Palpitation: brain, heart, and 'spirits' in the seventeenth century

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Palpitation, a word denoting the sensation of rapid or irregular heartbeat, was recognized in the medicine of antiquity, but my discussion relates to the work of the Oxford Scientists, beginning with William Harvey's *De Motu Cordis* in 1628 and culminating with Richard Lower's *De Corde* in 1669.

William Harvey's dedication of *De Motu Cordis*[1] refers to his 'opinion concerning the motion and use of the heart and circulation of the blood . . . confirmed by ocular demonstration for nine years and more . . . '. This little book, really a tract, *Concerning the Movement of the Heart and of the Blood in Animals*, has been referred to as the most important medical text ever written. Published in 1628 in Frankfurt-on-the-Main in a poorly printed volume of only 72 pages with two plates, *De Motu Cordis* generated a storm of protest in the world of philosophy and medicine. Harvey defended his work with a second small book published at Cambridge and at Rotterdam, *De Circulatione Sanguinis*, in 1640. In the opinion of Cohen[2], 'Harvey's work passes all tests for a revolution in science.' Although such accolades are awarded more frequently than justified, when Harvey is viewed in continuity with his teacher Hieronymus Fabricius ab Aquapendente (1537–1619) at Padua and Fabricius' predecessor Andreas Vesalius (1514–1564), the world of natural history did indeed experience a revolution. Harvey, a comparative anatomist and experimental physiologist in a world of theorizing physicians, combined patience, personal observation, and orderly experimentation with a fundamental grasp of human and comparative anatomy. Despite the Harveian revolution in physiology, the integration of Harveian principles into the practice of medicine was a long story.

ORIGIN AND CONDUCTION OF THE HEART BEAT: THE AURICULAR-VENTRICULAR RHYTHM

In his *Lectures on the History of Physiology During the Sixteenth, Seventeenth and Eighteenth Centuries*, Foster emphasizes Harvey's clear conception of the work of the auricles and the ventricles—ventricular filling during diastole, both ventricles emptying during systole, the blood moving in a circle ('which motion we may be allowed to call circular') from the left side of the heart, through the arteries, the tissues and the veins to the right side of the heart, and thence through the lungs to the left side of the heart[3].

In the words of Harvey 'Two sets of movement occur together, one of the auricles, another of the ventricles. These are not simultaneous, but that of auricles precedes that of the rest of the heart. The movement seems to start in the auricles and to spread to the ventricles.' The translator Leake comments that this was the first clear statement on the problem of the origin and conduction of the heart beat.

Harvey continues: 'These two motions, one of the auricles, the other of the ventricles, are consecutive with a rhythm between them like the mechanism in fire-arms, where touching the trigger brings down the flint, lights a spark, which falls in the powder and explodes it, firing the ball, which reaches the mark. All of these events because of their quickness seem to occur simultaneously in the twinkling of an eye[4].'

THE OXFORD SCIENTISTS

The turmoil during the latter portion of William Harvey's career reflected the condition of his country. As physician to Charles I, Harvey was caught up in the Civil War of 1642. As a result of the political and military chaos of the war, Charles I and his court fled London and moved to Oxford. Harvey reached Oxford with the King in December 1642, and remained there until the city surrendered to the Parliamentary forces in June 1646. While at Oxford, Harvey had a connection with Merton College in the nominal position of Warden.

Harvey's influence on the remarkable scientific group at Oxford during the mid-1600s is pertinent to the present story, but incompletely defined. Leake[4] raised the question in his Harvey chronology: 'Did he [Harvey] influence Willis, Highmore, Lower, or Wren?' A genealogy of teachers from William Harvey to the Oxford scientists—Thomas Willis, Robert Boyle, Richard Lower, Robert Hook, Christopher Wren—has been suggested. Figure 1 offers a time-line.

Thomas Willis, a graduate of Christ College in 1639, was an active member of the Trinity College group of natural philosophers as early as 1648, carrying on the experimental tradition of William Harvey[5]. His research

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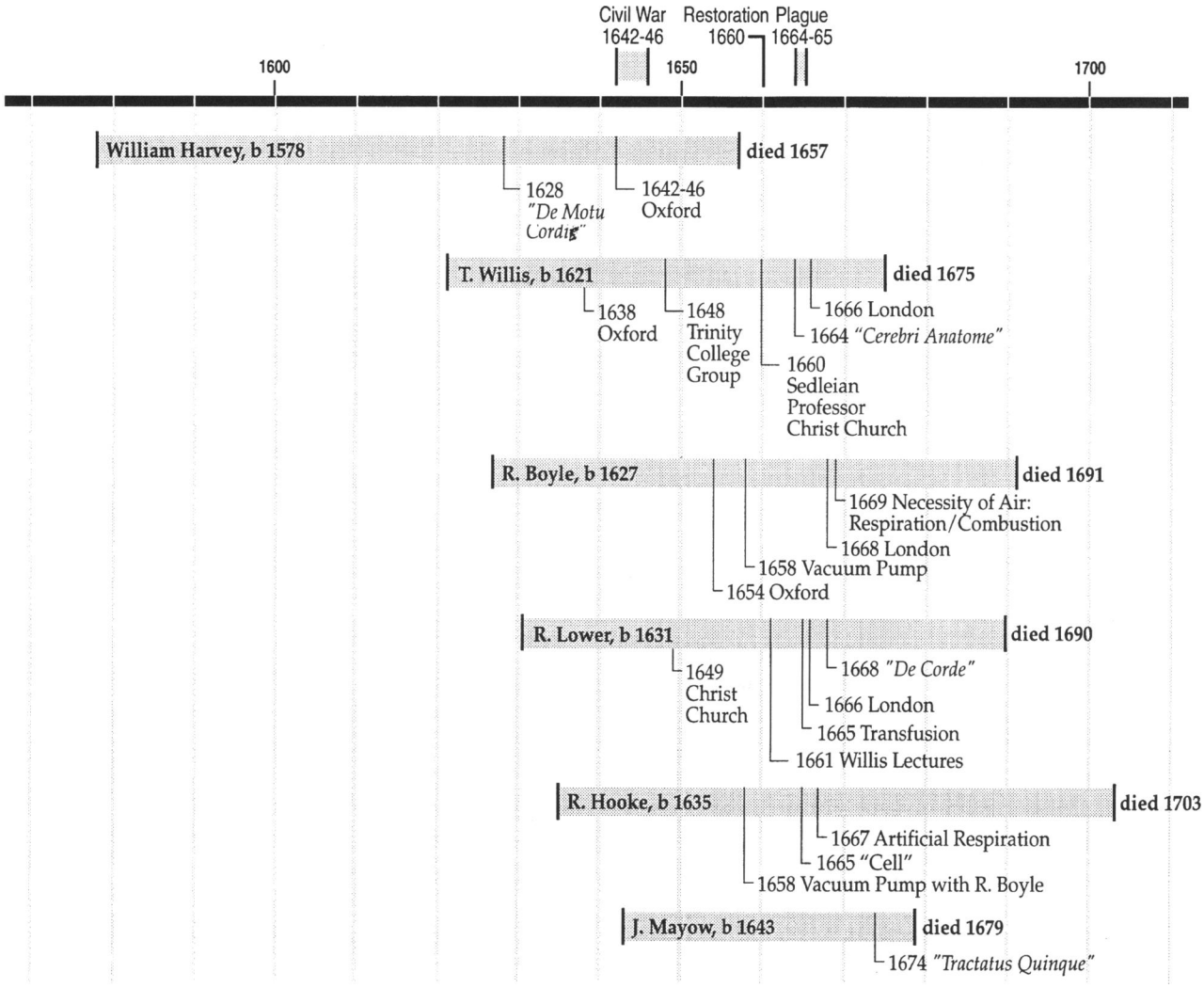

Figure 1 **A time-line of the Oxford scientists**

was stimulated by his appointment as Sedleian Professor of Natural Philosophy at Christ Church, Oxford, in 1660. Richard Lower, as pupil at Christ Church, collaborated with Willis in the anatomical dissections and animal experiments involving the nervous system that resulted in Willis' *Cerebri Anatome* in 1664. This complete account of the nervous system included a classification of the cerebral nerves; an account of the network of arteries at the base of the brain (the Circle of Willis) and the functional significance of their anastomoses; and descriptions of the distribution of nerves to the heart and the influence of the brain on the heart[5]. Willis acknowledges Lower's extensive contributions, and refers to him as a 'most learned Physician and highly skilful Anatomist'. In turn Lower, who became a lifelong friend, writes that his role was that of an assistant to Willis who planned, directed and checked all the research—thus setting straight the controversial record on relative contributions in the Willis–Lower collaborations[5].

Robert Boyle, a central figure in the Oxford scientific group is said to have been a friend of Harvey[6], but their scientific interactions are not well defined. Boyle, an Anglo-Irish physicist and chemist, is known as a father of modern chemistry and discoverer of one of the fundamental gas laws in 1662. Boyle conducted research at his own laboratories at Oxford from 1654 to 1668, and then in London from 1668 to 1691, separating chemistry from alchemy, giving the first precise definitions of a chemical element, a chemical reaction, and chemical analysis. According to the cardiopulmonary physiologist André Cournand, Boyle came next to Harvey as Richard Lower's teacher and adviser, and Robert Hooke was Lower's friend and fellow student at Christ Church[7].

TRACTATUS DE CORDE

Richard Lower was one of Oxford's great doctors. Translating his *De Corde*[8] Franklin noted that 'Through Harvey's discovery he [Lower] escaped, to an extent that even Harvey did not, from the dominance of older writers'[9]. According to Franklin, Lower had as good a

knowledge of the nervous system as any of his contemporaries, an outgrowth of his anatomic studies with Willis. His contributions to the understanding of the nervous system, the circulation, and respiration were multiple and substantial.

Lower's account of the difference in colour of the venous and arterial blood—'the arterial blood owes its red color to a mixture of air in the lungs, and . . . the venous blood owes its dark color to loss of air during its passage through the body'—was an important step in the history of respiration. Cournand credited Lower with proving that the function of the pulmonary circulation is the arterialization of the venous blood, and described Lower's text as 'one of the most important in the history of physiology, by the nature of the observations, the rigor of the experimental design and demonstrations, the simple and convincing form of the presentation, the honesty with which his previous error is admitted, and the candid expression of indebtedness to a fellow investigator . . . '[7]. Writing only 40 years after Harvey's book, Lower described the arrangement of the external and internal layers of the myocardium and the function of the pericardium, incorporating his knowledge of the nervous system, cardiac innervation, and the brain–heart interactions into his physiological explanations[9]. His quantitative estimations of the output of the heart and of the rapidity of the blood flow place him as the natural successor to Harvey and predecessor to Stephen Hales (1677–1761). Lower also used the term *relaxato venarum tono* to describe the effect of venous dilatation on the heart beat, an early insight into venous and vasomotor tone and control.

MOVEMENT OF THE HEART

Lower's chapter The Movement of the Heart in his *De Corde*[8] displays a remarkable appreciation of fundamental cardiac physiology. Like Harvey he differentiated auricular systole from ventricular systole and diastole, observing that the auricles were the first to move and not only provided the first impulses for the heart's motion but were 'the spark which sets off the whole'. Lower describes nerve branches distributed thickly all over the heart, and 'within the brain was a perpetual storeroom of animal spirits, so that there may be a continuous inflow of them into the heart'.

One of Harvey's most influential critics was the French philosopher René Descartes, who accepted Harvey's doctrine of the circulation of the blood but disagreed that the movements of the heart were due to contraction, maintaining that they involved internal fire or heat, and blood fermenting within the heart. Lower, in the subsection of this chapter Objections are Refuted, states: 'One perhaps may be surprised at the fact that after Harvey the distinguished Descartes, Hooghelande, and other famous men . . . have been in doubt if the Heart causes its own movement, or if it is not rather put into motion by the blood', and proceeds to give convincing reasons for rejecting Descartes' ideas, based on Harvey's experimental observations and his own.

PALPITATION—BRAIN, HEART AND 'SPIRITS'

Harvey used the word palpitation in *De Motu* in reference to a motion of the heart observed in his vivisection studies. Moving beyond his physiological observations, he expressed awareness that strong emotions have a physical effect on the body manifested in the behaviour of the heart: 'For every passion of the mind which troubles men's spirits, either with grief, joy, hope, or anxiety, and gets access to the heart, there makes it to change from its natural constitution, by distemperature, pulsation, and the rest . . . '[10].

Lower used the term palpitation to describe a symptom complex in a physiological setting, an important distinction. The interdependence of brain and heart is a recurrent theme in Lower's work. He notes that 'the movement of blood and the heart depends entirely on the brain'—a statement at odds with his experiments showing that excised hearts, emptied of blood, continue to beat. In fact, Lower used these observations to refute the concept that the movement of the heart was dependent on the blood. Lower then speaks of the *orderly movement of the heart* depending on the 'due inflow of spirits through the nerves, and so the movement of the heart will be very greatly changed by variation in their inflow.' Heart movements could be influenced by the 'incorrect nature' of these spirits or a diminution of their inflow[8].

The concept of *spirit* formed an important part of the Galenic tradition and of Western philosophy and medicine, and the word was used in various ways. Some writers used the term to indicate an essential or volatile principle, an activating factor within certain fluids that permeated the body, responsible for movement. Lower uses it to express a relationship, referring to substances that are carried to the heart and cause an effect: 'The heart is definitely a muscle and . . . receives spirits from the abundance of nerves which are inserted into it'. Lower describes the 'perversion' of the orderly movement of the heart that occurred in emotional states such as anger, joy and sudden fright, when these substances or spirits 'fly to the heart in excessive and unwanted amount or with a greater rush than usual, accelerate its movement very greatly, and excite and convulse it with bounding movements that are sometimes terrific. This condition writers have from time to time called by the diminutive term *palpitation*, not perhaps giving it adequate consideration . . . Once the substances or spirits have been ''driven into tumult and confusion'', and have been carried too hurriedly to the heart, they will thereafter

adopt the same path and movement, and will cause a similar spasm, to attack the heart. This can be seen in those subject to so called *palpitation*'[8].

Thus, the definition of palpitation as a symptom complex associated with the physiology of the circulation awaited Harvey's exposition of the circulation, the origin and conduction of the heart beat, and the auricular–ventricular rhythm. Then Lower integrated these circulatory events with the brain–heart connection, recognizing that perversion of the orderly movements of the heart was the cause of the symptom complex described as palpitation.

PERSPECTIVE

The Oxford group of scientists approached a wide spectrum of physical, physiological, and chemical problems, cognizant in certain instances of the clinical implications of their observations. Lower's emphasis on the innervation of the heart and his notion that excessive or unwanted amounts of bloodborne substances or spirits contributed to and accelerated the convulsing disorders of cardiac movement of the heart were profound insights.

Defining the 'next steps' after Harvey, the physiologist/historian Foster selected Robert Boyle's multiple contributions to physical and chemical science, Robert Hooke's experiments in 1667 showing that 'the essential business of respiration is carried on in the lungs', Richard Lower working with Willis in 1664, and his *De Corde* in 1669 extending Harvey's exposition of the circulation with the help of the new exact physics, and John Mayow's contribution at age 25 in 1668 to the knowledge of respiration, 'the entrance of something from the air of the pulmonary vesicles into the blood'. This dynamic phase came to an end when Boyle, Hook, Lower and Mayow—worthy children of the great Harvey—passed away, and for a long time none took their place[11].

PALPITATION—FROM 'ORDER' TO 'DISORDER'

In summary, the term palpitation and its meaning evolved along with the insights into the physiology of the circulation that resulted from Harvey's studies. Harvey's exposition of the sequence of the *orderly movement of the heart*, the origin and conduction of the heart beat, and the consecutive motions of the auricles and the ventricles, the *auricular–ventricular rhythm*, was the essential observation. Lower then extended Harvey's exposition of the sequence of the orderly movement of the heart, incorporating the concepts of the innervation of the heart as substrate, and the interactive role of the brain–heart connections, into his description of palpitation as a symptom complex with a physiological basis arising from a *disorder of the orderly movement of the heart*.

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