THE SPASMS OF JOHN HUNTER: A NEW INTERPRETATION

'By an acquaintance with principles we learn the causes of diseases.' John Hunter

JOHN HUNTER (1728–1793) suffered with angina pectoris for many years and eventually died of this condition. However, the post-mortem findings do not support the belief, commonly held, that his angina was due to an aortitis resulting from his earlier and deliberate self-inoculation with syphilis. Recent observations made on patients with symptoms similar to those which occurred in John Hunter encourage a new hypothesis to be put forward. However, it is important to first review the known facts beginning with the post-mortem.

THE POST-MORTEM REPORT MADE BY HIS BROTHER-IN-LAW (HOME, 1794)

> . . . the pericardium was very unusually thickened which did not allow it to collapse upon being opened. . . .
> The heart itself was very small, appearing too little for the cavity in which it lay, and did not give the idea of its being the effect of an unusual degree of contraction, but more of its having shrunk in size. . . . There were no coagula in any of its cavities. . . . The coronary arteries had their branches which ramify through the substance of the heart in the state of bony tubes which were with difficulty divided by the knife, and their transverse sections did not collapse, but remained open. The valvulae mitrales, where they come off from the lower edge of the auricle, were in many places ossified, forming an imperfectly bony margin of different thicknesses, and in one spot so thick as to form a knob; but these ossifications were not continued down upon the valve towards the chordae tendineae.
> The semilunar valves of the aorta had lost their natural pliancy, the previous stage to becoming bone, and in several spots there were evident ossifications.
> The aorta immediately beyond the semilunar valves, had its cavity larger than usual, putting on the appearance of an incipient aneurism; this unusual dilatation extended for some way along the ascending aorta, but did not reach as far as the common trunk of the axillary and carotid artery. The increase of capacity of the artery might be about one-third of its natural area; and the internal membrane of this part had lost entirely the natural polish, and was studded over with opaque white spots, raised higher than the general surface. . . .
> . . . but the internal carotid arteries, as they pass by the sides of the sella tursica, were ossified, and several of the ramifications which go off from them had become opaque and unhealthy in their appearance. . . .
> From this account of the appearances observed after death, it is reasonable to attribute the principal symptoms of the disease to an organic affection of the heart.

This information suggests that severe coronary and cerebral atherosclerosis was associated with probable mitral and aortic stenosis and a post-stenotic dilatation of the aorta rather than a coexistent luetic aortitis; and that all of these were factors which contributed towards his death.

However, the actual 'spasm' which ended his life cannot be defined on an anatomical basis although the further comments of Home (loc. cit.) are of interest.

> That organ [the heart] was rendered unable to carry out its functions, whenever the actions were disturbed, either in consequence of bodily exertion and affections of the mind.
> The stoppage of the pulse arose from a spasm upon the heart, and in this state the nerves were probably pressed against the ossified arteries, which may account for the excruciating pain he felt at those times.
> In the last attack, the spasm upon the heart was either too violent in the degree of contraction, or too long to admit of relaxation, so that death immediately ensued.

A new explanation of the pathogenesis of the spasms can be offered only after a

review of the symptoms which Hunter experienced and a description of the physical signs which he and others observed. The solution to the problem may be completed by evidence obtained from present-day patients whose attacks, similar in description to those of Hunter, were observed and monitored by radiotelemetric electrocardiography. This technique allows the continuous recording of a patient's electrocardiogram while he is completely mobile and unaware of the procedure and can therefore react in his normal manner (Holter, 1957).

A REVIEW OF THE SYMPTOMS AND SIGNS EXPERIENCED BY JOHN HUNTER: AS DESCRIBED BY HUNTER HIMSELF (1794) AND HIS BROTHER-IN-LAW (HOME, 1794)

About 1764, two leopards escaped and John caught them and carried them back to their den '. . . but as soon as they were secured, and he had time to reflect upon the risk of his own situation, he was so much agitated that he was in danger of fainting'. This event was probably sufficiently hazardous as to mean little on its own, but in the light of subsequent events it achieves much greater significance and makes Homes's statement that 'Mr. Hunter was a very healthy man for the first forty years of his life', not strictly correct.

In 1773, John suffered his first attack of angina pectoris.

> . . . at ten o'clock in the forenoon, I was attacked with a pain nearly about the pylorus; it was a pain peculiar to these parts [a comment which makes one wonder whether he had experienced this symptom previously] and became so violent that I tried every position to relieve myself, but could get no ease. . . . As I was walking about the room, I cast my eyes on a looking-glass, and observed my countenance pale, my lips white, and I had the appearance of a dead man looking at myself. This alarmed me. I could feel no pulse in either arm. . . . I continued in this state three-quarters of an hour, when the pain lessened, the pulse was felt. . . .

Here Home continues, '. . . several physicians of his acquaintance were sent for, Dr. William Hunter, Sir George Baker, Dr. Huck Saunders, Sir William Fordyce, all came, but could find no pulse. . . . in this state he continued for three-quarters of an hour, in which time frequent attempts were made to feel the pulse, but in vain; however, at last, the pain lessened, and the pulse returned, . . . in two hours he was perfectly recovered'.

These accounts provide the first major clue as to the aetiology and pathogenesis of the spasms.

Home's account continues, '. . . he enjoyed his health till the year 1776 . . . he was seized with a very severe and dangerous illness, in consequence of anxiety of mind. . . .'

Early in 1776, John had a strange illness which was closely related to his angina and which lasted ten days after which time, '. . . he got so well as to be able to stand without being giddy . . .'. Later that same year, in a letter to Jenner, John wrote, 'Not two hours after I saw your brother I was taken ill with a swimming in my head, and could not raise it off the pillow for ten days: . . .'. These symptoms are compatible with a prolonged and severe bout of postural hypotension. The cause of this was probably impaired cardiac output associated with a prolonged bradycardia the effects of this being aggravated by his mitral and aortic stenosis. It is interesting to note that during this attack, '. . . his pulse was generally about 60, and weak', and his symptoms were so severe that he '. . . was obliged to be fed as he lay'.

In April 1785, Home observed an attack and later wrote, '. . . the pain became

excruciating at the apex of the heart; the throat was so sore as not to allow of an attempt to swallow any thing, and the left arm could not bear to be touched, the least pressure upon it giving pain, the sensation at the apex of the heart was that of burning or scorching, which, by its violence, quite exhausted him, and he sank into a swoon or doze, which lasted about ten minutes, after which he started up, without the least recollection of what had passed, or of his preceding illness.' Home continues, 'I was with him during the whole of this attack, and never saw anything equal to the agonies he suffered; and when he fainted away, I thought him dead . . . the exercise that generally brought it on was walking, especially on the ascent, . . . the affections of the mind, that brought it on, were principally anxiety or anger: . . . what appeared extraordinary was, that the spasm did not come on equally upon all kinds of exercise'. This latter description is typical of the attacks experienced by the patient F. R. described below.

There is little doubt that John's attacks were due to myocardial ischaemia; his own description of them confirms this as well as providing an explanation as to their aetiology when it was stated, '. . . the feel of the sternum being drawn backwards toward the spine, as well as that oppression in breathing, . . . at these times the heart seemed to miss a stroke, and upon feeling the pulse, the artery was very much constricted, often hardly to be felt, and every now and then the pulse was entirely stopt'.

In 1789, a severe attack of giddiness was associated with both loss of memory and derangement of vision, '. . . the oblique vision', and subsequently the spasms became more frequent and were associated with impairment of memory. John, being conscious during the attacks, was aware of his severe memory losses which were usually transient.

John's attacks recurred with increasing frequency from 1790. One episode, in October 1792, was so severe that Home thought John was about to die.

One further observation is worth recording and was first noted by Jesse Foot (1794). In his attacks of angina, John had found a trick of breathing which gave him relief and which was re-enacted by patient E. C. as described below. '. . . by the exertions—which he constantly made, after the manner of something like a cough,—he seemed as if he solicited,—to set the circulation of blood a-going.'

THE SYMPTOMS AND SIGNS EXPERIENCED BY THREE PATIENTS WHO HAVE BEEN OBSERVED RECENTLY

1. F. R., a man, aged thirty-seven years, had experienced attacks of a dull aching pain across the chest for two years. The sensation radiated down both arms and produced a severe ache in both wrists. These symptoms occurred when he hurried and occasionally when he walked, especially when he was 'tensed up'. In addition, whenever he became emotionally upset by the behaviour of his children, the pains would be particularly severe and were preceded by a sensation of lightheadedness and occasionally he would become unconscious.

In the laboratory, a rigorous whole-body exercise test did not precipitate angina nor was the radiotele-electrocardiogram abnormal. After he had recovered from the effects of the exercise a discussion with him about a proposed cardiac catheterization procedure precipitated a typical attack. At the onset of this his skin became completely white and he complained of severe lightheadedness and stated he was about to lose

consciousness. After he had been lying supine for a few minutes his cerebral symptoms became less severe and he recognized that he had the chest symptoms which usually occurred during these attacks. The electrocardiogram (ECG) during this episode is shown in Figure 1.

2. E. C., a man aged forty years, had experienced attacks for four years which had become more frequent during the last twelve months. The attacks were of acute onset. In the beginning they were provoked only by heavy work but later they occurred at any time and especially when he was agitated. A typical episode would begin with a 'sharp' pain across the chest and this was associated with parasthesiae down the left side of the body including the head. As the attack continued he experienced a sensation of 'fading away' as though he had been 'switched off'. He had noted that if he kept moving during an attack he felt better and at other times if he lay supine for about two hours he would also recover.

A maximum tolerance exercise test was completed satisfactorily but during the recovery period, when in normal people vagal tone increases (Livesley, 1970), an attack occurred coincidental with the ECG changes shown in Figures 2a to 2f inclusive.

The patient became very pale and experienced his usual symptoms. His radial pulse was absent. The sinuatrial block which had developed was repeatedly, although only transiently, overcome by making the patient cough. Intravenous atropine was required to block the effect of the vagus and restore sinus rhythm with complete relief of the patient's symptoms.

3. L. N., a man aged fifty-three years, stated that thirteen years previously while he had been sitting, he had experienced the acute onset of a 'tightness' in the left forearm. The discomfort lasted about five minutes and spread as a 'vice-like' sensation over the whole of the left side of the chest. These symptoms were associated with profuse sweating, severe lightheadedness, nausea, angor animi and dyspnoea. One day later the discomfort in the left arm recurred and, as before, there was no obvious precipitating factor. When seen in March 1971, he stated that following the original attack he had developed progressive angina on effort.

The resting standard twelve lead ECG was normal with a heart rate of 60/minute. The only drug therapy the patient had received during the preceding two weeks had been trinitrin.

The maximum tolerance exercise test showed a normal resting record (fig. 3a) and after exercising for 115 seconds he stopped with breathlessness. The bipolar ECG chest lead now showed a heart rate of 155/minute and ST-segment depression of 2.5 mm (fig. 3b). After resting for 90 seconds he complained of chest pain and the ECG showed 2:1 sinuatrial block during periods of expiration when vagal tone increases (fig. 3c) (Livesley and Oram, 1971). His chest pain became more severe as the 2:1 sinuatrial block became more persistent (fig. 3d) and plane ST-segment depression developed (fig. 3e). When the patient had been experiencing pain for eight minutes, atropine 0.3 mg was given intravenously to relieve the sinuatrial block which was again intermittent. One minute after the injection, when the heart rate was 120/minute and there was no sinuatrial block (fig. 3f), the patient's pain had lessened considerably. After a further minute, the injection of a total of 0.6 mg atropine was completed to ensure perpetuation of the atropine blockade of vagal activity to the heart. Two

minutes later the heart rate had risen to 146/minute and the chest pain was becoming more severe and was associated with a greater degree of ST-segment depression (fig. 3g) indicating the development of a more severe degree of myocardial ischaemia at this fast heart rate similar to that present during the previous slower heart rate due to sinuatrial block.

As the heart rate continued at 146/minute the patient's pain became more severe and at this time he was lying supine and developed left ventricular failure as shown by orthopnoea and severe emotional distress. His symptoms were relieved within a few minutes by sitting him up and administering trinitrin sublingually.

COMMENT

The importance of hypoperfusion of the coronary arteries due to or associated with bradycardia in the aetiology of angina pectoris has been recorded previously (Benchimol and Goldstein, 1969) and this is supported by the historical accounts of angina and syncope (Parry, 1799; Trousseau, 1868; Mackenzie, 1908 and 1925; Allbutt, 1915). The degree of myocardial contractility and thereby aortic blood flow and tissue perfusion varies directly with the heart rate. This phenomenon was first noted in the experimental frog's heart (Bowditch, 1871), and has since been demonstrated in man (Livesley, 1972).

In the case of John Hunter, angina developed not only with a presumed tachycardia consequent upon exertion but also, and most severely during the attacks of pronounced bradycardia which occurred at rest and which may have developed in response to emotional stress. These three precipitating factors for angina have been shown to be operative in the patients 1–3 described above.

It is suggested that John Hunter's spasms were due to acute episodes of prolonged and severe bradycardia which by aggravating the effects of aortic and mitral stenosis resulted in hypoperfusion of the coronary and internal carotid arteries. As a result of their ossification these vessels were unable to constrict and offset the effects of hypoperfusion. Under these circumstances, bradycardia would be more likely to precipitate angina and syncope.

It has been shown that attacks due to disorder of sinuatrial activity with the development of bradycardia can be spontaneous and benign in nature during the patient's earlier life and that such a tendency can be familial and is probably inherited as an autosomal dominant characteristic with varying degrees of penetration (Livesley, Catley and Oram, 1971). This condition of sinuatrial disorder may only achieve clinical significance when episodes of bradycardiac hypoperfusion of tissues is aggravated by the development of valvular heart disease and obstructive atherosclerosis, particularly when this latter affects the coronary and cerebral arteries as was the case in John Hunter. In this connexion it is interesting to note that John's brother, William, died as a result of a 'stroke'. However, in the absence of more complete clinical data about him, it is only possible to speculate that he too had sinuatrial disorder but in a less severe form than his brother John.

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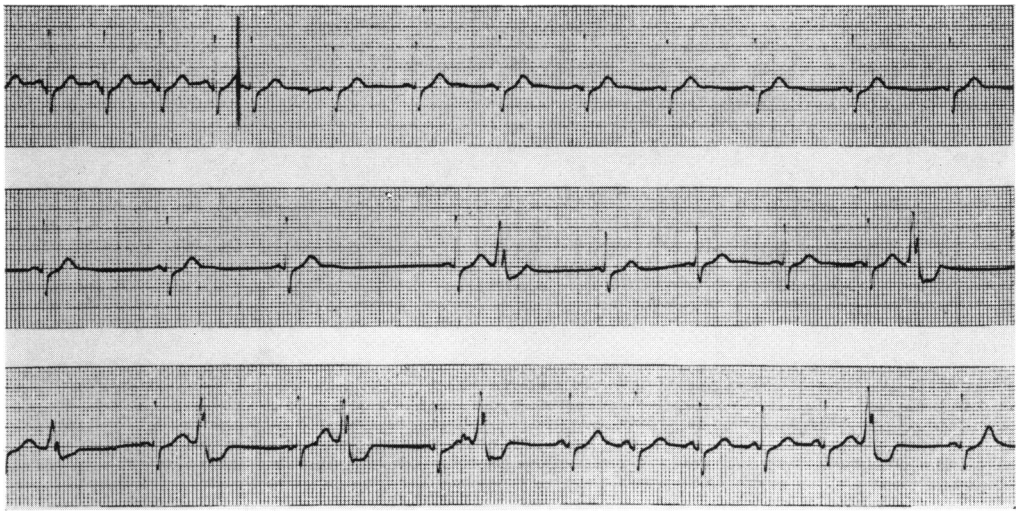

Figure 1
The resting control ECG is followed by serial records which show the bradycardia which was precipitated by emotional stress.

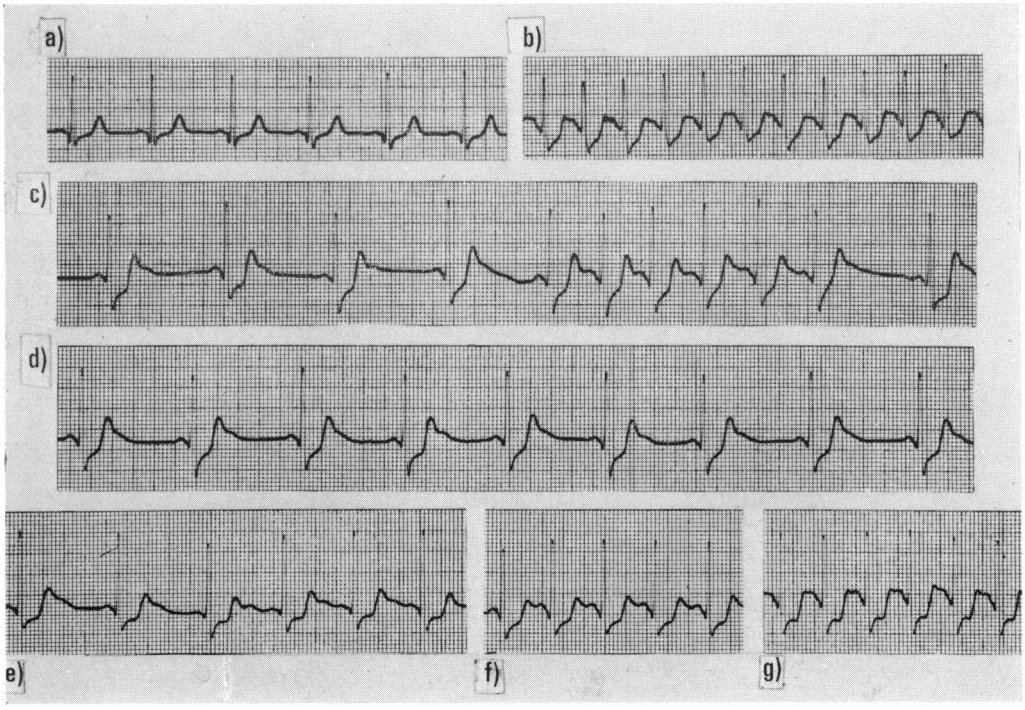

Figure 3
(a) Control ECG. (b) After exercise stress test. (c) Spontaneous development of 2:1 sinuatrial block (SAB) which initially varied with respiration. (d) Persistence of the 2:1 SAB. (e) Plane ST-segment depression. (f) Abolition of SAB after 0.3 mg atropine. (g) More severe ST-segment depression associated with clinical evidence of left ventricular failure after 0.6 mg atropine.

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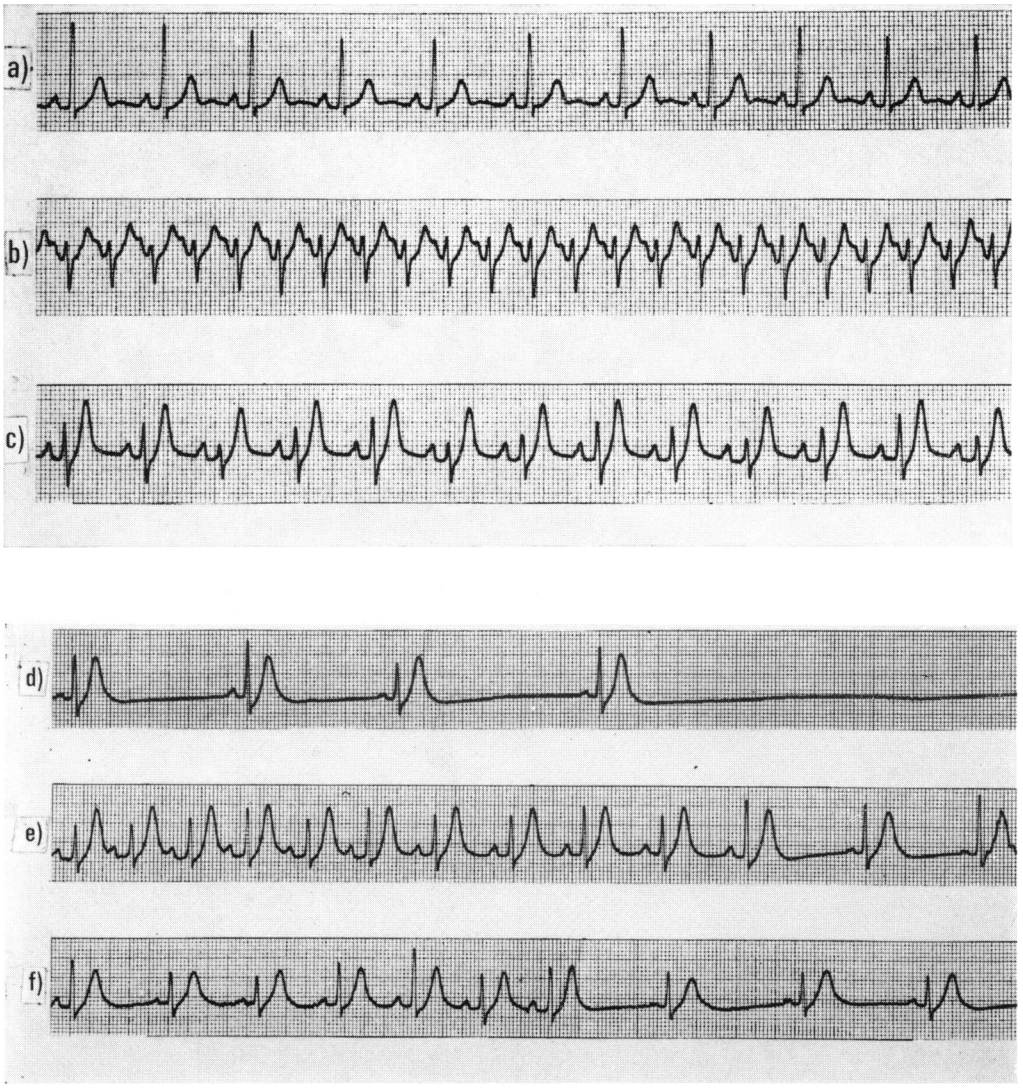

Figure 2

(a) Resting control ECG. (b) Peak heart rate after exercise stress. (c) After resting for one minute. (d) Record continuous with 2c and shows severe bradycardia. (e) An initial rise in heart rate in response to a sharp cough was followed by spontaneous slowing of rate. A further cough produced an artefact on the ECG and (f) a further transient rise in the heart rate which was again followed by spontaneous slowing of the rate.

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NOTES ON MEDICAL ORGANIZATION IN NINETEENTH-CENTURY TUNISIA: A PRELIMINARY ANALYSIS OF THE MATERIALS ON PUBLIC HEALTH AND MEDICINE IN THE DAR EL BEY IN TUNIS

LITTLE DETAILED information appears to be available about medicine or the organization of public health and medical services in most of Africa prior to the arrival of the european colonial powers during the nineteenth century. Tunisia, however, may be something of an exception to this rule. Indeed there is a very rich and unworked body of information dating from the nineteenth century in the Tunisian Archives on this very subject.

A preliminary analysis of these materials guides us to a better understanding of the Tunisian scene and more importantly convinces us that a small North African state had in fact, for its time, a reasonably advanced awareness of health matters and the nucleus of an organized public health service well before the French occupation in 1882. Although the government's early efforts at organization can hardly be described as successful or as a reflection of indigenous concern we still may safely