Origin of concept of ischaemic heart disease

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Geographic designations sometimes have been given to diseases such as the great pox, febrile conditions, diarrhoeas, anaemias, and itches, often in a pejorative sense by those in other nations, often unjustly. A just appellation would be "British disease" for ischaemic heart disease, because of the origin of the concept.

William Heberden was a prominent London physician when he described angina pectoris at a meeting of the College of Physicians in 1768. This classic description left little to be added from the standpoint of symptoms. Sudden death was mentioned as a complication. Heberden's practice was not hospital-based, so he had limited opportunity for postmortem examination of patients who had experienced the condition, or perhaps he seldom was consulted during the terminal illness. His paper on angina pectoris was published in 1772.¹ A popular magazine for the scholarly, *Critical Review*, published a complete account of Heberden's contribution in its March 1772 issue.² An interested reader recognised his symptoms as those described and noted that Heberden did not know the cause of the syndrome. The next month he wrote an appreciative letter to Dr Heberden in which he stated he had "never troubled myself much about the cause of it, but attributed it to an obstruction of the circulation or a species of rheumatism".³ He followed this remarkable speculation by a request that Heberden arrange a postmortem examination on his body, "if it please God to take me away suddenly". The letter was signed "Unknown" and less than three weeks later, early in May, Heberden was notified that the writer had died suddenly. He arranged for John Hunter, the great anatomist, pathologist, and surgeon, to do the examination. At the time, Edward Jenner was nearing the end of a two year term as a resident in Hunter's home and student of the master, and he attended the postmortem examination.⁴ Hunter found nothing to account for angina pectoris. In November of the same year Heberden reported to the College of Physicians that, "Since it was not due owing to any malconformation, or morbid destruction of parts necessary to life, we need not despair of finding a cure."

The identity of Heberden's "Unknown" corres-

pondent was not disclosed. Keele thought it was Dr John Haygarth.⁵ Recently this suggestion has been revived, and the desire was expressed for more knowledge of Haygarth.⁶ Haygarth was a distinguished physician in Chester, best remembered for his contributions to the knowledge of contagious disease.⁷ In addition, he reported a postmortem examination on a patient for whom he had made a diagnosis of angina pectoris, the paper being read at the College of Physicians in London in 1773, a year after the death of Heberden's correspondent.⁸ Angina pectoris was attributed in this case to a mediastinal abscess. Haygarth died in 1827. Review of obituaries in *Gentleman's Magazine* for deaths early in May 1772 does not reveal the name of any physician, surgeon, or apothecary, so it is likely that the "Unknown" was an inspired layman.⁹ Six possible candidates are listed but no clue is given, and Hunter's case-book is not helpful in this regard. The letter writer's desire to remain "Unknown" is fulfilled.

By a remarkable coincidence necropsy of another patient who had had angina was also done in May 1772.¹⁰ The patient was one of, "12 or 13 persons afflicted in this manner" seen by Dr John Wall of Worcester, a graduate of Oxford University, who was an outstanding physician in his area, an artist, and a founder of what is now the Royal Worcester China Company.¹¹ The number of patients seen by Dr Wall suggests that he may have noted the symptom before Heberden's original description. He carried out the first study of the natural history of angina pectoris, noting that one of his 12 or 13 patients was living, two had been, "carried off by other disorders; all the rest died suddenly". The reported case had been his first opportunity to secure a postmortem examination in a patient with angina, and necropsy showed aortic stenosis. With commendable caution, he stated, "It is possible that this condition of the semilunar valves may not be always the cause of the disease, though it seems not improbable that some malformation of the heart or vessels, immediately proceeding from it, may do so." Wall was the first to ascribe angina to heart disease. He wrote a letter regarding his findings to Heberden, who transmitted the report to the College of Physicians at the same November 1772 meeting at

which he presented his own case. Heberden demonstrated objectivity in arranging the presentation and publication of Wall's letter, even though it did not support his belief.

Another prominent London physician, Dr John Fothergill, first observed angina before 1756, at least 12 years before Heberden's presentation.¹² Fothergill was an Edinburgh graduate, a philanthropic Quaker, a friend of Benjamin Franklin, a botanist, and an apologist for the American colonists.¹³ Medically, he is best remembered for his description of *tic douloureux*. He appears to have suggested the cardiac origin of angina pectoris: "I have very seldom met with this disease, but that it was attended with an irregular and intermitting pulse, but often when the patient was free from pain and at rest." When one of his patients who had angina pectoris died in 1773 or 1774, he asked the prosecutor, "to attend to the condition of the heart". A small white cicatrix, "as big as a sixpence", was found near the apex of the ventricle. In the same paper is an unrelated clear account of the Pickwickian syndrome in two patients, 62 years before Charles Dickens's description of the fat boy, Joe. In 1776 another of his anginal patients died; Fothergill had John Hunter perform the necropsy, which showed mild mitral and aortic valvular disease and severe coronary artery disease.¹⁴ He made no aetiological speculations after the second case.

Still another distinguished physician, Dr Thomas Percival of Leeds, reported a necropsy on a patient who had angina but found nothing to account for the symptom.¹⁵ Percival is best remembered for his monumental work on medical ethics.¹⁶ Commenting on Percival's case, Heberden said, "The disease is neither owing to inflammation nor to any mal-conformation of the parts." In 1814, John Blackall collected a series of anginal patients who had had postmortem examinations.¹⁷ The first of these had died about 1774, and it is evident that this was a collected series, for Blackall was only 3 years old at the time of the first death.¹⁸ The physician in charge had corresponded with Heberden, who replied that early in the course of the condition there was no organic disease, but, "partook of the nature of a spasm". Heberden suggested that there was a, "contraction of the arch of the aorta or the arteries that go to the arm". John Hunter found severe calcific aortic stenosis in at least two patients who had suffered from angina, in addition to Fothergill's patient, but the notes in his case-book are not dated.¹⁹ James Johnstone, a fellow citizen of John Wall in Worcester, described "putrid" myocardium in an anginal patient who had died—apparently an acute myocardial infarction.²⁰ He first suggested functional impairment of the heart in this condition. "The symptoms of angina pectoris . . . plainly arose from, and were symptoms

of defect of the power of the heart," which was, "unfit for its office of carrying on the circulation of the blood." Another Johnstone, Edward of Birmingham, reported anginal pain during paroxysmal tachyarrhythmia in a patient who also had exertional distress.²¹

The stage was set for an original thinker, a 37 year old village practitioner, Edward Jenner of Berkeley, Gloucestershire. Early in 1786, Jenner was treating a Mr Carter for angina pectoris when the patient died.⁴ His famous account in a letter to Parry relates that Jenner thought a bit of plaster had fallen from the crumbling ceiling when he heard a grating sound as he cut into the heart. He was surprised to find that coronary calcification was responsible for the noise. Severe coronary disease with arterial obstruction caused him, "a little to suspect". He recalled John Hunter's dissection of Heberden's patient in 1772 and believed that the coronary arteries had not been examined. Shortly thereafter, Thomas Paytherus, a surgeon of Ross-on-Wye, invited Jenner and a mutual friend, Dr John Heathfield Hickes, to attend the postmortem examination of a patient who had angina.⁴ Jenner wagered that "coronary ossification" would be found but instead a "cartilaginous" obstruction of the coronary lumen was discovered. Paytherus did an endarterectomy, the intima separating, "as easily as a finger from a tight glove".⁴ Now Jenner was so sure that he knew the cause of angina pectoris that he soon wrote of his opinion to Heberden, who was John Hunter's personal physician. Jenner was concerned because his friend and mentor had angina and Jenner did not wish to alarm him. Jenner wrote, "the importance of the coronary arteries and how much the heart must suffer from their not being able duly to perform their functions. . . it is possible that all the symptoms may arise from this one circumstance".²² Surely Jenner realised the ischaemic origin of angina pectoris. Unknown to Jenner, Hunter must have recognised that aortic stenosis could cause angina and perhaps even that coronary artery disease might be responsible. He was aware of the ominous prognosis. If Heberden received Jenner's letter, it evidently made little impression.²³ At a Sunday soirée in London, Jenner subsequently predicted privately that Hunter had coronary artery disease, and this prediction proved to be correct in the 1793 postmortem study.⁴

Jenner's close friend, Dr Caleb Hillier Parry, of Bath, was familiar with Jenner's belief about angina pectoris, and in the spring of 1788, he had a necropsy performed on the body of Rev Mr S, who had had angina for some years.⁴ Severe coronary disease was found, and Parry reported the case to the Fleece (Gloucestershire) Medical Society in July 1778.²⁴ Unfortunately, the manuscript has not survived, but he gathered additional clinical material and added

Jenner's account of his experiences and Paytherus's case report and published them in 1799 in his monumental book on angina pectoris.⁴ Though he recognised that angina could occur in paroxysmal tachycardia and in valvular defects, reduction of blood flow through severely narrowed or occluded coronary arteries was proposed as the usual cause of angina. He not only believed that myocardial ischaemia was responsible for the symptoms, but that impairment of myocardial contractility occurred during attacks, an observation confirmed in recent years. Though he did not recognise the mechanism of action of the Valsalva manoeuvre, he found that it was beneficial symptomatically. He postulated that, "Death may at least ensue from a remedyless degree of irritability of the heart."

Details of the life of Dr Samuel Black are more obscure than those of the other major contributors to the ischaemic theory. He was born in 1764 and graduated in medicine at Edinburgh in 1786; he had been president of the Chemical Society as an undergraduate.²⁵ Black entered practice in Newry, Northern Ireland, probably in 1792, became a licentiate of the King and Queen's College of Physicians of Ireland, and, for a time, was a district health officer.²⁶ He published five scientific papers in addition to his MD thesis and a book on clinicopathological correlations.²⁷ Black died in Newry on 7 July 1832.

Shortly after opening his practice, Dr Black encountered a patient who had angina pectoris; the patient died in March 1793 after a clinical myocardial infarction. Necropsy showed, "a very unusually tender lacerable" heart and severe coronary disease. Black knew nothing of Jenner's and Parry's unpublished observations, but he thought that he had found a cause for angina pectoris. He communicated his findings to Dr Thomas Percival, who arranged a reading of Black's letter to the Medical Society of London in March 1794 and publication of the letter the following year.²⁸ In 1796 a second letter from Black was read to the same society, reporting another patient with similar findings.²⁹ Black came to conclusions remarkably similar to those of Parry. He wrote, "The primary and original cause of the disorder is, perhaps, in every instance, the ossification of the coronaries. . . the diseased state of the heart produces an impeded and weakened action of that organ." He thought the reason coronary involvement in angina pectoris had not been discovered previously was that, "The coronaries are small vessels, and do not lie altogether superficial, but are, in some degree, buried in the substance of the heart." In his book he summarised all of his experiences with angina pectoris and wrote, "I have no conception that this ossification is the only link in the chain of causation; but it is the only one we can see clearly." He thought that the

following groups were perhaps exempt from angina: the poor, the laborious, those who use strong exercise, the foot soldier, and the female sex, in his words. Finally, he believed that, "The application of chemical principles. . . may lead to the knowledge of remedies calculated to correct the diathesis, or perhaps remove the deposit." This remarkable vision, formed when chemistry was in its infancy, has not been fulfilled, but it is still viable. In his book, Black gave full tribute to Jenner and Parry, but there is no doubt that his observations were original.²⁷

The last chapter of the history of the origin of the concept of ischaemic heart disease was written by the brilliant young Glasgow pathologist, Allan Burns. In 1809, when Burns was 28 years old, he published his book, *Observations on some of the most frequent and important diseases of the heart*.³⁰ Though Parry's book was read widely in Britain and on the continent, as well as in America, its conclusions were not accepted generally. Burns endorsed Parry's views fully in his chapter, "On Disease of the Coronary Arteries and on Syncope Anginosa". He agreed with Parry that myocardial contractility is impaired during anginal attacks. Burns pointed out that the "power" of the heart is "augmented" by exercise in the healthy individual, and we, "increase the circulation in every part. . . . If, however, we call into vigorous action, a limb, round which, we have with a moderate degree of tightness applied a ligature, we find that then the member can only support its action for a very short time; for now its supply of energy and its expenditure, do not balance each other. Consequently, it soon, from a deficiency of nervous influence and arterial blood, fails and sinks into a state of quiescence. A heart, the coronary arteries of which are cartilaginous or ossified, is nearly in the same condition". This analogy, together with the observations of Jenner, Parry, and Black, form the basis of the concept of ischaemic origin of the symptoms of coronary artery disease.

William Heberden's description of angina pectoris in 1768 was followed by pathological studies beginning in 1772. Wall reported the first anatomical association with the symptom, and Fothergill and Johnstone made important contributions in case reports. Four young men, Jenner, Parry, Black, and Burns established the ischaemic theory of angina pectoris. This British team, working over a period of 23 years, clarified one of the most important heart problems of civilised man. It was approximately 120 years later that the leaders of the medical profession generally accepted the concept.

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