SPECIAL ARTICLE

William Harvey and His Contributions

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Life and Times

THE HARVEIAN Orator of 1662, probably Sir Charles Scarburgh but perhaps someone else who knew Harvey well, proclaimed that Harvey "thought again and again and for a long time how he could raise himself effectively from the ground and place his head among the stars and at last there settled in his mind the wish to embrace medicine." Harvey certainly succeeded in rising to a place amongst the stars, and the "ground," so to speak, from which he raised himself was Folkestone, on the strait of Dover, in Kent. Here, William Harvey was born on April 1, 1578, twenty years after the first Elizabeth had ascended the throne of England. William was the eldest son in a family of seven sons and two daughters. His father, Thomas Harvey, was a Turkey merchant as, subsequently, were five of Harvey's brothers.

Harvey was born into a world in ferment—intellectual, religious, social, economic, and political. Indeed, the year 1588, when young Harvey went off to King's School, Canterbury, was the year when the Invincible Armada of 132 vessels and over 3,000 cannon attempted its ill-fated invasion of England; Drake struck his most damaging blows in an attack that began off Calais, across the Strait from Folkestone.

Harvey attended King's School, Canterbury for five years. It was probably during this period that "there settled in his mind the wish to embrace medicine," for Sir Thomas Barlow has pointed out that the scholarship that enabled him to enter Caius College, Cambridge, in May 1593, was essentially a medical scholarship. Although he received his Arts degree in 1597, Harvey stayed on at Cambridge until Christmas, 1599, when his scholarship lapsed, but during his last three years, he was absent for various periods totaling sixteen months, presumably because of illness. Details of Harvey's activities at Cambridge are lacking, but since he retained his scholarship for six years, he probably fulfilled its conditions, among which were that he should first study subjects related to medicine and then subjects within medicine. The author of the recently discovered Harveyan Oration in speaking of Harvey's Cambridge days said, "He devoted himself assiduously to his studies and turned with greatest zeal to philosophy. After the manner of the ancient philosophers (as they say about Plato and Pythagoras) he thought that he should travel as widely as possible in the hope of acquiring thereby some of their teaching and wisdom. Therefore this genius, who was to become a second Aesculapius, did not continue to remain in this country." In 1600, the last year of the century of renaissance and reformation, Harvey proceeded to Padua to study medicine. He could not have chosen a better school, for the renowned north Italian University was the foremost scientific school of the sixteenth century. In Harvey's time, Galileo was its greatest genius. It was with the celebrated anatomist, Fabricius ab Aquapendente, however, that Harvey studied. Fabricius instructed him in the logic and technics of experiment and introduced him to the valves in the veins and
in chick embryology—subjects that were destined to be of great importance in the two fields of his subsequent publications. Various Harveian biographers have interpreted the exuberant language of Harvey’s 1602 Paduan diploma to be a testimonial to his brilliance as a student. But J. F. Payne commented, ‘‘Unfortunately it is nothing of the kind. This grandiloquent language was a common form, and occurs in several Paduan diplomas which I have seen. Every doctor was said to have answered ‘marvellously,’ and far surpassed the high expectations which had been entertained regarding him. Harvey’s diploma was neither more nor less than the usual one.’’

Harvey returned to England later in 1602 to be incorporated as Doctor of Medicine at Cambridge and to enter upon the practice of medicine in London. The England to which Harvey returned was a dynamic country. During the previous century English politics, economic well-being, and culture had been steadily changing. Under Elizabeth I, English nationalism welded the British into a single group. English ships had begun to sail the seas. England was rapidly becoming a world power in politics, in economics, in the arts and sciences. Two great movements from continental Europe had contributed their influences to the British—the Reformation from Germany and the Renaissance from Italy. In 1531 Henry VIII had renounced the Pope for political and personal reasons. During the century, the Reformation made this split permanent, and it was a Protestant England to which Harvey returned in 1602. From Italy, the Renaissance had stimulated artistic activity, particularly in literature. It was the age of Marlowe, Shakespeare, Ben Jonson, and Beaumont and Fletcher.

But most important of all there came from Italy a scientific attitude of mind, which was wholly new to the world. More than any other one factor, the experimental attitude was liberating Western Christendom from scholasticism. During the seventeenth century, this liberation was completed, and Newton produced the first great triumph of modern science. It is experimental science that differentiates western civilization from the rest of the world, and Harvey played an important role in the early progress and spreading of the new science. His contemporaries were Galileo, Kepler, Bacon, Gilbert, Stevin, Napier, Descartes, and a host of lesser men. Their successors completed the intellectual revolution that brought experimental science into being.

Whether or not Harvey had any notion of the circulation of the blood when he left Padua, is not known. In any event, he proceeded to practice medicine in London and the Royal College of Physicians elected him as candidate in 1604, also the year of his marriage. Three years later the College elected him a Fellow. St. Bartholomew’s Hospital appointed him Physician of the Hospital in 1609. The College of Physicians honored him in 1615 by appointing him Lumleian Lecturer. The appointment was for life, and Harvey was to give a series of anatomic and surgical lectures over a period of six years. Having completed the first series, he would then start on the second six-year cycle. His lecture notes for the 1616 series are still in existence and contain the earliest record of Harvey’s work on the circulation of the blood. Harvey gave these lectures in the week preceding Shakespeare’s death. During the next decade, Harvey continued to rise socially and professionally. James I, who had succeeded Elizabeth the year after Harvey returned from Padua, appointed him Physician Extraordinary to the King in 1618, and Francis Bacon was one of his patients. Harvey was not sympathetic to Bacon’s views on science, for John Aubrey records that Harvey admired Bacon’s ‘‘wit and style, but would not allow him to be a great Philosopher. Said he to me, He writes Philosophy like a Lord Chancellor, speaking in derision; I have cured him.’’

John Aubrey’s ‘‘brief biography’’ is the most extensive record extant of Harvey that was written by one who knew him. Aubrey did not become acquainted with Harvey until 1651, however, and did not set down his recollections until more than two decades after Harvey’s death. Those writing about Harvey, as well as others, usually label Aubrey as
“unreliable,” but his most recent editor, Oliver Lawson Dick, says, “he was sometimes inaccurate, it is true but he was never untruthful, and the distinction is a most important one.” Aubrey’s life of Harvey has its inaccuracies, but it contains more information about Harvey as a person than any other source. He was accurate when he wrote, “Ah! my old Friend Dr. Harvey—I knew him right well.” Describing Harvey, Aubrey says, “He was not tall; but of the lowest stature, round faced, olivaster complexion; little Eie, round, very black, full of spirit, his hair was black as a Raven, but quite white 20 years before he dyed.” “He was very Cholerique; and in his young days wore a dagger (as the fashion then was) but this Dr. would be to apt to draw out his dagger upon every slight occasion.” Sir Geoffrey Keynes thought that this description agreed well with the Harvey portrayed in his important discovery, a Harvey portrait of about 1622.

Late in 1627 Harvey became one of the eight Electors of the Royal College of Physicians. It was in the next year, 1628, when he was fifty years of age, that his greatest work appeared—the “Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus.” From 1628 to 1642 Harvey was a busy man writing, experimenting, traveling in Europe, performing his duties at St. Bartholomew’s Hospital, to say nothing of tending to his own practice about which Aubrey had heard him say, “that after his Booke of the Circulation of the Blood came out, that he fell mightily in this Practize, and that t’was believed by the vulgar that he was crack-brained.”

Charles I, who had succeeded James I in 1625, appointed him Physician in Ordinary in 1631, and his loyalty was to cause him great anguish and to cast a shadow over the last fifteen years of his life. When the Civil War began in 1642, Harvey sided with his King and spent most of the next four years in Oxford, the royal headquarters. At the start of the War his house in London was plundered, his goods and papers being destroyed, and “he often sayd, That of all the losses he sustained, no grief was so crucifying to him as the losse of these papers, which for love or money he could never retrieve or obtaine.”

After the fall of Oxford in July 1646, Harvey returned to London and resumed the practice of medicine. Although he was in his sixty-ninth year and afflicted with gout, he was quite active despite his being a royalist. He expressed his position when Dr. George Ent called on him at Christmas time 1650 and “asked if all were well with him? ‘How can it,’ said he, ‘whilst the Commonwealth is full of distractions, and I myself am still in the open sea. And truly,’ he continued, ‘did I not find solace in my studies, and a balm for my spirit in the memory of my observations of former years, I should feel little desire for longer life.’” The solace in his studies consisted of, among other activities, writing his “Exercitatio Anatomica de Circulatione Sanguinis,” published at Cambridge and Rotterdam in 1649 and probably in writing his “Exercitationes de Generatione Animalium” first published at London in 1651 and followed by three other editions printed in Holland the same year. Moreover, he may have written other treatises referred to in the “De Generatione” but never published.

During this period he was living in his brothers’ houses in London and in the country such as his brother Eliaj’s at Rochampton where, according to a great-niece, “he used to walk out in a morning, combing his hair in the fields.” He was requested to be President of the Royal College of Physicians in 1654 but declined because of advanced age and ill health. Three years later, on the third of June, 1657, he died, following a failure of that circulatory system which he had been the first to propose nearly thirty years earlier. John Aubrey, who “was at his Funerall, and helpt to carry him into the Vault,” described the end: “the morning of his death about 10 a clock, he went to speake, and found he had the dead palsey in his Tongue; then he saw what was to become of him, he knew there was then no hopes for his recovery, so presently sends for his brother and young nephe-wes to come-up to him, to whom he gives one
his Watch ('twas a minute watch with which he made his experiments), to another another thing, etc., as remembrances of him; made a signe to Sambrooke, his Apothecary, to lett him blood in the Tongue, which did little or no good; and so ended his dayes. The Palsey did give him an easy Fasse-port."

Harvey's Writings

Harvey published three major works of which the first, the "De Motu Cordis" of 1628, is, of course, the most important. The second, the "De Circulatone Sanguinis" (1649) consisting of two letters to Jean Riolan, is for all practical purposes a supplement to the "De Motu Cordis." The third, "De Generatione Animalium," appeared in four separate editions in 1651 as already noted. Sir Geoffrey Keynes' admirable "Bibliography" thoroughly describes the various editions of these works giving the locations of copies as well as the editions of "Opera Omnia" and several "Miscellanee." In all, Keynes lists some fifty-five different editions and translations of the first three titles of which forty-one are of the "De Motu Cordis"—evidence in itself of greatness.

Harvey's published writings are, however, but a segment of his total literary output, for there is reason to believe that perhaps as many as eighteen further treatises existed in manuscript in the seventeenth century. Today only two are known to be extant; both are volumes of notes, and both are in the British Museum. One, "Prelectiones Anatomiae Universalis" which is his Lumleian lecture notes of 1616, was published in 1886, but the other on muscle anatomy and the local motion of animals remained unpublished until the second part of it appeared in 1959.

Harvey as a Physician

Speaking of Harvey as a physician, the 1662 Harveian Orator declared, "He practised this art with such skill that it seemed as though he had not acquired the knowledge but had rather been born with it." Aubrey, on what at first glance might appear to be the other hand, reported, "All his Profession would allow him to be an excellent Anatomist, but I never heard of any that admired his Therapeutique way. I knew several practisers in London that would not have given 3d. for one of his Bills; and that a man could hardly tell by one of his Bills what he did aine at.'16

There is probably a good bit of truth in both the statements. Obviously Aubrey is referring to "cook-book" practitioners who bought up the prescriptions of others as though they were so many recipes. However, from the evidence available it would appear that Harvey practiced rational medicine, and his prescriptions would naturally have little appeal for recipe collectors.

Harvey did not introduce any important new therapeutic procedures, but he does seem to have been an able physician. Perhaps the best way to give a brief picture of him as a clinician is to cite one of his cases.

"The wife of a doctor of divinity was brought to me; a lady of a very tolerable constitution, but who was barren and having an extreme desire for progeny, had tried all kinds of prescriptions in vain. In her the catamenia appeared at their proper period; but at times, especially after horse exercise, a bloody and purulent discharge came from the uterus, and then, in a short time, ceased suddenly. Some considered the case as one of leucorrhoea; others, led chiefly by the fact that the discharge was not continually present, and in small quantities, but appeared by intervals and in abundance, suspected a fistulous ulcer; whereupon they examined the whole vagina by means of a speculum uteri, and applied various remedies, but in vain; when I was at length called to her. I opened the uterine orifice, and immediately two spoonfuls of pus came away of a sanious character and tinged with streaks of blood. On seeing this I said that there was a hidden ulcer in the uterine cavity, and by applying suitable remedies I restored her to her former state of health. But during the time when I was engaged in her cure, when the ordinary remedies did not appear to be doing much good, I applied stronger ones, suspecting as I did that the ulcer was of long standing, and perhaps covered by exuberant granulations. I

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therefore added a little Roman vitriol to the injection employed previously, the effect of which was to make the uterus contract suddenly and become as hard as a stone; at the same time various hysterical symptoms showed themselves, such, I mean, as are generally supposed by physicians to arise from constriction of the uterus, and the rising of 'foul vapours' therefrom. The symptoms continued some time, until by the application of soothing and anodyne remedies the uterus relaxed its orifice; upon which the acrid injection, together with a putrid sanies, was expelled, and in a short time the patient recovered." 17 Despite the fact that a modern gynecologist would not sanction the injection of so powerful an astringent as cupric sulfate into the uterus, the rationale of Harvey's treatment of this case is clear. Incidentally, Harvey says, "I have introduced this account from my 'medical observations'"—one of his missing manuscripts.

Harvey's ability as a practitioner was enhanced by his knowledge of pathology the value of which in application he thoroughly understood. He stated the purpose of his intention to print his "Medical Anatomy; or Anatomy in its Application to Medicine" (alias, also among his missing manuscripts) was that he might "relate from the many dissections I have made of bodies of persons diseased, worn out by serious and strange affections, how and in what way the internal organs were changed in their situation, size structure, figure, consistency, and other sensible qualities, from their natural forms and appearances, such as they are usually described by anatomists...and from pathology the use and art of healing, as well as occasions for the discovery of many new remedies, are perceived." 18

If Harvey's missing "Medical Observations" and "Medical Anatomy" were available, it would be possible to render a more complete evaluation of Harvey as a clinician. But the missing treatise which would be most exciting to have for this purpose was one supposed to be entitled "A Practice of Physick Conformable to his Thesis of the Circulation of the Bloud." But without these documents one can concur with Sir Thomas Barlow that Harvey was "an experienced pathologist, a learned physician, and that he had the qualifications of a good all-round practitioner." 19

Harvey's Contributions to Embryology

The "De Generatione Animalium" is the largest of Harvey's published writings. In Robert Willis's one-volume English translation, "The Works of William Harvey, M.D." 20 it occupies 444 pages while the "De Motu Cordis" has 86 pages and the "De Circulatione Sanguinis" but 55. The first three quarters of the book contain a discussion of chick embryology followed by a section on reproduction in the deer. It concludes with three relatively brief sections entitled "On Parturition," "Of the Uterine Membranes and Humours," and "On Conception."

The great and lasting interest in the "De Motu Cordis" has led to a neglect of the "De Generatione Animalium" which, it must be acknowledged, has its short-comings. In the 1930's, two qualified authorities, Joseph Needham and Arthur William Meyer, analyzed the book extensively, and their findings have not been superseded to any important extent. Meyer, whose investigation was particularly extensive and valuable, catalogues "such erroneous conclusions as that fertilization is due to an influence like that of the stars; that development begins even in unfertilized eggs; that an egg grows before the vital principle enters it; that nothing exists in the uterus of the deer until six weeks after mating; that the uterus generates the "ovum" of mammals; that nothing of the semen enters the mammalian uterus; that the mammalian fetus delivers itself, and that if it were expelled by the uterus it would present the feet instead of the head foremost; that the unborn infant sucks in utero, and that if it did not do so, it would not know how to nurse after it is born; that the human fetus swallows amniotic fluid for food and that its birth is due to hunger; that the fetal intestines contain excrementitious material identical with that formed from the ingestion of milk; that the
sexual products are not formed in the testes and ovary as commonly held in his time; that there is no placenta in the hog or horse: and so forth."²¹ Meyer's book is far from being negative in its conclusions as this quotation might indicate; it was chosen as an excellent succinct statement of Harvey's errors.

On the other hand, the following quotation from Needham is an equally excellent and succinct summary of Harvey's contributions to embryology.

"1. There can be no doubt that the doctrine omne vivum ex ovo was an advance on all preceding thought. Harvey's scepticism about spontaneous generation antedated by nearly a century the experiments of Redi. It is important to note that he was led to his idea of the mammalian ovum by observations on small embryos surrounded by their chorion and no bigger than eggs, for the follicle was not discovered until the time of Stensen and de Graaf, and the true ovum not till the time of von Baer.

2. He identified definitely and finally the cicatricula on the yolk membrane as the spot from which the embryo originated.

3. He denied the possibility of generation from excrement and from mud, saying that even vermiciparous animals had eggs.

4. He discussed the question of metamorphosis (preformation) and epigenesis, and decided plainly for the latter, at any rate for the sanguineous animals.

In addition to these achievements, there are others, perhaps less noticed hitherto, but equally important.

5. He destroyed once and for all the Aristotelian (semen-blood) and Epicurean (semen-semen) theories of early embryogeny. This was perhaps the biggest crash he made in the peripatetic teaching on development, but, in spite of it, Sennertus, van Linde and Sylvius adhered to the ancient views, and Cyprianus, in 1700, had the distinction of being the last to support them in a scientific discussion, though Sterne in Tristram Shandy, as late as 1759, referred to them in a way that shows they still lived on in popular thought.

6. He handled the question of growth and differentiation better than any before, anticipating the ideas of the present century.

7. He settled for good the controversy which had lasted for 2,200 years as to which part of the egg was nutritive and which was formative, by demonstrating the unreality of the distinction.

8. He set his predecessors right on a very large number of detailed points, such as the nature of the placenta.

9. He made a great step forward in his theory of foetal respiration, though here he did not consolidate the gain.

10. He affirmed that embryonic organs were active, and that the embryo did not depend on external aid for its principal physiological functions."²²

These statements of Meyer and Needham taken together form the best brief evaluation of Harvey as an embryologist that is available.

Harvey's Contributions to Cardiovascular Physiology

William Harvey was a life-long investigator of the cardiovascular system. His lecture notes of 1616 have a sufficient number of new observations on the heart and blood vessels to make it certain that he had been investigating them for some years. His great work, the "De Motu Cordis" of 1628, contains many more new findings, including his celebrated quantitative work. The "De Circulatione Sanguinis" of 1649 is essentially a supplement to the "De Motu Cordis" and has still further results that he had accumulated in the two decades following the publication of his masterpiece. An example of his continuing work is his repeated efforts to perform Galen's experiment of inserting a reed or tube into an artery and then tying a ligature about the artery over the tube. Galen had found that there was a pulse in the artery before he tightened the ligature but not afterwards. He concluded that the pulse was not the function of the blood within the artery but of the arterial wall. Something had gone wrong during Galen's experiment; perhaps blood clots formed in the tube. In Harvey's 1616 lecture notes he wrote "Galeni experimentum de
fistula Impossible,"' and twelve years later in the Introduction to the "De Motu Cordis," he said, 'I have neither made this experiment of Galen's, nor do I believe it can be done easily in the living body because of the excessive loss of blood from the artery."' However, in the "De Circulatione Sanguinis," he recorded that he had succeeded in doing Galen's experiment and found that there was a pulse beyond the tube after the ligature had been drawn up. But he did not cease investigations in 1649. Just before his seventy-third year in 1651, he wrote to P. M. Slegel of Hamburg telling of a new demonstration of the pulmonary transit—and in fact the only experimental demonstration of the pulmonary transit that Harvey contrived. He was truly a lifelong worker.

As has been mentioned, Harvey's Lumleian lecture notes of 1616 contain the earliest record of his work on the circulation. Sheets seventy-two through eighty of this ninety-eight sheet volume contain notes on the cardiovascular system with particular emphasis on the heart. It is perfectly clear from these notes that Harvey was lecturing on the circulation of the blood in 1616. He had already done much of the experimental work that he included in the "De Motu Cordis," some sections of which follow closely the outline of his notes. The last page reads in translation, "It is proved by the structure of the heart that the blood is continuously transferred through the lungs into the aorta, as by two clacks of a water bellows to raise water. It is proved by the ligature that there is a passage of blood from the arteries to the veins. It is therefore demonstrated that the continuous movement of the blood in a circle is brought about by the beat of the heart. Is this for the sake of nutrition, or the better preservation of the blood and members by the infusion of heat, the blood in turn being cooled by heating the members and heated by the heart?"

What caused Harvey to think of the possibility of the circulation of the blood, and when did it first occur to him? The second question cannot be answered with accuracy, but fortunately Robert Boyle asked Harvey the first question the only time he met him not long before Harvey's death. Harvey answered, "that when he took notice that the Valves in the Veins of so many several Parts of the Body, were so Plae'd that they gave free passage to the Blood Towards the Heart, but oppos'd the passage of the Venal Blood the Contrary way: He was invited to imagine that so Provident a Cause as Nature had not so Plae'd so many Valves without design that no Design seem'd more probable than that, since the Blood could not well, because of the interposing Valves, be sent by the Veins to the Limbs; it should be sent through the Arteries, and Return through the Veins, whose Valves did not oppose its course that way."'24

Harvey most certainly learned of the valves in the veins from Fabricius with whom he studied at Padua so that it is possible—indeed probable—that Harvey first conceived his idea of the circulation before he left Padua in 1602.

However, Harvey did not publish his renowned concept of the circulation, his greatest contribution to medical science, until 1628 in his "De Motu Cordis." The finished book printed in Latin at Frankfurt, Germany, has seventy-two pages. It appears from a reading of the "De Motu Cordis" that the entire book was not written at one time as Chauncey Leake has pointed out, for the style and spirit of some chapters are entirely different from other chapters. The introduction in which Harvey describes and ridicules the current theories of the cardiovascular system has a very vigorous and emotional style including a few expletives; it is quite unlike the rest of the book. Chapter IX entitled, "The Circulation of the Blood is Proved by a Prime Consideration" concludes with a reference to the anastomosis of veins and arteries and the statement that Harvey would now inquire into the subject. Chapter X called "The First Proposition Concerning the Amount of Blood Passing from Veins to Arteries, During the Circulation of the Blood, is Freed from Objections and Confirmed by Experiments"
contains nothing on anastomosis. However, Chapter XI, "The Second Proposition is Proven," constitutes a discussion of anastomosis. It is obvious that Harvey inserted Chapter X between Chapters IX and XI after he had originally written the latter two as successive chapters.

The book can be conveniently thought of as consisting of five sections: (1) introductory, (2) movement and function of the heart, (3) pulmonary transit, (4) systemic transit, and (5) supplementary arguments. Harvey included two dedications in the "De Motu Cordis;" one is to King Charles and the other "To His Very Dear Friend Doctor Argent the excellent and accomplished President of the London College of Physicians, and to other learned Physicians, his esteemed Colleagues." Dr. Argent was President of the College from 1625 to 1627. Therefore, Harvey probably finished the book for publication in 1627 and wrote the main body of the book during the previous year or more. In addition to the two dedications and the introduction, the "De Motu Cordis" has seventeen short chapters. First his friends had requested him to make known his discovery so that everyone could learn of it and next, he published it as a defense against ridicule. He also thought that he should publish the "De Motu Cordis" because Fabricius, his old professor, had written on nearly all parts of animals except the heart. And last he thought that by publishing his discovery he would open the path for others to make further progress. He was certainly correct in this opinion.

Chapters II through V are a remarkable analysis of the movement of the heart, arteries, and atria, and an equally remarkable analysis of the function of the heart. Harvey gives the first clear statement of the apex beat, of the muscular character of the heart, and of the origin and conduction of the heart beat. He also demonstrates that the pulse in the arteries is due to the impact of the blood ejected from the heart into the arteries as when "one blows into a glove," a phrase which he also used in his 1616 lectures. The current interpretation of the pulse following Galen was that it was a wave along the arteries originating from the motion of the heart; it was a phenomenon of the arteries and not of the pressure of the blood within the arteries. He correctly concludes in Chapter V that "the principal function of the heart is the transmission and pumping of the blood through the arteries to the extremities of the body."

Chapters VI and VII describe the pulmonary transit, the route that the blood follows in its passage from the veins to the arteries. Although Realdo Colombo had argued for the pulmonary transit seventy years earlier, some anatomists in 1628 still did not accept Colombo's thesis. Referring to Colombo, Harvey cites his observations and strengthens them with comparative anatomic demonstrations from lungless animals and embryology. These two chapters are the weakest part of the book, and it was not until 1651, as already noted, that Harvey devised an experimental demonstration of the pulmonary transit using a heart-lung preparation; Jan de Wale had contrived an experiment in a living animal a decade earlier.

Chapters VIII through XIV demonstrate the total circulation. Harvey employs three "Propositions" for his arguments: first, the amount of blood in the body must pass through the heart in a short time and that the amount of blood passing through the heart could not be supplied by the food consumed as would be the case according to the Galenic concept; second, the amount of blood going to the extremities is much greater than needed for the nutrition of the body; and third, the blood continuously returns to the heart from the extremities through the veins.

The first proposition is Harvey's famous quantitative work, the amount of blood ejected by the heart. To make his calculation Harvey had to measure the pulse rate and the amount of blood that the heart ejects with each beat. Here, he tackled a tough problem; even today there is no widely accepted figure for cardiac output. The determination of cardiac output is most difficult, and the various procedures for measuring it give results that vary as much as 25 per cent. The lowest figure, how-
ever—one dram, apothecaries weight—which Harvey used was only one-eighteenth of the lowest calculation accepted today. How could Harvey have made such a ridiculously incorrect measurement and at the same time use it to demonstrate such an important discovery?

It is a fairly simple matter to measure the pulse, but even here Harvey was inaccurate. He often uses a pulse rate of thirty-three per minute, about half the average rate in humans. Aubrey was quoted as reporting that Harvey while dying gave one of his nephews his minute watch which he had used in his experiments. If he did use a minute watch to time the pulse, he certainly must have obtained a figure higher than thirty-three per minute. And so he did, for in one calculation he reported that in some individuals the pulse is sixty-seven, one hundred, and one hundred thirty-three.

By using a pulse rate of thirty-three and one dram for the weight of blood ejected at each beat as the lowest estimate in his calculations, Harvey obtained a result, when he considered two or more beats, that was one thirty-sixth the lowest accepted value today. The difficulties of measuring cardiac output have been mentioned, but one cannot explain Harvey’s use of a thirty-three per minute pulse rate on the basis that it is a difficult measurement to make. The question, “How could Harvey have made such an important discovery by using such inaccurate measurements?” still remains to be answered.

The answer is that Harvey showed that the total weight of blood ejected over half an hour far exceeded the weight that would be supplied by food and indeed exceeded the total weight of blood in the body. His third calculation including man reads, “And so it may be inferred, that if at one beat the heart in man, the sheep, or the ox ejects but one dram of blood, and there are 1,000 beats in half an hour, in this interval there will have been 10 pounds 5 ounces [3,888 grams] expelled; if 2 drams at a single beat, then 20 pounds 10 ounces [7,776 grams]; if half an ounce, then 41 pounds 8 ounces [15,552 grams]; and if one ounce, the total would be 83 pounds and 4 ounces [31,104 grams] all of which would be transferred from the veins to the arteries [by the heart] in half an hour.” This calculation was a blow to the Galenic concept; it was obvious that the ingested food could not produce blood in these amounts. In his other calculation involving man, Harvey states, “In half an hour the heart will make more than 1,000 beats, in some as many as two, three, and even four thousand. Multiplying the number of drams ejected by the number of beats there will be in half an hour either 3,000 drams, 2,000 drams, 500 ounces or some other proportionate quantity of blood transferred into the arteries by the heart, but always a larger quantity than is contained in the whole body.” In this calculation the lowest weight, 2,000 drams, is equal to 7,776 grams, which is little above the blood volume of average man. The reason that Harvey could make such great errors in his measurement of pulse and stroke volume of the heart was that he employed the cumulative weight of blood ejected by the heart and the figure kept getting larger and larger. Using his lowest estimates, Harvey could have shown that in ten hours the heart would eject an amount of blood weighing more than the average man.27

Harvey’s demonstration of his second proposition, the amount of blood going to the extremities is much greater than needed for the nutrition of the body, is not as impressive because he does not use any specific weights. His arguments are largely inference. In the course of the discussion, however, he makes the important point that the blood must pass from the arteries to the veins in the extremities. By using the type of bandage around the upper arm that was used in letting blood, he showed that the veins would swell with blood but not the arteries. When he put the bandage on so tightly that the pulse in the artery stopped, the veins would not swell. From these observations he reasoned correctly that the blood entered the extremities through the arteries and passed to the veins.

It only remained for him to show that the flow of blood in the veins was toward the heart and not away from it as the Galenic
concept held. This he did by using the bandage around the upper arm that stopped the flow in the veins but allowed the pulse in the artery to continue. The veins, of course, would swell. Fabricius had pointed out that the little bumps in the swollen veins were the valves. Harvey showed that by pressing one's finger along a vein from below one valve to above the next valve and thereby forcing the blood up the vein that the blood did not return to the emptied section of the vein. This experiment is the only one illustrated in Harvey's book, and the illustrations are based on those in Fabricius' "De Venarum Ostiolis."

The last three chapters of the book contain philosophical and observational arguments supporting the circulation of the blood but which by themselves do not demonstrate it. For instance, he points out that the rapid spread of infections throughout the body is accomplished by the circulation. The Galenic concept of the flow of the blood could not explain this phenomenon.

Harvey's second publication, the "De Circulatione Sanguinis" of 1649, consists of two letters or "disquisitions" addressed to Jean Riolan, Professor of Anatomy at Paris, and is essentially a supplement to the "De Motu Cordis" which Riolan had criticized. The new experimental observations in the "De Circulatione Sanguinis" are important but do not have the great significance of Harvey's earlier work. The only quantitation in the "De Circulatione Sanguinis" is the measurement of equal volumes of blood in two cups.

What are the principal features of Harvey's discovery? The essential factors of the cardiovascular system that effect the circulation of the blood are, of course, the heart pumping the blood, the passage of the blood through the lungs and its return to the heart, and the similar passage through the extremities. When Harvey began his work, he already knew of the pulmonary transit. His contributions were an improved anatomic description of the heart and the discovery that the heart pumps the blood into the arteries. As for the vascular system, he showed that blood, pumped by the left heart, flowed out through the arteries to the extremities and returned through the veins to the right heart. Before Harvey, anatomists thought of the pulmonary transit as a route whereby the blood flowed from the veins to the arteries; it is not by itself a "circulation." Harvey, however, clearly established the total circulation of which the pulmonary transit is but one part. Harvey did not contribute any important anatomic discoveries of the vascular system. Indeed, he was unable to demonstrate the capillaries although he certainly tried to do so. It remained for Marcello Malpighi, born the year the "De Motu Cordis" was published, to make this important discovery. As for an explanation of the function of the circulation, Harvey was at a loss as the questions from his Lunian lecture notes indicate, and it is doubtful that a useful interpretation could have been developed in Harvey's time. "Yet," as John C. Curtis described the situation, "the phenomena of the very circulation used were so striking as to cry aloud for elucidation; for Harvey's own clinching statement that the heart drives into the aorta at least one thousand drachms of blood in half an hour, the reductio ad absurdum, which cut the ground from under the feet of his opponents, left him helpless in his turn to account for the need of so huge a flooding of the arteries."

It is important, however, not to think of Harvey's contribution solely in terms of discovery and description of anatomic structure and physiologic function. His greatest contribution was the development of the concept of the circulation that has been a most fruitful idea and still suggests new avenues of investigation—the real test of any concept.

Some three weeks after Harvey entered his eightieth year and a little more than a month before he died, he wrote a letter to John Vlaeckfeld, Physician at Harlem, which read in part, "But it is in vain that you apply the spur to me, at my present age, not mature but declining, to gird myself for any new investigation. For I now consider myself entitled to my discharge from duty. It will, however, always be a pleasant sight for

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me to see distinguished men like yourself engaged in this honorable arena." How pleased he would be if he could look in on the arenas of today!

References
7. Ibid. p. eviii.
8. Ibid. p. 128.

In the meantime this I know and declare to all men, that sometimes the blood passes in less, sometimes in more abundant quantitie, and the circuit of the blood is perform'd sometimes sooner, sometimes slower, according to the age, temperature, external and internal cause, accidents natural or innatural, sleep, rest, food, exercise, passions of the mind, and the like.—WILLIAM HARVEY. De Motu Cordis, 1628.
William Harvey and His Contributions
FREDERICK G. KILGOUR

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