Brief reference is given to hormone assays which have been carried out at King's College Hospital, and their possible prognostic significance indicated.

Premature termination of pregnancy before the end of the 37th week is recommended, and the relative places of caesarean section and induction of labour are discussed.

The importance of hyaline membrane disease as a cause of neonatal death and its possible relation to intra-uterine anoxia are explained.

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CLINICAL ASPECTS OF ATYPICAL CORONARY DISEASE*

BY

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It is generally agreed that more cases of coronary arterial disease are being recognized to-day than formerly. We know from Ryle and Russell (1949) that in Great Britain there has been an increase in the mortality from coronary disease in the post-war years, but the increase is less rapid than in the pre-war years. This increased mortality has occurred in spite of improved methods of treatment by anticoagulants, etc. Early and accurate diagnosis is therefore of fundamental importance, in order that the treatment can be started as soon as possible.

I propose to deal with atypical angina pectoris and with some of the clinical aspects of cardiac infarction.

Angina Pectoris

First let us remember that it was William Heberden who was the first to give, in 1768, a clear and accurate description of angina in a paper entitled, "Some Account of a Disorder of the Breast." In this paper Heberden showed that angina pectoris may occur with no physical signs and with an apparently normal cardiovascular system, and this has been recognized ever since his time. A diagnosis often has to be made on the history obtained from a patient.

The familiar picture of angina pectoris is that of pain in the centre of the chest radiating down into the left arm to the wrist. It is less well known, however, that the pain may radiate in other directions, or the case may present itself with different symptoms. In a series of cases investigated by me during a five-year period, pain extended from the chest into both arms in 17% of the cases.

In the "reversed" type the pain in all respects follows the classical pattern of angina pectoris, except for the distribution and radiation, which is the reverse of the usual. The patient complains that the pain starts in his left hand, wrist, or arm, or the left side of his neck, and radiates up into his chest, and is associated with the usual feeling of constriction in the chest.

Next, there is the patient who complains of a sensation of a band round his wrists or arms. On careful inquiry he may admit that it sometimes amounts to a pain; he may

not mention, unless asked, that it is directly related to exertion or is accompanied by a retrosternal pain. He may even have been treated as a case of neuritis or myofibrositis before a cardiac cause for his symptoms was suspected.

Quite a number of my cases have complained of a pain in the jaws or gums. One man said that he could not wear his dentures after a meal because of this pain; another man said that his jaws "ache at times."

It will be remembered that the word "angina" does not mean pain, but a strangling. There are the patients whose main concern is the choking or strangling sensation in the throat. An interesting example of this was a patient who reported to my out-patient clinic two years ago, and gave a history of a curious choking sensation in his neck, saying that he felt he was "breathing in cold air." This had been present for two months, and occurred only on walking; it had not interfered with his work, but he had noticed a pain across his chest, with slight dyspnoea, on exertion. At that time a diagnosis of atypical angina had been made. Two years later he gave a classical history of angina with considerable incapacity.

Several examples of angina have been sent to my clinic by doctors because they have been worried by the patient's complaint that the pain is worse after meals and they suspected some form of dyspepsia. A recent example of this was a carpenter, who found that his capacity for work was curtailed by his midday meal; he stated that he could do four times as much work in the afternoon if he went without his lunch. A full and carefully taken history revealed that this limitation of work was due to angina, which followed on slight exertion after a heavy meal.

The details of another patient, who experienced pain in his phantom hand, are of special interest. Two such cases have also been recorded by Sir Henry Cohen and Wallace Jones (1943). The man, aged 58, had had a gunshot wound of his left elbow in the 1914-18 war. After excision of the joint, sinuses and sequestra developed, so that amputation above the elbow had to be performed. Three months after the operation angina of effort developed; the patient complained that the pain radiated into the elbow and all the fingers of his phantom hand. When, six months later, he had an attack of coronary thrombosis, the pain followed a similar distribution in the phantom hand.

If young patients develop angina without any obvious cardiovascular disease the possibility of hypercholesterolaemia may be considered, although it is a very rare condition. I have recently seen two members of one family in which this interesting rarity existed. A Cypriot waiter, aged 24, attended my clinic complaining of severe angina pectoris of three months' duration. Since the age of 12 he had had yellow nodules in the skin (xanthomata). An electrocardiogram was normal, but after an exercise test it showed the classical E.C.G. changes of angina (depressed ST segments, etc.). His blood cholesterol was 650 mg. per 100 ml. His angina was considered to be due to deposits of cholesterol in his coronary arteries, and to be part of the general disease known as xanthomatosis tuberosum multiplex. He died two years later of cardiac infarction. His sister, aged 30, came to my clinic about this time; she had had skin nodules for eight years and angina pectoris for three years. Her blood cholesterol was 860 mg. per 100 ml. She died suddenly about one year later, whilst out shopping, as a result of coronary thrombosis.

These are some of the unusual types of angina. How, then, can we make a diagnosis in an atypical case? The answer is simple; it is by a most scrupulously taken history. Firstly, the method in which the patient gives his history is of great value; his whole manner of presentation is convincing, since he has no need to use the florid and exaggerated phrases that are so often associated with patients suffering from the neuroses. The patient is usually intelligent, and gives a definite history, showing how handicapped he now is, whereas previously he was a fit man. Moreover, there is an absence of inconsistencies in his history; there may be variations in the amount of exciting exercise, but

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the whole story rings true from beginning to end, and fits into a clear pattern of a man limited by his disability, for reasons which he does not understand. Secondly, the symptom (pain, discomfort, or constriction) is related to exercise and to a definite degree of exercise, and also to emotion; it is, in addition, influenced by heavy meals and a cold wind, each of which limits his capacity for exertion. Finally, the symptoms are almost always associated with a central chest pain, accompanied by a constriction in the chest, but this may well be overshadowed by the patient's concentration on a symptom in another situation, for which he presents himself.

Myocardial Infarction

Two aspects only of the problem of diagnosis of myocardial infarction are here dealt with. Firstly, are there any warnings of an attack of cardiac infarction, and, if so, what are they? The second aspect concerns the unusual manifestations of cardiac infarction—particularly the patient complaining of abdominal pain, and also the patient with the so-called silent or painless infarct.

Whereas the classical picture of cardiac infarction due to coronary thrombosis is the sudden onset of severe pain with shock and collapse, followed frequently by congestive heart failure, it is becoming increasingly recognized that certain warning symptoms may occur, which, if suitably treated, may result in the prevention or postponement of actual infarction of the myocardium.

Prodromal Symptoms Including "Indigestion"

The fullest and most recent study of the subject of premonitory pain was carried out by Mounsey (1951) at the British Postgraduate Medical School, Hammersmith. He came to the conclusion that it occurred often enough to form a recognizable clinical group.

I have made a careful study of my records of all patients seen for the first time during a recent five-year period, in whom a diagnosis of coronary thrombosis had been made; in particular, I have investigated any history of early symptoms or special features. These patients have either been under my care at University College Hospital as in-patients or have been seen in private practice. I have limited the investigation to in-patients and private cases because the notes of such patients are much fuller and more accurate than those of out-patients. Those patients who were so ill on admission to hospital that they were unable to give a complete history have not been included in the series. Three criteria have been used in the investigation: (1) the diagnosis of cardiac infarction must be clear, with a typical E.C.G., or confirmed at necropsy; (2) there must be clear evidence of the time at which the cardiac infarction took place; and (3) a good history of the events *before* the infarction occurred must have been obtained.

There were 23 cases out of 75 in the series with premonitory symptoms—that is, 30%. I have studied the details of the histories of these 23 patients to see if they can be grouped together in any way, and I feel that they might be put into the following three groups: (1) Angina of effort, of recent onset, or increasing in severity recently. (2) Constant sternal pain, roughly simulating angina in its site and radiation. (3) Attacks of sternal pain, quite unrelated to exertion, emotion, etc.

In the first group (angina of effort) sometimes the angina of effort is of recent onset; in others there has been a long history, but recently the incapacity has been progressively increasing over the last one to three months. This group consisted of five patients, of whom three died—a mortality of 60%, the highest.

In the second group (constant sternal pain) this symptom occurred up to three weeks, with an average of six days, before the onset of the coronary thrombosis. Radiation of the retrosternal pain occurred in all except one case; none had previously had angina of effort. There were six patients in this group and no deaths.

In the third group (attacks of sternal pain not related to effort or emotion) this symptom varied in duration between one day and one month, with an average of two weeks. The attacks were usually frequent and short-lasting. About one-quarter of the patients had previously had angina of effort, and these knew that this prodromal pain was a different one. Of the eleven patients in this group two died. There were also four patients who complained of excessive tiredness or feeling seriously ill prior to the onset of the attack of cardiac infarction.

I would like to refer here to the term "indigestion," which is in my experience not infrequently used by the patient, and sometimes by the doctor. It occurred in one-third of my patients' histories, and these cases have been included in groups 2 and 3. It is so easy for a patient, and even for a doctor, to attribute an upper abdominal or retrosternal pain to indigestion, especially if it is worse after meals or is associated with wind. Care must therefore be taken by a doctor in making such a vague diagnosis as "indigestion," or in accepting the patient's own label, in cases of hypertension, angina pectoris, etc., and in persons possibly liable to coronary occlusion. Perhaps this aspect might be illustrated by the history of a patient, a medical practitioner, who consulted me three days after he had had his premonitory attack: this consisted of pain which he attributed to an injudicious meal taken late at night. In the absence of signs of cardiovascular disease and on the strength of a normal electrocardiogram (and unfortunately ignoring the importance of a phrase used by him—namely, a "severe vice-like pain") I labelled it "flatulent dyspepsia." Six days later I was called out to see him in a typical attack of cardiac infarction, with classical E.C.G. changes; he recovered well and is now back at work.

The difficulties of recognition of these prodromal symptoms and of their significance is in no way underestimated. That they do occur in a fairly high percentage of cases of cardiac infarction (30% in this series) is generally agreed, but to recognize them *before* an attack of infarction may be almost impossible.

The mortality of patients with premonitory symptoms has been shown in all published series to be lower than the general average mortality, though there is insufficient evidence at the moment why this should be so. As regards the immediate mortality rate in the series with adequate histories recorded here, 20 of the 75 died (27%). Out of the 52 patients without any history of warning pain, 15 died (30%); whereas only 5 out of the 23 with premonitory symptoms died (22%).

It is important for us to look out for the cases with prodromata amongst our patients, and if we do we shall perhaps recognize them more frequently. It is well worth while in known cases of hypertension and of angina to arrange for a regular annual review of their condition, with detailed inquiries into any new symptoms; but care must be taken not to alarm the patient unduly.

Unusual Clinical Pictures

The two clinical pictures of cardiac infarction which are of greatest interest and most apt to lead to pitfalls in diagnosis are those presenting as an acute abdominal emergency and those cases in which pain is not a prominent symptom in the patient's history—that is, the so-called silent or painless infarct.

A case of coronary thrombosis presenting as an acute abdominal emergency calls for consultation and close co-operation between general practitioner, surgeon, and physician, because this condition may simulate, for example, a perforated duodenal ulcer or gall-stones. Some years ago I saw a surgeon who during the previous three days had had severe upper abdominal pain. Being a surgeon, he diagnosed his own case as "gall-bladder disease" or "partial volvulus." On account of this diagnosis that he had made he continued to do his full hospital work, including operations, until a few hours before he collapsed. When

seen by me he showed the clinical picture and E.C.G. changes of coronary thrombosis, from which he died two days later.

Help towards a correct diagnosis of myocardial infarction may be obtained by considering the age and sex of the patient, and the presence of any predisposing factor, such as hypertension, angina, etc. Conversely, a history of peptic ulceration or long-standing flatulence would point towards an abdominal cause for the pain. Whilst the abdominal pain may be so severe that it attracts the patient's attention as the major symptom, there is always, in my opinion and experience, some retrosternal pain, and this is a constant pain, never spasmodic or colicky; it is a valuable diagnostic feature of infarction. In abdominal infections a raised temperature would be expected, whereas in cardiac infarction fever is low and seldom occurs until some days after the onset. Breathlessness and cyanosis are less often seen in abdominal catastrophes than in cardiac lesions. In a large number of cases the immediate electrocardiogram will give diagnostic evidence of infarction, though the E.C.G. may have to be repeated two or three days later to be certain to exclude infarction.

My former chief, the late Sir Thomas Lewis (1933), wrote that "pain is not invariable" in coronary thrombosis. While this may be so in cases of sudden death from myocardial infarction, since no one can deny or confirm such an opinion, it is, in my experience, rare to find that a patient who has had an infarct has had no pain. In other words, a silent or painless myocardial infarct is exceptional.

What are some of the ways in which such patients may present themselves, and why is the attack often thought to be painless when actual pain frequently does occur? Some clinical conditions which should arouse our suspicions will now be considered.

Firstly, sudden onset of congestive heart failure occurring in a middle-aged person, especially if there is no immediate exciting cause, such as physical overwork or an infection, and where there is no obvious underlying disease, such as mitral stenosis or hypertension. Also, congestive failure without cardiac enlargement, in the absence of hypertension, is suggestive of coronary thrombosis in the appropriate age groups. Secondly, acute pulmonary oedema and left ventricular failure, especially with falling blood-pressure readings. Thirdly, unexplained irregularities of rhythm, such as heart-block and auricular fibrillation, etc. Fourthly, other signs of a failing heart, such as gallop rhythm, pulsus alternans, and Cheyne-Stokes's respiration.

The above four groups are examples of the type of case in which careful and full investigation may reveal that myocardial infarction is the underlying cause. Success in diagnosis often lies in remembering the possibility of coronary occlusion as a cause, and in watching for E.C.G. changes and late signs and complications.

While pain is almost invariably present at some time during the episode of myocardial infarction, it is often forgotten by the patient. This, I find, is often due to the fact that some other symptom predominates in the patient's memory. Usually it is dyspnoea; sometimes it is that he feels extremely ill; at other times he attributes the pain to wind or indigestion. It will be seen, therefore, that the attack may be labelled painless because the patient has omitted to mention the pain. The onus of eliciting a history falls on the doctor, and, as it may be difficult to obtain the story of the pain, it is necessary, in my opinion, to carry out an unhurried, careful, and thorough interrogation of the patient when he is fit enough; the value of such cannot be overestimated. Such questions as, Have you ever had any wind or indigestion? or, Why exactly did you or your relatives send for the doctor? will not infrequently bring out a story of pain, which had previously not been mentioned. It is well worth while trying to obtain experience in such history-taking without asking leading questions, and the time and trouble spent on getting such a history will be amply rewarded.

A recent example may be quoted to illustrate this difficulty. A works foreman, aged 46, consulted me for chronic bronchitis of six years' duration and increasing shortness of breath. The latter symptom had troubled him for only one month, limiting his activities to walking 200 yards on the level and preventing him from doing his job as foreman. On examination his dyspnoea appeared to be out of proportion to the degree of emphysema, and was attributed by me to a failing heart. Suspecting cor pulmonale as the cause, I took an E.C.G., and was somewhat surprised to find that it showed the classical changes of a recent posterior cardiac infarct. On inquiry about discomfort or pain in the chest, he then described the pain typical of ischaemic heart disease, which he had noticed during the last month or so. He had not mentioned it previously, as he thought it was tightness due to his bronchitis and his dyspnoea.

If we wish to look out for the atypical clinical pictures and for the prodromata of myocardial infarction, is there any guide to help us to recognize who are susceptible subjects? There are several classes of persons who are unduly vulnerable. They can be classified into three groups: (1) Those men over the age of 45 who have a family history of coronary disease or hypertension or who are found to have abnormal electrocardiograms. (2) Patients with certain diseases—for example, high blood pressure, diabetes mellitus, angina of effort; those who have already had one attack of cardiac infarction, etc. (3) Those in certain occupations, such as those shown by Ryle and Russell to have a high mortality—for example, physicians and surgeons; proprietors of wholesale businesses, judges, barristers, and solicitors. These are occupations requiring a high degree of mental activity, and also considerable anxiety and stress in their performance.

If, therefore, in these vulnerable subjects we look more carefully for the prodromal group of symptoms, and for variations in the classical clinical picture of coronary disease, we may achieve a greater accuracy in diagnosis and, with the aid of modern anticoagulant and other methods of treatment, help to lower the mortality of this serious disease. Finally, a word of warning must be given about the risk of causing undue alarm to a nervous or otherwise healthy person, and turning him into a cardiac invalid. We have to steer between the Scylla of missed diagnosis on the one hand and the Charybdis of the risk of producing cardiac invalidism or neurosis on the other.

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"If the telephone rings between 11.30 p.m. and 8 a.m. the chances are even that the physician will encounter a parturient woman, a corpse, or a sufferer from biliary-tract disease, respiratory infection, or injury," writes W. W. Forbes in an article in the *New England Journal of Medicine*, July 14, 1955, analysing 200 consecutive night calls in a Massachusetts "family type" practice. In 65 cases the complaints were those attendant on birth or death, and of the remaining 135, 48 were of non-traumatic pain and 23 of injury. 16 were paediatric calls, an unexpectedly low number, and 10 of these had upper respiratory infections. Adequate diagnosis was made in all but 2 cases, which proved to be hysteria presenting as backache, and cholecystitis. The telephoned description of the symptoms proved a reliable clue to diagnosis, though the degree of illness was largely exaggerated. Definitive therapy was carried out in 172 of the 185 living patients: sedatives were given to 40% of the cases, antibiotics to 6%, and minor surgery to 14%. The author reports that 22 of the calls were unnecessary, 21 should have sought earlier or later help, and 3 should have been handled by a dentist.