Review

John Hunter: on heart disease

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In August 1777 John Hunter was preparing for a trip from London to Bath in the hope that he might find some relief from angina pectoris. His brother in law, Everard Home, was to maintain his surgical practice and William Bell, a talented artist-surgeon, was a member of the Hunter household.¹⁻³ Hunter instructed these two assistants to prepare a catalogue of his museum of comparative anatomy and pathology during his absence. This was a formidable task because there were hundreds of specimens, many of which were accompanied by scant or no descriptions. By reference to manuscript notes and labels on jars, Home and Bell were able to identify and catalogue much of the material, but many specimens in the pathological section required Hunter's presence for proper organisation and description. More immediate concerns must have demanded Hunter's attention in November after his prolonged absence, and Home's entry into naval service the next year may have prevented attention being paid to the catalogue, but Hunter did not forget it. In the last year of his life (1793) he was about to turn his attention to this important work, after the planned publication of his classic *A Treatise on Blood, Inflammation and Gun-shot Wounds*.² He did not live to see the book published, nor was the catalogue completed. Hunter's distinguished nephew Dr Matthew Baillie and Home were executors of his estate, the principal asset of which was the museum.³ After much effort they were able to persuade parliament to purchase the collection in 1799. It was presented to the Company of Surgeons, soon to become the Royal College of Surgeons. Unfortunately, parliament did not specify that all relevant notes and manuscripts were to be included in the purchase, and they were retained by Home.⁴ William Clift, a 20 year old who had been a resident assistant for 20 months before

Hunter's death, continued to live in the Hunter household until the time of transfer of the museum and he was named as its curator after the move.⁴ During the years between Hunter's death and the sale of the museum, Clift was in extreme poverty because of Anne Hunter's straitened circumstances, but he used part of what little money he could save to buy paper, so that he could transcribe those of Hunter's notes that most interested him. Much later these notes were useful in the completion of a catalogue.⁵

About 30 years after Hunter's death, Sir Everard Home said that he had burned all of Hunter's manuscripts, notes, and letters in accordance with Hunter's orally expressed wish.⁴ Being a great collector and preserver Hunter must have known that the usefulness of an undescribed collection of specimens would be limited, so it seems likely that it was his intention to destroy the original notes and manuscripts. It took Home 30 years to comply with the alleged instructions. Home stated that he spent a great deal of time compiling a catalogue of the museum, but there is no evidence to support his claim. Later, after a series of bitter exchanges with the board of curators of the Hunterian Museum and the board of trustees of the Royal College of Surgeons of England, Home made two presentations of Hunterian manuscripts. Clift soon transcribed many of the medical notes into a series of five bound volumes, recording some of Hunter's experience in the practice of medicine and surgery as well as descriptions of postmortem examinations.⁶ Unfortunately, most of the latter were limited to his experience before 1783, most of the observations of his last decade having been lost or burned. Hunter said that he had done "thousands" of postmortem dissections, of which the recorded material and the museum specimens can only be a fraction.³ Eventually, with the guidance of Clift's compilation, Stanley and Paget were able to assemble a catalogue of the museum in 1848.⁷ Subsequent editions, the last of which was published in 1966 and 1972, have clarified some of the problems in organisation of the

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specimens.⁸ Fortunately most of the pathological material was not damaged by the bombing of the Hunterian Museum in the second world war, although there were other extensive losses.

An additional handicap is that Hunter's notes on postmortem examinations, unlike those of Morgagni, were not intended for publication.⁹ Most are simply anatomical descriptions, with only occasional inductive reasoning. The general arrangement of the Hunterian Museum specimens probably influenced Matthew Baillie in the organisation of his classic, the first modern textbook of pathology, published in the year of Hunter's death.¹⁰ Keele has reviewed the Hunterian Museum specimens of cardiovascular pathology.¹¹

Because the written records of Hunter's many contributions to biology and medicine are incomplete, a review of his knowledge of a restricted area, that is, diseases of the heart, may give a better indication of the depth of his genius. In Hunter's time relatively simple concepts such as congestive heart failure being a specific type of dropsy, the rheumatic origin of much valvar disease, and coronary disease as a cause of angina pectoris had not been published, and clinical examination of the heart was usually confined to checking the pulse. John Hunter was not a bookish scholar, and he was free to make original observations, uninhibited by what "authorities" had stated. Although Volume III of Alexander's translation of Morgagni's great work on pathology was dedicated to "Dr Hunter," and it has been stated that this was John Hunter, it is obvious that John's brother, William, was the physician honoured in the preface.⁹

Congenital heart disease

Congenital malformations of the heart had been occasionally noted but little reported before 1750. William Hunter described three cases in 1783, one of which was what is now called tetralogy of Fallot; however, the description is not complete.¹² In 1781 a 13 year old cyanotic patient of Richard Pulteney died of dysentery.¹³ Necropsy showed an inter-ventricular septal defect and a pulmonary ring that was "much smaller and more firm than is usual." John Hunter mentioned that he had seen this patient—apparently meaning that he was present at the dissection.⁶ Hunter wrote of the "imperfect construction of the heart" saying that "there is a communication between the right and left side, kept up after birth" and that "cases of this kind frequently occur."⁶ To supplement Pulteney's description, Hunter stated that there was dextroposition of the aorta in addition to pulmonary stenosis and inter-ventricular septal defect. Thus Hunter recognised

the essential features of tetralogy of Fallot. Although he indicated that such lesions were commonly encountered, no other cases are recorded in his preserved papers and there are no examples in the museum. When in 1787 Hunter saw a 16 year old girl with cyanosis who was a patient of Caleb H Parry he predicted a poor outcome; he also expressed his wish to know the findings of a post-mortem examination if the prognosis prove to be accurate.³ It is not known whether she died soon afterwards or outlived Hunter.

The other congenital defects that Hunter described were relatively simple. He mentioned canalis arteriosus (ductus arteriosus) and the foramen ovale "... as much open as in the foetus."² It is likely that some of the latter abnormalities were interatrial septal defects. He also studied the structure of the heart in various animals and said that "the foetus of the class possessing four cavities may be classed with the mixed, having but one auricle, by communication between the two and also one ventricle by means of a union of blood although not in the same way (viz ductus arteriosus). The passages are shut up almost immediately after birth, or at least the canalis arteriosus, which immediately prevents the foramen ovale from producing its former effects; therefore it is not so necessary that it should be shut up in the adult."² There is no doubt that Hunter, the evolutionary theorist, recognised the embryological similarity of the human fetal heart to that of lower forms of animal life. He described "transposition of the viscera" without reference to a specific case. Hunter also recognised bicuspid aortic valves and speculated on the congenital origin of the condition in several patients.⁶ One additional case was that of a 14 year old boy who had congenital aortic stenosis, although Hunter did not state the aetiology. Finally, he had one case of two superior vena cavae.

Valvar heart disease

The museum contains 12 specimens of valvar heart disease, but curiously only one with isolated mitral valve disease. Hunter's first resident student, Edward Jenner, however, reported a case of isolated mitral stenosis at the first meeting of the Fleece Medical Society in 1788.¹⁴ There are also 12 descriptions of valvar disease in volumes III and V of Clift's transcriptions of Hunter's notes. Only two of these definitely refer to museum specimens. The notes in volume I:127 and volume III:80 related to specimen P 286, and the description in III:79 is that of specimen P 287. It is evident that Hunter considered isolated aortic valvar disease in the aging adult as being distinct from mixed valvar lesions. He

thought that with advancing years men especially lose elasticity of the aorta and that in diastole the blood "throws" the aortic leaflets shut and, as a result "the valves become thicker and are often very irregular and bony." The result is that "more blood is allowed to regurgitate into the ventricle, than in a regular circulation."² Only in recent years has isolated aortic stenosis in the aging adult been considered to be non-rheumatic.

Hunter did not speculate on the cause of mixed aortic and mitral valvar lesions. Jenner, who often corresponded with Hunter, related valvar disease to the residual effect of rheumatic fever, and talked on this subject at the Fleece Medical Society in 1789, but because his letters to Hunter have not been preserved it is not known whether he communicated this concept to his mentor.¹⁴⁻¹⁶ Dr David Pitcairn, a friend and one of Hunter's personal physicians, has been credited with proposing the same aetiological hypothesis as Jenner at about the same time, but Pitcairn was not a medical writer. The claim for Pitcairn rests on a footnote in the second edition of Baillie's textbook of pathology.¹⁷ It appears that Baillie was discussing cardiac enlargement rather than valvar disease specifically. It is possible that Pitcairn was more restrictive in his speculation, and he may have mentioned this belief to Hunter, but this is not known.

Pericarditis

Eight of the museum specimens show pericardial disease and four postmortem descriptions are given in Clift's transcriptions. Several cases were probably localised pericardial adhesions, and several were examples of acute pericarditis. One specimen in the museum is the "heart of a man who had died of a fever and violent pain and oppression of his breast. The whole heart is covered with gluten, from inflammation which made the pericardium adhere." A woman had a large bloody pericardial effusion with active disease of the visceral pericardium. Hunter said that "the heart and pericardium looked as if they had been torn by cats."⁶ A third case, a young man, died of a fever and was found to have a bloody pericardial effusion as well as non-sanguineous ascites. A young woman had pericardial effusion associated with tubercles of the lung. The Earl of Bristol, although he had no apparent cardiac symptoms and his death was not cardiac in cause, had a small heart with a diffusely adherent pericardium.

Endocarditis

The only definitely dated cardiac case dissected by Hunter after 1783 is that of a six and a half year old

boy who died in 1793, the year of Hunter's own death. He had palpitation from the age of three years and an apical thrill had been noted. A fever was followed by coma and death. Hunter found the mitral and aortic valves to be "shriveled and thickened" as well as calcified, and the aortic valve was bicuspid. The chordae tendinae "had a number of small bodies like granulations growing on them."⁶ Death was caused by a cerebral haemorrhage. Bacterial endocarditis seems to have been the terminal illness; however, the bacterial origin of some infectious diseases was not recognised in Hunter's day. A museum specimen shows active endocarditis involving the mitral and aortic valves with ruptured chordae, and another specimen shows calcific aortic stenosis with a small active vegetation in one cusp. In another specimen numerous small bodies were found to be adhering to prominent fasciculi but the description does not strongly suggest endocarditis.

Cardiac enlargement

In nine cases in Hunter's casebook an increased heart size was the most impressive finding. In one (a 13 year old girl) other gross findings may have been omitted inadvertently. In two cases there had been irregularity of the heart for several years before death. In one other patient the pericardium was "furred over with some coagulable lymph." This may have represented uraemic pericarditis. Hunter mentioned pallor of the myocardium in one case ("like the flesh of veal"). The remaining four cases occurred in men who had no abnormality described except for enlargement—in two instances Hunter stated that the heart appeared "sound" except for the size.⁶ He said that "we see every day enlarged hearts... and yet no visible mechanical cause existed."² Probably these were examples of cardiomyopathy or hypertensive heart disease, but indirect blood pressure could not be measured for another century.

Arrhythmias

In addition to the two necropsy cases mentioned above, Hunter reported one patient with an arrhythmia whom he had seen both clinically and at necropsy. He described attacks of paroxysmal tachycardia with a rate of 160 beats per minute. Attacks could last "for weeks" but might "leave him all at once." An apical scar was found at necropsy. The coronary arteries were not mentioned. He seems to have examined a 13 year old girl both clinically and at necropsy. She had palpitation since infancy; the heart rate was "inconceivably rapid." She developed congestive heart failure and died, and dissection showed appreciable cardiac enlargement, but the

heart was not otherwise described. Two 16 year old girls were seen clinically and mentioned in Clift's transcriptions. In one the heart rate was 192–216 beats per minute during attacks. The other girl probably had valvar disease; she had an apical thrill and her carotid artery pulsated visibly. The noise of her heart during paroxysms was audible to others. The left radial pulse was absent and the arm was weak and "black" during attacks. Another remarkable case was that of General Robertson who had a heart rate of "not thirty-six in the Hour."⁶ He was dropsical, jaundiced, and asthmatic. Hunter said that "his pulse was not quite 3 strokes in five minutes; it was not more than 8 strokes in a quarter of an hour."

Cardiac function

Hunter recognised that the heart could be diseased without having an adverse effect on general health. He thought that "the heart may be in some degree disordered in its action; is therefore to be considered as a local agent very little affecting the constitution sympathetically, except by means of failure in its duty."² He seems to have confused angina pectoris and dyspnoea due to congestive heart failure at least in some instances.^{2,6} He believed that "when the heart ceases to act, or cannot get rid of its blood. . . respiration ceases, or is performed so imperfectly as to have nearly the same effect. . . In such inspirations I conceive that so little air is taken in as hardly to reach the cells of the lung, so as to be able to influence blood circulating to those cells."² Two observations may have impressed on Hunter the importance of apnoea. He was apnoeic during an episode of severe coronary pain or at least he had to force himself to breathe.² Also he had observed at least two patients who had Cheyne-Stokes respiration, which he may have attributed to heart disease.⁶

Hunter had a rational concept of left ventricular ejection. He stated that in the relaxed state at necropsy the left ventricular volume was about four ounces. In life under normal conditions he thought that the diastolic volume might be three ounces, of which two ounces might be expelled during systole. He believed that increased cardiac output could result from increase in the heart rate or from augmentation of contractility. Increased diastolic filling was not mentioned. When the left ventricle was diseased Hunter speculated that increased cardiac output could result only from increased heart rate.

Ischaemic heart disease

Early in the spring of 1772, a 51 year old man read a summary of William Heberden's published description of angina pectoris in the literary magazine *Crit-*

Fig 1 Thinning and scarring of the incised apex of the left ventricle and an endocardial thrombus, as well as many postmortem thrombi (specimen P 150, Hunterian Museum, Royal College of Surgeons of England).

ical Review.^{18,19} He recognised the similarity to his own symptoms and wrote to Heberden that "I have never troubled myself much about the cause of it, but attributed it to an obstruction of the circulation, or a species of rheumatism." Believing that sudden death was likely, he left instructions that Dr Heberden be notified "if it please God to take me away suddenly" and gave permission for "an examination of my body, as will show the cause of it." His premonition was fulfilled less than three weeks later and Heberden engaged the "experienced and accurate anatomist, Mr J Hunter, to open the body." Nothing was found to account for angina; Heberden concluded that angina was not due to an organic disease.¹⁹ Edward Jenner attended this necropsy, performed near the end of Jenner's two year residence with Hunter, and the negative findings must have bothered him. Years later, after he had ascribed angina pectoris to coronary artery obstruction, he wrote that he was "almost certain that the coronary arteries were not examined" in the case of Heberden's correspondent.²⁰ No record of the dissection has been found among Hunter's preserved manuscripts. Heberden gave a report of this case to the College of Physicians in November 1772 and also presented correspondence from Dr John Wall, the Worcester physician, indicating that aortic stenosis was responsible for angina pectoris in a patient in whom necropsy was performed. Most of Wall's patients with angina had died suddenly.²¹ These communications were not published until 1785.

John Hunter's records show that he performed necropsies on at least three cases of ischaemic heart disease before that of Heberden's correspondent, and many of his notes are not dated. Two of the

three cases had ventricular aneurysms and the third had an apical scar and an endocardial thrombus (fig 1). The circumstances of death were not described in a man who had experienced paroxysmal tachycardia, one man died suddenly, and the third man had experienced a stroke (ventricular thrombus and possible cerebral embolus). In the latter case (in 1770) Hunter reported that “when I cut into the right ventricle I found the coronary artery as it goes between the auricle and ventricle, ossified.”⁶ He made no comment on the coronary disease, and whether he correlated it with the clinical presentation is not known.

On 13 March 1775, Mr Rook, a 54 year old man who had angina pectoris, died suddenly “in a sudden and violent transport of anger.” His physician, the eminent John Fothergill, suspected that angina pectoris was due to disease of the heart, and he asked John Hunter to “open” the body.²² Hunter found calcific aortic stenosis and mitral valvar disease and that two coronary arteries “from their origin to many of their ramifications upon the heart, were become one piece of bone.” The degree of arterial narrowing was not stated. Although Hunter’s notes

indicate that Mr Rook had “felt frequent pain in the arms” still “there was nothing very remarkable in his case worth taking notice of.”⁶ Perhaps Heberden and Fothergill had not yet impressed Hunter with the symptoms and importance of angina pectoris. This was at least the second case of “ossification” of the coronary arteries encountered by Hunter.

A specimen (P 1150) in the Hunterian Museum shows a thrombus in a thickened anterior descending artery. The date of death of the patient is unknown, no clinical description was given, and the specimen does not correspond to any preserved description in Hunter’s postmortem observations. This specimen is attributed to Hunter in the latest catalogue, which states that the thrombus probably occurred postmortem.⁸ If the heart was in the original collection, Hunter must have believed that the thrombus was important. The specimen also shows ischaemic cardiomyopathy (fig 2). Another undated record refers to the findings in the case of Mr Almack who is said to have had “gout” in the extremities and stomach and died of a stroke. Non-articular “gout” was a common diagnosis at the time. At necropsy the “heart was extremely flaccid and flabby; and, as it were, half putrid.” It is possible that Mr Almack had acute myocardial infarction with cerebral embolisation.

It is curious that evidence of ischaemic heart disease was not recorded in any case after 1775 except for that of Mr Coxwell, whose notes are undated, but it is probable that he died in 1782 or later.²³ This man had angina pectoris associated with calcific aortic stenosis, but the coronary arteries were not mentioned. As noted previously, Hunter’s records contained little information on necropsies performed after 1783 although he remained an active pathologist.

Hunter’s symptoms of coronary disease started in 1773 with an attack of severe epigastric pain accompanied by pallor “...the appearance of a dead man.”² The maximal pain lasted for 45 minutes and he was “perfectly recovered in two hours.” Subsequently he did well, but in the spring of 1777 he had severe vertigo, from which he recovered slowly, and angina pectoris became a problem at this time. He was advised to go to Bath for spa therapy and, while there, Jenner diagnosed angina pectoris.¹⁶ Improvement was slow and he continued to have angina for the remainder of his life.² In 1785 he had another prolonged episode of pain and exertional angina was accentuated. He visited the spa at Tunbridge Wells for two weeks and Bath for one month. Jenner was concerned about Hunter’s condition when he saw him in Bath in 1785, and Jenner’s friend, Caleb H Parry, a Bath physician, gave Hunter sound medical advice.²⁰ The following

Fig 2 Dilated fibrotic left ventricle in coronary artery disease (specimen P 1150). The emphysematous changes in the myocardium occurred after death. The coronary lesions described in the text are not shown.

spring, Jenner recognised the relation between angina pectoris and coronary disease, but did not inform Hunter because he did not want to disturb his friend.²⁰ Hunter's biographers point out that he was aware of the possibility of sudden death and undoubtedly he associated angina pectoris with disease of the heart.^{1 3 24-26} From his necropsy experience, he may have related angina to aortic stenosis and even speculated on the role played by "ossified" coronary arteries, although there is no evidence to support such a speculation. Hunter's angina was severe in 1789 and probably for the next four years of his life. He had nocturnal pains as well as exertional discomfort. Hunter died suddenly on 16 October 1793 and necropsy confirmed Jenner's prediction that coronary artery disease would be found.^{2 20} Hunter's wish that his heart should be preserved was not honoured.⁴

Although many of Hunter's manuscripts are lost, and few inferences are recorded in his descriptions of postmortems, it is clear that he had remarkably advanced insights into the nature of heart disease. Some of his observations were published by his nephew Matthew Baillie in his epochal textbook of morbid anatomy. Baillie also used anatomical drawings of William Bell and William Clift, both protégés of Hunter. Hunter influenced the thinking of Jenner and Parry in a way that led them to propose and develop the ischaemic theory of angina pectoris. He was instrumental in introducing a new era in British medicine. John Hunter left a message for us: trust careful personal observations rather than authoritative opinion, if there is a conflict.

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