. This was very strenuous as he was a hammerman. The blood Wassermann was negative.

When first seen he complained of pain in the chest. This was situated behind the sternum and radiated down the inner border of the left arm. He was moderately collapsed; his face was pale, and he was perspiring freely. There was no vomiting; he was very restless. There was little dyspnoea. The temperature was 98 deg.F. The respiratory rate was 26 per minute.

The pulse was very feeble at the wrist; the rate was 80 per minute and it was regular. There was marked sclerosis of the radial vessels. The blood pressure was 140/90 mm.Hg.

The apex beat was situated in the sixth interspace 10'4 cms from the left sternal border; while the heart measured 14'2 cms in the fourth interspace. The cardiac enlargement seemed to be mainly towards the left. The heart sounds were very faint, especially at the base of the heart. No cardiac murmurs were heard.

Measures were taken to counteract shock, he was given $\frac{1}{30}$gr Morphine hypodermically and omnopon gr$\frac{1}{2}$ orally every four hours. Next day he had rallied from the shock. The pulse rate was 98 beats per minute and the temperature was 99 deg.F. He was

CASE NO. 9. (Continued)

still very restless and complained of incessant pain in the praecordium.

On account of his home conditions he was removed to hospital.

In June 1935 he was discharged from hospital with the diagnosis of coronary thrombosis. The electrocardiogram was not personally inspected but it was described as follows;-

Ten days after admission the electrocardiogram showed a " cove " shaped T wave in L III with a high take off of the R S - T interval. T was inverted in L I

This patient was very breathless after his discharge from hospital. He attempted to resume work but found that he was unfit for the strenuous exercise. He began to suffer from praecordial pain after exertion. The blood pressure was 156/98 mm.Hg.

In June 1936 a year after leaving hospital he was still easily tired and he still suffered from angina on effort. The blood pressure was 162/ 102 mm.Hg.

This was a typical attack with subsequent incapacity for work.

CASE NO.10. D. D. AGED 63. A BUSINESS MAN.

This patient had good health up to the time of the present illness. He had no previous angina and no previous breathlessness. The patient was thin and below the average height. On examination three months before the attack nothing abnormal was made out. The pulse rate was regular, 76 beats per minute. There was no thickening of the radial vessels. The blood pressure was 135/98 mm.Hg.

In November 1934 the patient while out walking was suddenly seized with acute praecordial pain radiating down the inner border of the left arm. He managed to reach home where he collapsed.

On examination the patient was pale and perspiring freely; there was no vomiting. The pain seemed to be situated below the lower border of the sternum and it radiated down the left arm and over the posterior aspect of the shoulder joint. The temperature was 97'6 deg.F. the respirations were 27 per minute but there was no dyspnoea. There was a little cyanosis around the lips. The pulse rate was 86 beats per minute; there was an occasional extra-systole. The pulse volume was small, and indeed the pulse at the wrist was difficult to palpate. The blood pressure was 100/80 mm.Hg.

The apex beat was in the fifth interspace lateral to the midclavicular line, and about 9 cms from the left sternal border. The heart dulness was not enlarged. The heart sounds were very faint and muffled. There was a short systolic murmur at the aortic area. An occasional extra-systole interrupted the

CASE NO. 10. (Continued)

regular rhythm of the heart. There was nothing abnormal on examination of the lungs.

The patient was treated as usual. Lacarnol was given in addition to Morphia.

The patient recovered from the shock in twenty four hours but the pain persisted as a dull ache for three days. The temperature on the second day was 99'6 deg.F. on the third day it was 99'8 deg.F. on the fifth day it was 100'2 deg.F. and it became normal on the 8th day. The pulse rate varied between 78 to 100 beats per minute; on the fifth day the extra systoles increased in number so that an intermission in the pulse appeared about every twenty beats; later however they disappeared completely. The blood pressure on the second day was 100/82 mm.Hg. on the fifth day it was 114/82 mm.Hg.

A very faint friction rub was heard on the second day over the apex but it was not made out on any subsequent examination.

The patient progressed very well; he was out of bed after six weeks. His blood pressure at this time was 122/88mm.Hg. The heart sounds were much louder; the action of the heart was regular. He was able to resume business four months after his attack. He was much less active but had no dyspnoea on moderate exertion, and no effort angina. He had some stiffness and pain in the left arm for nearly six months after his attack but this gradually passed off and at the end of this period there was no limitation of movement of the left shoulder joint. An electrocardiogram taken after his illness by a cardiologist was

said to confirm the diagnosis of coronary thrombosis. No details of the exact findings are known.

Two years after the attack he was in good health.

CASE NO. 11. MISS MARGARET PATTISON. AGED 64. HOUSEKEEPER.

This patient suffered from breathlessness and a sense of constriction in the chest six months before the onset of the acute attack. There was nothing of importance in her past history.

When first seen she was very breathless and easily tired. She was a small thin nervous woman. She was rather pale and had cyanosis of the lips and ears. The pulse rate at this time was regular at 78 per minute but it was very full and bounding in character. There was some sclerosis of the radial vessels. The retinal vessels were tortuous. The Wassermann reaction was negative. The blood pressure was 210/140 mm.Hg. The heart was enlarged to percussion, mainly to the left side. The apex beat was in the sixth interspace 11'2 cms from the left sternal border. The breadth of the heart was 14'4 cms in the fourth interspace while the upper border of the heart was in the third interspace. The heart sounds were pure at the apex although the first sound was rather more muffled than normal. The second aortic sound had a loud ringing quality; there was a short localized systolic murmur over this area.

The patient was put on treatment with nitrites. She gradually improved in the next few months.

She took suddenly ill six months after the date of the first examination in November 1932. Suddenly while in bed about 9 p.m. a sudden severe pain appeared in the chest radiating down the left arm. The patient was very restless; she was pale and collapsed and had vomited once. The respirations were rapid,

jerky and rather irregular. The rate was 29 per minute. The lips and ears were cyanosed.

On examination the pulse was hardly palpable at the wrist. It was regular and the rate was 74 beats per minute. The temperature was 98 deg.F. The blood pressure was 115/74mm.Hg. The apex beat was impalpable; there was no alteration in the size of the heart from the previous examination. The heart sounds were hardly audible; they were very faint and muffled; at the apex the first sound was especially weak. The ringing 2nd aortic sound had disappeared.

There was no hepatic enlargement. At the lung base some crepitations were present. The urine contained a trace of albumen. The remainder of the examination was negative. Despite the administration of Morphine at frequent intervals the acute pain persisted for forty-eight hours and after this it was replaced by an ache which persisted for a further three days. The temperature on the second day of the illness was 98'2 deg.F. on the third day it was 99 deg.F. and on the fifth day it was 99'6 deg.F. After this it gradually declined to normal.

The pulse rate remained steady between 76 and 84 per minute.

The blood pressure on the second day was 123/80 mmHg. on the third day it was 127/80 mm.Hg. and on the fifth day it was 132/82 mm.Hg. After the patient rallied from the shock she improved gradually. She was in bed for eight weeks.

Three months later she was able to get about but her

CASE NO. 11. (Continued)

exercise tolerance was poor and angina of effort was present. The blood pressure was 162/108 mm.Hg. and the heart sounds were much more emphatic. The accentuated second aortic was again present.

In December 1936 she was well but her activity was still greatly diminished because of breathlessness and effort angina.

CASE NO. 12. MR. ESKOVITCH. POLISH JEW. AGED ABOUT 50. (SALESMAN)

The history of this patient was obtained from his relatives as he was semi comatose when first seen. He had always been healthy but about three months before the onset of the present illness he had begun to be breathless on exertion; he had however never complained of any angina. His weight had been gradually increasing over the last year.

The attack came on with great suddenness; while talking to a friend in the street he suddenly became pale, complained of pain over the lower part of the chest, and collapsed on the ground. He was seen about thirty minutes after the onset of the attack.

He was a stout man of average height. He was obviously very ill. He was lying tossing about in bed complaining of a sensation in his chest; it did not seem to be so much an acute pain as a sense of constriction or oppression. He was deathly pale and the pallor besides being facial was also easily seen in the extremities. The breathing was shallow and rather irregular. There was no pain on respiration. The temperature was 97'0 deg.F. The respirations were 24 per minute. The pulse was impalpable at the wrist.

The systolic blood pressure was about 70 mm.Hg. No diastolic reading could be obtained. The apex beat could not be felt. The heart dulness appeared to be within normal limits. The heart sounds were inaudible.

There were moments when the patient appeared to

rally but eventually he became comatose and died about two hours after the onset of the attack.

A post-mortem performed by the police surgeon confirmed the diagnosis of coronary thrombosis.

No details of the post-mortem findings are available.

CASE NO. 13. MR. WATSON. AGED 72. COMMERCIAL TRAVELLER.

This patient was first seen on January 1932 when he complained of breathlessness on exertion. He was a tall, thin very active man who had always been in good health. There was nothing of importance in his past history. The pulse rate at this examination was 84 beats per minute, the respirations were 18 per minute and the blood pressure was 186/120 mm.Hg. There was pronounced thickening of the radial vessels but the retinal vessels appeared normal.

The apex beat was in the sixth interspace 10 cms from the left sternal border while the breadth of the heart in the fourth interspace was 12'2 cms. The cardiac enlargement was mainly towards the left. The heart sounds were of good tone; the second aortic sound was emphatic. There were no murmurs.

The remainder of the examination was negative. The urine was normal and the Wassermann reaction was negative. The patient was put on to routine treatment Tab. Glyc. Trinit. t.i.d. were given.

About six months later while the patient was sitting in his chair two and a half hours after a meal, he suddenly had acute pain in the chest. He collapsed immediately and had to be assisted to bed. He was seen about two hours after the onset of the attack. He was pale and perspiring freely; the lips were blue. He had no vomiting or dyspnoea. He was very restless. The pain was confined to the chest; he could not localize it exactly but it seemed to be behind the lower edge of the sternum.

CASE NO. 13. (Continued).

The temperature was 98'0 deg. F. The respirations were 26 per minute, while the pulse rate was regular at 82. The radial pulse was hardly palpable. The blood pressure was 105/78 mm.Hg.

The apex beat was faintly perceptible to palpation in the sixth interspace. There was no alteration in the cardiac dulness from the previous examination. The heart sounds were very muffled, the first sound at the apex being almost inaudible.

The patient gradually rallied from the shock; on the second day the temperature rose to 98'0 deg.F. and on the 8th day it was 101'4 deg.F. It was normal by the twelfth day. The pulse gradually improved in volume and was easily palpable by the fourth day. The rate varied between 72 and 86 for the first week. The blood pressure on the second day was 112/82 mm.Hg; on the fifth day was 115/82 mm.Hg. and was the same on the tenth day.

The pain lasted for two days. The patient was out of bed in six weeks' time. He was unable to resume business as he was easily tired out on exertion. The blood pressure was 148/102 mm.Hg. The heart sounds were clear and the emphatic second aortic sound was again present. The diagnosis was confirmed by an electrocardiogram taken in hospital.

In July 1936 he came complaining of "indigestion". It was evident that this was angina of effort; the pain came on after the patient ascended a hill or employed any unusual exertion. It was situated in the chest and had no radiation. As a rule it lasted for three or four minutes. The blood pressure was 156/110 mm.Hg.

CASE NO. 14. MR. PATERSON. WATCHMAKER. AGED 72.

This patient took suddenly ill on 14th November 1936. He had previously been in good health, and was able to go for long walks every day. He was a stout man of medium height. On the night of the onset of the illness, he felt well on going to bed. While in bed before he was asleep, sudden pain set in under the sternum. There was no radiation from the chest. He put the pain down to "indigestion", but on the following morning the pain still persisted.

When seen on the following morning he was pale, collapsed and sweating. There was no vomiting. He was very restless. There was no cyanosis and no dyspnoea. The pain was accompanied by a sense of constriction in the chest. The pulse was very feeble at the wrist; the rate was 82 per minute, and the rhythm regular. The radial arteries were sclerosed. The temperature was 98'0 deg.F., and the respirations 20 per minute. The patient was not greatly prostrated and was able to rise from bed.

The blood pressure was 98/76 mm.Hg. The apex beat was impalpable. The heart did not seem to be enlarged; the cardiac dulness measured 12'2 cms in the fourth interspace. The heart sounds were very distant but were audible over the whole of the cardiac area. There were no murmurs. He was not seen personally on the second day of his illness; however at this period the collapse had passed off but the pain persisted; it seemed to come in paroxysms and morphine had little effect in soothing the pain. The patient was extremely restless, and when unattended attempted

CASE NO. 14 (Continued)

to rise from bed.

On the third day the pulse rate was 78 per minute and the pulse could be more easily felt at the wrist. The heart sounds were still very distant. There was no friction rub. Examination of the abdomen was negative. There were a few crepitations at each base.

The paroxysms of pain still continued despite morphine gr½ every four hours hypodermically. During the pain the patient became extremely restless and sometimes maniacal. He attempted to struggle from his bed. On the fourth while apparently quiescant he was left unattended for a few minutes. The patient rose from his bed to visit the lavatory where he was found dead on the floor.

A patient with recurring paroxysms (status anginosus); the resistance of the pain to the usual sedatives was a noteworthy feature and recalls Levine's statement that for some cases Chloroform has to be administered.

CASE NO. 15. WILLIAM THOM. AGED 59. HAIRDRESSER.

This patient had been in good health until 10th February 1937. On this date he complained of pain in his chest which came on after he had been out walking at night. The weather was exceptionally cold, and he said that he first felt the pain after he had been out walking for half an hour. The pain persisted throughout the night; it was very severe and made him very restless; however there was no collapse. In the morning he was well enough to leave his house to receive medical advice.

There was nothing of interest in his previous history; he had always been healthy except for an attack of indigestion two years before. There was no record of his blood pressure before the attack. When seen on 11th February 1937, the patient was pale and easily breathless on exertion. He had no pain and apparently had recovered from his attack of the previous night.

The pulse was of poor volume but the rate was regular at 82 beats per minute. The respirations were 24 per minute; the temperature was 98'6 deg.F. The blood pressure was 100/64 mm.Hg. There was some arterial thickening.

EXAMINATION OF THE HEART.

The apex beat was in the fifth interspace in the midclavicular line, 10 cms from the left sternal border. The breadth of the heart dulness in the fourth interspace was 12'2 cms The heart sounds were distant; there were no murmurs. The second pulmonic was louder than the second aortic sound.

There was no hepatic enlargement.

CASE NO. 15. (Continued).

The remainder of the physical examination was negative. There was nothing abnormal found on examination of the urine.

The patient was sent home to bed. Two days later he was comfortable; there was no pain. The pulse rate was 84 beats per minute; the temperature was 99'4 deg.F. and the leucocyte count was 18,400 cells per cm. The blood pressure was 100/70 mm.Hg.

On the third day he felt so much better that he rose from bed and went out at night for a short walk. (the patient could not be convinced that his condition was not an attack of indigestion)

On returning home he sat down to fill his pipe but collapsed and died within five minutes.

No details of the post-mortem are available but the police surgeon certified death as being due to coronary thrombosis.

In this case the patient had no premonitory symptoms before the attack. The pain came on apparently after exercise. It seemed severe but passed off completely in twelve hours; at this time he was able to walk about without discomfort. The low blood pressure was an important point in the diagnosis; the heart sounds were faint but not inaudible. There seems to be no doubt that the onset of the infarction was marked by the attack of severe thoracic pain; it was remarkable that he could move about so freely twelve hours after the attack.

In studying first the factors which influence the occurrence of infarction in any particular site on the wall of the ventricle, it is necessary first to remember certain anatomical facts. There is no need to give a full description of the coronary vessels, this has been done in several excellent monographs and papers by Spalteholz (12) Gross (13) Campbell (14) Whitten (15,16). Their findings are in very close agreement.

The blood supply to the auricles is of little importance, except in relationship to the collateral circulation.

THE LEFT CORONARY ARTERY runs to the left and bifurcates under cover of the left auricular appendage into the left circumflex division, and the left anterior descending branch. The latter vessel forms the main blood supply to the anterior surface of the left ventricle. It runs down in the anterior inter-ventricular furrow, passes round the apex and anastomoses with the posterior descending branch of the right coronary artery at the lower third of the posterior inter-ventricular furrow. The circumflex branch of the left coronary artery continues along the auriculo-ventricular groove and it eventually supplies a portion of the posterior surface of the left ventricle.

THE RIGHT CORONARY ARTERY runs to the right and emerges between the roots of the aorta and pulmonary artery. It passes around the right border of the heart (margo acutus) and at that point on the posterior aspect of the heart where the auricles and ventricles meet (Crux) it gives off the posterior descending branch. The right coronary vessel as it runs transversely is usually known as

the right circumflex artery. The posterior descending branch runs down in the posterior inter-ventricular furrow, anastomosing with the termination of the anterior descending branch of the left coronary artery. The main vessel continues from the crux for two thirds of the way down the posterior surface of the left ventricle, where it terminates. Thus the blood supply to the left ventricle is divided between the two coronary arteries and mainly between the anterior and posterior descending branches of each artery. The left coronary artery supplies most of the anterior aspect of the left ventricle, and the right coronary artery most of the posterior aspect of the left ventricle. The blood supply to the ventricles is given by Whitten (16) as follows:-

" THE LEFT CORONARY ARTERY supplies the entire anterior surface of the left ventricle, the adjacent third of the anterior surface of the right ventricle, the apex of both ventricles, all of the inter-ventricular septum at the apex, the anterior two thirds of the septum above that point and the left half of the posterior surface of the left ventricle. It supplies also the anterior papillary muscles, and the lower portion of the posterior papillary muscles of the left ventricle, and most of the anterior papillary muscles of the right ventricle.

THE RIGHT CORONARY ARTERY. supplies two thirds of the anterior surface and all of the posterior surface of the right ventricle with the exception of the apex. It supplies the posterior surface of the inter-ventricular septum except at the apex, and the adjacent half of the basal three fifths of the left ventricle. It supplies the posterior papillary muscles of the right ventricle, and generally, the upper portion of the posterior papillary muscles

of the left ventricle."

From the above description the theoretical site of the infarction can be predicted when any particular vessel is obstructed. Obstruction of the left anterior descending branch leads to an infarction situated on the anterior aspect of the left ventricle, and it may include the apex of the heart, an adjacent strip of the right ventricle, and sometimes a portion of the inter-ventricular septum. This is the ANTERIOR INFARCTION. Infarction of the right coronary artery usually leads to obstruction of its two terminal divisions. The infarction is situated in the basal region of the left ventricle. This is the POSTERIOR BASAL INFARCTION.

When the left circumflex artery is obstructed then the infarction is usually found on the lateral aspect of the left ventricle, the LATERAL OR MIDVENTRICULAR INFARCTION.

The majority of infarctions of the heart fall into one of these groups. Infarctions of the right ventricle are usually small and associated with infarctions of the left ventricle; Saphir (17) and his associates had only one case of right ventricular infarction in twenty-four cases of myocardial infarction. Appelbaum and Nicolson (18) examined one hundred and thirteen cases of myocardial infarction and found only eight cases of infarction of the right ventricle. Thus for all practical purposes myocardial infarction is mainly confined to the left ventricle.

What are the factors which lead to this predominance of left ventricular infarction?

Whitten (16) has described a difference between the vessels supplying the two ventricles. This writer points out that the left ventricle can, as regards its blood supply, be divided by a plane passing between the branches of the anterior descending branch of the left coronary artery, and the terminal branches of the right coronary artery. The former vessel supplies the anterior aspect of the left ventricle mainly, while the right coronary artery supplies the posterior basal region of the left ventricle. The branches supplying the right ventricle spread out in a manner parallel to the long axis of the heart. The branches supplying the left ventricle leave the main vessels at right angles, pass perpendicularly through the myocardium and under the endocardium turn at right angles parallel to the endocardial surface where they end in small arterial twigs. Whitten considers that this method of supply immobilizes the parent vessels in the case of the left ventricle, while in the case of right ventricle the blood vessels have considerable mobility. Also the commencement of the left coronary artery is immobilized by the anterior descending branch, while the right coronary artery is free at its commencement and is able to expand considerably if its wall is diseased. Whitten considers that the lessened mobility of the vessels supplying the left ventricle is an important factor in deciding their liability to obstruction.

Gross (13,19) has also described this difference between the blood supply to the two ventricles; he says that the condition follows the hypertrophy of the left ventricle which comes on with increasing age. The differences in the blood supply to the ventricles are well seen in the illustrations to

Whitten's (15) paper and the photographs in Gross's (13) monograph.

Certainly, thrombosis is relatively uncommon in the first part of the right coronary artery. The question can be further studied by comparing the frequency of obstruction of each of the coronary vessels.

In cases of coronary thrombosis following on arterio--sclerosis of the vessels, all writers are agreed that the left coronary artery is more frequently obstructed than the right coronary artery. In Parkinson and Bedford's (20) series there were thirty-seven cases of left sided obstruction to eighteen cases of right sided obstruction. In Barnes and Whitten's(21) series there were twenty-five cases of the former to eleven cases of the latter. These writers consider that many cases of posterior infarction are small and are missed at post-mortem. The anterior descending branch of the left coronary artery is the commonest site of obstruction. This was the site of thirty-nine out of a total of forty-nine cases in a series reported by Levine (22)

This writer finds that the usual site of thrombosis is 2 cms distal to the origin of the left descending branch from the left coronary artery. The right coronary artery is the next most frequent site. According to Saphir (17) and his associates, the obstruction more frequently involves the terminal ventricular branches than the terminal branches of the posterior descending branch. The left circumflex artery is not often obstructed alone.

It is thus seen that the common sites of obstruction lead to infarctions of the left ventricle; the anterior infarction is commonest, the posterior basal infarction next in frequency and the midventricular infarction least common of all three.

There is another difference between the two ventricles, the effect of which on the relative frequency of the site of infarction, is difficult to estimate. Anrep and Segall (23) have stated that the blood flow during the systole of the ventricles is arrested, at least in the left ventricle, where the intra-ventricular pressure is greater than in the right ventricle. Probably, as will be shown later, the flow is not arrested, but only the velocity of the flow is diminished, the volume of the flow not being much changed. Thus the velocity of the flow would be diminished more in the left ventricle during systole than in the right ventricle. This might have some effect in predisposing the left ventricle to infarction, especially if the vessels were sclerosed.

The pathology of the arterial disease has some bearing on the site of the infarction. The above statements apply when the coronary vessels are the seat of arterio-sclerosis. When however myocardial infarction follows on the presence of syphilis (usually syphilitic aortitis), the right coronary artery is more frequently occluded than the left. In a series of syphilitic cases reported by Bruenn (24) the right coronary artery was occluded eight times for every single left sided occlusion.

It may be concluded that left ventricular infarction is more common than right sided infarction because the common sites

of coronary thrombosis lead to infarctions on the left ventricle. This may be due to differences in the arterial supply to the ventricles. The first part of the right coronary seems to be little liable to obstruction. In addition there are probably differences in the haemodynamic conditions in the walls of the two ventricles; although the left ventricle seems to have a more profuse blood supply than the right, the fluctuations in the circulation of the left ventricle, in response to external stimuli, are probably more extensive.

EXTENT OF THE INFARCTION. The infarction rarely corresponds in size to what would be expected theoretically. An infarction may range from the size of a penny to an area which extends over most of the surface of the heart. The collateral circulation tends to overlap from the area of the sound vessel into that of the obstructed vessel. Several factors influence the effiency of the collateral circulation. These are (1) age (2) variations in the distribution of the coronary vessels, (3) the presence of disease in the coronary vessels, (4) and closely connected with (3) is (4) the rate of closure of the coronary vessels, (5) the condition of the myocardium, (6) the systemic blood pressure, (7) site of the obstruction in the coronary artery.

(1) AGE CHANGES in the coronary vessels have been studied by Gross (13). Müller(quoted by Gross (13)) has shown that at birth both ventricles are of approximately the same weight; up to fourth decade the left ventricle rapidly increases in weight as compared with the right ventricle; and after the fourth decade the left ventricle still increases, but more slowly. Associated with

this left ventricular preponderance as regards weight, there is an increased blood supply to the left ventricle. Gross's (13) and Campbell's (14) results are mainly in agreement. In another paper by Gross (19) the various stages of the development of the blood supply to the ventricles and the septum can be easily followed in the illustrations (photographs of injected hearts). Thus at birth there is an equally generous blood supply to each ventricle. Fat vessels are absent and so are the septal vessels. By the second decade the blood supply to the left ventricle is a little more abundant than to the right ventricle; septal vessels and fat vessels are small and there is little tortuosity of the main trunks. Gradually, through the third and fourth decades of life, the left ventricular preponderance of the blood supply increases, while the septal vessels and the fat vessels develop. At the fifth decade the main trunks show some tortuosity. By the sixth and seventh decades the septal anastomoses are free while the fat vessels are pronounced. At the eighth decade arterio-sclerotic changes appear in the main trunks while the septal vessels and the fat vessels are large. Whitten (16) however says that the left ventricular preponderance is absent after the tenth year. Gross (19) has discussed the results of other investigators and it seems that their varying results are due to imperfect technique in injecting the coronary tree.

The question concerning the anatomical channels whereby the collateral circulation is carried on in cases of myocardial infarction, will be discussed later. Gross (13) thinks that the heart of an old person is better able to withstand an infarction than is the heart of a young person, because in the

latter the collateral channels are relatively undeveloped. Gross's anatomical findings can probably be accepted but his conclusions on the ability of the heart of an old person to with--stand an infarction are more doubtful. In Levine's (1) series the average age of recovery was less than the average age of death. Although the anastomoses are well developed in old age this increase in the collateral circulation is probably offset by other factors; e.g. disease of the vessel walls and myocardial fibrosis. The former would tend to diminish the blood supply and the latter might obliterate some of the smaller twigs.

(2) VARIATIONS IN THE DISTRIBUTION OF THE CORONARY VESSELS probably account for many variations in the size and site of the infarction. Variations in the coronary vessels are very common, especially in the ultimate distribution of the smaller branches. Gross (13) gives a full description of the usual variations in his monograph. One important variation is that in which both descending branches arise from the left coronary artery. It can be seen that obstruction of the left coronary artery in this case would lead to a much more extensive infarction than in the usual arrangement of the descending branches. To take another example, it is known that in 92% of cases the ramus septi fibrosi arises from the right coronary artery. The ramus septi fibrosi supplies the A - V node. The right coronary is not often obstructed. However if the ramus septi fibrosi arose from the left coronary artery (as occurs in 8% of cases) then it would be liable to be obstructed along with the obstruction of the main trunk of the left coronary artery. Disturbances of rhythm might then occur

from interference with the blood supply of the A - V node.

(3) THE EXTENT OF ARTERIAL DISEASE is bound to effect the site and extent of the infarction. Atheroma is the usual condition found at post-mortem; syphilis is a much rarer cause while other conditions are rarely the cause of coronary occlusion. The condition of the arterial wall is also bound up with the fourth factor; the rate of closure of the coronary vessels.

(4) WHEN COMPLETE OCCLUSION OF THE CORONARY VESSELS IS PRECEDED BY A GRADUAL DEGREE OF NARROWING

then the infarction is not likely to be so extensive as it would have been if no previous narrowing had taken place. Any gradual narrowing of the parent stem will allow the collateral anastomoses time to develop and so limit the extent of the infarction which follows on the complete closure. In cases of atheroma of the coronary trunk some degree of narrowing is frequently present before complete obstruction supervenes. Gradual occlusion leads to fibrosis of the myocardium; a considerable degree of fibrosis is frequently found post-mortem in cases of sudden complete occlusion. This benefit developing from previous gradual narrowing may be counteracted by the arterio-sclerotic changes in the collateral vessels, and by the replacement of the muscle of the heart wall by fibrous tissue. Several cases of complete occlusion of both coronary vessels at their ostia are on record. Most of these cases were due to syphilitic aortitis and in all of them the occlusion developed gradually and the patient died slowly, usually from congestive failure. Leary and Wearn (25) described cases in which both vessels were completely occluded in

syphilitic aortitis. Cannon (26) Carr (27) Albutt (28) have described very similar cases. It is thus well established that provided the occlusion is gradual, both coronary vessels may be completely obstructed at their origin without myocardial infarction supervening on the closure.

(5) Recent investigations by Wiggers (29,30) and his associates gives the MUSCLE OF THE HEART an important role in maintaining the coronary flow especially in the capillary bed. It is difficult to assess the effects of any fibrosis of the myocardium. Presumably the fibrosis may obstruct some of the smaller capillaries; fibrous tissue needs less blood than cardiac muscle, so that in any fibrous area the capillaries will be few in number.

(6) The SYSTEMIC BLOOD PRESSURE is important in keeping up the coronary circulation. The coronary flow is increased by raising the systolic blood pressure (Anrep (31)) However so many other factors complicate hypertension in cases of coronary occlusion that it is difficult to say what effect the raising or lowering of the blood pressure will have on the coronary flow. Presumably, if the coronary vessels show some degree of obstruction, elevation of the blood pressure will help them to fill properly.

(7) There is also a relationship between the extent of the infarction and the site of the obstruction in the vessel, but this is not always so close as might be expected. This can be seen from the two post-mortem reports in the present series. In case No.8 the obstruction was in the anterior descending branch of the left coronary artery and yet the area of infarction was larger

than in case No.7 where the infarction was in the main stem of the left coronary artery. Post-mortem reports are full of such discrepancies.

A vessel may be suddenly obstructed without any infarction being found in the area of the vessel; in this case the vessel was probably functionless before its obstruction. The obstruction of a vessel may cause an infarction in the area supplied by another vessel. Saphir (17) and his associates have described two cases of this nature; in these cases thrombosis of the circumflex branch of the right coronary artery caused an infarction in the area supplied by the left coronary artery. The right coronary artery must have been supplying the area of the left coronary artery, this latter vessel having become functionless because of arterial disease. Probably small obstructions are not uncommon. It is easy to imagine a condition where the arterial supply to a portion of the heart is so diminished that the obstruction of a small twig would be enough to precipitate an infarction. These cases are probably those which at post-mortem show no signs of thrombosis in the larger vessels.

We have thus discussed the factors which govern the extent of the infarction after coronary obstruction. It will be seen that it is impossible to calculate the exact effects of any one of them. The very varying effects of coronary artery obstruction can thus be understood.

Coronary thrombosis has been produced experimentally by the intra-venous injection of acetylcholine (Hall Ettinger and Bonting) (32). At present there seems to be no practical

application of this finding.

Obstruction of the coronary sinus has been little investigated. Apparently ligation of the sinus does not lead to much cardiac disturbance. Gross,Master and Silverman (33) ligated the coronary sinus in dogs and found that the heart became dilated and engorged. Subsequently the R - T interval became elevated while the ventricular deflection became notched and deflected downwards. The T wave became inverted and there was temporary slowing of the heart. It is remarkable that coronary sinus ligation should have so little effect on the heart when one considers the effects of venous obstruction elsewhere,e.g. in the femoral vein.

It tends to support the view that under certain circumstances a large amount of the venous blood can reach the heart chambers by the thebesian system. Under normal working conditions it has been estimated that 40% of the blood entering the coronary arteries does not leave by the coronary sinus (Markwalder and Starling (34))

THE CORONARY CIRCULATION AFTER MYOCARDIAL INFARCTION.

Reisman and Harris (35) describe a case where recanalization of a coronary vessel occurred after thrombosis, but from the post-mortem report it is doubtful if the vessel regained its function. Probably once a coronary vessel is thrombosed it never functions again. In the first few days after infarction there is always likely to be some extension of the infarction due to surrounding oedema and haemorrhage obstructing the collateral vessels.

It may be said that after myocardial infarction all the main factors which maintain the coronary circulation are unfavourably influenced.

One of the most important sequences of cardiac infarction is a fall in the systemic blood pressure. Anrep and Segall (23) have shown that the coronary flow is greatly influenced by changes in the systemic blood pressure; decrease in the pressure causes decrease in the coronary flow and vice versa. According to Levine,(1) (page thirty of his monograph), the fall in the blood pressure is greatest in these cases in which hypertension was present before the attack and it might be expected that in these cases the coronary circulation would be more embarrassed than in these with normal pressure before thrombosis. In any case the fall in the blood pressure is important in diminishing the coronary flow. If the infarction is extensive it will affect the pumping action of the left ventricle and diminish the cardiac output. Increasing or decreasing the cardiac output also influences the coronary circulation in the same way as the alterations in systemic blood pressure, although the two actions are independent (Anrep and Segall)(23).

The heart rate has no influence on the coronary flow. However any disturbance of rhythm is likely to interfere with the coronary circulation; a tachycardia will lessen the diastolic interval, during which the coronary vessels fill, while any pronounced bradycardia, as in complete heart block, will still further diminish the cardiac output and general failure will include also the coronary circulation.

The infarcted area affects the intra-mural circulation in another manner.

Green,Gregg and Wiggers (57) have demonstrated that "the changing resistance within the ventricular walls, and the variations of aortic pressure during each cardiac cycle, constitute continually opposing forces which determine the velocity of flow from moment to moment, but one or other dominates at different times during each heart beat."

The ventricular muscle contraction begins to influence the cycle early on in systole (during isometric contraction); when the muscle is destroyed by infarction one of the chief forces in regulating the coronary flow is lost. Other factors being equal, this would tend to increase the coronary flow through the area of infarction.

There are other factors which influence the coronary flow but they are probably of little importance in coronary thrombosis. Thus a diminuation of the oxygen saturation of the blood accelerates the coronary flow, especially after the figure falls below 50%. Changes in the carbon dioxide content from 3% to 7% and an increase in the pH of the blood increase the coronary flow (Anrep. (31)). The absorption of tissue products from the area of the infarction is said to be the cause of the fever and the leucocytosis after infarction. Metabolites cause a very varying effect on the coronary flow e.g. histamine dilates the coronary vessels of the cat but constricts the coronary arteries of the rabbit. The absorption of tissue products is not likely to influence greatly the coronary flow after coronary thrombosis as

the other factors present are of much greater importance.

There is little definite information in the literature concerning the period for which the total blood supply can be cut off from cardiac muscle without causing death. This period varies with the different tissues of the body; it is well known that in the case of nerve tissue the period is very short, probably not more than five minutes. In Tennant and Wiggers (36) experiments the ligatures around the coronary vessels were released after being tied up to periods of two hours, and contract--ility returned to the ischaemic area. Sutherland Dial and Harris (37) found that no demonstrable changes were present in an area of experimentally produced infarction until at least ten hours had elapsed from ligature of the vessel. Tennant et alia (38) found that eight hours after ligation, oedema of the interstitial tissue appeared along with fat droplets in the myocardial fibres. Tennant and Wiggers (36) give no information in their paper as to the period during which contractility will persist in the ischaemic area. However the period during which the blood supply may be cut off from the myocardium without permanent damage to the muscle fibres is probably of short duration. By the time histological changes described by Sutherland Dial and Harris (37) have set in, the muscle has been dead for some time. It seems likely that total deprivation of blood from an area of the myocardium for more than one hour will lead to necrosis of the muscle cells. The chief importance of this finding is in estimating the beneficial effects of vaso-dilator drugs.

THE EFFECT OF THE INFARCTION ON THE WORKING OF THE HEART.

The area of the infarction is useless in maintaining the cardiac output, and no doubt part at least of the fall in the blood pressure is due to failure of the myocardium, especially as infarction is so common in the left ventricle. If the patient survives the acute stage of the attack he may die later from insufficiency of the myocardium, manifested clinically by symptoms of congestive failure. This may come on immediately, or at a considerable interval, after the attack. This indicates that the ventricle has not enough force to maintain the systemic circulation properly, such an extensive portion of the heart muscle being replaced by fibrous tissue. The infarction may involve the conducting system of the heart; this will be discussed later under the clinical section. Marked disturbances of rhythm are not common in myocardial infarction.

(Tennant and Wiggers(36)) have shown that the function of heart muscle which is first impaired by loss of blood supply is contractility. These investigators clamped the ramus descendens artery of the dog, and by means of a myograph they obtained a curve from the ischaemic area. They found that the curve obtained was an inversion of that obtained over normal ventricular muscle. The inversion began one minute after the ligation of the artery. They concluded that one minute after the production of an ischaemic area, the contractility in that area is either absent or extremely feeble. They also concluded that the muscle fibres of an ischaemic area stretch, instead of contract, during ventricular systole.

Irritability and conduction are little altered in the ischaemic area; after experimental production of such an area the heart was stopped by vagal stimulation; on applying induction shocks to the ventricles it was found that they were propagated across the ventricles in a normal manner and were unaffected by the presence of the ischaemic portion of ventricular muscle. It seems therefore that anoxaemia produces as its first effect on cardiac muscle, an interference with the property of contraction.
The infarcted area is usually regarded as a functionless portion of the contracting ventricle, and the consequent loss of power of the ventricle is due thus to loss of that part of the ventricular muscle which is involved in the infarction. (This resembles Craib's (46) view, that the electrocardiographic changes after myocardial infarction are due to loss of that part of the ventricular component represented by the infarcted area).

However Tennant and Wiggers (36) show that the loss of the power of the ventricle after infarction may also be due to loss of power following stretching of the ischaemic area by the intra--ventricular pressure, i.e. some of the total intra-ventricular pressure is used in expansion or stretching of the infarcted area. Tennant and Wiggers' results only apply to the immediate results of myocardial infarction. The formation of fibrous tissue sets in about three weeks after the onset of the infarction. Rupture of the heart however is not so common as might be expected from Tennant and Wiggers' results.

We thus find that when an infarction appears in the heart wall the output of the heart is diminished from interference with the force of contraction and from stretching of the infarcted area by the intra-ventricular pressure. The contractility of the affected area is lost early; the relationship between the aortic pressure and the peripheral coronary resistance is altered, as the contraction of the infarcted area is lost.

CAUSES OF DEATH IN CORONARY THROMBOSIS.

The only two post-mortem results in the present series are of cases which died in the first twenty four hours after the onset of the attack. Death however, is always liable to occur suddenly, especially in the first three weeks. As regards the pathological causes of death within the first three weeks, there are three common causes; (1) Rupture of the heart. (2) extension of the thrombosis. (3) embolism.

Other conditions which may cause death, but have little or no pathological signs are:- (1) ventricular fibrillation, (2) auriculo-ventricular dissociation, (3) shock and various reflex conditions, eg: carotid sinus reflex.

(1) RUPTURE OF THE HEART.

This may occur in the first three weeks when the infarction is friable, or later when in the scar in the mayocardium gives way. The usual time for early rupture is about the tenth or eleventh day. Cases No.1 and 2 were probably cases of cardiac rupture. The infarction is friable up to about the third week. The actual rupture may seem to be related to movement although in some cases

this is so slight that it would not appear to put much strain on the infarcted area, (eg: case 2). About this time the patient is often feeling so much better that he is inclined to move about too freely. This occurred in No.1 and 15. who died suddenly within twelve days of the attack after surviving the first forty eight hours. Levine (1) on page 103 of his monograph says that 6% of cases of coronary thrombosis die of rupture of the heart. Harvey is said to have reported the first case in 1647. Recent analyses have appeared by Davenport (39) Beresford and Earl (40) and Salzmann (41). The tear may be very small. Haemopericardium is usual but not invariable. Beresford and Earl (ibid) state that the blood does not always come from the heart chamber but sometimes from the heart wall. These authors consider that hearts which are the subject of considerable fatty infiltration are more liable to rupture because of the well known tendency of degenerated fat to liquefy. They consider that the main force causing rupture is the intra-ventricular pressure. There are however probably other factors as yet unknown which lead to rupture; the intra-ventricular pressure no doubt plays an important part but rupture and aneurysm of the heart are not very common; if the intra-ventricular pressure was the main cause of rupture it is difficult to see what would prevent rupture occurring in nearly every case of infarction. There must be some other factor which diminishes the effect of the intra-ventricular pressure on the infarction.

Davenport (39) analysed the literature and he gives the frequency of rupture at difficult sites as follows:-

Left Ventricle.	79'8%	Right auricle.	5'3%
Right Ventricle.	10'7%	Left auricle.	1'8%

and miscellaneous cases 2'4%.

As cardiac rupture is usually a sequel to cardiac infarction the greater frequency of rupture of the left ventricle is what would be expected as this is the common site of infarction. Auricular rupture is found in younger persons (Clowe and Gorham(42) Death may ensue suddenly; sometimes the patient survives for a few hours. Rupture of an aneurysm of the heart some time after infarction may cause sudden death. Nine cases out of one hundred and fifty cases of infarction showed a cardiac aneurysm (Appelbaum and Nicolson (18)) and in a series of thirty four cases reported by Saphir (17) and his associates six aneurysms occurred. Small aneurysmal dilatations over fibrous areas are not uncommon but they cause no symptoms.

Rupture of the inter-ventricular septum appears to be uncommon; from post-mortem reports septal involvement is frequent so that it is remarkable that rupture of the septum is not more common.

There were two cases of inter-ventricular rupture in Appelbaum and Nicolson's (18) series of one hundred and fifty cases of infarction. Freeman and Griffen (43) reported two cases; one of the patients lived one and a half days, but this is exceptional; the formation of a communication between the two ventricles usually leads to sudden death.

The muscular component of the septum is most marked at the lowest portion of the septum where infarction is most frequent. This must protect the septum from rupture. Apparently the septum does not often rupture at the time of the infarction, but may do so about ten days after the infarction has set in.

Bickel and Moser (44) under the title of "perforating infarction of the inter-ventricular septum" describe two cases in which a perforation was found post-mortem in the inter-ventricular septum. In each case there was a large infarction on the ventricular wall. In the first case the patient gave a typical history of coronary thrombosis. He died three weeks from the onset of the illness; the infarction was situated on the anterior wall of the left ventricle and the perforation was on the apical end of the septum. The second case was what would be called a painless infarction; onset with signs of cardiac failure and death in three weeks time. The infarction was situated posteriorly, due to obstruction of the right circumflex coronary vessel, while the perforation was found high up on the posterior aspect of the septum. An infarction confined entirely to the septum must be a rarity.

Inter-auricular rupture is very rare. There is said to be only one reported case (Marshall H.T. quoted by Swineford)(45)

(2) EXTENSION OF THE THROMBOSIS.

It is impossible to estimate the number of patients who die from a progressive extension of the thrombosis, as there is no way of determining the size of the infarction at its onset. Many cases die in the first three weeks in which no rupture is found to explain the cause of death.

One would expect that a progressive extension of the thrombosis would be likely in coronary thrombosis. A certain amount of extension must take place in the first few hours, until an area is reached in which the collateral circulation is sufficient for the nutrition of the myocardium.

Extension of the thrombosis is common in other similar conditions e.g. in cerebral thrombosis where the gradual development of the thrombosis gives rise to a typical progression in the symptoms. The oedema and haemorrhage around the infarction will tend to interfere with the collateral supply and increase the tendency for the thrombosis to extend beyond the original area. The lower--ed blood pressure will tend further to diminish the coronary flow. This extension might lead to ventricular fibrillation or sudden auriculo-ventricular dissociation. The development of the status anginosus is said to be due to extension of the thrombosis. This occurred in case No.14.

(3) EMBOLISM may follow myocardial infarction; this may occur shortly after the attack, or at a considerable interval, when the coronary incident has been forgotten. The emboli may be systemic or pulmonic. Out of a total of two hundred and eighty-seven cases of infarction there were forty-nine cases of embolism in Connor and Holt's (47) series. Twenty-one of these cases had pulmonary embolism, while the systemic emboli occurred mainly in the cerebral vessels (twenty-one cases). Other sites of embolism are the renal vessels (eight cases) the popliteal, retinal, femoral and brachial arteries. Emboli may occur in both the pulmonary and systemic systems at the same time, while a paradoxical embolism may occur through a septal defect. The embolism comes from mural thrombi on the endocardial aspect of the infarction.

VENTRICULAR FIBRILLATION is usually said to be the common cause of death in the first few hours after myocardial infarction. It is frequently seen after experimental coronary ligation (Smith 4.) (ligation in the dog) and de Waart,Storm and Koumans (48) (in the monkey - "Macaca Irus") It is rather an indefinite clinical entity. Wiggers (49) has studied the experimental production of ventricular fibrillation and has treated it successfully with calcium injections. These experimental investigations at present have little clinical application although on their basis Hooker (50) has advised the use of calcium injections in cases of electric shock. Ventricular fibrillation is said to be due to ischaemia of the ventricle. If the ventricle fibrillates in diastole the coronary circulation is augmented, if in systole it is decreased (Anrep (31)) This does not seem to have any practical application in coronary thrombosis. Ventricular fibrillation is an uncommon cause of death from other diseases. Turner (51) investigated the mechanism of death of the human heart using electrocardiographic methods, and he found that in 70% of cases death of the heart was preceded by idio-ventricular rhythm. This occurred in all types of cases, independent of the age and mode of death.

Death may occur from shock alone, but this in the present series did not seem to be the cause of death. It is difficult to distinguish between the symptoms of shock, and those which are due to ventricular failure, but in the present series peripheral failure seemed to be an additional factor in all those patients dying within a short time of the onset of the attack. Shock itself does not seem to lead to any alterations in the myocardium. It would be interesting to study the histological

conditions in the heart muscle in other conditions of shock e.g. after severe accidents etc. The fall in the blood pressure in many of these conditions is as extreme as in coronary thrombosis although of course, of a less permanent character.

Sudden death in cardiac disease is sometimes said to be due to carotid sinus reflex. This reflex is usually stimulated by a rise in blood pressure, not by a fall, as occurs in coronary thrombosis. Stella (52), working with the heart-lung preparation, has demonstrated that the coronary flow is diminished by a fall of pressure in the carotid sinus.

COLLATERAL CIRCULATION.

This is a problem of the greatest importance in coronary thrombosis, and much controversy exists as to how a collateral circulation can be established. It seems possible that if closure is gradual, complete occlusion of both coronary arteries may be compatible with life (Leary and Wearn(25)) although these cases are of the nature of pathological curiosities.

However some patients will die from a small branch obstruction, while in others a larger vessel may be occluded with impunity. Cohnheim considered that the coronary vessels were, anatomically, end arteries, while Pratt (53) has considered them to be 'functional' end arteries. Gross, Campbell, Whitten have shown that the anastomoses within the heart wall are very widespread Wearn (54) has described the extent of the capillary bed; this writer says that each cardiac muscle fibre is in relationship to at least three capillaries. Gross has described the gradual develop--ment of the septal and fat vessels with increasing age.

The blood supply to the heart is unique; the actual supply is profuse, and also it is the first vessel to receive the arterial blood from the left ventricle, but its source is rather precarious. The two coronary vessels arise close together at the beginning of the aorta so that any pathological process implicating the first part of the aorta is likely to involve both vessels. There are no obvious collateral channels which may then develop to bring the blood to the heart from a distance, and, suspended in its pericardial sac, it has much less chance than other organs of developing accessory vessels. The heart itself will go on

removing oxygen from the blood until it is completely de--oxygenated (Anrep (31). A surprising fact is, that the literature gives the most meagre accounts of the collateral circulation in the cases of coronary occlusion and myocardial fibrosis. There seems to have been little systematic study of this question. Many speculations are advanced, some of them lacking any definite foundation.

The only possible routes for a collateral supply to develop are as follows:-

(1) Extra-cardiac anastomoses.

(2) Reversal of the coronary circulation.

(a) Thebesian circulation.

(b) Reflux through the coronary sinus.

(3) Anastomoses in the heart between the coronary branches.

The last factor only operates when a branch is obstructed; if the main coronary vessel is blocked at its origin it will be unlikely that the other vessel could completely supply the whole heart unless the first vessel by reason of disease had gradually lost its function before complete closure supervened. The cases of complete closure of both vessels cannot be explained by the anastomoses between the coronary branches; it is obvious that they must have some other method of developing anastomoses.

EXTRA-CARDIAC ANASTOMOSES.

There are two main methods by which extra-cardiac anastomoses may develop, (a) by anastomoses of the coronary arteries, fat vessels and vasa vasorum of the aorta. (b) by pericardial adhesions.

Hudson,Moritz and Wearn (55) studied the anastomoses around the heart and the great vessels, by the injection of various substances,(indian ink, lamp black and colloidal graphite). These injections were made into the coronary arteries.

It was found that a very extensive extra-cardiac anastomosis exists through the fat vessels and it is also marked where the parietal pericardium meets the main vessels, especially over the area of the pulmonary veins and the venae cavae. This anastomosis develops with advancing age. Other anastomoses develop mainly (1) around the root of the aorta, (2) around the base of the pulmonary artery, (3) around the pulmonary veins, (4) around the ostia of the two venae cavae, (5) and at the intervascular pericardial reflections. The last mode of supply is the least important.

Branches run directly from the coronary arteries into the adventitia of the aorta. The vasa vasorum of the aorta can be injected as far as the diaphragm. Vessels also run along the pulmonary artery as far as the lung; the branches to the pulmonary veins run in the pericardial reflections and anastomose with bronchial and mediastinal vessels. Large auricular branches of the coronary arteries run along the pulmonary veins.

There is an extensive network along the parietal pericardium and the coronary vessels ultimately become connected with arterial branches accompanying the phrenic nerves, branches of the internal mammary arteries, anterior branches of the thoracic aorta and bronchial arteries.

Thus the heart is connected by means of these channels with a very widespread area. The coronary vessels may communicate with these extra-cardiac vessels via the vasa vasorum of the aorta, through the fat vessels or along the pericardial reflections.

The results are all based on injection experiments; no case has been discovered in the literature where these channels were enlarged in the human subject.

(b) Pericardial adhesions may convey an extensive blood supply to the myocardium. Moritz et al (56) investigated the vascularity of adhesions in the human subject and came to the conclusion that they might be important channels for carrying blood to the heart muscle. Beck and Tichy (58) and H.F. Robertson (59) produced artificial cardiac adhesions. Robertson found that on cutting such an adhesion an area of necrosis appeared in the heart wall. He found no development of the extra-cardiac channels after experimental ligation of a coronary trunk. O'Shaughnessy (60,61) has recently devised an experimental method of increasing the collateral supply using an omental graft, while Beck (62) has lately operated on the human subject with the intention of causing pericardial adhesions and thereby augmenting the blood supply of the heart.

THEBESIAN CIRCULATION.

It has long been known that small communications run into the myocardium from the chambers of the heart. Vieussens first described them in 1705 and two years later Thebesius also gave a description of them, and they are generally called after his name, veins of thebesius. In cases of cardiac infarction their chief interest lies in the possibility of blood reaching the heart muscle through these channels. It is necessary to examine what is known about the anatomy of these channels before their use in this manner can be discussed.

According to Gross (13) these channels are found in both auricles and ventricles and along the inter--ventricular and inter-auricular septa. They appear on the endocardial surface of the heart as small pits, varying in size, but averaging about 2mm in diameter. They are probably the remains of the primitive inter-trabecular circulation which communicated in the embryo with the heart chambers, (Grant and Regnier (63)). In the adult mammalian heart these inter-trabecular spaces are obliterated with the development of the coronary arterial system. Communications between the cavities of the heart and the venous system are found in many animals, in cats, dogs, and fish (Grant and Regnier) and in the rabbit.(Grant (64)) and an anomalous human heart has been described by Grant (65) in which there was a primitive inter-trabecular system communicating with the cavity of the heart.

From Grant and Regnier's description of the development of the coronary system it is evident that the coronary

arterial system develops at a much later date than the venous system, and is not thus likely to have any connection with the venous system.

Pratt (53) in 1898 made a series of experiments on the extirpated mammalian heart. He inserted a cannula into one of the ventricles of the cat's heart and closed the other openings of the heart. This cannula was connected with a reservoir of blood; when blood flowed through the cannula so as to distend the ventricle, the ventricle began to contract and, if a coronary vein was cut, blood emerged from the vein although no blood could be obtained after cutting a coronary artery. If Ringer's solution was used in place of blood no contraction of the ventricle resulted. From these experiments Pratt concluded that sufficient blood could reach the myocardium from the thebesian system alone; he also concluded that no communication exists between the thebesian system and the arteries, except via the capillaries. Pratt considered that mechanical distention of the ventricle would not of itself explain why the heart beats when the ventricle is distended by the blood introduced through the cannula. However it seems likely from Pratt's experiments that mechanical distention might have played the greatest part in causing the ventricles to contract.

Tissue culture has advanced so much since Pratt's time that it is not now remarkable to learn of pieces of tissue or portion of organs maintaining their function for long periods, even when completely isolated from the body. It seems certain from Pratt's experiments that blood flowed from the ventricular cavity

into the venous system via the thebesian system, but this might easily have been a mechanical effect following on the contraction of the ventricle, this contraction having been set up by mechanical distention of the heart chamber. Pratt's work suffers from another disadvantage; in his experiments the cat's heart was not working against any resistance as it was extirpated from the body; the conditions of the experiment are therefore somewhat artificial.

Grant and Viko (66) investigated these communications by injecting their orifices through a fine needle. They found that only the coronary veins could be injected from the thebesian openings unless the injected material was fine enough to pass the capillaries, in which case the material might reach some of the smaller branches of the coronary arteries. Saline injected into the coronary artery or vein could be seen to emerge from the thebesian orifices, but any thicker material failed to reach the thebesian system. These authers concluded therefore, that, while communication could take place from the heart cavities to the venous system, there was no direct communication between the thebesian system and the arterial system. It is obvious, if Grant and Viko's conclusions are accepted, that the thebesian system would be of little use in keeping up a collateral supply when the coronary vessels are occluded.

In 1928 Wearn (54,67) published the results of some experiments in which he perfused the coronary arteries of the human heart with indian ink. He came to the conclusion that direct communications exist between the arterial and thebesian systems; he also brought out the point that the thebesian flow was less after perfusion of the beating heart than after perfusion of

the inactive heart. In the former case the dye tended to run into the capillary system, in the latter case into the thebesian system.

In further descriptions of these vessels in 1933, Wearn (68) and his associates described the communications in greater detail. They injected the human heart and subsequently made plaster casts and photographs. They described:-

(1) a branch of the coronary artery, the arterio-sinusoidal vessel, which gradually loses its wall and becomes endothelial lined as it runs through the myocardium. This channel is now the myocardial sinusoid, (apparently the same structure as the intertrabecular space of Grant and Viko (66)). The myocardial sinusoid runs a tortuous course among the muscle fibres, and eventually opens by a small orifice into one of the heart chambers.

(2) Wearn and his co-workers also described a small artery, the arterio-luminal vessel, which runs directly through the myocardium and opens into the lumen of the heart chamber without the intervention of any capillary system. Thus it is evident that these writers consider that the arterial system communicates directly with the chambers of the heart.

Bohning, Jochim and Katz (70) injected into the beating heart an emulsion of bacteria. The injection was made into the superior vena cava, and the organisms were later recovered from a widespread area, including the sinusoidal spaces, the capillaries, and blood from the coronary sinus.

It is difficult to decide between the contending opinions of these authors. Some of the discrepancies arise from the use of injection material of varying thickness; Saline can be seen to flow from the thebesian orifices when injected into the coronary artery (Pratt), but this does not prove that blood could take a similar course. On embryological grounds a communication between the arterial and thebesian systems is extremely unlikely. However the illustrations in Wearn's latest paper are more convincing than in some of the previous papers, and it might be said that a prima facie case for the presence of direct arterial luminal communications has been made out. The literature concerning any pathological alterations in the thebesian channels is extremely meagre; in fact the only case in the literature in which such alterations are mentioned seems to be that described by Bellet,Gouley and M'Millan (69). This case will be discussed later. However if the possibility of these communications being present is granted, then it is necessary to examine how the circulation could be carried on by means of these channels. Most writers are discreetly silent about this and vaguely mention theories of 'reversal of the blood flow' and 'to and fro' movements in the thebesian system.

Most writers, in considering the use of the thebesian system as an alternative route for the heart's blood supply, assume that this blood will be obtained from the heart cavities i.e. there will be a reversal of blood flow in the thebesian system. This certainly seems to be the opinion of Wearn (67) Leary and Wearn (25) Bohning et al (70) Bellet et al (69).

We will discuss first the case of a boy sixteen years of age which has been reported by Bellet, Gouley and M'Millan (69). This boy had tuberculous myocarditis which had occluded both the coronary sinus and the coronary arteries, and had also destroyed two thirds of the right ventricle and three quarters of the left ventricle. In the wall of the right ventricle there were large numbers of sinusoidal channels which diminished in number towards the outer aspect of the wall of the ventricle. These channels communicated freely with the venous system but communications with the arterial system were indefinite. These authors considered that the venous system was first obstructed by the tuberculous process and that during this period arterial blood was forced into the thebesian system. These channels became dilated and when the arterial system was later involved in the pathological process, the channels formed the only communication through which blood could reach the myocardium. They are unable to say whether blood entered the myocardium from the heart chambers during systole or diastole but they thought that the circulation was of an 'ebb and flow' nature.

It is necessary to point out that in this case over a half of the total ventricular muscle had been destroyed by caseation.

It is doubtful if such a degree of destruction would be likely to occur as a common event even in the most advanced cases of myocardial fibrosis.

Bohning, Jochim and Katz attempted to work out a theory of the working of the thebesian circulation. They said that, if the thebesian vessels supplied the heart, this must occur during the diastolic period. These writers say,'at the onset of relaxation the pressure around the intra-mural vessels will be less than in the heart cavities and in the superficial coronary veins, so that a reflux of blood could occur'. This postulates a sort of suction action such as Katz (71) has described in the filling of the heart. Bohning et al further consider that this suction action into the intra-mural vessels from the heart chambers, will be greatly augmented when the arterial inflow is diminished (such as occurs in disease of the coronary arteries). They say that when the blood flow is gradually diminished by coronary closure, the blood flow during the relaxation period of the heart would tend to be reversed.

There are many objections to this theory. Objections to the theory that filling is likely to be diastolic are numerous although almost an equal number of points could be raised against a possibility of filling during systole as was postulated by Kretz (quoted by Bohning et al). The statement of these writers that the intra-mural pressure at the beginning of diastole is less than the pressure in the heart chambers must be regarded as a very doubtful point, even when there is diminished arterial flow due to disease.

The peripheral coronary pressure is greatly dependent on the muscular contraction of the ventricle, (Green Gregg and Wiggers (57),and the myocardium would have to be extensively

diseased before a reversal of flow to any degree could be established. In any case the thebesian orifices are so small, and so very tortuous is the passage that it is difficult to visualize any efficient suction action being employed. Even in the enlarged state reported in the case of Bellet, Gouley and M'Millan (69) it is doubtful if the channels could receive sufficient blood to maintain an efficient circulation. Bohning et al say that this filling action begins 'at the onset of relaxation', presumably meaning at the onset of isometric relaxation. Filling at this period would seem to be very unlikely because (1) the ventricular pressure at this period is low and falling rapidly (although this point mainly relates to the alternative theory that the intra--ventricular pressure fills the thebesian system without any suction action), and (2) the ventricle is a closed chamber i.e. no blood is reaching the ventricle from the auricle. Wright(72) says that probably some blood remains in the ventricle after the completion of ventricular systole, but,even so, the quantity will be small and it would appear to be of little use in filling the thebesian system and supplying blood to the myocardium. Indeeed according to Wiggers and Maltby (21), the ventricle has no cavity at isometric relaxation, the walls of the chamber being in apposition; if this is correct, then any regurgitation of blood into the thebesian system at this period of the cardiac cycle would be impossible. The only other period that might be indicated by the phrase 'onset of relaxation' might be the period immediate--ly following the maximum ejection phase, but this would be a systolic filling of the thebesian system. The ventricular

muscular contraction is then certainly tending to pass off, and the intra-ventricular pressure is falling but no efficient suction action would then be likely. The only likely period is at the onset of isometric relaxation where a change in the peripheral pressure takes place owing to the passing off of muscular contraction. It has been demonstrated above that there are objections to fixing this point as the time of filling the thebesian system by suction action. We are thus unable to accept this theory of the American authors.

However others appear to consider that the thebesian vessels might be filled by the intra-ventricular pressure alone. (Leary and Wearn (25)). It is obvious that on this theory a reversal of the flow in the thebesian system could only occur during diastole, when the intra-ventricular pressure is great enough to force blood into the thebesian system. This could not occur during systole as the muscle of the ventricle is then con--tracting and would form a barrier to any reversal of the blood flow. The ventricle fills mainly during the early stages of diastole; however it is doubtful if the intra-ventricular pressure during diastole could be great enough to force blood through such small orifices as the thebesian veins. It would appear then, that by any of the above methods any marked circulation in the thebesian system demanding a reversal of the blood flow, is extremely improbable, at any rate to any extent which could form a basis for nourishing the myocardium.

However it has not been mentioned by any of these writers that the thebesian system might still play a less important

part in maintaining the collateral circulation. If only a branch of the main coronary vessel is blocked, and if Wearn's (67,68) conclusions on the anatomical distribution of the thebesian connections are correct, it can be seen that blood might utilize these connections under certain circumstances. Arterial blood entering through a main coronary ramus might pass into the venous system of the heart, via the thebesian channels, and then reach the capillary bed from the venous side. A circulation could then be established from the coronary artery through the thebesian system, venous system, capillaries, and also the lumen of the heart. Wiggers and Cotton (30) have shown that systolic arrest of the circulation in the ventricle does not take place, and that during systole, the blood is still flowing at a decreased velocity in the myocardium. Wearn (54) has shown that in the inactive heart a large quantity of the perfusing fluid flows into the heart chambers, via the thebesian system, while in the beating heart the fluid reaches mainly the capillary bed and little escapes from the thebesian orifices.

Perhaps the conception may be advanced of a continuous circulation in the heart wall. Wearn (54) has shown the enormous extent of the capillary bed. Perhaps in some circumstances the arterial blood can be brought relatively quickly through the capillaries and drained away by the coronary sinus. Other streams, much slower in movement, and unaffected by muscular contraction, may exist along the sinusoidal channels which connect capillaries, veins and the heart chambers. A similar condition exists in the splenic circulation; the blood may be brought through

the organ rapidly when necessity requires it, or it may flow sluggishly through the alternative route among the cells of the splenic pulp. Barcroft and Stephens (73).

This view accepts the conclusions of Wiggers and Cotton(30) that there is no systolic arrest of the coronary circulation.

Hochrein (100) also denies that there is any "systolic check" (systolichen hemmung).

It seems unlikely that such an important organ as the heart will be deprived of blood for even a short period of the cardiac cycle. Doubtless the velocity of the blood flow in the coronary vessels is greatly diminished during systole. Anrep and his associates however, maintain that "the blood supply to the heart during systole is negligible" (Anrep and Saafeld(74). The two latter investigators planned experiments, using both the heart--lung preparation and the whole animal. The coronary artery was clamped for a short period at different intervals in the cardiac cycle, and the effect of this clamping on the coronary outflow was noted. They found that during systole no alteration in the coronary outflow followed clamping of the coronary artery, but that following clamping during diastole the outflow was greatly diminished. They argued from this finding that there was no active coronary flow during systole as the clamping of the coronary artery did not alter the coronary flow; and also, as the clamping during diastole diminished the coronary flow, then the main flow in the coronary vessels occurred during diastole. However such an experiment would not record a sluggish flow through small sinusoidal capillaries,and this might continue during the systole of the heart and be unaffected by the contraction of the ventricle.

Such a circulation would be comparatively unaffected by coronary arterial disease, and might be sufficient to nourish the myocardium although the reserve of the latter would be greatly diminished. It seems unlikely that the heart muscle actually 'massages' the blood out of the heart wall during systole as was suggested by Porter (76). The contraction of the ventricle acts more as a resistance to the coronary flow, this resistance varying at different periods of the cardiac cycle.

(b) Batson and Bellet (77) have reported a case in which they considered that the myocardium might have been supplied by means of a reversal of the blood flow in the coronary sinus. This would take place by means of the right auricle forcing blood through the coronary sinus so that it could escape from the thebesian orifices. However the period in the cardiac cycle when there is a positive pressure in the auricle is of short duration. During ventricular systole the pressure in the coronary sinus rises (Anrep et al(78)) so that no flow reversal could take place during this period. Also the blood from the left auricle would be venous in character and although the heart will remove oxygen from the blood until it is completely de-oxygenated, it is doubtful if the venous blood would carry sufficient nourishment for the myocardium.

The idea of a reversal of flow in the coronary sinus is not new. Pratt (53) in 1898 considered that this might be of importance in pathological states. However as experiments were performed on isolated cats hearts they throw little light on what occurs in the intact heart. For these reasons it is concluded that a reversal of flow in the coronary sinus is unlikely to play a

part in restoring a collateral supply.

(3) ANASTOMOSES BETWEEN THE BRANCHES OF THE CORONARY ARTERIES.

These are the most important channels of additional supply when the obstruction occurs in a main branch of the coronary tree. The most important anastomosis between the coronary arteries occurs across the interventricular septum which is very vascular, especially in old age. Gross (13) lays great stress on the anastomoses between the fat vessels which are also more prominent in old age. These latter vessels also connect with the extra-cardiac channels. The anastomoses around the A - V node are very free. They have been described by Kugel(79,80)

The main anatomical connections between the branches of the coronary vessels are as follows:-

There is a free anastomosis between the anterior descending branch of the left coronary artery and the anterior branches of the right coronary artery. A similar anastomosis exists on the posterior aspect of the heart between the posterior descending artery and the left circumflex vessel. The ramus ostii cavae superioris forms a wide anastomotic circle in the sulcus terminalis with branches from its own side (right coronary artery), and auricular branches from the opposite side. The ramus septi fibrosi usually from the right coronary artery, runs towards the A - V node and sends branches to the septal area which anastomose with vessels from the left coronary artery. According to Campbell (14), this vessel has seven separate connections. The ramus ventriculorum superior runs also from the right coronary artery, and anastomoses in the upper portion of the

interventricular septum. Ramus cristae supraventricularis, Campbell (14), from the right coronary artery, anastomoses with septal branches of the left coronary artery.

The left coronary artery gives off a twig (usually from the ramus descendens) which passes around the root of the aorta. The upper septal vessel is often large and anastomoses with the other septal vessels including the ramus septi fibrosi. The arteria anastomotica auricularis magna (Kugel(79) arises from the left coronary artery and anastomoses with vessels from each circumflex vessel. In addition there are profuse capillary connections under the endocardium and in the papillary muscles.

This is the anatomical arrangement of the main collateral channels. It might be expected that with such a profuse blood supply the heart would be well able to stand a sudden arterial obstruction. However, clinically this is not the case; although there is available a large reserve supply it seems that the heart muscle has the greatest difficulty in keeping up the circulation in any part of its wall which is suddenly rendered ischaemic.

No doubt this is partly due to the many factors altering the peripheral coronary flow, the most important of these factors being the peripheral coronary resistance due to the muscle contraction. There are few investigations concerning the efficiency of the collateral circulation in the myocardium.

It is well known that if after ligation of a branch of the coronary artery, the peripheral end of the vessel is opened, blood oozes from it. (Anrep and Hausler(81) Wiggers

and Green (82.83). These two groups of investigators differ in the amount of blood which will flow from the peripheral end- 0'5 cc.to 0'7 cc. per minute according to Wiggers and Green and greater amounts according to Anrep and his associates. However Wiggers and Green have shown that, even if the peripheral end of the vessel is opened simultaneously with ligation of the main trunk, there is still a diminution of contraction in the ischaemic area. We are thus left with the fact that although the myocardium is well supplied with blood the collateral circulation seems to be of very little utility in the presence of sudden occlusion of the main trunk.

Anrep and Haüsler found that the quantity of blood which issued from the peripheral end of the clamped coronary artery was much greater than that found in the experiments of Wiggers and Green. The former give the blood flow as 1'8 cc. to 7'2 cc. per minute. This blood flow comes from the collateral circulation; Stella (84) has shown that it does not come from the thebesian veins.

Under certain experimental conditions, when the aortic pressure is much greater than the perfusion pressure in a branch of the coronary artery, a reversal of the coronary flow may occur, but such conditions are unlikely to occur clinically.

The capillary bed is very extensive. The capillaries are usually described as surrounding cardiac muscle fibres. In 1899 Meigs (85) published a paper describing the presence of capillaries penetrating the individual muscle fibres. The writer considered that this was only a feature of

the adult heart and that in early life such capillaries were absent. He considered that they developed by a process of inclusion. No further investigations or reports of capillaries penetrating the individual muscle fibres appear in the literature, although Meigs's observations are noted by several writers.

All the methods by which blood may reach the heart have now been discussed. In cases of complete occlusion of both main trunks there is probably a combination of circumstances which may maintain the nourishment of the heart muscle for some time. The blood will come from extra-cardiac sources and perhaps the thebesian system may play a small part. These cases however are rare and in myocardial infarction we have to deal usually with obstruction of a main branch. On a basis of what occurs in other sites one would expect the main collateral supply to come from the other coronary artery. However, as already mentioned, unless the collateral supply is gradually improved by previous narrowing of the vessel, sudden occlusion is likely to lead to a sufficient diminution in the blood supply to lead to infarction.

The collateral circulation of itself will not be sufficient to avoid this. In fact Tennant and Wiggers (36) conclude that "if an extensive collateral circulation has not developed before total occlusion, the muscle in the zone affected is not likely to survive"; clinical experience seems to confirm this statement.

It might be thought that the extra-cardiac anastomoses would be of use, as they drain such an extensive area.

However the pathological evidence of the development of these channels in coronary occlusion is disappointing. They do not seem to have been seen enlarged in the human subject, although they must convey some blood in cases of complete stenosis of both coronary vessels at their origin. Even in experimental coronary ligation the extra-cardiac channels do not seem to alter. It is unlikely that the thebesian channels are of much utility by means of any 'suction action' or 'reversal of flow' in their channels. They may play a part in forming an alternative route for arterial blood from the coronary arteries. It may thus be said that in cases of coronary occlusion the myocardium is mainly dependent on the collateral circulation in the area of the infarction; furthermore, unless this is abnormally developed before occlusion, it is not likely to be sufficient to prevent the onset of infarction. Other outside factors, e.g. extra-cardiac channels are only of utility after the passage of a certain period; they develop slowly.

FACTORS IN THE ETIOLOGY OF CORONARY OCCLUSION.

Sudden occlusion in a coronary vessel may be due to (1) thrombosis in the lumen of the vessel, (2) embolism occluding the vessel. Thrombosis is much more common than embolism, and as far as could be judged, there were no cases of embolism in the present series. Out of the total of fourteen cases, one case(No.7) was associated with syphilitic aortitis. This was confirmed at post-mortem. This patient was the youngest in the series. As far as is known the remaining cases were associated with arterial

degeneration. The W.R. reaction was negative in all these cases in which there was an opportunity for obtaining blood for this test, with the exception of case No.7. They nearly all gave evidence of arterial changes in the peripheral or retinal vessels. None of them showed glycosuria. The post-mortem was done personally in two of these cases. One of these cases was (No.7) in which the syphilitic lesion of the aorta was present.

We can discuss the mechanism of coronary thrombosis as follows:-

LOCAL FACTORS.

(1) Changes in the arterial wall.

(2) Changes in the systemic blood pressure.

(3) Changes in the aortic valves.

(4) Changes in the wall of the aorta.

EXTRINSIC FACTORS.

(1) Alterations in the blood itself.

(2) Extra-cardiac reflexes.

LOCAL FACTORS.

(1) Changes in the arterial wall. This is certainly the main factor in precipitating an attack of coronary thrombosis, especially in cases following on atheroma of the coronary vessels. The degenerative process in the wall of the vessel acts by causing a rough portion on the vessel wall where a thrombus is likely to form. It also acts by slowing the blood stream. These two factors will explain nearly every case of thrombosis occurring in cases of coronary atheroma; thrombosis in other conditions is not so easily explained. There are three main causes of arterial

disease in coronary thrombosis. (1) atheroma of the coronary vessels. (2) syphilitic disease of the aorta. (3) diabetes.

Coronary thrombosis occurs as a rare event in the course of some other diseases e.g. rheumatic fever (Karsner and Bayless (86)) but these cases are all uncommon. Atheroma is by far the commonest cause; even syphilis is not often the cause of myocardial infarction.

In case No.8 of the present series the post-mortem findings were typical of coronary thrombosis following arterial degeneration. This patient, with little previous ill health, suddenly collapsed and died. The infarction was the typical anterior infarction, haemorrhagic in colour and due to obstruction in the left coronary artery. The coronary tree was extensively calcified; the vessel wall, when it was cut open, split into bony spicules. The aorta showed many atheromatous patches although the coronary orifices were not apparently narrowed. The arterio-sclerosis was widespread in this case, and involved most of the peripheral vessels, and also the cerebral vessels. Nearly all the cases in the present series showed some degree of thickening of the peripheral vessels, and the majority showed some degree of hypertension.

It is not intended here to discuss the etiology of coronary atheroma or as it is usually called in the American literature--coronary sclerosis. The term covers several conditions, atheroma, arterio-sclerosis, and congenital medial sclerosis. However attention must be drawn to a group of cases in which coronary occlusion sets in usually at a comparatively

early age and in which no peripheral arterial degeneration is evident. Cases of this description are noted in most of the larger series reported in the literature. Usually these cases are found to have an arterial degeneration confined entirely to the coronary tree, and many of these patients have a hereditary history of sudden death. Coombs(87) lays stress on examining the medial wall of the coronary vessel otherwise the vessel may be classified as normal. Congenital medial sclerosis may involve the coronary vessels and may be associated with sudden death. (Kissane and Fidler (88)).

ATHEROMA causes infarction by providing a roughened area over the inner aspect of the arterial wall. This favours a formation of thrombosis at this site. Atheroma also causes slowing of the blood stream by narrowing the vessel lumen. Usually both factors are combined together. What actually precipitates the formation of the thrombosis is still doubtful. Some of the causes discussed under "extrinsic factors" may actually bring about the attack.

(2) SYPHILIS is an uncommon cause of myocardial infarction. Case No.7 of the present series is a fairly typical example of infarction following on syphilitic aortitis.

In this case,the first part of the aorta was covered over by irregular elevated areas which overhung the coronary orifices. The coronary vessels were perhaps a little distorted by the syphilitic lesion in the aorta, but no very obvious narrowing of the vessels could be made out.

There were no signs of arterio-sclerosis in the coronary system and the heart (apart from the infarction) appeared normal; the heart valves were normal, and the syphilitic process did not extend to their surfaces. The thrombosis occurred in the left coronary artery, in an apparently normal portion of the coronary tree.

The events which lead up to myocardial infarction in syphilitic aortitis are much less clear than in atheroma of the coronary vessels. The coronary orifices are not uncommonly involved in syphilitic aortitis, (Saphir and Scott(75)) give the percentage involvement as 33%, but syphilis of the aorta is a rare cause of myocardial infarction, (page 12 of Levine's monograph (1)). In Parkinson and Bedford's series (20) there were ten possible cases of syphilis in one hundred cases of infarction and the disease was only known certainly to be present in five out of the ten cases. Indeed the coronary orifices may be completely closed by syphilitic aortitis and yet infarction may not occur. Cannon (26) has described two such cases, the patients dying in each case from cardiac failure. Leary and Wearn's (25) cases were similar. Albutt (28) also mentioned the possibility of complete occlusion taking place without myocardial infarction. Carr (27) says that, in his series of syphilitic aortitis, the coronary orifices showed definite signs of narrowing in 10%. Martland (89) gives the figures as 15% in his series, and Bruenn's (24) figures are 33'1%.

From this it appears that while the coronary orifices are not unfrequently implicated in the syphilitic

process,the tendency is for this process to bring about gradual narrowing only. In myocardial infarction, following syphilitic aortic disease, other factors must be present. Primary syphilitic involvement of the coronary vessels is rare. (Levy (90). Even Warthin (91) considers that, while the smaller branches may sometimes be involved, the main trunks always escape.

Leary and Wearn (25) drew attention to the fact that only the intra-aortic portion of the coronary arteries is usually found to be implicated in syphilitic aortitis; i.e. coronary involvement in syphilitic aortitis is only an incident in the aortic spread of the disease. It never seems to spread along the coronary vessels from the aorta. Martland (89) has confirmed this observation. Martland also mentions cases of congenital high origin of the coronary arteries. These vessels would be mainly likely to be implicated in syphilitic aortic disease. Warthin (91) considers that, along with syphilitic aortitis, it is usual to find a certain degree of coronary sclerosis. This is likely enough to be present in many cases of syphilitic disease, especially in older patients, and may not have any connection with the luetic infection in the aorta. However Warthin explains that the arterio-sclerosis in many of these cases may be an arterial reaction to the process in the aorta, i.e. syphilis indirectly causes the arterio-sclerotic changes.

This is a view which it is difficult to confirm; certainly in case No.7 of the present series no arterio-sclerotic changes were found in the coronary vessels. In older cases of

syphilitic aortitis, the presence of arterio-sclerotic changes in the arterial wall is probably incidental to the age of the patient.

The part played by DIABETES in the etiology of coronary thrombosis is still doubtful. Diabetes is frequently associated with arterial degeneration; this might lead diabetic patients to be liable to thrombosis in the coronary arteries but only because of the arterial degeneration which is present. Whether diabetes could otherwise predispose to coronary thrombosis is still not settled. It is well known how the myocardium is dependent on a supply of glucose for its nourishment; in diabetes this is either deficient? or if present in adequate supplies, it is not properly utilized. There is no evidence that this disturbance in the nutrition of the myocardium will predispose to coronary disease. Hochrein (100) thinks that insulin is a factor in regulating the coronary flow. According to this writer the coronary flow is diminished both by an excess and a diminution of insulin in the blood.

Glycosuria is found frequently? in patients suffering from myocardial infarction and in some of the cases reported by Levine (1) there was considerable difficulty in the diagnosis as the patients were comatose when first examined. In the majority of cases the glycosuria clears up in a few days. It is probably an expression of the general systemic upset which follows the infarction; transient glycosuria is commonly found in other conditions, e.g. hemiplegia. Levine (1) (page nine of his monograph) found that the age incidence of thrombosis in diabetic

subjects was almost the same as the age incidence in non-diabetic patients.

Blotner (92) however considers that coronary thrombosis is more common in diabetic than in non-diabetic patients. In seventy-seven fatal cases of diabetes, myocardial infarction accounted for ten per cent of deaths.

Coronary thrombosis may occur in hypoglycaemic states. Cases are mentioned by Herrick (93) and Blotner.

These are the commonest conditions which alter the coronary arterial wall. In atheroma, and probably also in diabetes, the alteration in the arterial wall is the most important factor in producing the thrombosis. In syphilis, the involvement of the arterial wall is of much less importance, and in this disease other factors play a part.

CHANGES IN THE ARTERIAL BLOOD PRESSURE.

The coronary blood flow is greatly dependent on the arterial pressure (Anrep and Segall (23)) The actual raising of the blood pressure such as is frequently associated with arterio-sclerosis, does not of itself appear to predispose to coronary thrombosis. In the present series hypertension was present in the majority of cases before the attack, but Levine(1) considers that low blood pressure is as common before an attack as is high blood pressure. Persistent low blood pressure might predispose to infarction, as this would, other factors being equal, diminish the coronary flow.

It is difficult to produce hypertension experimentally under conditions comparable to the occurrence of hypertension in the human subject. Coronary thrombosis apparently is not usually related to a sudden elevation of the blood pressure; the reverse is indeed the case, and lowering of the blood pressure sometimes seems to bring on the attack. Gregg (94) has recently investigated the effects on the coronary flow of acute hypertension experimentally produced, either by compression of the aorta or by the intravenous infusion of adrenalin. It was found that the total minute coronary flow, the diastolic, and systolic coronary flow, all increased with the raising of the blood pressure, but that the main increase was in the diastolic flow.

The increase in the systolic flow was due mainly to increased velocity of flow, and this was due to the fact that the systolic coronary resistance rose much less than the aortic pressure during the experimental production of the hypertension. It will be remembered from the work of Wiggers and Cotton (30) that the peripheral coronary resistance,(due to muscular contraction), and the height of the aortic pressure, are the two main factors which regulate the coronary flow. They are antagonistic to one another and each factor predominates at different stages of the cardiac cycle. In one of Gregg's experiments, on causing acute hypertension by compression of the aorta, the ratio of the maximum coronary systolic resistance to the aortic systolic pressure decreased from 73% to 59%.

The diastolic flow is greatly augmented on experimentally

raising the blood pressure. This is due to prolongation of the diastolic interval and to the higher aortic pressure during diastole.

The intravenous infusion of adrenalin leads to very similar results, but the systolic coronary resistance remains at a higher level than in compression of the aorta. This high systolic coronary resistance may reduce the flow in the ventricle during ventricular systole to a marked degree. However, comparable states following the administration of adrenalin in the human subject are not likely to occur. These experiments are of interest as showing what the results of the sudden rise in the blood pressure are on the different phases of the coronary flow. The increase in flow is mainly diastolic. The difficulty in the human subject is to determine the part played by the peripheral coronary resistance. It is useless to know what is the effect of one factor e.g. the aortic pressure, when the other factor, i.e. the peripheral coronary resistance, is still unknown.

CHANGES IN THE AORTIC VALVES.

Disturbances of the function of the aortic semilunar valves will affect the coronary circulation. These changes are much more likely to occur in syphilitic disease than in atheroma. Indeed the changes in the semilunar valves in the latter condition are probably only of minor importance; syphilis is the most important cause of damage to the aortic cusps. In Bruenn's (24) series of cases of syphilitic aortitis involving the coronary orifices, 87% of cases also showed valvular disease. Aortic valvular disease may alter the coronary flow by (a)

destruction of the aortic cusps and less of their action in filling the coronary orifices and (b) through incompetence or stenosis of the valves altering the pressure in the first part of the aorta.

(a) Halliburton (95) quotes Brücke as stating that the coronary orifices are closed during ventricular systole by the aortic valves.

This view does not now seem to be accepted. Other writers consider that the aortic cusps direct the blood towards the coronary orifices. There does not seem to be any experimental evidence in support of this theory. If the cusps have this action then their destruction by disease might alter the coronary flow.

(b) Many writers believe that the diastolic pressure is the most important factor in maintaining the coronary flow. These writers therefore consider that the low diastolic pressure which is seen in aortic incompetence will diminish the coronary flow. Certainly a regurgitation of blood past the semilunar valves will diminish the pressure in the aorta at that period of the cycle when the main coronary inflow takes place. Wiggers and Maltby(21) have shown that any regurgitation of blood into the ventricle in aortic incompetence, is not compensated for by a backflow of blood from the thoracic aorta, as by the time that the regurgitation occurs, some of the blood expelled from the heart during systole has already left the thoracic aorta and has reached the peripheral vessels.

Smith Miller and Graber (96) made an investigation in which they introduced a cannula into the coronary sinus of the dog and studied the effect of artificially altering the blood pressure by clamping the abdominal aorta. They also studied artificially induced aortic regurgitation. They came to the conclusion that the important pressure which governed the coronary flow was the diastolic pressure, even when the systolic pressure moved in the opposite direction to the diastolic pressure.

Laplace (97) investigated a series of cases of aortic incompetence and came to the same conclusions as did Smith and his associates. Gregg (98) has recently investigated the effects of experimentally produced aortic insufficiency, arterio-venous communications and aortic stenosis. This investigator was able to reconstruct curves showing the simultaneous alterations in the aortic pressure, peripheral coronary pressure, velocity of the blood flow and the mean blood pressure. His conclusions confirm those of Smith et al that the fall in the aortic pressure during diastole in these conditions is solely responsible for the decreased coronary flow in diastole. This decrease in flow is considerably compensated by an increase in the systolic coronary flow due to a lowering of the systolic peripheral coronary resistance in relationship to the aortic pressure.
(These are the two main factors in altering the coronary flow).

Gregg (98) found that aortic stenosis also caused a diminished coronary flow because in this condition there is a high systolic peripheral coronary resistance compared with the aortic pressure.

Thus disease of the aortic valves might theoretically bring about a diminished coronary flow and predispose to myocardial infarction. However, valvular disease seems to play a small part in coronary thrombosis. Marked aortic valvular disease is not frequently present clinically in coronary thrombosis. Aortic incompetence of syphilitic origin frequently? leads to sudden death but an infarction is not often found post-mortem. Rheumatic aortic valvular disease is not associated with myocardial infarction or even frequently with angina pectoris. It seems likely that valvular disease plays a small part in the causation of the majority of cases of coronary thrombosis, but in some syphilitic cases it may have some effect in diminishing the coronary circulation. The actual pulse pressure itself has little effect in determining the extent of the coronary flow. (Gregg (94).

Laplace (99) reported the case of a patient, aged 35 years, who developed an arterio-venous aneurysm in the femoral region, following a bullet wound. The development of this aneurysm was followed by signs of cardiac failure. On pressure over the aneurysm the blood pressure rose and the heart rate slowed. There was a low diastolic pressure, although the mean systemic pressure was within normal limits. After operative treatment the signs of cardiac failure disappeared, and the pulse pressure became within normal limits. According to Laplace the enlargement of the heart was due to inadequate coronary flow. In this case, of course, there was no valvular disease but the low diastolic pressure might have been the cause of the altered coronary flow, and thus led to cardiac failure. Whether actual lowering of the diastolic

pressure, apart from aortic incompetence, will be enough to seriously interfere with the coronary circulation is doubtful.

CHANGES IN THE WALL OF THE AORTA.

The elasticity of the aortic wall diminishes with advancing age. During ventricular systole the heart forms a rigid attachment to the aortic arch, and after the ejection phase there is a certain amount of recoil in the aorta. This recoil is said to have some effect in filling the coronary vessels. Hochrein (100) considers that eddies and swirls in the first part of the aorta are important factors in filling the coronary system. Atheroma involves the aorta in a patchy manner and mainly affects the intima of the vessels. No doubt this process causes loss of elasticity and roughening of the arterial wall but syphilis which attacks the artery from the outside is much more likely to cause marked weakening of the wall. In these cases the loss of the elasticity of the aorta may be an important factor in diminishing the coronary flow.

Thus in atheroma of the coronary arteries it is the condition of the vessels themselves which leads to the thrombosis, while in syphilis there are several varying factors, namely, narrowing of the vessel lumen, loss of elasticity of the aorta, and alterations in the haemodynamic conditions in the aorta. It is difficult to explain how (as happened in case No.7 of the present series,) the thrombus should form in a healthy portion of the coronary artery and not at the mouth of the vessel where the narrowing was most evident. The site of the formation of the thrombus must have been where the diminution of the

coronary flow was most acute; it is thus evident that a thrombus can form even when the arterial wall is healthy.

ALTERATIONS IN THE BLOOD.

At present there is no evidence that there is any alteration in the blood itself in coronary thrombosis. Alterations in coagulability might predispose to thrombosis. Syphilis itself does not seem to alter the coagulability of the blood. Riesman and Harris (35) mention the occurrence of coronary thrombosis in polycythaemia. Some writers have thought that the increased use of intra-venous injections may predispose to coronary thrombosis. Spinal anaesthesia has been associated with a few deaths from coronary thrombosis (Saphir et al (17). Extra-cardiac reflexes may play an important part in the latter occurrence.

EXTRA-CARDIAC FACTORS.

The actual onset of the infarction seems, in many cases, to be related to some extra-cardiac event. In case No.2 the attack came on during sleep. This is a common finding among other series. It may be related to exercise (case No.15) but this is not so common. In case No.7 the attack came on after a meal. Case No.4 is of interest. This patient had always been healthy and active; a few days before the attack the heart had been examined as a routine measure although she had no cardiac symptoms. Apart from the accentuated second aortic sound (the systolic blood pressure was 200 mm.Hg.) nothing much abnormal was made out. The patient was confined to bed to

determine the effect of rest on the blood pressure. The attack came on a few days after her confinement to bed. The onset of the thrombosis at the period of confinement to bed may have been coincidence but as the patient was so well before the attack the possibility must be considered that the rest in bed altered the coronary circulation. This may have followed on a fall in blood pressure or there may have been a reflex diminution in the coronary flow.

An experimental investigation into the effect of sleep on the coronary circulation is hardly possible; however it is well known that the heart beats slower, and the blood pressure falls, during sleep. Probably therefore the coronary flow is diminished during sleep. This might explain why so many cases come on during sleep. Riesman and Harris (35) think that the occurrence of a nightmare might precipitate an attack, especially according to Martland (89) in the syphilitic cases.

Coronary thrombosis may come on after a meal. Digestive disturbances may seriously upset the action of the heart. Cowan (101) has recently described cases of paroxysmal auricular fibrillation due to gastric disturbances; according to this writer gastric flatulence is the commonest cause of extra-systoles. Wayne and Graybiel (102), in an investigation into the factors in angina pectoris, found that the attack was not brought on by distention of the stomach by air, even when considerable displace--ment, visible in an X-Ray photograph, resulted. However, a meal precipitated the angina in many cases so that these writers conclude that there is a reflex action from the stomach to the heart. The actual distention does not seem to be the main factor.

Jackson and Jackson (103) have recently elaborated a theory that the main pain of angina is referred from the oesophagus, and is related to inco-ordination and stretching of the walls of this passage. They believe that distention of the stomach is the commonest single cause which brings on an attack of coronary thrombosis. There is no doubt that the views of these writers have much clinical evidence for their support, although they probably go too far in ascribing all angina cases to oesophageal disturbance.

Many cases are reported in the literature in which the attack of thrombosis was associated with flatulent distention of the stomach; the eructations of air which are associated with attacks of angina are well known. Relief of pain is frequently associated with the eructation of gas. According to Jackson and Jackson (103) the relief of the pain comes on a short time before the passage of the gas, and is due to the beginning of the relaxation of the oesophageal and gastric spasm, the cessation of which finally completely relieves the attack. Ryle's (104) view that the air in these cases is swallowed seems to be, from personal observation, the correct one. The attack of pain seems to set up a spasm of the oeosophagus with inco-ordinate sttempts at swallowing, so that air is carried into the stomach.

However no doubt a reflex action from the stomach may precipitate the actual attack of thrombosis. Greene (105) has shown how the heart responds to distant stimulation, and this might lead to the actual thrombosis, when arterial disease is present.

Wilson and Finch (106) have shown that drinking cold

water alters the T. wave of the electrocardiogram.

During digestion a decrease in the coronary circulation would be expected; however Essex (107) and his associates have shown that the coronary flow in the dog is increased after a meal.

It seems that conceptions of the heart's response to external stimuli have hitherto been too limited. The heart is thought of as reacting to certain stimuli, e.g. stimulation through its nerve supply, through alterations in the systemic pressure and distention of the heart chambers. These are all definite stimuli which directly affect the working of the heart. Greene (105) has recently investigated the alterations in the coronary flow which follow on external stimuli. This author records the flow from the coronary sinus by means of a modification of the morawitz cannula.

Stimulation of the central end of the sciatic nerve by faradic shocks led to pronounced coronary dilatation in most cases, sometimes however, preceded by a diminution of the coronary flow for a short interval. This reaction seemed to be independent of alterations of the heart rate and the blood pressure, which in most of these experiments were little marked. In some cases coronary vaso-constriction was the chief reaction. Atropine had no effect on the coronary flow reactions.

Cutting the sciatic nerve led to vaso-constriction; cutting the skin at operation led to coronary vaso-dilatation.

The sciatic nerve is a mixed nerve containing many different types of fibres. The branch from the sciatic nerve to the vastus lateralis was isolated, (it is a motor nerve), and on

stimulation of its central end it was found that a coronary dilatation of 10% had occurred. Stimulation of the coeliac plexus caused considerable dilatation of the coronary vessels.

Greene noticed that the type of the reflex varied to some degree with the strength of the stimulus; strong stimulation tended to produced vaso-constriction while mild stimuli produced vaso-dilatation. Stimulation of the central ends of the phrenic nerves and the central end of the branches of the vagus usually produced dilatation of the coronary vessels.

Thus we have the conception that the heart reacts to whatever stimulus is applied to the body, no matter where this stimulus is situated. Stimuli from the areas of the special senses may also affect the heart. These were not tested in the present investigation but Greene (105) says that it is certain that these areas will also bring about changes in the coronary vessels.

It is only recently that the conception of reflex action has been widening; it is now known how widespread are the reflexes which have to do with the maintenance of posture. These reflexes are all unconscious. Barcroft and Stephens (73) have shown how diminution in the size of the spleen follows on emotion. Probably similar reflexes prepare the heart for the slightest movement, visceral action (e.g digestion) or emotional effort. These results may help to answer Albutt's ironical question "How can a spring up three stairs, an effort at stool, or a walk against the wind, constrict the coronary arteries?"

Exercise causes a great increase in the coronary flow. Comparatively few cases of coronary thrombosis seem to be

related to increased exercise. Some patients take their attack when out walking but it is uncommon for the attack to come on after hard or excessive exercise. The onset of exercise might cause a temporary inadequate flow if coronary vessels were diseased, and thus lead to infarction.

EMBOLISM OF THE CORONARY ARTERIES is rare and is frequently only an incident in another disease e.g. acute endocarditis. In these cases the infarction may become infected. An embolism may occur from vegetations in the aorta or on the heart valves. This may be a piece of atheromatous material or, in syphilitic cases, a piece of the vegetation may become detached and plug the orifice of one of the coronary vessels. (Levy (90).

Both in cases of thrombosis following on atheroma, and in cases of syphilitic aortic disease, there are a considerable number of cases in which an infarction is found post-mortem but no evident thrombosis of the coronary vessels is present.

Saphir (17) and his associates studied a series of thirty-four cases of recent infarction. In three of these cases no thrombus could be found in the coronary vessels. In these cases the thrombosis may have occurred in such a small twig that it was overlooked at post-mortem, or the thrombosis may have occurred in a vessel remote from the site of the infarction. It seems likely that in a heart where the circulation has been reduced by arterial disease to a minimum, the obstruction of an insignificant twig may be enough to upset the balance of the circulation and thus lead to infarction. In other cases, before

the onset of infarction, the area may be entirely supplied by a distant vessel, the vessel which previously supplied the area being functionless following the arterial disease. Then occlusion of the distant vessel would lead to infarction in an area remote from its usual distribution. Saphir et al (17) consider that gradual narrowing of the vessel wall may itself be sufficient to cause infarction without any thrombus formation. These writers record cases of sudden death in which a recent thrombus was found in the coronary vessels but no infarction was present. There were three of these cases in Appelbaum and Nicolson's (18) series. These cases probably died so suddenly that no infarction had time to form.

C L I N I C A L S E C T I O N.

In many cases of coronary thrombosis there is no previous history of any cardiac trouble and in other cases the previous symptoms are so slight that they cause little disturbance to the patient.

Five of the present series gave no previous history of heart disease. In the remaining cases the patient had noticed some slight symptoms e.g. breathlessness or indigestion, but had been little inconvenienced.

BREATHLESSNESS on exertion seems to be the commonest complaint prior to the attack. The patient's exercise tolerance diminishes; and he became easily breathless on exertion. This was the only previous symptom in two cases (3,4). The breathlessness seems to come on rapidly; in both cases it had come on only three months before the attack.

ANGINA of effort was present before the attack in three cases, (Nos. 3,5,11). These cases also had varying degrees of dyspnoea on exertion. In case No.2 the pain was well marked but not severe; in case No.5 the pain was slight but was associated with a very disturbing sense of constriction in the chest. In none of these cases was the pain of great severity; not so severe as the angina which has followed the attack e.g. in case No.13. Case No.2 had had a previous attack of coronary thrombosis so that in only two cases could angina be traced as a prodromal symptom of coronary occlusion. The angina in all cases was related to exercise.

Thus breathlessness on exertion is one of the most important symptoms before the attack. It was present in five patients to a marked degree and to a slight indefinite degree in four others. This probably explains why coronary thrombosis so frequently occurs without any previous history of cardiac disease.

Angina does not seem to be such an important prodromal symptom as has been supposed. It is frequently absent, and if present does not indicate whether or not the patient will suffer from coronary thrombosis. Many cases of angina have been personally observed in which despite frequent and severe attacks of angina pectoris, no deterioration in the patient's condition could be noticed over a considerable period of years. The comparatively large number of patients in this series who had no previous pain before the onset of the attack is important. From the study of the single symptom of angina, it seems impossible to predict what patients will develop thrombosis and what patients will escape. Many patients will have no pain before the attack. If however a patient suddenly begins to have breathlessness associtaed with constriction and oppression in the chest on exertion, and there is no evidence of valvular disease the possibility of an infarction setting in is always to be remembered, especially if the patient is over fifty years of age.

Other writers give different figures. In Parkinson and Bedford's (20) series the majority of the patients had previous angina. Previous angina occurred in 62% of Levine's(1) series and in 38% of Connor and Holt's (47) series.

All the patients with angina in the present series had a definite degree of dyspnoea on exertion. Cowan has suggested that the patients with angina but no dyspnoea have a relatively intact myocardium.

AGE AND SEX.

In the present series, the youngest patient was a man aged 36 years (case No.7) while the oldest patient was a man 78 years (case No.2) who had survived a previous attack two years before. The youngest case (No.7) had syphilitic aortitis. It is frequently said that the younger cases of coronary occlusion are syphilitic in origin. However arterio-sclerosis may occur in young subjects, sometimes as a sequel to hereditary arterial degeneration, and this degeneration may be confined to the coronary vessels. Levine (1) mentions a case of thrombosis in a woman aged 39 years, while cases with a familiar tendency to arterial degeneration are described by Musser and Barton (110), and Coombs (87).

Coronary thrombosis is usually a disease of middle age. In Levine's series the average age was 64 years. In Connor and Holt's (47) series the maximal incidence was between 56 and 60 years of age. The figures of the present series correspond most closely with those given by Saphir and his associates(17). They found that the maximal incidence was between 61 and 65 years. In Connor and Holt's series (loc.cit) 75% of the cases had their first attack before 61 years of age.

It is thus seen that coronary thrombosis is not a disease of old age but one of middle life. This age incidence

may be explained from a consideration of the findings of Gross(13). Round about the fifth decade the main coronary vessels become tortuous and the septal anastomoses and the fat vessels begin to become prominent. These develop gradually, until in old age they are a prominent feature. Arterio-sclerosis in old age will be associated with prominent anastomotic channels in the septum and in the sub-epicardial region, so that the arterial degeneration will be offset by the rich anastomoses. However, if arterial degeneration sets in about the age of 50 years it will find the heart badly prepared. The anastomotic channels are just beginning to develop. Thus arterial changes will have a more serious effect at this age and will be more liable to culminate in thrombosis.

All writers are agreed that coronary thrombosis is more common in men than women. Only two of the present series were females. 84% of Connor and Holt's series(47) were males. Cowan's (108) figures were very similar- 87% males.

The higher incidence of thrombosis in males is probably due to the higher incidence of arterio-sclerosis in this sex.

The patients in the present series were mainly of the working class so that it is difficult to judge whether employ--ment has any effect on the occurrence of the disease. It might be thought that manual workers e.g. labourers, would be especially liable because of the strain put on the heart during their work. However many of the so called 'brain'workers also die from this condition; lawyers and physicians seem to be particularly liable

to coronary thrombosis and a general impression is that the disease is more common in those whose work is largely mental.

Levine (1) states that stout overweight persons are more liable to coronary thrombosis. Six out of the present series of fifteen cases might be classified under this heading. The series is too small for any definite findings. However it is noteworthy that all the patients in this group died from the attack.

The effect of tobacco on the heart is still a matter of speculation. Many writers have considered that it may play a part in the causation of arterial disease. Thrombo--angiitis obliterans in particular has been ascribed to heavy smoking. There is no doubt that many people have an idiosyncrasy to nicotine. Cowan (109) has described a case of angina pectoris due to cigarette smoking. It is such a common habit that definite proof of its relationship to any particular disease is difficult to obtain. Riesman and Harris (35) found that one quarter of the cases of coronary thrombosis were heavy smokers. Maddock,Russell and Coller (111) have recently shown that tobacco smoking can produce vaso-constriction of the vessels of the extremities. Cigarette smoking in a series of healthy adults produced a decrease in the peripheral skin temperature, and an increase in the blood pressure and the heart rate. The above authors found that Jews were especially liable to these disturbances and they ascribed this to the sensitivity of their temperament.

There can be no doubt that tobacco smoking has a very varying influence on different people. It is interesting to enquire from non smokers the reasons for their refusal to adopt the habit. It will be found that these persons think that smoking upsets them; this frequently is of the nature of a gastric upset or sometimes palpation follows on the use of tobacco. Many of these patients are probably sensitive to the use of tobacco and instinctively refrain from smoking for this reason. Thus in certain cases it may be a factor in altering the coronary circulation.

PREVIOUS HYPERTENSION.

It is not easy to estimate the frequency of high blood pressure before an attack of coronary thrombosis. In White and Bland's (112) series 25% of the patients had hypertension before the attack. The figures given by other writers are, Connor and Holt (47) 34%, Parkinson and Bedford (20) 41%, Levine (1) 40%, and Saphir et al (17) 38%.

In the present series it was known that high blood pressure was present before the attack in six cases. In two cases the pressure was subnormal before the attack. Of the remaining cases (six in number) in which the blood pressure was not known before the attack, arterio-sclerosis was marked in most of them so that some degree of hypertension was probably present in most of these cases. Of the patients with subnormal pressure before the attack (cases 2 and 10) one of the patients (case No.2) had a previous attack of coronary thrombosis, so that in only one case (No.10) was it known that low blood pressure was present

before the onset of the attack. A general opinion was gained that hypertension is more frequently present before coronary thrombosis than a normal or subnormal blood pressure. In the hypertension group the average systolic reading was about 180 mm.Hg.

It is difficult to say what effect the high blood pressure had on the course and development of the individual cases as so many other factors complicate the picture. One might think that on physiological grounds the circulation in the coronary vessels would be probably better maintained when the systemic blood pressure was elevated.(Anrep et al (78)), but the best recovery in this series was made by the patient with subnormal pressure before the onset of the infarction.

ARTERIO-SCLEROSIS was found in eight cases of the present group, judging mainly from the brachial, radial and retinal vessels. All the present series, as far as could be judged, were a sequel to degenerative arterial disease except in case No.7 in which syphilitic aortic disease was present. In Parkinson and Bedford's series (20) 36% showed peripheral arterial thickening while in all the post-mortem reports of Saphir and his associates (17) arterio-sclerosis was present in some degree. In 47% of these cases it was classified as severe.

Coronary disease is rarely associated with gross valvular disease. Levine (1) in his monograph reports as a curiosity a case of infarction associated with mitral stenosis; myocardial fibrosis may give rise to cardiac symptoms before the thrombosis sets in.

Dilatation of the aorta occurred in 55% of Parkinson and Bedford's (20) series and 26% of this series showed a soft systolic aortic murmur, said to be an indication of aortic atheroma. This murmur was present in several cases in the present series. Persistent auricular fibrillation is rarely complicated by coronary thrombosis Levine (1). In case No.1 of the present series, the fibrillation before the attack had evidently supervened on myocardial fibrosis. The onset of the attack did not apparently alter the fibrillation. Some other conditions may lead up to an attack but they are mainly curiosities.

Coronary thrombosis is a rare sequel to rheumatic fever (Karsner and Bayless (86)). These authors have shown that in an acute rheumatic infection, the walls of the coronary vessels are not infrequently involved in the inflammatory reaction, such as is seen in the myocardium. Actual thrombosis is however rare.

SYMPTOMATOLOGY.

The following description is based on the observations of the present series.

ONSET OF THE ATTACK.

The attack was sudden in its onset in all cases. Frequently the attack came on in bed while the patient was asleep (four of the cases in the present series). In some it came on after a meal (case No.7) and sometimes when out walking in the street e.g. (cases Nos.8,10,15). Cases are reported by Levine (1) in which exertion precipitated the attack but this is less common and did not occur in the present series. One case (No.4) occurred while the patient was confined to bed as part of the treatment for her high blood pressure. In some others the patient was sitting at the fireside, or had retired to bed but had not yet gone to sleep.

The severe pain which accompanies a typical attack is one of the characteristic features of the disease. In all the present series the pain was of a very severe character. It varied a little in intensity among the different cases. It seemed to be greatest in severity in cases No.7 and No.14. In the former the pain was entirely epigastric. In this case there was continous pain from the moment of the original attack. In case No.14 the course of the pain was rather different. It seemed to come on in paroxysms at frequent intervals (status anginosus), and this persisted for three days despite the administration of opiates. As regards the actual

severity of the pain this was probably the most acute case. The pain radiated down the inner border of the left arm in six cases, to the shoulder alone in one patient (case No.1), and to the epigastrium in one case (No.7). In the remainder the pain was confined to the chest (in one case the distribution of the pain was not known as the patient was unconscious when first seen, Case No.8).

Thus the pain was usually referred along the inner border of the left arm. Of these patients in which the pain was confined to the chest, it was usually felt behind the sternum. As a rule the patient was unable to locate the exact site of the pain and usually indicated the whole of the lower part of the thorax when asked to point to where the pain was situated. It was frequently associated with a sense of constriction or oppression. In one case(No.12) a sense of oppression was the predominant feature. In this series there were no cases in which the pain was felt in the neck, jaw or opposite shoulder although such cases have been recorded by other writers. The so called 'painless' cases will be referred to later. Minor degrees of coronary occlusion, only distinguishable by electrocardiographic records, are probably not so uncommon and pass unnoticed under various headings e.g. intercostal neuritis, dyspepsia and indigestion. Hamburger (148) has drawn attention to the group which resembles digestive disturbances.

When the vital position of the heart is considered it is easy to understand how widespread pain may arise from disturbance in the organ. The exact reason of the varying distribution of the pain is not yet known. There seems to be at present no correlation found between the radiation of the pain and the site of the infarction. It has been suggested that epigastric radiation is due to distention of the pericardial sac. This however was not present in case No.7 of the present series, and the idea does not seem to be supported by the post-mortem reports of other writers.

The pain of ordinary angina, either of the effort type or the paroxysmal (spontaneous) form, and the pain of cardiac infarction are probably of similar origin. The pain is due to muscle ischaemia (or anoxaemia). In effort angina this is a temporary occurrence; in thrombosis it is permanent; angina pectoris is closely related to myocardial infarction as regards the actual attacks. The electrocardiographic changes during an attack of angina may be very similar to those seen after coronary occlusion. Generalized anoxaemia will produce similar changes in the electrocardiogram (Kountz and Hammouda)(113), Katz et al(114). Thus the pain is probably due to anoxaemia of the myocardium. Ischaemic muscle frequently causes intense pain. A good example is seen in ischaemic contracture of the forearm following injuries in the region of the elbow joint; in this condition the circulation to the forearm is impeded by a swelling, usually in the region of the antecubital fossa. This swelling consists of blood, oedema and sometimes a displaced bone

fragment, and the circulation may be further impaired by fixing the elbow in a position of acute flexion. In this case the contracture is preceded by very severe pain in the forearm muscles. Similar results have been obtained by experimental methods (M'William and Webster (115)). In the human subject other factors besides anoxaemia of the heart muscle probably play a part. This was the conclusion of Katz et alia who found that a degree of anoxaemia sufficient to cause electro--cardiographic changes resembling those of coronary thrombosis, did not cause any cardiac pain. Anrep and Segall (23) have shown that there is a reflex action through the vagus, whereby increased coronary flow follows an increased output of the heart. In angina this reflex action may be interfered with and thus pain occurs. The pain is not likely to arise from the infarction itself, as this portion of the myocardium is dead. However there is the possibility that the infarction may give rise to pain by irritating the surrounding healthy muscle. At the border of the infarction there is considerable oedema and haemorrhage and this may press on surrounding nerve endings. A similar condition is seen in gangrene of an extremity, where the gangrenous portion, itself insensitive, gives rise to pain by its irritation of the living portion.

Tennant and Wiggers (36) have demonstrated that the ischaemic portion of the ventricle which follows on occlusion of the left anterior descending ramus in the dog, is stretched during ventricular systole by the intra-ventricular pressure, and they conclude that this stretching might be the cause of the pain

during myocardial infarction. They do not say, however, whether they consider that the pain originates in the infarction itself or in the surrounding healthy muscle.

Clifford Albutt's view that cardiac pain was aortic in origin is not now so generally accepted. Sutton and Lueth (116) found experimentally, that occlusion of the coronary artery caused pain, a fall in blood pressure and vomiting, while stretching of the aortic wall caused dyspnoea but no pain.

It is not intended to discuss the route by which the painful sensations are conveyed from the heart. This is only of importance in cases of angina where relief of the pain may be given by surgical measures.

The radiation of the pain is usually said to be an overflow along the sympathetic connections of the heart. Many types of fibres run together in the sympathetic and vagus nerves. Greene (117) has shown that many sympathetic fibres run in the vagus bundle. Woolard (118) has demonstrated the presence of fibres running from the heart towards the great vessels, and these ultimately reach the vagus. These fibres however may be sympathetic and leave the vagus trunk later. Sutton and Lueth (116) have recently described a new experimental method. They made a pericardial fistula, brought the anterior descending ramus of the left coronary artery to the surface of the chest, passed a ligature around it and then closed the chest wall leaving the artery on the external aspect. It could be occluded at will by pulling on the ligature, and the effect of this on the behaviour of the animal (dog) could be studied. White, Garrey

and Atkins (119) using this method found that unilateral removal of the stellate ganglion did not prevent pain on tying the ligature. Even bilateral removal of the stellate ganglion, and removal of the sympathetic as high as the subclavian artery and as low as the first dorsal ramus did not prevent painful sensations. The only procedures which prevented pain were (1) removal of the stellate ganglia on each side with removal of the associated upper thoracic ganglia. This was also successful in human subjects. (2) Bilateral section of the upper spinal roots (anterior and posterior) also prevented pain. Bilateral section of the vagi did not prevent pain.

Mayne and Katz (120), using a similar method, found that the plexuses on the posterior mediastinum had also to be removed. From these findings the widespread connections of the heart can be seen and it can be understood how pain in infarction and in angina may be referred to a considerable distance from the heart.

In contrast to the pain of angina, the pain of infarction is persistent. The average length of the acute pain in the present series was a little over twenty-four hours, but in the majority of cases a dull aching sensation persisted for a few days, often up to a week. The pain persisted unabated in one case for twenty-four hours and in another case (No.14) it was present in paroxysms for three days. Apart from this last case, when the pain of the attack had passed off it did not return, even in those cases which died on the tenth or eleventh day. Actual

rupture of the heart or ventricular fibrillation does not seem to be associated with any additional pain. Indeed rupture of the heart is often a painless event.

SHOCK is usually a prominent feature of an attack of coronary thrombosis. In some cases it is slight, in others the patient is reduced to a state of extreme prostration. In case No.10 where low blood pressure was present before the attack, the systolic fall was less than the average systolic fall of the hypertension cases, and in this case the degree of shock was not so well marked as in the other cases of the series. In case No.14 despite recurrent paroxysms of pain, the shock was only moderate in amount. On the other hand, in the fatal cases e.g.case No.12, the degree of shock was often extreme. So that a slight degree of shock may mean a severe or a mild attack,but extreme shock is always a grave sign. The extreme degree of shock may be a remarkable feature; within a few minutes the patient becomes completely collapsed, pallor appears on the face and in extreme degrees spreads to the extremities; the face is ashen or leaden in color; an important sign is the cyanosis of the lips, ears and nails which is frequently present. In other states of shock e.g. in perforation of a viscus, or in biliary colic, the lips are usually white. Cyanosis of the lips in the presence of extreme shock should always raise the suspicion of coronary thrombosis. The face becomes covered with cold perspiration, and often the patient is semi-comatose. Vomiting is not uncommon and may be recurrent. Cases Nos. 3,5,6, vomited once, while case No.7 vomited repeatedly. There was no vomiting in the remainder.

It is probably an expression of the general shock. The temperature is usually subnormal. The extent of the pallor is an important feature. As Lewis (121) has pointed out, facial pallor is an expression of nervous shock, often due to pain, such as occurs in many varied conditions e.g. biliary colic, vaso-vagal attacks and in emotional states of fright,etc. General pallor however is an expression of circulatory failure. The present series bears out the significance of generalized pallor. All the cases which showed pallor of the limbs proved fatal. Case No.12 is typical of this condition. Here the paleness of the whole body was easily seen.

There are several conditions which bring on the condition of shock. No doubt the severity of the pain is an important factor. Severe pain lowers the blood pressure; the picture is very typically seen in an attack of biliary colic or after a bad fracture. In the cases of 'painless' infarction the symptoms of shock are usually absent. The presence of the infarction itself lowers the blood pressure because it interferes with the action of the heart, especially as the majority of infarctions involve the left ventricle which is the pump for the systemic circulation. It is difficult to separate these cases in which the symptoms are due to circulatory failure and these in which, although shock is present, the ventricle is adequate for the work of maintaining the circulation. One method of distinguishing the two groups, i.e. extent of pallor present, has already been mentioned. The height of the systolic pressure during the attack is not a trustworthy guide although a systolic

pressure below 75 mm.Hg. is a bad sign. Many cases with systolic pressure round about 90 mm.Hg. recover, while some with higher pressures succumb.

The absorption of 'metabolites' from the area of infarction is not likely to be the cause of the immediate collapse after cardiac infarction, although their absorption may predispose to the persistence of a state of shock. The absorption of these substances, probably analogous in composition to histamine, is said to cause the rise in the temperature a few days after the infarction. In the present series there has been no evidence of the delayed toxic shock which is such a fatal event in some surgical conditions, especially following extensive burns. (Wilson)(122). This condition of toxic shock is said to be due to absorption from the burned area.

DYSPNOEA.

This is frequently present but it is not a sign of much diagnostic importance. There does not seem to be any typical alteration in the breathing during an attack of thrombosis. The respiratory rate is frequently accelerated, usually the rate lies between 20 and 25 respirations per minute. Some of the severe cases may show irregular, jerky respirations, often shallow, and sometimes sighing in character. Cheyne-Stokes breathing appeared as a terminal event in one case (No.3), and was present during the convalescent stage of another patient (Case No.5). The breathing is frequently irregular but it does not have a sudden 'catch' in it such as is seen in pulmonary conditions. The pain was not aggravated by deep respirations in any of the present

cases. The dyspnoea is no doubt partly due to the severe pain; it is seen in other painful conditions. However in the graver cases oxygenation of the blood must be interfered with and this probably explains the shallow, sighing breathing seen in these patients. A diminished flow of blood through the respiratory centre leads reflexly to acceleration of the respiratory rate.

CYANOSIS, is mainly confined to the lips, ears, and finger nails. None of the present series showed extensive cyanosis. This is confined usually to cases which already suffer from congestive failure.

The urinary output is diminished. This occurs in other conditions associated with severe shock. In some cases it may be an indication of cardiac failure with congestion.

Sugar is not infrequently found in the urine. There were no cases of glycosuria in the present series.

Albumen is sometimes found. Only one case in the present series showed a slight albuminuria. Usually this also disappears in a few days. Renal disease is not frequently associated with coronary thrombosis. A persistent albuminuria may precede the onset of congestive failure.

FALL IN THE BLOOD PRESSURE.

In eight cases (Nos. 1,2,4,5,6,10,11,12) the blood pressure was known before the attack. Of this group No.2 and No.10 had subnormal readings before the attack while the other group had elevated readings. The remaining cases whose previous readings are not known, all had low pressures during the attack.

The fall in the blood pressure is a characteristic feature of coronary thrombosis. In the group with subnormal pressures the average fall in the systolic pressure was 37 mm.Hg. and the fall in the diastolic pressure was 19 mm.Hg. In the hypertension group the average systolic fall was almost exactly 90 mm.Hg. while the diastolic fall averaged 56 mm.Hg. for four readings,as in the remainder no diastolic reading could be obtained.

These figures confirm Levine's (1) statement (page 30 of his monograph) that the fall in pressure is greatest in cases of previous hypertension. This however is only to be expected as the hypertension group have their pressures elevated above the normal for the patient, and the onset of the infarction is likely to reduce the blood pressure in all groups of cases to a level common to them all.

It is difficult in such a small series to estimate the relationship between the severity of the attack and the extent of the fall in the blood pressure.

The greatest recorded fall was in case No.3, where the systolic pressure fell 122 mm.Hg; no diastolic pressure was recorded. This patient died from the attack. The next greatest fall was in case No.4 (105 mm.Hg). This patient survived for over a year. Both these patients had systolic readings of over 200 mm.Hg. before the attack. Probably the actual extent of the fall has little effect on the prognosis although the impression has been gained from these cases that symptoms are more severe in the cases with hypertension before the attack of thrombosis. Thus in cases Nos. 2 and 10 who had low pressure readings before the

attack, the symptoms were much less severe than in the hypertension group.

The actual level to which the blood pressure falls is of some importance. All the patients in whom no systolic readings could be recorded shortly after the onset of the thrombosis, died from the attack. In other cases who died, the systolic readings were 84 mm.Hg. (case No.1) 100 mm.Hg.(case No.2) and 78 mm.Hg. (case No.3) The remaining patients who survived (Cases Nos. 4,5,10,11,12)had as the lowest reading of the group 95 mm.Hg.(case No.4) Thus a systolic pressure below 80 mm.Hg. is a serious sign, but round about 95 mm.Hg. recovery or death seems equally likely.

Coombs (123) put stress on the pulse pressure as an indication of the severity of the attack. According to this writer a persistent low pulse pressure is a bad sign. The present series is too small to confirm this statement, especially as in many of the fatal cases no diastolic readings could be obtained. The lowest pulse pressure recorded was 20 mm.Hg. in case No.10. This patient recovered. The average pulse pressure after the attack was 27mm.Hg.

By the fifth day the pulse pressure increases by about 10mm.Hg. This seems to be mainly due to a rise in the systolic reading. The pulse pressure increased in both the fatal and non-fatal group. By the tenth day the pulse pressure is stationary, and only increases gradually after this period. It rarely reaches the same level as before the attack. In none of the present series did the systolic or diastolic pressures regain

the same level as before the attack, e.g. in case No.4, the systolic pressure was 30 mm.Hg. less than the reading before the attack, while in case No.5 it was 35 mm.Hg. less. Case No.10 had the nearest approach to the level prior to the thrombosis. Six months after the attack this patient's systolic reading was short of the original pressure by 13 mm.Hg.

The fall in the blood pressure after the attack is due both to shock and ventricular failure. In some cases shock seems to be the main feature. In cases in which both the above factors are combined, probably the lowest levels of the pressure are recorded. An increase in the systolic reading soon after the attack is probably a good sign as it shows that the fall was mainly due to shock. The amount by which the systolic reading after a few months' time, falls short of the original pressure may indicate the extent of myocardial damage.

Feil and Katz (124) found that the ligature of the coronary artery in the dog did not lead to a permanent drop in the blood pressure. On this finding it would appear that the pain is the main factor in lowering the pressure, and not the actual impairment of the wall of the heart. However the remainder of the myocardium in Feil and Katz's experiments would be healthy; in the human subject it is frequently impaired by associated fibrosis.

PAINLESS INFARCTION.

Cases of painless infarction are mentioned by most writers. There were no cases of this description in the present series. Small painless infarctions are probably not uncommon.

Some of the larger infarctions are nearly painless, owing to the suddenness of the patient's death.

There is,however, another group in which a painless infarction can occur. This is in myocardial infarction in patients suffering from congestive failure. In these cases the onset of the infarction may easily pass unnoticed; it is painless and may only be associated with an attack of dyspnoea. "If a failing heart which is not due to either rheumatism or syphilis, suddenly goes downhill more rapidly with cardiac asthma, pulmonary oedema, a fall in the systolic blood pressure, feeble apex beat, and perhaps gallop rhythm, then cardiac infarction should be suspected". (Herrick (93). The attack of dyspnoea marks the time when the infarction sets in. "Sudden dyspnoea may be the only symptom of coronary thrombosis". (Saphir et al). The diagnosis in these cases may be made by the electrocardiogram but often the infarction may remain unsuspected until the post-mortem.

At present there seems to be no explanation of why the occurrence of painless cases should be mainly confined to the group of patients with congestive failure. It would be expected that an infarction of the myocardium would always be painful, no matter what was the condition of the heart. Shock is also absent in these cases.

EXAMINATION OF THE PATIENT.

It is agreed by the majority of writers that the diagnosis of a typical case of coronary thrombosis is easy; some of the less severe cases, or those complicating cardiac failure, can

only to be diagnosed with certainty by the use of the electro--cardiogram; even a fully developed severe attack may present atypical features which lead to difficulty in diagnosis.

The general appearance of the patient has already been discussed.

In coronary thrombosis the temperature begins to rise twenty-four hours after the attack. In this series the temperature did not often exceed 101 deg.F. and the peak of the rise usually occurred about the seventh or eighth day. In most cases the temperature was normal by the tenth day, even in cases which subsequently died.

There is usually an increase in the respiratory rate.

The pulse is frequently impalpable; it is always at least of very poor volume. It is accelerated, the average reading being about 90 beats per minute. The rhythm is regular; one case in the present series had auricular fibrillation before the attack and the irregularity of the pulse persisted after the attack. One patient had bradycardia (case No.4) with a regular rhythm. Transient irregularities are not infrequent after myocardial infarction.

EXAMINATION OF CARDIO-VASCULAR SYSTEM.

The apex beat is feeble and may be impalpable. Percussion of the heart may be considerably hampered by the restlessness of the patient. In those cases of this series in which the heart was examined before the attack, it was evident that clinically no cardiac enlargement followed as a result of the

attack.

This view is confirmed by a recent report of Horine and Weiss (125) who investigated a series of cases to find out if the onset of infarction altered the size of the heart.

Cases of coronary thrombosis have, as a group, a tendency to enlargement of the left side of the heart, due probably to associated high blood pressure. It is common to find the apex beat in the sixth interspace well outside the mid--clavicular line. Pericardial effusion complicating coronary thrombosis might cause considerable enlargement of the cardiac dulness; pericardial effusion however, is a rare complication.

AUSCULTATION OF THE HEART.

The most striking feature of auscultation is the great weakening of the heart sounds. The heart sounds were inaudible in two cases of the present series (Nos. 3 and 12) both of whom died; in case No.7 the heart sounds were only audible at the base, and in case No.6 at the apex. In the other cases the heart sounds were very faint. The absolute silence over the heart is very striking; the first sound at the apex is always muffled and very short. In the present series the second pulmonic was usually louder than the second aortic; this was more noticeable because several cases had accentuated second aortic sounds before the attack.

Extreme weakness of the heart sounds is probably an unfavourable sign. Both cases with complete absence of any cardiac sounds died. However several patients had very distant

sounds and yet recovered so that the prognosis cannot be judged entirely on this finding.

There were no cases of gallop rhythm in the present series, although they are reported in the writings of other observers. Associated cardiac murmurs are uncommon. Cases Nos.5,8,10,11 had a short systolic murmur over the aortic area.

PERICARDIAL FRICTION was heard in case No.10 on the third day, over a small area in the region of the apex beat. This friction rub persisted for five days. When present, the friction rub is one of the best signs of cardiac infarction. It is not often detected. Saphir (17) and his associates report a series of thirty-four cases of myocardial infarction verified at post-mortem; pericarditis was a clinical finding in only five of these cases. In Parkinson and Bedford's (6) series of twenty-eight cases of myocardial infarction case No.14 is the only one which mentions the occurrence of pericardial friction, although all of the cases in this series were not examined by the writers immediately after the attack. Some degree of fibrinous pericarditis is not infrequently seen over the area of the infarction at post-mortem, so it is difficult to understand the rarity of the clinical signs of pericarditis. It might be thought that, when a friction rub is present, the infarction will probably be situated on the anterior aspect of the ventricle. However, in the series reported by Saphir et alia the infarction was posterior in half the cases in which a friction rub was

present. In pericarditis from other conditions, the friction rub is rather variable and often alters with the position of the patient. The same variability seems to account for the inconstant findings in coronary thrombosis. If the patient was systematically examined both at short intervals and in altered positions, the clinical signs of pericarditis might be oftener detected. Pericardial effusion is rare as a clinical finding, although of course haemopericardium is sometimes found post-mortem, usually resulting from cardiac rupture. According to Bickel and Moser (126) a loud murmur in the fourth or fifth left intercostal spaces resembling the murmur of mitral incompetence, is associated with a perforation of the interventricular septum.

EXAMINATION OF THE RESPIRATORY SYSTEM.

This may be completely negative. The breathing is frequently loud and harsh. When congestive failure is present crepitations are frequently found, especially at the bases of the lungs, and in these cases oedema may be present elsewhere. Some cases have moist sounds at the bases even in the absence of congestive failure. These cases are probably a sequel to left ventricular failure and are due to a temporary congestion. In favourable cases this soon passes off. Even the air intake may be deficient e.g. in case No.7 where the signs at the base of the lung led to the diagnosis of pneumonia being seriously considered.

Levine (1) records a case (No.11) in which the attack began as an attack of pulmonary oedema.

ABDOMINAL EXAMINATION.

This is frequently negative in cases of coronary thrombosis. In case No.1 there was hepatic enlargement; this patient had auricular fibrillation before the attack but no signs of general cardiac failure. The liver may be enlarged after an attack of thrombosis if congestive failure supervenes on the attack. There seems little confirmation at present for the statement, which is sometimes made, that hepatic enlargement, with slight icterus following an attack of coronary thrombosis, indicates that the infarction is in the right ventricle.

Cases of coronary thrombosis with abdominal pain may lead to difficulty in the diagnosis at the time of the attack. A considerable number of cases are mistaken for acute abdominal conditions.

Levine and Tranter (10) were the first to draw attention to the resemblance between myocardial infarction and acute abdominal disease. These authors reported two cases in which the symptoms were almost entirely abdominal, and indeed one of the patients was subjected to a laparotomy. It is an unfortunate error of diagnosis to mistake a case of coronary thrombosis for an abdominal condition, as the laparotomy destroys the patient's chance of recovery. In a review of the literature on this subject, variations are found in the clinical picture. In many cases the pain is both thoracic and abdominal, with a radiation down one or more arms. Rigidity is often present and if vomiting is frequent the resemblence to abdominal disease may be close. However, if the pain is also thoracic this should give

some indication of the possibility of the condition being cardiac in origin. Those cases in which the pain is entirely epigastric may give rise to considerable difficulty. Case No.7 of the present series was in this class. This patient had well marked rigidity in the epigastric region associated with severe abdominal pain. The patient was definite that he had no painful sensations in the chest. In this case there was no radiation to the arms. The patient had also vomited several times. There was no hyperaesthesia of the abdominal wall and no tenderness on deep pressure. Abdominal rigidity is a fairly frequent occurrence in some thoracic conditions e.g. a fracture of the lower ribs. In coronary thrombosis it may be present even when the pain is entirely retro-stenal (see case No.2 of Parkinson and Bedford's series (6)). Apart from pain, rigidity seems to be the commonest abdominal finding in coronary thrombosis. It may however be absent even when the pain is epigastric and associated with vomiting (case No.17 in the series of Parkinson and Bedford (6)). Tenderness is apparently the least common finding. In No.15 in Parkinson and Bedford's series there is no mention of rigidity but slight tenderness and distention of the abdomen was present. Thus although pain and rigidity may be present, tenderness is unusual, and this may be of help in the differential diagnosis. Deep tenderness is uncommon, and hyperaesthesia is not likely ever to be present as it is in the main only a sequel to peritoneal inflammation. As far as can be made out from the cases of coronary thrombosis described in the literature there seems to be no relationship between the site of the infarction

and the radiation of the pain. In the present series (case No.7) the infarction was situated on the usual anterior site on the left ventricle.

Doumer (128) has discussed the cases of abdominal pain complicating myocardial infarction. He reports two cases in which the pain was purely abdominal and this led to the mistaken diagnosis of abdominal disease. In his second case the only clinical finding was a bradycardia, although the electrocardiogram showed a prolonged P - R interval and the negative T wave in Lead 1.

An impression is gained from the study of reported cases, that the mortality is greater in these patients with marked abdominal symptoms than in the typical cases. The above mention--ed cases of Doumer both died as did the cases of Levine and Tranter, while a fatal ending occurred in these reported by Parkinson and Bedford. Coombs (123) found in an analysis of his own cases that the mortality was slightly greater in these cases with abdominal pain.

The remainder of the examination is usually negative.

The blood Wassermann should be determined if the patient survives the first twenty-four hours. An electrocardio--gram is not often available as an emergency measure, although in America it seems to be more widely used in this connection. There is no doubt that it may sometimes prove the deciding factor when the diagnosis is difficult.

There is a rapid leucocytosis in myocardial infarction. The leucocyte count is only available in a few of

the present series and in these patients it is recorded too late to be of much value. The leucocyte count rises about one and a half hours after the onset of the infarction and is one of the best signs of coronary occlusion. Generally it is above 10,000 per cm. of white cells. Out of seventy-four cases reported by Levine (22) only four had a total leucocyte count below 10,000 per cm. It does not often rise above 34,000 per cm. A high leucocyte count is said to indicate a poor prognosis (White (130)). The count is highest on the second or third day after occlusion. Goodrich and Smith (131) have demonstrated that the polymorphonuclear count shows a shift to the left.

After the first twenty-four hours the patient usually begins to rally. The shock gradually passes off; the blood pressure and the temperature rise. The rise of the temperature begins within twenty-four hours and remains elevated sometimes for a week. It does not often exceed 101 deg.F. There is no typical behaviour as regards the heart rate, but it may vary considerably in the first week. After this it is frequently steady. In the present series the heart rate was usually about 100 beats per minute. The behaviour of the blood pressure will be described later. In cases in which death ensues within the first twenty-four hours the patient gradually passes into a state of coma. This latter period is usually short and the patient seems to be sensible up to a short period before death. Cheyne--Stokes breathing may set in. None of the present series recovered from this state of coma although recoveries are mention--ed in Levine's series (1). The onset of epileptiform

convulsions usually indicates complete heart block.

COMPLICATIONS AND SEQUELAE.

Ventricular fibrillation and cardiac rupture have already been described. The most important remaining complications are (1) Embolic phenomena. (2) Disorder of rhythm and conduction. (3) Cardiac failure.

EMBOLIC PHENOMENA.

There were no cases of embolism in the present series. It is however not an uncommon sequel to myocardial infarction.

The emboli came from mural thrombi, formed on the endocardial aspect of the infarction. In most cases the embolism is detached in the first few weeks after the infarction, but cases are reported in which the embolism appeared at a much later date. Willius (132) has described cases in which the embolic phenomena were the chief symptoms of coronary occlusion. The emboli gave similar symptoms to those occurring as a complication to other conditions.

It is rather surprising that embolism is not more frequent in coronary thrombosis. Probably the fact that the endocardial surface of the infarction is frequently covered by a layer of healthy tissue prevents the formation of a thrombus.

DISTURBANCES OF RHYTHM AND CONDUCTION.

Excluding ventricular fibrillation, marked disturbances of rhythm and conduction are not frequent after coronary occlusion. Levine (1) on page thirty-five of his

monograph states that minor transient degrees of disturbance are probably not uncommon, but serial electrocardiography is needed for their indentification. Many of these disturbances are of little clinical importance.

EXTRA-SYSTOLES.

These are of little significance. Out of one hundred and forty-five cases of coronary thrombosis Levine had thirty-five cases of recurrent extra-systoles. Case No.5 of the present series had extra-systoles in the fourth week after an attack of pulmonary oedema, but they disappeared in a few days.

In Parkinson and Bedford's (20) series of one hundred cases of coronary thrombosis, two showed paroxysmal tachycardia, five showed paroxysmal fibrillation, one showed fibrillation and flutter, and three had paroxysmal flutter. There was a case of complete block and one of partial block. It is thus seen that these disturbances are uncommon.

Case No.1 in the present series had fibrillation before the attack. No clinical difference could be made out after the attack.

The only other case in the present series in which a disturbance of conduction appeared was in case No.4 who died two hours after the attack. This patient's pulse rate was recorded a few days before the attack and was found to be regular at seventy-two beats per minute. When she was seen half an hour after the attack the pulse rate was regular at forty-two beats per minute. The bradycardia, associated with the muffled heart sounds

gave a striking clinical picture. The heart rate was maintained at the slow rhythm until just before death. At the time of the examination it was thought probable that she was suffering from complete heart block; however without an electrocardiographic record of the auricular rate it could hardly be definitely stated whether this was a case of complete auriculo-ventricular dissociation or a partial two to one heart block. Complete heart block is rare, while Levine on page 35 of his monograph says that a two to one block is not infrequent.

COMPLETE HEART BLOCK IN CORONARY OCCLUSION.

It is surprising that this is a rare event in coronary occlusion. Levine had only two cases in his series of one hundred and forty-five cases of coronary occlusion. Both cases died. Other cases have been reported by Ball (127) Frothingham (133) Hansen (134) Sanders (135) Schwartz (11). The latter writer reports a series of fifteen cases many of them having unusual symptoms. The A - V node is supplied in 92% of cases from the right coronary artery by the ramus septi fibrosi. There seems to be a little evidence to support the theory that complete block is more common in right than in left coronary occlusion.

The case reported by Sanders was that of a physician whose pulse rate fell to forty-four beats per minute, after the attack. He died on the third day and the electrocardio-gram showed a T_3 type of curve which is indicative usually of a posterior infarction.(Barnes and Whitten (7,8). Levine's case was due to obstruction of the left coronary artery. The cases of

Hansen and Frothingham, were all T_3 in type while many of Schwartz's group also showed a T_3-Q_3 type of curve. In two of Schwartz's group, although the infarction was posterior, the left circumflex was found occluded at post-mortem. The writer explains these cases by saying that they belonged to the group (8%) of patients whose A - V node is supplied by the left coronary artery. Many of Schwartz's cases had epileptiform seizures. Some of his cases are remarkable. Case No.1 of his group had a pulse rate of only twelve to sixteen beats per minute. Case No.4 had ten beats per minute as the pulse rate, while case No.5 had only a rate of six beats per minute. Many of these cases ultimately recovered. His treatment with large doses of adrenalin will be described later.

PARTIAL HEART BLOCK.

This may simply be a delay in conduction shown by a prolongation of the P - R interval. Blocks in the ratio of 2'1 or 3'1 are not uncommon. Case No.4 was probably a partial heart block. Various types of branch bundle block or arborization block may set in. Many of the phenomena are transient. Heart block seems to be more common in chronic myocardial fibrosis than in acute coronary occlusion.

PAROXYSMAL VENTRICULAR TACHYCARDIA.

There were no known cases of paroxysmal tachycardia in the present series. It is however an important complication as proper treatment may save the patient's life. Lewis (136) described the condition in 1909, and it has frequently

been seen after experimental coronary occlusion. There were two cases in Parkinson and Bedford's (20) large series of one hundred cases of myocardial infarction. Levine and Fulton (137) published a series of cases of paroxysmal ventricular tachycardia and they found that in one fourth of the cases there was a history of coronary occlusion. Strong and Levine (138) and Robinson and Herrman (139) have papers on this subject, while individual cases are reported by Hamilton and Hurwitz (140), Schwab (141), M'Millan and Bellet (142), Elliot and Fenn (143), Prinzmetal and Kellog (144), Allan (145), and Davis (146). The paroxysms come on suddenly and disappear without any obvious cause. The longest paroxysm noted in the literature was that described by Hamilton and Hurwitz in which the paroxysm lasted for thirty-five days. This patient recovered. Some cases are said to ensue on the administration of digitalis (Schwab;Davis).

The paroxysms, if continuous, soon lead to death. In Levine and Fulton's series six out of eight cases died. The average duration of life in Prinzmetal and Kellog's series was twenty-four days. When the paroxysm is present there is great collapse and dyspnoea. In tachycardia of ventricular origin, although the heart is apparently regular, careful auscultation may sometimes detect a slight irregularity. In auricular tachycardia, the heart is absolutely regular. The irregularity in the ventricular rate can also be seen in the electrocardiogram.

Vagal pressure has no effect in ventricular tachycardia. Clinically the most important sign is that described

by Gallavardin. This consists in counting the jugular pulse; if it is beating at half the ventricular rate then a diagnosis of ventricular tachycardia is almost certain. The sign is of value if no P waves are seen on the electrocardiogram. The ventricular complexes during the paroxysm should resemble those seen in ectopic beats between the paroxysms. The auricular rate should be seen in the electrocardiogram to be slower than the ventricular rate and independent of it. If the onset of the paroxysm is recorded, it may be evident that no auricular activity preceded the first ventricular complex. Death occurs from ventricular fibrillation. Paroxysmal or permanent auricular fibrillation may ensue on coronary thrombosis. It does not seem to alter the prognosis. (Levine (1) page 88).

PAIN IN THE SHOULDER AFTER MYOCARDIAL INFARCTION.

This complication was first noted during the convalescence of case No.6. Three weeks after the onset of the infarction the patient began to complain of pain in the left shoulder, mainly situated over the outer and anterior aspect of the joint. The pain was constant, of a boring character and aggravated by abduction of the shoulder joint. There was marked limitation of abduction. In the early stages the arm could not be raised further than a right angle and the patient was unable to dress himself. The pain persisted for six months. The movements at the shoulder-joint gradually improved but a little limitation was still present a year after the onset of the infarction.
This condition gave rise to much anxiety, and worried the patient

much more than the cardiac infarction had done. At this time there was no record of this complication in the literature, and the reports of the larger series did not mention it. It was put down at the time to a co-incident rheumatic infarction.

However a very similar case was seen a few months later (case No.10). The pain in this patient began about two weeks after the infarction, and the patient had the same difficulty in abducting the arm. However the limitation of movement was much less in this case. The pain was mainly situated over the bicipital groove. The condition lasted for nearly four months and then gradually passed away. No limitation of movement was found six months later. As the condition occurred twice in this small series it might have been thought that it must be a common occurrence.

In February 1936, a short article appeared by Edeiken and Wolferth (147) describing shoulder pain after coronary thrombosis. These authors published a series of cases (fourteen in number) who complained of shoulder pain after myocardial infarction. In this group the pain was usually in the right shoulder but in three cases it was in the left shoulder. In three cases the pain commenced immediately after the attack, but in one case it did not begin until sixteen weeks from the attack.

The pain in the present cases probably began shortly after the attack, within seven days of the infarction, but in the early stages it was thought to be only the referred pain from the thrombosis and little attention was paid to the condition. It was only when movements of the arm were tried that it was

recognised that a definite local condition was present in the region of the shoulder. Edeiken and Wolferth give details of a case in which the pain lasted for five years.

The two cases of the present series were not X-rayed; this was done in some of Edeiken and Wolferth's series but the findings were usually negative. Some showed slight osteo-arthritic changes in the vertebrae.

Edeiken and Wolferth note the intractibility of the complaint.

None of the two present cases had effort angina after the attack so that no connection between angina and shoulder pain could be made out. Edeiken and Wolferth found that usually movement did not aggravate the pain; it did so in the two cases now reported. Two patients of Edeiken and Wolferth had a 'trigger zone' over the deltoid; no trace of this was found in cases Nos. 6 and 10.

Edeiken and Wolferth state that the condition is probably a causalgia, although they admit that no vaso-motor symptoms could be found in their cases.

The two cases of the present series do not support this view. The condition seemed to be due to limitation of the shoulder joint, mainly in the movement of abduction. In case No.10 there seemed to be a degree of muscular contracture mainly involving the deltoid muscle; in case No.6 in addition there seemed to be some intra-articular adhesions.

A possible explanation is as follows:-

When a patient has an attack of coronary thrombosis he is advised to move about as little as possible; in addition he is

usually severely shocked and incapable of much exertion. If the pain is referred to the shoulder joint the patient will hold the arm as still as possible from an instinctive desire to prevent aggravation of the existing pain. In addition there is probably a reflex adductor spasm.

By the third week a certain amount of intra-articular adhesions may have formed, associated with a contract--ure of the shoulder muscles. especially the deltoid and to a lesses degree the supraspinatus and the infraspinatus.

D I A G N O S I S.

The diagnosis is usually easy; if however the attack is a mild one, the electrocardiogram may alone decide the diagnosis. Some severe cases are difficult to diagnose especially if the patient is comatose when first seen, or if the pain is mainly abdominal.

The previous history is of importance when available; there may be a history of increasing breathlessness or of effort angina. If the previous blood pressure is known then the fall which accompanies the onset of thrombosis is an important diagnostic point. The cyanosis of the lips and ears contrasts with the facial pallor. The pain in a typical case is retrosternal; the radiation is important and the persistence of the pain is a typical feature. The leucocytosis sets in one and a half hours after the onset of the thrombosis.

The muffling of the heart sounds is characteristic when associated with sudden collapse. If a friction rub is present this is an important aid to the diagnosis.

Coronary thrombosis must be diagnosed from spasmodic or paroxysmal attacks of angina pectoris. There was little difficulty in doing this, in this series. The collapse was always very profound and the pain persistent. However mild attacks of coronary thrombosis may resemble attacks of angina pectoris. The pain is very similar in the two conditions but in angina pectoris the pain is of short duration and unattended by the severe

symptoms of shock seen in coronary thrombosis. The duration of the pain may be an important point in the diagnosis. If the pain lasts more than a few minutes then coronary thrombosis should be suspected. This is well seen in case No.15. This patient came home from his evening walk with pain in the chest, evidently of a very severe character. He was treated by hot fomentations; the pain was so much better the following morning that he was able to visit the doctor. When examined, this patient showed few of the classical signs of coronary thrombosis; the heart sounds were weak but audible over the praecordium; there were no signs of collapse, and the patient appeared to have recovered completely from the attack. The systolic blood pressure was however 98 mm.Hg. This patient was sent home to bed and died suddenly three days later, a myocardial infarction being found post-mortem. If it had not been for the prolongation of the pain throughout the night and the low blood pressure the case might easily have been mistaken for angina pectoris. No doubt an electrocardiogram and a blood count would have helped in the diagnosis, but facilities for these were not available when he was first seen.

The onset of angina pectoris may be referable to exercise, emotional attacks etc; in coronary thrombosis the attack usually comes on while the patient is at rest, but this is not invariable as is seen by case No.15 when the pain came on when the patient was out walking. The pulse rate during an attack of coronary thrombosis is usually slightly increased but there is no characteristic feature; in certain types of angina the pulse rate slows during the attack. The muffling of the heart sounds only

occur in coronary thrombosis.

The two respiratory conditions which most closely resemble coronary thrombosis are pulmonary embolism and pneumonia. In these two conditions dyspnoea is a prominent feature, and the thoracic pain is related to the breathing. The examination of the lungs will show the presence of a commencing consolidation in pneumonia. However considerable difficulty may be experienced in distinguishing pneumonia and coronary thrombosis. This can be seen in case No.7 where crepitations and diminished breath sounds were present at the base of one lung. However the temperature in case No.7 was subnormal.

There are several conditions indistinguish--able from coronary thrombosis even with the help of an electrocardiogram. Rupture of a cardiac aneurysm, or of an aortic aneurysm, may resemble coronary thrombosis very closely.

Many cases of coronary thrombosis resemble some form of abdominal disease. Levine and Tranter(10) were the first to draw attention to the difficulty in the diagnosis. In 1918 they reported two cases, one of which was subjected to laparotomy with a fatal result.

Confusion in the diagnosis may arise in two different groups of cases.

First a patient may have angina pectoris for many months before the attack of thrombosis. This angina is referred to the abdomen and is put down to digestive disturbances. These patients are usually elderly and complain of dyspepsia. In the larger series of cases it is remarkable

how often 'indigestion' is present before the attack of thrombosis. Indeed both the prodromal angina or the actual attack is often considered by the patient to be of gastric origin, (e.g. Cases Nos.5,14,15). Hamburger (148) has discussed the group of cases in which chronic 'dyspepsia' is complained of before the attack. This writer says that these patients often have slight dyspnoea, slight praecordial pain on exertion, or after a meal, and may have slight left ventricular enlargement and high blood pressure. Some cyanosis of the lips and ears may be present. The pain in this type of case is however, without the periodicity of peptic ulcer.

The diagnosis in the second group of cases has already been referred to when discussing the symptomatology of coronary thrombosis with abdominal pain. In this group the actual attack of thrombosis resembles an acute emergency, usually a perforated peptic ulcer, acute pancreatitis or acute intestinal obstruction. The possibility of acute abdominal pain being due to a cardiac condition is likely to be overlooked as the abdominal pain concentrates attention entirely on the abdomen. As the treatment of most of the abdominal condition is surgical, the diagnosis cannot be delayed too long. An electrocardiogram may be the deciding factor in a doubtful case, but it is not often available. The most important thing in the diagnosis is to remember that coronary thrombosis may have abdominal symptoms; if this is done few mistakes will occur; the majority of mistakes in the diagnosis are due to incomplete examination of the patient, as the possibility of a cardiac lesion is overlooked.

As regards the experience with the case of the present series, the absence of abdominal hyperaesthesia is an important feature in distinguishing an abdominal from a cardiac condition. Hyperaesthesia usually indicates peritoneal inflammation and is usually a marked feature of a perforated viscus or acute pancreatic necrosis. Intestinal obstruction may give rise to considerable difficulty as superficial tenderness is usually absent in this condition.

At present there seems to be no confirmation in the literature of the statement of Riesman and Harris (35) that slight jaundice and hepatic enlargement in coronary occlusion indicate obstruction of the right coronary artery, if signs of congestive failure are absent.

HEMIPLEGIA may be the first indication of myocardial infarction Willius (132). The embolism comes from the site of the infarction.

ELECTROCARDIOGRAPHIC CHANGES IN ACUTE CORONARY OCCLUSION.

It is not proposed to discuss these changes in any detail as few of the present cases give continuous electro--cardiographic records. Isolated electrocardiograms are not of much interest, it is the serial development of these changes which are of most importance.

The literature on this subject is extensive and many experimental methods have been devised to study the various factors which produce the characteristic changes of myocardial infarction. Unfortunately each investigator devises an experimental method of his own, and no confirmation of many of

the experiments is obtained. Most of the experiments fail to take into account all the variable factors, so that very conflicting results are recorded. For instance, different animals are used by different investigators. The majority of them use the dog as the experimental animal, but apes, cats and rabbits are also employed. It is obvious that the results are not comparable with each other, and certainly not with the human subject, in whom the heart, owing to the upright posture, will have a different relationship to the thorax than the heart of a quadruped. Other variables are, the position of the leads, and the influence of external factors e.g. respiration. Craib (46) says that "it may be pointed out that clinical variations in the T waves due to localized necrosis in the human heart, are not to be compared with monophasic curves experimentally obtained from exposed and partly injured hearts directly led off from injured and uninjured regions respectively".

Fortunately the recent controversy about heart block which has arisen between the classical theory (Lewis) and the new theory proposed by Wilson and his associates (149), has little influence on the electrocardiographic findings in coronary thrombosis.

Attempts have been made to localize the site of the infarction from the electrocardiogram (Barnes and Whitten(7,8), Barnes (150). From the literature it appears that sometimes an estimation of the site may be inferred from the electrocardiogram but it is by no means always accurate (Gilchrist and Ritchie(151), Saphir et al (17)).

The actual alteration in the working of the heart, which is responsible for the electrocardiographic changes in coronary thrombosis, is still undecided. Craib(46) says that the changes are due to failure of the injured region to contribute its normal component to the electrical field. This would appear to be the simplest explanation. Some consider that the electrocardiographic findings are an expression of a disturbance of the blood supply to the heart as a whole (Saphir et al (17)). Wilson (9) and his associates think that the relationship of the infarction to the epicardial or the endocardial aspect of the heart is the most important factor. Others think that interference with conduction or local anoxaemia are of importance.

The typical electrocardiographic changes of coronary thrombosis have been produced experimentally in many conditions and they are sometimes seen as curiosities in other conditions besides coronary thrombosis, e.g. pneumonia, pleurisy and pericardial effusion.

A patient may survive several attacks of coronary thrombosis but a second attack is usually fatal. The only patient with a second attack in the present series (case No.2) died on the eleventh day of the illness.

PROGNOSIS.

Many cases of coronary thrombosis die so suddenly that little can be attempted in the way of treatment. The majority of writers exclude these cases from their statistics so that the mortality rate appears much lower than it really is. The present series contained several cases which died within the twenty-four hours. (cases Nos. 3,4,7,8,12) so that the mortality rate in this series is probably unusually high. If however the cases which died in the first twenty-four hours are excluded it can be seen that by this time the patient has a fair chance of recovery as only four cases died after this interval. (cases Nos. 1,2,14,15). The cases which died in the early stages all had attacks of great severity, but some of the patients who died after the first twenty-four hours had comparatively mild attacks. Thus it may be seen that mild symptoms do not necessarily indicate final recovery.

The prognosis in any case of coronary thrombosis is grave, as it is impossible to determine whether the patient will avoid the many dangers which ensue on onset of the infarction. The patient may die from ventricular fibrillation immediately after the attack; or later the thrombosis may extend. Rupture of the heart, auriculo-ventricular dissociation may follow. An embolism may appear in the pulmonary or systemic circulations. Later a cardiac aneurysm may follow, or if the ventricular muscle is inadequate, congestive failure may set in. These factors are all intangible. Usually severe shock is a bad sign. If the systolic blood pressure is below 80 mm.Hg. the

prognosis is grave.

The extent of the pallor is an important sign. If it is generalized it is usually due to circulatory failure, and is not merely a symptom of shock. Inaudibility of the heart sounds usually indicates a severe attack, but this sign varies in different patients. Some cases have greatly weakened heart sounds before the attack, usually as a sequel to fibrosis of the myocardium.

An impression is got that the prognosis is better in cases where the blood pressure is subnormal before the attack but the present series is too small for a definite opinion. White and Bland (112) say that previous hypertension does not affect the prognosis. Transient disturbances of rhythm do not affect the prognosis, and even the onset of auricular fibrillation may make little difference to the patient. Partial heart block cases do badly (Connor and Holt (47)) and complete heart block is usually fatal although Levine (1) mentions a case described by Bell and Pardee which recovered. Ventricular tachycardia is soon fatal if the paroxysm is not amenable to treatment. Signs of congestive failure indicate a poor prognosis.

Parkinson and Bedford (48) say that if the patient survives the first twenty-four hours he has an even chance of recovery. The present series tends to confirm this; if the patient survives two weeks his chances of recovery are good. All the patients in the present series who survived for fourteen days were alive six months later.

As regards the remote prognosis the majority of patients die from cardiac trouble. This occurred in twenty-four out of sixty-six patients (Cowan (108)). The average duration of life after an attack is given by White and Bland (112) as 1·5 years. Out of thirty-three patients who survived the attack thirteen died in the first two years (Cowan (108). Single cases have been recorded as having survived for much larger periods e.g. fifteen years (Cowan). John Hunter lived for twenty years after myocardial infarction. Many of the patients die suddenly at work or in the street. Case No.2 of the present series survived an attack for two years before dying from a second attack. Three patients in the present series are alive two years after the attack. The mortality in the second attack is 29% compared with 16'2% in the first attack. (Connor and Holt) (47).

None of the present patients were completely restored to health. They all lost their previous activity and had to walk slowly. Three patients (cases Nos. 5,11,13) had effort angina after the attack. Nearly all the cases had some degree of dyspnoea on exertion. Only case No.10 of the present series resumed work after the infarction. Thirty-eight cases out of Cowan's (108) series of sixty-six patients resumed work.

As regards the present series, coronary thrombosis proved a much more serious cause of permanent incapacity than in the larger reported series. All the surviving patients were, with one exception, so badly crippled that further work was impossible.

T R E A T M E N T.

The following description is based on the treatment given to the patients in this series. It is difficult in coronary thrombosis to assess the value of any particular line of treatment. Some theoretical considerations will also be discussed.

The immediate treatment consists in combating the shock. The patient is put to bed; if badly shocked it is unnecessary to undress him completely. Warmth is supplied by hot bottles or the electric cage.

Morphine relieves the shock by relieving the pain; a hypodermic dose of $\frac{1}{3}$gr. is usually required, and may need to be repeated several times. It is usually stated that there are no contra-indications; however in one case it seemed to be responsible for a rapid deterioration in the patient's condition (case No.4), probably through its effect on the respiratory centre. In the present series two hypodermic administrations were usually sufficient for the acute stage, until opium could be administered by the mouth. This was usually given in the form of omnopon gr$\frac{1}{4}$. four hourly. Later the omnopon was administered only at night.

Absolute rest must be enforced for at least three weeks. The patient must have everything done for him. It is remarkable how a slight movement may precipitate a sudden collapse. In this series, if the cases which died in the first twenty-four hours are excluded, the remaining fatalities were associated with some degree of movement.

Many old patients require very careful watching; some

of them do not fully recognise the gravity of their condition, and after the period of shock has passed they tend to move about too freely. Cases Nos. 1 and 14 were of this type. The former patient, when unattended, wished to smoke his pipe but fell unconscious when attempting to reach it. Case 14 rose when unattended and was found lying on the floor of the lavatory. In case 2 the movement which preceded the fatal collapse was very small; the patient merely turned his head towards the feeding cup.

Stimulation has not been adopted as a routine measure. It would appear undesirable to alter the blood pressure or the heart rate. Case No.5 was given two teaspoonfuls of Brandy at bed-time but it was discontinued as it made him restless. Camphor, caffein, euphyllin, and theophylline and muscle extracts have been all used in this series but no definite benefit could be made out from the use of these drugs. There are many incalculable factors in a case of coronary thrombosis and it is difficult to assess the effect of drugs on these factors. Ephedrine was used in case 2 (gr$\frac{1}{4}$ t.i.d.). The therapeutic effect of the drug was doubtful in this case, but the patient died on the day following the withdrawal of the drug.

EFFECT OF DRUGS ON THE CORONARY CIRCULATION.

The effects of drugs on the coronary flow are dependent on many factors. To understand the effects of drugs it is essential to examine the various influences which regulate the coronary flow. Recent investigations on the coronary circulation have been made by Hochrein (100) in Germany, by Anrep (78) and his associates in Britain, and by Wiggers and his associates in America. Hochrein's views are not accepted by Wiggers or Anrep. The German writer's views are revolutionary. He considers that the main coronary filling takes place during ventricular systole, that the coronary flow is almost entirely related to the cardiac output and that eddies and swirls in the first part of the aorta influence the coronary flow.

His results are probably due to a defective technique; many varying factors have to be taken into account in estimations of the blood flow in the coronary arteries, in the coronary sinus or in the peripheral coronary vessels.

Anrep uses an electrical method for his estimations and Wiggers uses an optical method. Many of their results agree closely, and indeed the main difference between these investigators is in the interpretation of the results.

Anrep (78) and his associates find that during ventricular systole the coronary flow comes to a standstill. This view has been widely accepted, but it seems rather unlikely that the blood flow should altogether cease in such an important organ as the heart.

Wiggers and Cotton (30) investigated the condition

of the coronary circulation during ventricular systole, and came to the conclusion that the coronary flow decreases with the onset of contraction and that this is due to compression by the muscle of the ventricle. The flow increases as the aortic and coronary pressures reach a summit; it remains steady until the period of isometric relaxation, when suddenly there is a greatly increased flow, owing to the relaxation of the ventricular muscle. The coronary flow maintains itself during diastole but gradually falls off towards the end of this period. This view is a contradiction of that of Anrep. However Green,Gregg, and Wiggers (57) published a study of their own curves and also those of Anrep. They point out that in both sets of curves the contraction of the ventricular muscle during systole affects the velocity of the flow and not the volume of the flow. Thus the coronary flow is not actually diminished during ventricular systole, but only the velocity of the flow is altered. This opens up a new conception of the circulation in the heart wall. This conception is more easily understood than that which postulated a temporary arrest of the coronary circulation. The coronary circulation is continuous and has a cycle of its own.

The two factors which regulate the coronary cycle are (1) aortic pressure (2) the contraction of the ventricular muscle which gives rise to a factor--peripheral coronary pressure. These are two opposing forces each in ascendance at different periods of the cardiac cycle. Green,Gregg, and Wiggers (57) indeed estimate that during the systole of the ventricle the myocardium receives approximately three-quarters as much blood

as during an equivalent period of diastole, although of course the total flow in diastole is greater because of the larger diastolic interval. During systole the blood which has entered the coronary circulation is not held up, but moves on through intra-mural capillaries.

It follows from the above findings that alterations in the pressure head in the larger coronary vessels are not directly conducted to the peripheral capillaries. This finding alters all the previous ideas about the effects of drugs on the coronary circulation. Indeed, whatever alterations may be caused in the aorta or in the larger coronary vessels themselves, they are unlikely to be directly communicated to the smaller peripheral vessels. It is even doubtful if a drug which changes the coronary circulation through the nerve supply of the heart will be able to alter the calibre of the smaller vessels. Woolard (118) has shown that in all probability these smaller arteries have no direct nerve supply.

It is apparent that a drug may increase the coronary circulation by a vaso-dilator or vaso-constrictor action through the nerve supply of the heart; or the drug may act directly on the smaller vessels in the myocardium. Anrep and Segall have shown that alterations in the heart rate do not affect the coronary flow, but that alterations in the cardiac output are directly related to the coronary flow. In addition many drugs alter the systemic blood pressure and thus alter the coronary flow. Indeed Wiggers and Green (82) consider that many drugs apparently increase the coronary output mainly through this action on the

systemic blood pressure. In addition, as has been described above, there is the factor of coronary peripheral resistance. This is due to the contraction of the ventricular muscle and is mainly dependent on the intra-ventricular pressure. This factor is very difficult to estimate in the majority of experiments, and at present little is known about its variations.

Cruickshank and Subba Rau (152)investigated the reactions of isolated systemic and coronary arteries to the application of various drugs. Their investigations can have little application to the living heart. A similar objection applies to experiments performed on denervated heart-lung preparations.

There are several experimental methods by which increased coronary flow may be demonstrated. The majority of investigators rely on estimating the flow from the coronary sinus; others have produced an area of ischaemia by ligating the coronary artery, and watching the alteration in the size of the ischaemic area which follows on the administration of the drug; probably the method which is most free from the influence of external factors is that of Wiggers, who by means of a myograph applied to the ischaemic area, studied the effects of drugs on the contractile function of the muscle fibres in the ischaemic area. Drury and Smith (153) and Drury and Subbal (154) viewed directly the alterations produced by certain drugs on the heart of the tortoise.

The purine base derivatives have been extensively used as coronary vaso-dilator drugs. Gilbert and Fenn (155) published in 1929 the results of an investigation into this

subject,estimating the variations in the flow from the coronary sinus, and then taking these estimations as evidence of alteration in the coronary circulation. Caffein sodium benzoate, theocine sodium acetate, and theophylline ethylenediamine (Euphyllin) all produced an increased coronary flow. Theocine sodium acetate produced the most marked increase. However their experiments show that this increase was accompanied by a fall in the blood pressure. This itself will diminish the coronary flow and must greatly counteract any vaso-dilator action that may be possessed by these drugs. Many of the investigators themselves realize that the method of estimating increased coronary flow by estimating the changes in the flow from the coronary sinus, has certain disadvantages. The method may estimate changes in the coronary circulation as a whole; it is not absolute evidence that there is dilatation of the peripheral vessels. In myocardial infarction, interest lies in the changes in the circulation over a localized area of the heart. Markwalder and Starling (34) have shown that only 60% of the blood entering the coronary system can be recovered from the coronary sinus; it is assumed in these experiments that the 40% loss from the output at the coronary sinus is constant under all experimental conditions. If a drug diminished the peripheral coronary resistance this would cause increased coronary flow although there might be very little active vaso-dilatation.

Fowler, Hurewitz and Smith (156) have recently (1935) published the results of an experimental investigation into the action of theophylline ethylenediamine. The drug was

administered intra-venously, the experimental animals used being dogs. These workers first ligated the anterior descending branch of the left coronary artery along with the attendant vein. An area of cyanosis appeared in the area supplied by the ligated artery, and this was fully developed in five minutes time. The theophylline compound was then administered and the changes in the cyanotic area were observed. The cyanotic area became indistinct one minute after the administration of the drug, diminished gradually in size and in some cases disappeared completely so that the cyanotic area became indistinguishable from the normal ventri--cle. In another series of experiments they ligated the coronary artery in nineteen dogs, ten of which were used as controls. The remaining nine dogs were given theophylline ethylenediamine after ligation of the coronary artery. In six weeks the dogs were killed. The area of fibrosis at the site of the infarction was smaller in those dogs which had received the drug than in the control animals. However although the cyanotic area diminishes after the use of this drug, this does not indicate that the function of the muscle in the cyanotic area is restored. The actual haemodynamic action in the ischaemic area is still a matter of doubt. Wiggers and Green (82) say that observations of the changes in colour and outline of the ischaemic area are untrust--worthy signs of improved collateral circulation.

Another point of importance is, that in the above experiments, the drug was administered intra-venously, very shortly after the ligation of the artery. This is not done in the human subject, and would seem to indicate that to have any benefit

the drug must be administered shortly after the onset of infarction. There seems to be no experiment on the period of time for which cardiac muscle can exist with its blood supply cut off. This period is probably short. In the experiments by Fowler and his associates the administration of theophylline ethylenediamine caused a tremendous fall in the systemic blood pressure. This is certain to counteract any vaso-dilator effect that the drug may have, as the coronary flow is closely related to the systemic pressure. (Anrep and Segall). In some of their experiments they counteracted the fall by the administration of 50% glucose solution, but even then the average fall in pressure after the administration of the drug was 6-12 mm.Hg. Fowler and his co--workers make no mention of any difference in the size of the ischaemic area, as regards those cases in which there was a big fall in blood pressure and those in which the fall was small. These investigators say also that theophylline ethylenediamine causes an increase in the rate and amplitude of the cardiac contractions. If this increased the peripheral coronary resistance, as seems likely, then the vaso-dilator effect would be of little value. From their experiments it seems that the vaso-dilator effect lasts for about 1½ hours. Subsequent administrations have comparatively little effect. Whether this period would be sufficient to keep up the nutrition of an infarcted area is doubtful. In a subsequent paper Smith, Rathe, and Paul (157) describe clinical benefit from the use of the drug. Many other papers have appeared on the action of these drugs on the coronary flow; most of the investigators work with the heart-

-lung preparation. The results show that under these conditions the purine base derivatives have a vaso-dilator effect. Heathcote's (158) paper seems to have been the earliest in the English literature; he noted that these drugs altered the heart rate and the blood pressure, and he concluded that the alterations in the coronary flow were the result of a true vaso-dilatation, and were not a consequence of alterations in the rate of the heart or changes in the blood pressure. Stolland et al (159) confirmed the findings of Gilbert and Fenn that theophylline ethylenediamine increases the coronary flow, but the increase is much greater in the denervated preparation than in the intact animal.

Wiggers and Green (82) investigated the effects of various drugs on an ischaemic area. Their technique is complicated. They were able to canalize the ramus descendens of the dog below the site of the ligature. It is well known that blood flows from the peripheral end of the ligated vessel, and it has been proved that this must come from the collateral vessels. (Stella (84)). Wiggers and Green found that the theophylline group had little effect on the collateral flow. The nitrites caused a slight decrease in the peripheral coronary resistance (due probably to the lowering of the intraventricular pressure which follows on the lowered blood pressure after administration). This might cause an increased coronary flow, but it is probably offset by the fall in the blood pressure. Wiggers and Green by means of the myograph studied the effect of drugs on the contract-ility of the muscle in the ischaemic area. The use of

theophylline, theobromine, nitrites, oxygen administration and adrenalin were all useless in restoring the function of contraction although this readily returned when the ligature was released.

Probably those experiments which deal with isolated ischaemic areas are of more value than those which deal with the heart as a whole. A small area of the mammalian heart will probably always act in the same manner no matter what species it comes from. The heart as a whole may behave very differently in different animals. For instance histamine dilates the coronary vessels in the cat and constricts them in the rabbit. (Anrep)31).

Gruber, Olch and Blades (160) have published the results of investigations on the production of myocardial damage following the intravenous injections of certain drugs. The purine base derivatives caused no myocardial injury unless adrenalin was given after their administration; adrenalin alone caused marked degenerative changes in the myocardium. In 40% of the animals (rabbits) 0'2 cc. of 1'1000 solution caused myocardial changes. This was said to be due to alterations in the systemic blood pressure and to direct toxic action of the drug on the myocardium.

ACTION OF MUSCLE EXTRACTS, ETC.

Frey (161) was the original discoverer of the so called 'cardiac hormone' which is a substance of pancreatic origin secreted in the urine. It is well known under the trade name of 'padutin' (Bayer). This substance is said to have a vaso-dilator

effect on the coronary arteries. Greene (162) investigated the effect of intravenous injection of this substance by estimating the variations in flow from the coronary sinus. The drug increases the flow from the coronary sinus, but its administration is attended by a fall in the blood pressure which may equal 41% of the original reading. Greene mechanically equalized the blood pressure so that the effect on the coronary system alone could be estimated. There was a pronounced increase in the coronary flow after the administration. The reaction is of short duration; from the tables published in this paper, it can be seen that there is little acceleration of the heart after the use of this drug. Some of the experiments showed a diphasic reaction, dilatation being followed by constriction.

Elliot and Nuzum (164) investigated the effect of the insulin free extract of the pancreas and the urinary hormone described by Frey, on the coronary flow. They came to the conclusion that both substances are similar in composition. Intravenous injection is associated with a fall in blood pressure; the cardiac hormone only acts when given intravenously. In the rabbit's heart an increase in the coronary flow is produced. These preparations also inhibit the pressor action of adrenalin.

Stoland et al (159) found that an insulin free pancreatic extract caused an increased coronary flow of from 4% to 125% in the denervated specimen, but in the intact animal the results were very varying, and even a decreased flow might result.

A muscle extract (lacarnol) is employed in the same way as the cardiac hormone. Greene found that this drug causes a pronounced coronary dilatation, but the fall in blood pressure is not so pronounced as in the case of the 'cardiac hormone'.

The use of adenosine was attended with similar results; this also caused vaso-dilatation but little fall in the blood pressure.

Greene (162) considers that the above results are brought about by the action of the drugs on the vaso-motor nerve supply to the heart.

Wedd (163) has recently investigated the effects of the administration of certain choline derivatives. These results vary greatly. The drugs cannot be used clinically in their present form, as they are very toxic.

Adenylic acid causes increased coronary flow (Wedd and Drury)(165). Sulzer (166) investigated the effects of alchohol on the mammalian heart. In his experiments there was little fall in blood pressure after the administration of alchohol, but the coronary flow was always decreased.

The therapeutic results from the administration of so called coronary vaso-dilators have been found to be disappointing; recent investigations in the physiology of the coronary circulation explain the complexity of the factors determining the coronary flow, and rather decrease, than increase, the likelihood of any of the above mentioned drugs having any therapeutic effect. By administering a coronary vaso-dilator in coronary occlusion there are two objects. The first is almost certainly unobtainable i.e.

to restore the circulation to the infarcted area so that the muscle survives. Even if the circulation could be completely restored to the ischaemic area it is doubtful if the heart muscle would survive unless the circulation was restored within a few hours. As at present administered the above drugs are useless for this purpose; the majority of them are administered clinically by the mouth; it is doubtful if they are absorbed unchanged into the blood stream; many of them have a very transient effect and a large number of them cause also a fall in the blood pressure which probably outweighs their coronary vaso-dilator effect.
The collateral circulation makes little attempt to supply an ischaemic area. Sutherland and Dial (37) have shown that the temperature of an ischaemic area remains low despite vagal or sympathetic stimulation although it will soon rise when the ligature is released. Wiggers and Green (82,83) have shown how contractility in the ischaemic area is still absent after the administration of vaso-dilator drugs.

A second object in administering a coronary vaso--dilator drug is to limit the extent of the infarction. The experiments of Fowler already quoted indicate that this might be possible. At the periphery of the infarction the nutrition of the myocardium will be precarious, and an increased flow at this point may limit the spread of the infarction. Tennant et al(38) however, have shown that where an infarction is experimentally produced by coronary ligation there is some oedema but little haemorrhage; where however the ligature is released after being tied for over half an hour the blood flows into the infarcted area

and produces a haemorrhagic infarction. It might therefore be undesirable to force blood into an area of infarction. In the present state of therapeutic knowledge, therefore, little can be expected from drugs in coronary thrombosis. The routine administration of theophylline or theobromine may help to limit the infarction.

The nitrites are contra-indicated in the early stages as they cause a fall in the blood pressure. In the present series they have been found useful in relieving the effort angina which sometimes follows an attack of thrombosis.

Alchohol was given at night to three patients but had little benefit on their condition. It would be contra--indicated from the results of Sulzer's experiments.

Lacarnol was given to four patients, all of whom survived but no definite credit could be given to the drug.

The patient will require little food until he is over the initial shock. Fluid only will be administered for the first forty-eight hours. Glucose is useful as it is easily assimilated. Taken by the mouth it has probably no direct action on the myocardium although it is sometimes used intra-venously in cases of congestive failure,

Distention of the stomach is to be avoided; some--times a simple carminitive mixture may help the patient. When the acute pain has passed off, the patient can take a light diet.

An enema is given after the first forty-eight hours are passed. A simple laxative should be employed after this as any straining at stool might precipitate a fatal collapse.

Glycosuria and albuminuria are treated on the usual lines if present. Usually the urine clears up in a few days time.

After the third day a pillow should be placed between the left arm and the body for a few hours each day to prevent the occurrence of any stiffness of the shoulder joint. Digitalis is usually contra-indicated in coronary thrombosis; if congestive failure sets in this drug may be employed. Pulmonary oedema is treated by atropine, morphine and oxygen. It is not necessarily a sign of approaching cardiac failure. (case No.5). There were no cases of ventricular tachycardia in this series. Quinidine sulphate is used and very large doses may be required. Levine (1) on page 99 of his monograph records cases in which very large doses of quinidine sulphate were given five times a day, before normal rhythm was restored..

If complete heart block sets in, then adrenalin should be administered. This was tried in one case of the present series (case No.4) but there was no change in the pulse rate. In view of a recent article by Schwartz (11) the dose administered was inadequate. This writer advises the administration hypodermically of doses up to 1cc. of 1'1000 solution of adrenalin hydrochloride. When the patient is over the attack he advises ephedrine hydrochloride gr.$\frac{1}{4}$ t.i.d. up to 1gr. t.i.d. He records several cases where the symptoms recurred after the withdrawal of the ephedrine. Its administration may be required for a long period. Schwartz finds that atropine is of little use. It was given to case No.4 of the present series without any obvious change.

The patient should be kept in bed for from six to eight weeks. This allows the coronary anastomoses to develop and helps the damaged myocardium to recover.

When the patient first gets up, his exercise will be greatly limited. Connor (167) advises graduated exercises. Progress is always slow and exercise tolerance is usually greatly diminished. Later attacks of angina may require treatment. Tab. glyc. Trinit is probably the most useful drug. Syphilitic cases may be given antisyphilitic treatment, but caution is needed. Stiffness of the shoulder will require massage, manipulations and radiant heat.

Only one case in the present series resumed his normal work. (case No.10).

Surgical treatment in order to improve the blood supply of the heart muscle has been attempted successfully by Beck (62) and a theoretical operation has been planned by O'Shaughnessy (60,61). The operation, which attempts to improve the blood supply by pericardial adhesions, or by omental trans--plants, is a very severe one.

Beck had one death in his group of four cases. The difficulty is to foretell what cases of myocardial fibrosis or arterio-sclerosis are liable to coronary thrombosis. Comparatively few cases of fibrosis are seized by thrombosis; and at present there seems to be no mode of differentiating between the two groups of cases.

Cox and Robertson (129) have recently (1936) published an experimental investigation into the effect of removal of the stellate ganglion on the function of the dog's heart. Ten dogs had stellate ganglionectomy done before coronary ligation, and ten had only coronary ligation performed. In the first group only one dog died shortly after the operation while in the second group two died shortly after operation from ventricular fibrillation, while three others died suddenly in the first few weeks after operation. The area of infarction was smaller in the first than in the last group.

From this the writers conclude that bilateral stellate ganglionectomy would be likely to reduce the mortality of coronary occlusion by eliminating the sympathetic reflex arc and promoting absolute rest of the heart.

This operation at present would seem to have little practical application. As a prophylactic measure it is open to the same objection as Beck's operation, namely that the patient is subjected to a severe procedure without knowing whether in any particular case it is necessary since all cases of coronary sclerosis do not develop coronary thrombosis. During an attack of coronary thrombosis the patient is obviously too ill for any operative procedure.

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