CORONARY DISEASE

PASSAGES FROM THE HARVEIAN ORATION*

BY

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For many years I have been especially interested in cardiology, and I have been impressed, like many others, by the increasing prevalence of coronary disease. Even during so short a period as the last twenty years this increasing prevalence seems to be beyond question. In the year 1926, 64,465 persons died in this country of all forms of heart disease. Ten years later this number was almost doubled—126,584, to be exact. The figures for coronary disease are even more startling—1,880 died in 1926, 14,095 in 1936, and 19,496 in 1939. The crude death rate from all causes per 1,000 persons living fell from 22 in the decade 1851–60 to 12 in 1930, and has subsequently remained almost stationary at about that figure. The similar crude death rate from heart disease, and especially from coronary disease, has risen in a spectacular fashion during this period, and particularly during the last twenty years. In the case of coronary disease the figures increase rapidly year by year—48 per million living in 1926, 148 in 1930, 473 in 1939.

Part of this rapidly increasing death rate from coronary disease is no doubt attributable to the increasing age of the population. In 1900 there were 1,750,000 persons over 65 years of age in Great Britain; in 1937 there were over 3,750,000. It is true that the standardized death rate, corrected for ageing, for policy-holders of the Metropolitan Life Insurance Company of New York shows a 70% decline for diseases of heart, arteries, and kidneys in the years 1940–5, as compared with 1911–15. But this astonishing decline in mortality is for ages 1 to 74. When the figures for the different age groups are examined it is clear that the improved mortality affects chiefly persons up to the age of 25, and is no doubt attributable, in part at least, to more efficient treatment of the acute infections which are largely responsible for cardiovascular and renal deaths in this lower age group. Between the ages 35 and 64 the standardized mortality among men shows little or no decline in the past two decades, and there is in fact an increased mortality now as compared with the level reached in the early nineteen-twenties.

The crude death rates in America, without correction for increasing age of population, have increased as they have done in this country: thirty-five years ago cardiovascular diseases accounted for less than one-quarter of all deaths; now they account for nearly a half.

The Increase in Coronary Mortality

Part of this mounting coronary mortality has been ascribed by some to increasing accuracy of certification. But I cannot believe that this can play a very important part. The position here is very different from that in bronchial carcinoma, for example, where accurate diagnosis is largely dependent on refinements of investigation such as are afforded by bronchoscopy and radiography. Angina pectoris is one of the easiest of all diseases to recognize. Its clinical features have been well known to every doctor since Heberden recounted them before this College in 1768. In most cases electrocardiographic and radiographic investigations are superfluous diagnostic aids.

Certainly the clinical recognition of coronary thrombosis has till recently been hidden from us. Though first well described clinically by Herrick in 1912, its diagnosis did not become widespread in America till about 1920. Curiously enough, it was not until 1925 that McNee brought to the notice of physicians in this country the clinical picture of coronary thrombosis as first described by the American cardiologists, and the rapid increase in the certification of deaths from coronary thrombosis since that date must be partly attributable to this. Even so, I have the impression that coronary thrombosis is far more prevalent than it was. Looking through my notes of patients seen twenty or thirty years ago, I come across occasional cases where I failed to recognize the coronary thrombosis which now, on paper, is the obvious diagnosis. But such cases are

surprisingly infrequent. It is interesting to read Mackenzie's notes of Case 112, one of the 160 case records in his book on angina pectoris (1923). He describes this as "one of the most puzzling cases I have met." It is now evident to us that this patient suffered from at least two attacks of coronary infarction, the second associated with pericardial friction, and that six months later the consequent myocardial degeneration brought on three attacks of acute pulmonary oedema, the last fatal.

It is odd, too, that coronary thrombosis figures so infrequently in the post-mortem reports of thirty years ago, despite the fact that the very astute morbid anatomists of those days were fully alive to the existence of this condition.

Consider, too, the clinical experience of great physicians of the past. In his book on angina pectoris James Mackenzie states that "380 patients consulted me for angina pectoris." Osler in his *Lumleian Lectures* (1910) says: "It is a disease for seniors to discuss, since juniors see it but rarely; indeed, I had reached the Fellowship before I saw a case in hospital or in private practice. During ten years I did not see a case at the Montreal General Hospital and only one case at the University Hospital, Philadelphia. . . . A consultant in active practice may see 10, 15, or more cases in the course of a year, and this is about the figure reached in this country by a consultant with recognized cardiovascular leanings." He goes on to say that he has now seen 268 cases, which included 42 "of the mild neurotic or pseudo form." Contrast these figures with those of the modern cardiologist, who counts his coronary patients by thousands rather than by hundreds, and remember that there was but one James Mackenzie, and one William Osler, whereas the modern cardiologist's name is legion! During the ten years 1898 to 1908 Sir Richard Douglas Powell saw 96 cases of angina, 26 of which he classified as vasomotor angina. Surely Osler, Mackenzie, and Douglas Powell were at least as competent to diagnose angina pectoris as are physicians of this generation!

Increasing Prevalence of Coronary Disease

What is the explanation of the increasing prevalence of coronary disease? In an attempt—and I confess at once a vain one—to find some answer to this question, I have analysed the notes of 1,000 cases of coronary disease, including both coronary occlusion and angina pectoris, seen in consulting practice. I have notes of approximately another 1,000 cases which I have not analysed. I was careful to include only those cases where I was reasonably certain that coronary disease was present. And here may I put in a plea for the abandonment of such terms as angina minor, angina innocens, and, worst of all, pseudo-angina? Either the patient has angina or he has not. If he has, we believe that some portion of his myocardium is ischaemic, usually as a result of coronary atherosclerosis, with or without a coronary thrombosis or a subintimal haematoma. Syphilis is a rare cause of true anginal pain, and embolism a rarer cause still. A severe anaemia may play a part, probably in association with some degree of coronary atherosclerosis, for I have never seen a severe anaemia cause angina in a young subject, though this happens quite commonly in the more elderly. Alastair Hunter, however, has described 12 cases of anaemic angina, of whom ten were women and five were aged 40 or less, the youngest being 31, which certainly suggests that anaemia alone may cause anginal pain.

Anginal pain is sometimes a symptom of rheumatic heart disease, but I have not included such cases in my series because in my experience they do not conform to the clinical picture of the atherosclerotic type, though we know that rheumatic infection may produce somewhat similar coronary changes. I have never seen a coronary occlusion complicate rheumatic heart disease, nor do I feel that anginal pain in a young rheumatic subject has the same serious significance as in the atherosclerotic patient.

We can conceive of the possibility of spasm of a healthy coronary artery producing a localized myocardial ischaemia with consequent coronary pain; but we have no proof that this does in fact ever happen, though we may suspect that an unstable vasomotor control may play a part in the clinical picture of the patient, familiar to us all, who suffers, perhaps for years, from anginal paroxysms of great severity provoked by trivial physical effort, and especially by emotion. Physical

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examination may be surprisingly negative, and consequently these patients are often regarded as cardiac neuropaths till at last the diagnosis of organic coronary disease becomes only too clear, perhaps as a result of the sudden and unexpected death of the patient.

Some years ago I used to diagnose "vasomotor angina" not infrequently in patients who complained of anginal pain of typical distribution, this pain being provoked by effort, but especially by emotion, without physical signs of organic cardiovascular disease and with a normal electrocardiogram. Sometimes there was evidence of vasomotor instability, such as easy flushing, or Raynaud-like phenomena, or a history of migraine. But increasing experience has convinced me that sooner or later these patients present undoubted evidence of organic coronary disease. If the same amount of effort constantly provokes substernal pain or even discomfort, however slight, and if this discomfort disappears promptly with rest, I think we may assume with confidence some degree of coronary obstruction, however negative the findings may be.

As for that large heterogeneous group of so-called "false angina," we can only speculate as to the explanation of their pain, feeling assured that it is not of coronary origin. Many of them are suffering from a cardiac anxiety state. There is an interesting, and sometimes a diagnostically difficult, group of patients, usually women, who suffer from severe paroxysms of precordial, usually not sternal, pain, which may radiate into the arms, back, or jaws. These paroxysms may be provoked by emotion, or there may be no obvious exciting cause. They come after rather than during effort, and they are usually widely spaced, with periods of robust health without limitation of physical effort between them. The subjects of these attacks, though sometimes temperamental, are often quite stable psychologically. Their symptoms are very real and severe, and may indeed be quite alarming. Possibly these paroxysms may be due to spasm of the oesophagus or the cardiac sphincter. X-ray confirmation of this is obviously difficult to obtain, though I understand that William Evans has made some interesting kymographic observations on this class of case. Diagnosis is made more difficult here by the fact that nitroglycerin gives relief; but perhaps it does so by relaxing gastric or oesophageal and not coronary spasm.

I submit that in the differential diagnosis between true angina and these non-coronary pains careful history-taking is even more important than physical, including instrumental, examination, and that the characteristic and constant relationship between anginal pain and effort is fundamental.

Personal Statistics

Turning now to my own statistics, out of 1,000 cases 779 were males and 221 females, giving a female/male ratio of 1:3.5, which seems to be about the usual ratio found in the literature, though in a recent report from the Mayo Clinic on 3,440 anginal patients the female/male ratio was 1:4.3. This far heavier incidence of angina in males than in females has never, so far as I know, received a satisfactory explanation. In the past no doubt women led a more sheltered life. But certainly to-day no one would contend that men work four times as hard as women; in fact, some might argue that the reverse is true. I have not been able to satisfy myself that the incidence of angina in women has increased of recent years as compared with that in males. If smoking plays an important part in the causation of coronary disease, which I doubt, we should certainly expect a more equal sex incidence during the next ten years or so.

Nor is there any satisfactory explanation of the unquestionably heavier incidence of coronary disease in the non-hospital as opposed to the hospital population.

As to age incidence, my figures are much the same as those of the Mayo Clinic:

	Under 30	30-40	40-50	50-60	60-70	70-80	80 +
Females ..	0	1.3%	11.7%	29%	39%	15%	4%
Males ..	0.25%	3.2%	14.6%	33.9%	36%	11.1%	1%

Approximately 70% of all these patients were aged between 50 and 70 at the onset: 58% of women and 48% of men were

over 60 at onset, which confirms the general impression that coronary disease tends to become manifest at a later age in women than in men. In 26 males the age at onset was under 40, in 2 under 30, the youngest being 26. There were only 3 women under 40 and none under 30.

It has become evident that coronary disease in young subjects is not so rare as used to be thought. During the recent war French and Dock have reported 80 cases of coronary disease in American soldiers aged 20 to 36, and Newman 50 cases of coronary occlusion occurring in Service men and women in this country aged 35 or less: 22 of Newman's patients were under 30, the youngest aged 20. At necropsy atheromatous changes were found, in several instances accompanied by extensive calcification. Stolkind reported four personal cases of angina in children, and collected a further 25 cases from the literature. Many of these cases occurred in rheumatic children, and in some the evidence of angina was not very convincing.

Aetiological Factors

Family history plays a notorious part in the aetiology of cardiovascular disease, and it did so in almost exactly half my cases. But this leaves another 50% of patients whose coronary disease cannot be attributed to inheritance.

Stress, mental or physical, is often thought to be responsible for early cardiovascular death, and coronary disease has been brought into the ever-increasing ambit of psychosomatic disease. But do people really work harder or live more strenuous lives than their grandfathers did? I sometimes doubt it. Certainly we eat and drink much less than they did. I have looked carefully through the histories of my patients, and in only 20% of them do I find evidence of subjection to outstanding stresses. Many of them in fact seem to have lived remarkably placid and sheltered lives. Dr. Paul White of Boston, on a recent visit to this country, told us that in the first edition of his book *Diseases of the Heart* a sentence emphasizing the relationship between angina and stress was in italics, in the second edition in ordinary print, and in the third deleted! Nor am I familiar with the "coronary disease personality," as described, at some length, by Arlow.

Tobacco has long been thought to be a factor in the causation of arterial spasm, and there seems to be convincing experimental evidence of this. Numerous workers have demonstrated that the smoking of two cigarettes usually lowers the peripheral skin temperature, diminishes the peripheral blood flow, and raises the systolic, and still more the diastolic, blood pressure. It is said that these changes may occur not only during the smoking of the cigarettes but sometimes for as long as 30 minutes subsequently. This is depressing information to the smoker, but he will be encouraged to hear from Goetz that very similar results are obtained if the subject is alarmed, or asked to do a difficult sum, or even to take a series of deep breaths. Goetz concludes that the driving of a car in traffic would produce more adverse circulatory effects than the smoking of several cigarettes in an armchair at the club!

I always advise sufferers from intermittent claudication to stop smoking, usually without any amelioration of their symptoms. But very occasionally the results are dramatic, and I have seen relapse occur if smoking is resumed. So far as so-called "tobacco angina" is concerned, I have never encountered such a condition, and certainly I have never seen angina cured by stopping smoking. Statistically 17.6% of my coronary patients were non-smokers, 42.6% smoked moderately—i.e., not more than 20 cigarettes a day—39.8% were heavy smokers. As a control I investigated the smoking habits of a small series of non-cardiac cases, and found much the same figures.

Coronary disease persisted for more than twenty years in 11 of my patients, for more than thirty years in 2 of them. The record duration was fifty-two years, in the case of a lady who had her first attack of angina at the age of 30; she was leading quite a busy life at the age of 80, though still liable to angina whenever she walked. She died suddenly at the age of 82.

It has long been known that quite extensive coronary disease is compatible with an active life, and need not necessarily be associated with angina. In fact, this used to be put forward as an argument against the view that angina is due to coronary ischaemia. Coronary occlusion often antedates angina. It did so in 225—i.e., 22.5%—of my cases. Yet before coronary

occlusion can occur there must almost always be coronary disease. Moreover, a remarkably complete functional recovery is possible after a coronary occlusion. One of my patients played vigorous games after a coronary occlusion at the age of 39. He had a second attack at the age of 48, and, against advice, was playing tennis regularly two years later, without any angina. Now at the age of 58 he is at work, plays golf, and mows his lawn without cardiac symptoms.

It is quite common for coronary disease to be entirely latent till sudden death occurs. Prof. Hume of Newcastle tells me that since 1911 he has performed or attended post-mortem examinations on 160 miners who had died suddenly and unexpectedly in the pit or in close proximity to it. The cause of death in each instance was coronary atheroma, and the majority of the men had been working regularly, without complaint, up to the moment of their fatal collapse. Only 40 had premonitory symptoms. In one case there was a clear history of an attack of coronary thrombosis two years previously, after which he had resumed his normal work in the mine and continued it till his sudden death. In approximately 50% of the 160 cases there were old fibrotic scars in the heart muscle.

The explanation of coronary disease without symptoms is presumably that a wonderfully efficient collateral circulation may be formed if arterial obstruction develops sufficiently slowly. As Lowe and Wartman point out, "complete obstruction may, gradually produced, effect no disturbance whatever in the blood supply to the tissue. On the other hand, should the parent vessel supplying the anastomotic circulation become suddenly blocked, the area deprived of blood supply will be much greater than that following blockage of a similar vessel in a normal circulation." Hence, presumably, the sudden fatal attacks in Hume's coal-miners with previously symptomless fibrotic hearts. In this way, too, we find an explanation for the fact that, on the whole, angina in those over 70 runs a more benign course than it does in those under 60.

Relation between Hypertension and Coronary Disease

Investigating this relationship, I classified my cases as having a normal blood pressure where the readings were below 160/100, moderate hypertension those above these figures but below 200/120, gross hypertension where these last figures were exceeded. Throughout the entire series, in 44.6% the pressure was normal, in 33.7% moderately increased, and in 21.7% grossly increased. Excluding those cases in which an existing or recent coronary occlusion was thought to be responsible for a low blood pressure, the figures were: normal tension 30.6%, moderate hypertension 42.3%, gross hypertension 27.1%. So that nearly 70% of my anginal patients without coincident or recent coronary occlusion were hypertensives. These findings surprised me, for I had not realized that the proportion of hypertensives was so high. In a recent paper Fisher and Zukerman say that in the literature hypertension antedating coronary occlusion has varied between 33 and 73%. Of their own 108 cases of coronary occlusion, hypertension antedated the occlusion in 65% of the women and 39% of the men. They point out that though negroes are more prone to hypertension than whites, they show a significantly lower incidence of coronary disease. Nevertheless, one cannot help suspecting that there may be some aetiological factor in common between hypertension and coronary disease. But, unhappily, in spite of all the intensive investigation of hypertension during the last decade, fruitful though it has been, we are still abysmally ignorant of its aetiology: in the words of Harvey, "All we know is infinitely less than all that still remains unknown."

The London County Council allows the staff of its public health and social welfare departments to have free medical treatment at its general hospitals, but not at its mental hospitals. The reason for this restriction is the long-term nature of institutional care associated with mental illness. It is considered, however, that this does not apply to many types of nervous disorder which are in particular dealt with at the Maudsley Hospital, and therefore free treatment is now to be provided there, subject to review in individual cases, as at the general hospitals, when recovery is not effected in twelve months.

DEFICIENCY NEUROPATHIES OBSERVED IN MADRID DURING THE CIVIL WAR (1936-9)*

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Among the 3,116 patients suffering from deficiency diseases studied at the Institute of Nutritional Hygiene in Madrid during the Spanish Civil War we selected 98 cases with serious nervous disorders, as we were greatly impressed with their not showing the slightest signs of any skin symptoms connected with pellagra.

"Painful-feet" Syndrome

The most frequent symptoms in these cases were typical acro-paraesthesias occurring mostly in the toes, but also appearing in many cases in the finger tips (patients complained of "pins and needles"; "as though I had ants under my nails"). Generally, together with these acro-paraesthesias there appeared some much more alarming phenomena—patients complaining of "terrible prickings" and "horrible stabbing pains" in the hands and feet or in other parts of the limbs (calves, thighs, and forearms). Sometimes after the appearance of these new symptoms or coincidentally there arose what, owing to their close resemblance to the causalgia described by Weir Mitchell, Morehouse, and Keen in wounds of the peripheral nerves, we have called *causalgic symptoms*. Some of the more intelligent or self-observing patients began to notice that their feet had become peculiarly sensitive to heat and unable to bear it. As soon as their feet were placed near a stove they began to notice "pains, and a very troublesome feeling of discomfort." They found that when night came, and especially when in bed, their feet, which during the day had mostly been "insensible and cold as ice," began to feel "very hot like fire." They got to feel as though their feet were on hot coals, and to experience an atrocious sensation of burning which obliged them to push their feet out of the bed and let the cool air of the room get to them, to walk barefoot on the floor, or to wrap their feet in cloths wrung out of cold water. At the height of their illness the patients presented a special sensitiveness of the skin of the affected parts, so that in addition they could not bear the slightest touch on them. But patients also complained of an acute sensation of cold in the extremities often alternating with these causalgic sensations ("my feet and legs are very cold," "my feet are like ice"). Often this sensation of cold became painful, and they spoke of "cold pains inside the feet." Some described the succession of these phenomena very graphically ("I feel as you do when you put your hands into the snow; first I feel very cold about the feet, and then they get warmer and warmer, until I can't bear the heat of them any more, and they burn me").

Other Symptoms

These signs of "painful feet" were predominant, but any or all of the following, discussed in greater detail by Peraita and Grande (1941), were observed in this series: adynamy, depression, lacrimation, insomnia, forgetfulness, reduced acuity of special senses, perniat erythema, hair and nail loss, girdle sensations, amenorrhoea, impotence, polyuria, changes in mucosae and in the motor functions of the gastro-intestinal tract, micturition, and sweat regulation. It was interesting to contrast the rarity of peripheral motor defects and cardiac and skin lesions with the frequency of both cutaneous and proprioceptive sensory changes. Little classical pellagra was observed but no true beriberi, and while neither purified vitamin B nor nicotinic acid was effectively curative of the nervous lesions success was obtained with 90 g. dry yeast daily by mouth.

REFERENCE

Peraita, M., and Grande, F. (1941). *Avitaminosis y Sistema Nervioso*, Servet, Madrid.

* Abridged for publication.