James Mackenzie and coronary heart disease

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SUMMARY. Sir James Mackenzie's writings, especially his *Diseases of the Heart,* suggest that ischaemic heart disease, including myocardial infarction, was common in England at the beginning of the twentieth century.

Introduction

THE immediate stimulus to writing this paper was Yellowlees' James Mackenzie Lecture, in which he states that: "The failure of Mackenzie and his contemporaries to recognize acute infarction was simply because it was not there" (Yellowlees, 1979a). This led to a brief exchange of letters in which I maintained that a study of Mackenzie's work showed that myocardial infarction was common in the 1890's and early 1900s (McCormick, 1979 and Yellowlees, 1979b). This paper attempts to prove my thesis.

Mackenzie's *Diseases of the Heart*

In 1914 Henry Frowde and Hodder and Stoughton published the third edition of James Mackenzie's *Diseases of the Heart.* This edition contains many illustrative cases, as Mackenzie says, "to give practical proof of the views expressed in the text". There are 92 of these cases and they are so detailed and so well written that in many instances we may have little difficulty in making a diagnosis.

Forty-two of these cases bear the diagnosis angina pectoris. Mackenzie used this term to describe the characteristic pain of myocardial ischaemia and did not distinguish between angina of effort, which he certainly recognized, and the angina of infarction, which he did not fully understand.

Some of the characteristics of the 42 cases are outlined in Table 1. Eight are not acceptable as ischaemic heart disease. Case one is a beautifully described effort syndrome. Case five is a case of pericarditis with pneumonia. Cases 37 to 42, grouped together by Mackenzie, all had syphilitic aortitis with angina.

This leaves 34 cases which are acceptable as ischaemic heart disease. Eight of these were women. This gives a male:female ratio of just under 3:1. The average age of the women was 59 as compared with an average age of 53·5 for the men.

Of the 34 cases, 26 were seen by Mackenzie in general practice; three were seen after he became a cardiologist; in the remaining five cases information about when he saw them is not available. For comparison, we can note that he saw four of his six cases of syphilitic aortitis as a cardiologist.

Nineteen of the 34 died of their disease, six of them suddenly. Twenty-two are reasonably likely to have infarcted. One of the most remarkable features of this series is that in some instances Mackenzie was able to remove the heart. The hearts were then sent to London to be examined by a pathologist, usually Sir Arthur Keith. Nine postmortem reports are recorded.

Selected case histories

It would clearly be inappropriate to reproduce in full all the relevant case histories. Anyone who is interested in the subject must refer to Mackenzie's work. I have included two full histories, one with and one without a postmortem report.

I have chosen case 25 because the postmortem report concentrates on embolic phenomena and makes little reference to the coronary circulation. It is difficult to be sure that this patient had an infarct and I have indicated this in Table 1, but the history and postmortem are consistent with infarction, deep vein thrombosis and multiple embolism.

I have chosen case eight as an example of a history without postmortem findings, yet which still allows a confident diagnosis.

Case 25: angina pectoris—postmortem report

"Male. Aged 52. He consulted me on 11 March 1903, for a pain in his chest and arms which had suddenly seized him an hour before. He was a foreman engineer and had led a temperate healthy life. For some months before his present illness he had been feeling weak and easily tired on exertion, but he continued his very active life in spite of that. He had been at his work for an hour when he was seized with the pain, which was at first of great severity. It began over the lower part of the sternum, struck up into both arms and his fingers tingled. I saw him an hour later. The pain abated but

Table 1. Characteristics of the 42 cases reported in Mackenzie's *Diseases of the Heart.*

Case	Sex	Age at onset	Seen in general practice	Ischaemic heart disease	Myocardial infarction	Died (S = suddenly)	Postmortem carried out
1*	M	18	+	−	−	−	−
2	M	42	+	+	−	−	−
3	M	47	+	+	+	−	−
4	M	41	+	+	+	−	−
5**	M	23	+	−	−	+	+
6	F	46	+	+	−	−	−
7***	F	48	+	(+)	−	−	−
8	M	47	+	+	+	−	−
9	M	49	+	+	(+)	−	−
10	M	59	+	+	+	−	−
11	F	54	+	+	(+)	−	−
12	F	55	+	+	+	−	−
13	M	58	−	+	+	−	−
14	M	55	+	+	−	−	−
15	M	63	+	+	−	−	−
16	M	66	−	+	(+)	−	−
17	F	74	+	+	+	+	+
18	F	62	+	(+)	(+)	+S	
19	M	60	?	+	−	−	−
20	M	67	?	+	−	+	+
21	M	62	+	+	−	+	−
22	M	54	+	+	−	+	+
23	M	46	+	+	−	(+)	−
24	M	43	+	+	+	+	+
25	M	52	+	+	(+)	+	+
26	M	51	−	+	+	+S	−
27	M	58	?	+	−	+	−
28	M	?	+	+	+	+	+
29	M	52	+	+	−	+	+
30	M	48	+	+	+	+S	−
31	F	60	?	+	+	+	+
32	M	65	+	+	(+)	+S	−
33	M	43	+	+	+	+S	−
34	F	68	+	+	+	+	−
35	M	57	+	+	+	+	+
36	M	60	?	+	+	+S	−
37	M	35	−	Syph	−	−	−
38	F	43	−	Syph	−	−	−
39	F	41	+	Syph	−	−	−
40	M	35	−	Syph	−	+	+
41	F	42	+	Syph	−	+	+
42	M	35	−	Syph	−	+	+
Total for ischaemic heart disease	M:26 F: 8		26	34	22	19	9

(+) Denotes uncertainty over diagnosis
*Effort syndrome
**Pericarditis pneumonia
***Paroxysmal nocturnal dyspnoea

was still present. He was a short, powerfully built man, and his face was greyish white in colour. The pulse was full and regular, 64 beats per minute. The heart was normal in size and the sounds were low and soft. At the base and mid-sternum there was a systolic murmur.

"I first gave him an inhalation of nitrite of amyl, which increased the rate of the heart and softened the pulse, but gave him no relief. Then he had an injection of morphia, and afterwards the pain gradually passed off. After a week's rest he got about and gradually resumed his work. He had to avoid any strenuous effort, as he became at times very short of breath and the pain would tend to return. He remained fairly well until 17 January 1905, when he had another attack while sitting at tea in the evening after his day's work. He was feeling quite well, when a curious tingling sensation began in his chest, a vague sort of painful feeling in his arm. This passed off, and 10 minutes later the pain started with great severity across the middle of the chest, passed into the left chest and up into the left side of the

head and neck, and into the left arm. While the pain continued he broke into a profuse perspiration. Whiskey and hot water gave a little ease and the pain suddenly subsided after half an hour. He was very weak after the attack, but he felt better on the twenty-second. On the twenty-third he was seized with a slight attack when walking out. That evening he had a severe attack, which began about seven o'clock and persisted with varying severity till I saw him at half-past nine. His face was grey and pinched, and beads of perspiration stood out on it. The pulse was rapid and hard. I gave him amyl of nitrite to inhale but the relief was slight and transient. I tried chloroform, but he could not bear the sense of suffocation, so I gave him an injection of half a grain of morphia from which he got relief after a few minutes. From this time the attacks of pain were so readily induced that he was obliged to keep in bed and obtain relief by the use of chloral and morphia. Gradually he became weaker and was unable to rest in bed, and had to sit up and go to sleep with his head resting on a table. Swelling of the legs and Cheyne-Stokes respiration set in. Towards the end of March he began to expectorate small clots of blood. The pulse had been persistently increased in rate, up to 120 per minute, until he died on 1 June 1905 at the age of 54. The heart was large and full of blood, the lungs were congested and had numerous infarcts. There were also infarcts in the kidneys. The veins and venules of the heart were distended. The arteries of the heart and aorta showed a slight thickening of the intima, but the muscle-coat was hypertrophied. There was a remarkable thickening of the base of the mitral cusp, but no stenosis. The tricuspid orifice was reopened. The right ventricle was hypertrophied and dilated, the left dilated and atrophied. There was a considerable degree of degeneration of the muscle fibres and a slight degree of fibrosis."

Case 8: angina pectoris

"Male. Born 1857. The patient had always enjoyed good health, but noted that in 1904 to 1905 he could not go uphill quickly without a sensation of tightness being felt across the upper part of the chest. This, however, was slight, and gave him no concern. On 25 November 1905, he visited some houses that were being built (he was a master builder); the day being cold, and feeling somewhat chilly, he seized a spade and for an hour dug up earth and threw it into a cart. He did this with a good deal of energy. He then examined a few partially built houses, running up and down a great many steps. On his way home he became conscious of pain in the chest, and, as it continued to increase in severity, he called on me. I examined him carefully, and found a slight dilatation of the heart with an impure first sound. The blood pressure was 130 mm Hg. On his way home the pain increased in severity and after he reached home it became very violent. My colleague saw him and prescribed opium, which relieved him. When I saw him next morning, he gave a graphic account of his sufferings. He said: "In the tram coming home the pain got worse, and after getting home it became so severe that I felt that I was going to die. The pain spread from my chest down my left arm to my little finger. You asked me when I saw you yesterday, if I felt any gripping sensation, and I did not know what you meant, but by George! I know now. When the pain was at its worst I felt my chest suddenly seized as in a vice, and I rolled on the floor in agony. The pain and the gripping eased off for a time and then came again. This continued till I got the opium. This morning I awoke all right, but at 10.30 that gripping sensation came on and held me tight for 10 minutes. I dared not move for fear the awful pain should come on, and I felt every minute it was about to come, and I was in such terror of it that the sweat poured off me."

"For some weeks slight attacks continued to occur, but after treatment, mainly by rest, they gradually subsided, and in three weeks he was able to go about with comfort, except when going up a hill, when he felt a tight sensation coming into the chest and a curious feeling that the pain would come on if he did not stop. I kept the patient under observation for two years and repeatedly examined him, but, save for an occasional extrasystole, I could never detect anything abnormal. His blood pressure was always about 130 mm Hg. I have seen him at rare intervals, and in 1913 he reports that he keeps in fair health and has never had any return of the violent pain."

Case 17: angina pectoris due to senile changes — postmortem report

"Dr Keith examined the heart. There was great dilatation of the auricles and compression of the ventricle. The ventricular muscle was very friable. The orifices and valves were normal. The coronary arteries showed much atheroma with calcareous patches, yet not so great as to severely cripple the circulation in the heart. The right coronary artery was more affected than the left."

Case 20: angina pectoris due to senile changes — postmortem report

"Dr R. T. Williamson examined the heart and reported that there was well-marked calcification along the margin of the aortic valves. There were a few calcified patches of atheroma in the aorta immediately above each aortic cusp and around the orifices of the coronary arteries. Both coronary arteries were very atheromatous and presented numerous calcareous patches in their walls. The right coronary artery for about two inches was almost completely calcified. The heart muscle appeared but little affected."

Case 22: angina pectoris, great exhaustion, death — postmortem report

"The heart was removed and sent to Dr Keith, who reported that the left ventricle had been hypertrophied

but is now dilated, especially the apical two thirds. There are no areas of fibrosis, but the muscle fibres are small and very brown. The aorta is dilated. There is a considerable degree of endarteritis of the coronary artery, leading to a reduction of the lumen, at parts to half the normal. The aorta is also affected, especially at the origin of the coronary arteries, which instead of measuring 3-4 mm in diameter measures only 1·5 mm. The mitral valve is slightly thickened and shortened, probably from the same affection as the arteries. The mitral orifice is slightly dilated, and also the aortic orifice. The septum is stretched and shows perforation. The sinoauricular node is large and contains much fibrous tissue. Taenia terminalis hypertrophied."

Case 24: angina pectoris, Cheyne-Stokes respiration, pulsus alternans—postmortem report

"Professor Keith's report on the heart stated that it was similar to Case 35, except that the ventricle was hypertrophied and the arteries more sclerosed. The whole heart was slightly increased in size. The valves were quite healthy, except that the mitral was slightly thickened. There was intense endarteritis, especially of the left coronary artery, the lumen of which was much diminished. The anterior interventricular artery was occluded. The apical half of the left ventricular muscle was much fibrosed, the subendocardial and the subpericardial fibres being least affected. There was some fibrosis of the taenia terminalis."

Case 28: angina pectoris, cardiac aneurysm, rupture of the heart—sudden death

"On the postmortem examination the heart was found to have ruptured, the pericardial sac being full of blood. There was a small aneurysm, the size of a marble, in the wall of the left ventricle, where the ventricular cavity was separated from the pericardial sac by a thin wall consisting only of pericardium and endocardium. In this thin wall there was a narrow slit. The coronary artery was very atheromatous. The external anterior thoracic nerve was found to be lying under the place (over the second rib) that had been so tender to pressure during life."

Case 29: angina pectoris—postmortem report

"At the postmortem examination the heart was found very flabby, and the walls of both ventricles were soft and friable. There was well marked atheroma of the coronary arteries. In many places the arteries and their branches were calcified. Microscopic examination of the cardiac muscle (left ventricle) revealed fatty degeneration."

Case 31: angina pectoris, with severe pain in the left arm—postmortem report

"The patient died . . . . . from heart failure and Dr R. T. Williamson examined the heart for me and found marked atheroma and calcification of the coronary arteries and extensive fibrous changes in the muscle of the left ventricle."

Case 35: angina pectoris, with Cheyne-Stokes breathing, pulsus alternans—postmortem report

"Musculature-hypertrophied, but the apical half of the ventricle is fibrosed and dilated; large premortem clot adherent to the anterior wall of the left ventricle. Thickness of wall at base, 18-22 mm; over the fibrosed area, 6-8 mm. The musculature at the mouth of the superior vena cava is hypertrophied. Taenia terminalis is hypertrophied, and under the microscope shows many fibres atrophied and fibrosed.

"Valves and orifices—mitral cusps thickened; tricuspid, pulmonary, and aortic healthy. Auriculoventricular orifices smaller than normal, due to tonus or contraction of the musculature of the base.

"Arteries—patches of atheroma in aorta, especially at orifices of coronary arteries. Intense endarteritis of left coronary artery, diameter 6 mm, lumen 2·5 mm; the interior is especially thickened. The right coronary artery is not so much affected. All the arteries of the heart above 1·5 mm in diameter are affected if they lie outside the musculature of the heart; if surrounded and supported by the musculature they are less affected. The anterior interventricular artery was most affected, while the artery to the auriculoventricular bundle from the right coronary was more like a needle-prick. Sinoauricular node, less musculature (more fibrosed) than in health, still not marked. The auriculoventricular bundle is normal in size, and its fibres and cells are normal."

These relatively few case histories do not represent the totality of Mackenzie's experience; they simply give us an idea of the criteria he used in making the diagnosis of angina. We can better judge the extent of his experience from his book *Angina Pectoris* (Mackenzie, 1923).

In this book he was able to record the ages at which 284 patients died where the death was "due directly to the condition which caused the angina". (Interestingly the commonest age of death was 61 to 65.) He was able to say that: "On going over my notes I find records of the 380 patients who had consulted me for attacks of angina pectoris. I have no doubt a great many have died whom I have not been able to trace". This suggests a personal experience of at least 380 cases and probably many more.

It is interesting that so many of his illustrative cases of angina derive from general practice. By comparison, his 13 illustrative cases of 'auricular flutter' were all seen as a cardiologist.

Discussion

We have ample evidence that Mackenzie was familiar with ischaemic heart disease and that the disease he saw so commonly as a general practitioner is the same

disease that we see today. The clinical presentation was the same, it was commoner in men, and men developed the disease at a younger age than women. It frequently did, and does, lead to sudden or unexpected death. How can this be reconciled with the failure to recognise myocardial infarction as a common event until comparatively recently?

The major reason is that cardiologists see only those cases which are referred. Hospital experience of a disease does not necessarily reflect its incidence or prevalence in the community. This was beautifully illustrated by Loudon *et al.* (1953) who pointed out that admissions to the Radcliffe Infirmary with the diagnosis myocardial infarction rose threefold between 1949 and 1951. This increase was a response to the idea that anticoagulants provided useful therapy.

It is difficult to understand the reluctance of morbid histologists to relate the narrowing of the coronary arteries to pathophysiology and the morbid changes of infarction. However, as most mortality from this disease occurs outside hospital, very few were in the privileged position of Sir Arthur Keith. The histologists would have examined the hearts of those who died in hospital. Apart from coroners' inquests, they would presumably have had little opportunity to examine postmortem those who died in the community.

The evidence I have adduced from Mackenzie's work must cast some doubt on the wisdom of those who, believing ischaemic heart disease to be a new disease, look exclusively for aetiological factors which are peculiar to the latter part of this century. It may well be that the disease is indeed commoner than it was, but this is a question that can never be satisfactorily answered. Nonetheless, it was also common in the 1890s and early 1900s.

Re-reading Mackenzie is a humbling experience; it should be compulsory.

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