WELLCOME PRIZE in the HISTORY OF MEDICINE.

1957.

"HARVEY'S TREATISE ON THE CIRCULATION OF THE BLOOD".

by

In the year 1615 at the age of thirty seven Harvey was chosen to deliver the lectures on anatomy and surgery at the College of Physicians. It is generally believed that in the very first course of these lectures he presented a detailed account of the views concerning the circulation of the blood which have since made his name immortal. The circulation continued to form one of the subjects in the lectures on anatomy, but Harvey did not publish his arguments until 1628 when he brought out his celebrated treatise on the "Motion of the heart and Blood". Thus for many years Harvey had gone on demonstrating his hypothesis concerning the circulation of the blood to his learned gathering, illustrating it by new and additional arguments and freeing it from the objections raised by the more astute of his colleagues. Harvey's masterpiece bears the full title of "Exercitatio anatomica de motu cordis et sanguinis in Animalibus", but is generally abbreviated to "De Motu Cordis". It was published in Frankfurt on poor paper and was full of printer's errors. As an example of book production it ranks very low, but as a clear, brief and logical account of the author's researches it is beyond praise.

Before discussing the content and significance of the work let us first of all consider the character of the man who wrote it and the intellectual climate in which it was conceived. The main outlines of Harvey's character are clearly evident in his works; indeed few scientific writers are so revealing. A love of truth is predominant and there is no commoner word in "De Motu Cordis" than "truth". Like all great discoverers he seems to have had a flair for truth -
truth -"that fanaticism of veracity", which Huxley alluded to. As
will later become apparent, it must have required much moral cour-
age to attack the Galenic stronghold. Furthermore, the appearance
of "De Motu Cordis" gave a decided and severe check to his profession-
al prosperity. John Aubrey relates that he had heard Harvey say
that after his book on the "Circulation of the Blood" came out he
fell mightily in his practice; 'twas believed by the vulgar that he
was crack-brained and all the physicians were against him'. Many
years later the same writer comments that 'although all his profess-
ion would allow him to be an excellent anatomist, I never heard any
that admired his therapeutic way. I knew several practitioners in
the town that would not have given threepence for one of his bills
(prescriptions) and who said 'that a man could hardly tell by his
bills what he did aim at'. So has it often been with those who have
added to the sum of human knowledge. There was no doubt that Harvey
was prepared to follow the truth into what ever unpopularity or person-
al sacrifice it might lead him.

His patience is evident not only from the nature of his experi-
ments, but also from the reluctance to make them public. In this
he was like Darwin, who waited twenty nine years for the result of
a single experiment, and all of whose work was published after he was
fifty. In his slowness to publish he was like other great men of his
own time and of the next century - Galileo, Bacon, Newton, Cavendish
and Gauss; but how different from us today with our "preliminary note;
and disputes on precedence in discovery. A discoverer who waits years
before publishing what he is firmly convinced in his own mind is a
a new idea, not to say a great discovery, must be possessed of that calmness of mind and abnegation of self which we associate with the true philosopher. A discoverer who is prepared to wait so long as to give opportunity for criticism and to deal with objections must indeed be modestly wedded to the truth.

Harvey also had a great reverence for nature, which seems to be with him synonymous with reverence for the Creator. Such quotations as "There is nothing either more ancient or of higher authority than Nature" and, again, "In Nature, just as there is nothing lacking, so there is nothing superfluous" reveal what appears to be a truly religious feeling in the face of nature.

Charity, using the word in the scriptural sense, is another essential Harveian characteristic. Contrast Harvey with Galen. Like many other Greeks, Galen had an immense feeling of intellectual superiority. Consequently, his chief fault was that he believed himself to be acquainted with the "final cause" of nature, the reason why things are as they are. By arrogating to himself such divine omniscience he marred his real greatness. His belief was that God had made all organs of the body as perfect as possible for their functions. Now the object of physiological research is to discover, by mainly experimental methods, how living beings perform their various functions. If experiments are planned with skill and care, if fortune be with the physiologist, and if he interprets the result of his experiment without bias, he will be able to make contributions of worth to his science. In this did Harvey exceed. But if, like Galen, the experimenter considers that he already knows the general scheme
scheme of nature, he will be much more liable to error, less enthusiastic, and less likely to advance his subject. Galen was an operator of consummate skill and ingenuity, but his experiments would have carried him to a less superficial greatness if only he had rid himself of his preconceived notions of nature's processes. He made many important discoveries which aided physiology, but he also left many ideas which retarded its subsequent development. Dramatically opposite to Galen's arrogance is Harvey's humility and love of truth. Indeed, the comparative absence of opposition to Harvey's discovery was, no doubt, partly due to the disarming modesty with which, like Lister, he gave it to the world; just as on the contrary Pasteur's aggressive cocksureness aroused the resistance of his contemporaries.

But Harvey's gift of character and intellect, notable though they were, would not alone have enabled him to make his great discovery, and, like all innovators, he owed much to his predecessors. It is not usually difficult to trace the pedigree of great ideas - Einstein's theory is, perhaps, an exception - for discoveries rarely spring fully grown like Minerva from the head of Jove.

However much the renewal of classical learning in the 14th, 15th, and 16th centuries may have furthered the development of letters and of art, it had anything but a favourable influence on the progress of science. Scientific investigation was almost wholly restricted to the study of the writings of authors like Aristotle, Hippocrates, Ptolemy and Galen, and it became the highest ambition to explain and comment upon their teachings, almost an impiety to question them. Independent inquiry, the direct appeal to nature, were thus discouraged,
discouraged, and indeed looked upon with the utmost distrust if the result ran counter to what was found in the works of Aristotle or Galen. The spell of ancient authority was broken by the anatomists of the 16th century, who determined at all costs to examine the human body for themselves, and to be guided by what their own observations revealed to them.

Harvey was not the only experimentalist of the early 17th century; there were many others, of whom Galileo (1546 - 1642) was the greatest. Galileo and Harvey were contemporaries during the greater part of their lives, and were some years together at the famous university of Padua. Experimentation was in the air. Harvey, therefore, must be regarded as having been not altogether unfortunate in the climate of opinion in which his discovery came to birth. It has not always been so, of course. It is possible for a discovery to be born into an uncongenial mental climate, as Servetus and Semmelweiss, to mention only two examples, found to their cost. In Harvey's case the time was ripe for the man. Standing between the 16th and 18th centuries, the 17th partook both of the credulity of the one and the scepticism of the other. It owed much to the Renaissance and more, perhaps, to the Reformation. It was a time of great awakening and renewal.

Bacon's "Advancement of Learning", first published in 1605, was so immediately popular that Harvey must have known of it. He would then be aged 27 and had been back from Padua for 3 years. Much of the argument of this great work is directed to show that a reform of method
Seratus was burned at the stake for questioning Roman Catholic church doctrine, while, with the beheading of Charles I at the head of the Episcopal Church, was free from fear.
method in the pursuit of knowledge is necessary. "Where there is much controversy, there is at many times little inquiry". "For as things are now, if an untruth in nature be once on foot, what by reason of the neglect of examination and countenance of antiquity, and what by reason of the use of the opinion of similitudes and ornaments of speech, it is never called down". The "Novum Organum" was published in 1620. As with the "Advancement", extracts are given which show that it also is just such a book as would help to form a mind like Harvey's. "The subtlety of experiments is far greater than that of the sense itself. I contrive that the office of the sense shall be only to judge of the experiment and that the experiment shall judge of the thing". We are warned not to pin our faith to the syllogism, for the premisses being only words, often there is no firmness in the superstructure, our only hope lies in true induction based on the results of experiment. In spite of the fact that Harvey never makes any reference to Bacon's writings it is worth recalling that Bacon was a blatant hypochondriac much in favour of medical attention, and that Harvey was his physician. It just was not possible for Harvey to be unaware of Bacon's revolutionary ideas on scientific reasoning. Then there was Gilbert. Both for professional and family reasons Gilbert must have been well known by Harvey. In the first words of his famous book "On the Magnet" (1600) are: "In the discovery of secret things and in the investigation of hidden causes, stronger reasons are obtained from mere experiments and demonstrated arguments than from probable conjectures and the opinion of philosophical speculators"
speculators of the common sort." This book is responsible for the word "electricity" and made Gilbert the founder of experimental philosophy in this country. Also in the year 1600, John Napier, who was constructing the first table of logarithms, made a mathematical invention that is unique in its usefulness and simplicity - he invented the decimal point. In that year (according to Sir Edmond Chambers) Shakespeare's "Merchant of Venice" was first published and "Julius Caesar" and "Hamlet" were written. It was in that year that Harvey (according to a conversation recorded by Robert Boyle) noted that the direction of the valves in the veins tells a story that directly contradicts the dogma that had been unchallenged since the days of Aristotle and Galen.

Scepticism and doubt, the active doubt that Goethe praised, were replacing credulity and degeneration. Men were learning to trust reason rather than authority, to assert liberty of individual judgement, to set the natural above the supernatural, and to look to the future rather than to the past. The imagination of the age had been kindled by the Copernican Theory and by the new orientation of man to the universe which it brought about, as well as by the geographical discoveries of the preceding epoch. The century owed much also to its great poets. It has been well said by Buckle that it was no accident that Shakespeare preceded Newton, for the poets not only stimulated the imaginations but led men back to Nature. Finally, it was an age indebted to its philosophers, to Bacon, Descartes, and Spinoza especially, who created a spirit of scepticism and inquiry.
inquiry. Stimulated by their ideas, more men than ever before were turning away from the barren controversies of religion and devoting themselves to scientific pursuits, and these men animated and encouraged one another.

The practical results of the new outlook were also becoming apparent. Modern anatomy had already come to birth only a generation before Harvey. In 1543 Vesalius published at Basel the book which revolutionised anatomy, "De humani corporis fabrica libri septem". This beautifully illustrated and wonderful work was important to physiology in that it gave the first complete and reasonably accurate description of the whole human body. The reception given to it was, however, discouraging and, apart from publishing a second edition in 1555, Vesalius did little further. What he had done was sufficient in any case, for at the age of 28 he had removed the anatomical authority of over a thousand years. He also made more direct contributions to physiology, for in a short chapter at the end of "De humani corporis fabrica" he gave a concise description of the technique and results of experiments in living animals. After accurate study of the anatomy of the cadaver, he wrote, one should proceed to examine the functions of organs, or to acquire data from which these functions can be deduced, in the living animal.

Chemistry was emerging from alchemy, just as astronomy had already done from astrology, nor was the revolt seen only in science. It was being carried by Bacon into philosophy, by Hobbes and Glanvil into metaphysics, by Cromwell into politics, and by Harrinton and Algernon Sydney.
Algernon Sydney into the theory of government. In short this was a time when anything seemed possible.

**DISCOVERY OF THE CIRCULATION OF THE BLOOD.**

In the extensive literature on the discovery of the concept of the circulation of the blood appear many claims that various men other than William Harvey (1578 – 1657) were the true discoverers. Those who deny the originality of Harvey's discovery very often confuse the idea of movement of blood with the idea of its continuous motion in a circle. It would seem that even from the most remote past mankind had recognised the blood to be in motion. We have this fact re-echoed to us by all antiquity, and it is even particularly referred to in various passages from that grand observer of his age, Shakespeare. For example, Brutus says to Portia –

"You are my true and honourable wife;  
As dear to me as the ruddy drops  
that visit my sad heart";

And again by the bedside of the murdered Gloster :-

"See how the blood is settled in his face  
- Oft have I seen a timely-parted ghost,  
Of ashy semblance, meagre, pale and bloodless,  
- Being all descended to the labouring heart,  
Who in the conflict that he holds with death,  
Attracts the same for aidance against the enemy;  
Which with the heart there cools, and ne'er returneth  
To blush and beautify the cheek again -  
- But see, his face is black and full of blood," etc.

These passages have actually been quoted to prove that Shakespeare was familiar with the concept of the circulation; indeed there have been those who have argued that Shakespeare had his knowledge from
from Harvey himself with whom for several years at least he was contemporaneous. However, Shakespeare probably referred to nothing more than the accredited opinion that the blood was in motion within the vessels, particularly the veins. In ancient times the veins were regarded as the principal vessels of the body. Indeed, the veins alone were believed to contain true blood, whereas the arterial blood was believed to be small in amount, and to be different from that in the veins. The arterial blood was believed to be mixed in some way with the vital spirits, for which the arteries were the proper conduits.

Prior to Harvey the liver was considered to be the central organ of haemopoiesis and to be the source of all the veins or blood vessels proper. The heart in its capacity as the generator of heat and the vital spirits was viewed as the mere cistern of the blood, the blood was propelled from the heart by the act of inspiration, and returned to the heart during the act of expiration. The principal flow was believed to be mainly determined by "certain excitations there inherent or specially set up". By and by, however, the liver was given up as the origin of the venous system generally. Nevertheless, such anatomists as Jacobus Sylvius, Realdus Columbus, Bartholomaeus Eustachius, and Gabriel Fallopius may be found opposing Vesalius in regard to the origin of the vena cava, and asserting that it arises in the liver, not from the heart, as that great reformer in modern anatomy had maintained.

In the progress of anatomical investigation, the valves in the interior of the heart, at the root of the pulmonary artery and the
the aorta, and in the course of the peripheral veins were described and their probable uses and actions surmised. The generally accepted idea was that they served to break or moderate the force of the current in the interior of the vessels or chambers where they were encountered. However, it must be conceded that Berengarius of Capri had already said with respect to the cardiac valves that the effect of the tricuspid valve must be to prevent the blood in the right atrium from escaping into the right ventricle; whereas the function of the pulmonary and aortic semi-lunar valves, he declared, from their position must be to prevent the regurgitation of the blood from the great arterial trunks into the heart. Fabricius, Harvey's teacher, may be said to have perfected anatomical knowledge in regard to the valves of the veins, but he by no means first directed attention to their existence or discovered them, as is generally asserted. So thorough was his knowledge of the valvular elements of the vascular system that it is really astonishing that he should not have had clearer ideas on the function, among other things, of the pulmonary veins, and should have continued a rigid adherent to the prejudices which prevailed before his time. Fabricius could observe and he could describe, but he lacked the combining intellect and the imagination that leads to new discoveries. Though he did little himself to advance the sum of human knowledge, Fabricius proved a tooth in the wheel that has since put in motion the whole machinery of modern medical science.
Another much disputed point in the anatomy of the cardiovascular system was the state of the interventricular septum; whether it was permeable or impermeable. The reason for the great importance attached to this point was connected with the ancient, and, in Harvey's time, generally accredited hypothesis of the Three Spirits—the natural, the vital, and the animal. This hypothesis necessitated the intermixture in the heart of the two kinds of blood that were appropriate to the two ventricles and to the arteries and veins respectively. The different bloods were, moreover, believed to meet in the cavities of the cranium, thorax and abdomen and then to return from these organs to the heart by the way they came for a fresh supply of the now exhausted or enfeebled spirits. Spirits in adequate amounts were believed to be essential for the accomplishment of all the functions of the body.

Galen, the founder of this hypothesis, in order to obtain the necessary admixture of the two kinds of blood, described the partition between the two ventricles either as perforated like a sieve, or as filled with depressions of sufficient depth to enable them to be viewed as constituting a kind of third ventricle, presumably to accommodate each order of spirits with its own particular "office" or "workshop". With the revival of anatomical knowledge in modern Europe, however, the porous nature of the interventricular septum came under suspicion (Berengarius, 1521) and was eventually denied (Vesalius 1555). In the first edition of his book "De humanicorporis fabrica libri septem" Vesalius noted that the interventricular septum was covered on both
both sides with pits, but that not one of these, so far as the senses could perceive, penetrated from the right to the left ventricle. He wondered at the art of the creator, who caused blood to pass through invisible pores. However, in the second edition Vesalius no longer let Galen's authority sway him, he had become frankly sceptical, and he did not see how even the smallest particle could be transferred from the right to the left ventricle through the septum. Another means had therefore to be found for securing the necessary admixture of the two kinds of blood in order to comply with the accepted origin of the three vital spirits.

Such was the state of anatomical science and physiological belief on this particular point when Michael Servetus came upon the stage, and suggested the transit of the blood through the lungs from the right side of the heart to the left, with a view to meeting the difficulty which the undeniable solidity of the interventricular septum opposed to the admixture of the two kinds of blood. Consequently, Servetus's idea seems to be nothing more than a suggestion or proposition as a means of overcoming a difficulty. It is as though he had argued that if you cannot go straight through, then why not go round. The following passage from "Restitutio Christianismi" of Servetus, 1553, illustrates this point:— "The vital spirit has its origin in the left ventricle, the lungs assisting especially in its generation. It is a subtile spirit. It is engendered from the mixture that takes place in the lungs of the inspired air with the elaborated subtile blood which the right ventricle of the heart communicates to the left. But/
But this communication takes place, not by the middle septum of the heart, as is commonly believed, but by a remarkable artifice; the subtile blood of the right side of the heart is agitated in a lengthened course through the lungs, whereby it is elaborated, from which it is thrown a crimson colour, and from the vena arteriosa (pulmonary artery) is transfused into the arteria venosa (pulmonary vein); it is then mixed in the arteria venosa itself with inspired air, and by the act of expiration is purified from fuliginous vapours, when, having become the fit recipient of the vital spirit, it is at length attracted by the diastole. Now, that the communication and preparation take place as stated through the lungs, is proclaimed by the various conjunctions and communications of the arterial vein with the venous artery. The remarkable size of the arterial vein (pulmonary artery) confirms this, a vessel which could neither have its actual constitution nor dimensions, nor transmit such a quantity of the purest blood direct from the heart itself, for the mere nourishment of the lungs. Neither would the heart supply the lungs in such proportion, (especially when we see the lungs in the embryo nourished from another source) by reason of those membranes or valves which remain unopened until the hour of birth, as Galen teaches. The blood, consequently, from the moment of birth, is sent, and in such quantity is sent, for another purpose from the heart into the lungs; from the lungs also it is not simple air that is sent to the heart, but air mixed with blood is transmitted through the arteria venosa (pulmonary vein). In the lungs consequently does the mixture take place. The crimson colour is imparted to the spirituous blood by the lungs, not by/
by the heart. There is not room enough in the left ventricle of the heart for so important and so great an admixture; neither is there space there for the elaboration into the crimson colour. Finally, the septum medium seeing that it is without vessels and properties, is not adapted to accomplish that communication and elaboration, although something may transude through it".

The discussion in this passage from Servetus obviously concerns the generation of the vital spirit, not the pulmonary circulation - that is all together a secondary consideration. His mention of "numerous communications" between the pulmonary artery and the pulmonary veins is plainly conjectural; neither he nor anyone else for a century saw such communications. The course through the lungs, then, as suggested by Servetus, was a mere hypothetical proposal for getting over the difficulty of the solid, or nearly solid, interventricular septum. He obviously had no idea how a transfusion around the septum could be effected. The transmission of the blood from the right to the left side of the heart as proposed by Servetus is in fact no great improvement on the old efflux and reflux, like the tides of Euripus, betwixt Attica and Eubaea. He had no conception of a circle of the blood beginning and ending in the heart. On the contrary he regarded the liver as the fountain head of the blood; and if he has any reference to a moving power in connexion with the heart, it is nothing more than the diastole or dilatation of the organ that is named - a passive state therefore considered as an active and efficient cause, which is absurd.
The book in which this account of the pulmonary circulation is found has a most curious history. All copies of it, except one, were burned with Servetus. This copy became the property of D. Colladon, one of his judges. After passing through the library of the Laudgraus of Hesse - Cassel it came into the hands of a Dr Mead, who undertook in 1723 to issue a quarto edition of it, but before completion the sheets were seized at the instance of Dr Gibson, Bishop of London, and destroyed. The Duc de Valise is said to have given four hundred guineas for the original copy, and at his sale it brought three thousand eight hundred and ten lire. It is now in the National Library at Paris. It may well be questioned, therefore, whether the discovery of Servetus was ever known to the anatomists, including Harvey, who wrote after his death.

Realdo Columbus (1516 - 1559) published posthumously his "De re Anatomica" six years after Servetus died, in which he shows that he clearly understood the valves of the heart, and describes the passage of the blood through the lungs. The blood, he says, once it has entered the right ventricle from the vena cava, can in no way return since the tricuspid valves are so placed that while they permit a ready passage to the stream inwards, they effectually oppose its return. The blood having passed from the right ventricle into the vena arteriosa or pulmonary artery is unable to flow back into the ventricle for it is opposed by the semi-lunar valves situated at the root of the pulmonary artery. Thus, the blood, once mixed with the air in the lungs and so in some manner acquired the nature of a spirit, is/
is carried by the arteria venosa or pulmonary vein into the left ventricle. From there the blood passes into the aorta and is transmitted to all parts of the body.

Taken so far, this looks very like an exposition of the circulation of the blood as understood today, although Columbus still insists that the blood must be made to participate in the nature of spirit before it enters the arteries and is not the same blood as that contained in the veins. However, deeper research into his writings makes it clear that Columbus could never have conceived any proper idea of the circulation. For example, he continues like Galen, to regard the liver as the origin of all the veins. The vasa eportae (portal vein), he maintains, arises by innumerable roots from the liver and carries blood from there to the stomach, spleen and intestine so that it may carry nourishment in the first case, black bile in the second, and in the third serve the double function of supplying nourishment to the intestines and, further, by a kind of imbibition, to obtain nutritive matter which is taken back to the liver for haemopoiesis. The vena cava he describes as arising from the convex aspect of the liver, and by its ramifications carries the blood that is required to nourish and maintain every part of the body. This of course is enough to condemn him, but when in addition we find that Columbus denies the muscular nature of the heart we can justifiably say that he could have had no true conception of the greater or systemic circulation.

A third and much more serious precursor of Harvey as the discoverer has been brought forward in the person of Andreas Caesalpinus of
Andreas Caesalpinus of Arezzo, justly renowned as the earliest of botanists. The account which he gives of the passage from the right to the left side of the heart is essentially the same as that given by Columbus. From the right ventricle the blood passes into the pulmonary artery and from this by numerous anastomoses into the pulmonary veins, which transmit it to the left ventricle. Quite properly he points out that it is absurd to call the pulmonary artery by the name of vena arteriosa merely on account of it departing from the right ventricle; it is a true artery and is analogous in all respects to the aorta. The title of arteria venosa given to the pulmonary vein is likewise no less ridiculous inasmuch as this vessel, though it ends in the left ventricle, has all the properties of other veins. All this is very reassuring and when one notes that he actually used the word "circulation" in regard to the passage of the blood through the lungs, one begins to sympathise with the claims of Caesalpinus which have been taken up with enthusiasm, not to say bitterness, in Italy. In 1876 his statue was erected with much pomp and speech making in Rome and an inscription was placed upon it recording that he was the first discoverer of the circulation of the blood. However, our faith in the extent and accuracy of his knowledge begins to waver when it is learnt that in his works Caesalpinus speaks of the arteries ending in nerves, of the septum of the heart being permeable, and its valves acting imperfectly and of the veins carrying blood to the body for its nourishment. The statements made by Caesalpinus, which at first sight point to his knowledge of the circulation, are altogether discounted on perusal of his works, and it becomes/
becomes impossible to believe that he had any clear idea of the circulation as we understand it today. As with Servetus and Columbus the misconception has no doubt arisen from the interpretation of isolated passages in the light of what we now know regarding the circulation. Moreover, it is impossible to believe, seeing how well the works of Caesalpinus were known, that, had he ever been regarded as putting forward in them the doctrine of the circulation as we now understand it, such a new and startling view would not have attracted the attention of the distinguished anatomists who were contemporaries or immediate successors. But that none of them ever for a moment see any such doctrine in the works of Caesalpinus is shown by their writings and by the surprise with which Harvey's discovery was received. In addition to the confusion already mentioned between the movement of blood, which has been accepted from the earliest of times, and its movement in a circle it must also be explained that a good deal of confusion has arisen between the passage through the lungs of some blood, and the passing through the lungs of the whole mass of it. It is difficult to believe, on taking a broad view of all their statements on the subject, that any of Harvey's predecessors realised that the whole mass of the blood was continually passing through the lungs. Had they done so it is difficult to see how the systemic circulation should have escaped them. But of this they certainly had no idea.

We may admit all this previous knowledge without its detracting from the greatness and merit of Harvey's work. Although the same anatomical facts and even a glimmering of the pulmonary circulation may /
may have been present in the minds of his predecessors or contemporaries, yet the genius, the spark of originality by which was discovered the proper relation to one another of the former, the true significance and meaning of the latter, belongs to Harvey and to him alone. Moreover, some of the foremost grounds of Harvey's claims to rank as a discoverer are very commonly overlooked. We always associate his name and fame with the development of the ultimate fact of the circulation of the blood. But Harvey, as a step to the conclusion, first demonstrated the heart as the means by which the circulation was effected; and he further showed that there was but one kind of blood, common to both arteries and veins. Up to this time the heart was regarded as the passive cistern of the blood and the factory for the vital spirits; it was not known as the effective instrument in any efflux or reflux of blood, or even of any lesser circulation that had been previously asserted or conjectured. The moving power was still the respiratory act. Harvey may thus be said to have first launched, and he also essentially completed the physiology of the heart's actions. The circular motion of the blood followed as a necessary corollary. Even in the title of his immortal work the "motion of the heart" has precedence; the chapter in which he first enters properly on his subject (Chapter ii) is devoted to the heart's action.

In his introduction, and by way of clearing the ground, Harvey exposes the views of preceding physiologists, ancient and modern, in regard to the accredited physiology of the thoracic viscera together with /
with comments which prove it a mass of unintelligible and irreconcilable confusion. He claims therefore, that there is room for another interpretation, compatible with reason and anatomical fact and capable of experimental confirmation. When he first attempted to analyse the motions of the heart and to understand its uses from the dissection of living animals, he found the subject so beset with difficulties that he was almost inclined at one time to say with Fracastorius that these motions and their purpose could be comprehended only by God. By degrees, however, by repeating his observations, using greater care and giving more concentrated attention, he at last discovered a way out of the labyrinth and a means of explaining simply all that had previously appeared so obscure. Great pleasure and satisfaction will reward the reader who follows the author through the different steps of his argument until the conclusion is reached. The inference presents itself as inevitable, namely, that the blood must circulate in one determinate course, in the body as in the lungs, incessantly. Yet it must be remembered that Harvey left the doctrine of the circulation as an inference or induction only, not as a simple demonstration. He adduced certain circumstances and quoted various anatomical facts which made a continuous transit of blood from the arteries to the veins a necessary consequence. He never saw that transit and indeed his idea of the way in which it was accomplished was defective. He had no notion of how the arteries end by uninterrupted continuity or by an intermediate capillary network in the veins. Harvey, who laid great stress upon comparative anatomy, used a "magnifying glass" to study the prototype of the heart in insects, shrimps, and other creatures /
creatures, but he was not familiar with the microscope. It was left to Malpighi in 1661, and to Leeuwenhock in 1674, to supply the proof of the existence of the capillaries which Harvey presumed to exist as 'pores in the solid parts, permeable to the blood, connecting the arteries with the veins'. (De Motu Cordis, Chapter xi).

The appearance of Harvey's book on the Motion of the Heart and Blood seems to have attracted the attention of all the better intellects among the medical men of Europe almost immediately. There can be no doubt that Harvey's conclusions took the medical world by surprise - it was not prepared for such a proposition as a ceaseless circular movement of the blood, with the heart for the propelling organ. Let it be once more emphasised that the latter point was just as great a novelty as the former. Coming unexpectedly and differing so widely from the ancient and accepted notions, it is not surprising that Harvey's views were at first rejected almost universally. The older intellects who occupied the places of authority regarded them as idle dreams and upon the faith of this conclusion Harvey was looked upon by laymen as a crack brained innovator. After two years had elapsed a young physician, Primrose by name, published an essay which may be regarded as a defence of the physiological ideas of Galen against the innovations of Harvey. Primrose had been a pupil of Joannes Riolanus, professor of anatomy at the university of Paris, and had doubtless listened to his master's demonstration of the absurdity of the Harveian doctrine of the circulation. His essay is memorable for any characteristic rather than that of a candid spirit in pursuit of truth. His arguments are not based on fact
fact or experiment but upon the precepts he had learned from his teacher and the texts of the ancients. Not surprisingly Harvey deigned him no reply.

The next to assail the Harveian doctrine of the circulation was Parisanus, a physician of Venice. His instruments were again the authority of Galen and the ancients generally. Nearly at the same time as Parisanus, Caspar Hofman, the learned and laborious professor of Nuremberg, attracted particular attention both in his teachings and writings as the opponent of the Harveian doctrine. The opposition here is the more remarkable since Hofman had shaken himself quite free from the authority of Galen and, as Slegel says, even admitted the lesser circulation of the blood through the lungs. This, however, must have been at a later period of his life for in his works up to Harvey's time the idea he had of the motion of the blood may be gathered from his likening it to a lake or sea agitated by the wind, the veins being the conduits of the nutrient blood, the arteries of the vital spirits. Hofman was an adversary whom Harvey held worthy of notice and he took advantage of an opportunity to visit Hofman at Nuremberg to demonstrate his new ideas before him. Hofman, however, remained entirely unconvinced, although towards the end of his very long life he did begin to show some signs of yielding.

Joannes Veslingius, professor at the university of Padua and one of the best anatomists of his time, addressed two letters to Harvey in which he politely but candidly states his objections to the new doctrine. One great difficulty with Veslingius was the striking difference between the colour of the arterial and the venous blood. It did not seem possible /
possible to him that the blood which was bright scarlet in the arteries could be the same as the dark-colored fluid which is found in the veins.

There were also the clinicians who asked what was to be the use of this teaching, and if it was not just really an ingenious piece of academic fiction. Harvey's anticipated answer to this is somewhat disappointing as it is so non-specific - "many questions in medicine, physiology, and therapeutics can be answered by the truth we have declared, on which I might expatiate, but my whole life would not suffice for the completion of the work". However, Harvey refers on several occasions to his "Medical Anatomy, or Anatomy in its affilia
tion to medicine" and perhaps this manuscript like his notes on the Generation of Insects, was lost when the college library was destroyed by fire, or when his rooms in Westminster were raided by a mob during the Civil War.

But the theory of the double circulation was not to meet opposition only. Roger Drake, a young Englishman appeared as an enlightened advocate of the Harveian views. In the same year H. Regius (Leroy) of Utrecht came forward with further evidence in favour of the doctrin of the circulation. Still more illustrious advocates of the Harveian circulation presented themselves in Werner Rolfink (1641), professor of anatomy at Tena, and the celebrated Renatus Descartes. Rolfink, from his position and popularity as a teacher, had immense influence in disseminating the new doctrine over Europe. Descartes, in his "Discours de la Methode" (1637) accepted Harvey's principles. Francis Glisson /
Francis Glisson reinstated the liver in correct perspective in his classical work *Anatomiæ Hepatis*, 1654. As early as 1639 the renowned Francis de la Boë (Franciscus Sylvius) was giving demonstrations of the circulation in dogs to his class at Leyden. The most helpful of the critics, however, were those who took the trouble to repeat Harvey's experiments rather than merely argue about them. Such a one was Herman Corning, of Helmstadt, whose book, "De Sanguinis Circulatione" (1643), brought strong support to the doctrine, as also did the work of Hendry Power, one of the first to use the microscope, whose experiments are described in his *Microscopical Observations on the Lamprey*, 1664. There can be no doubt that this was the only true way of appraising Harvey's work, by repeating his experiments, by applying to his results the method which he himself used to obtain them.

The controversy on the circulation had been carried on up to this time abroad rather than at home. Harvey seems to have won over to his side all the men of his own country who, by their professional standing might have been expected to array themselves against him. His lectures at the College of Physicians had apparently satisfied all his contemporaries. But now one of Harvey's own countrymen, Sir Guy Ent stood forward as a vindicator of the circulation from the misrepresentations and misapprehensions of its adversaries. Ent's work is entitled "An Apology for the Circulation of the blood, with a reply to Amylius Parisanus" (1641). In his letter to Harvey which prefaces the work, Ent explains that he first thought of making Primrose the particular object of his animadversions, but as this opponent /
opponent had already been very effectively dealt with by Henry Leroy he preferred taking Parisanus to task. Ent's apology is undoubtedly a learned though a rather pompous and pedantic book. Parisanus and Ent make a wonderful contrast of personalities - the former greatly ignorant of physical science and without power of utterance opposed by one gifted with eloquence and full of energy. It is said that no man who had attained the age of forty years was found to adopt the doctrine of the circulation - it had to win its way by the support of the youthful and unprejudiced spirits of the age.

Finally, twenty years after the publication of the "Exercitatio de Motu Cordis et Sanguinis", Joannes Riolanus, the younger, produced his "Encheiridium Anatomicum et Pathologicum" in which he makes a vain attempt to supplement the Harveian doctrine by a new and most extraordinary one of his own, very ingonorous and most unlikely. Harvey's genius could surely have felt no real respect for the illogical intellect of Riolan; yet Harvey was in want of a good occasion for a further development of his views and so he seized on the Parisian professor, respectable from his position in the university and as physician to the queen mother of France, and made him his vehicle - his placard bearer. Riolan is by no means totally opposed to a circulation of the blood, but he would only allow it in certain arbitrary regions into which he divided the body. The nature of his ideas can be gathered from Harvey's comments on them in his First Disquisition, addressed to the Coryphaeus of Anatomists, as he politely designates /
designates the Parisian professor.

Having disposed of the original notions of the author of the "Encheiridium Anatomicum et Pathologicum" in his first disquisition, Harvey in his second disquisition returns to his own views which he proceeds still further to illustrate and confirm by additional arguments, observations and experiments. Riolan never replied to Harvey nor did he attempt to vindicate his views. His doctrine had no abettors and never bore fruit.

Harvey must now have seen his views assured of general acceptance at no distant date. In the same year in which he himself answered Riolan, Dr James de Baek of Amsterdam published his work on the heart (1649), which is written entirely in harmony with the Harveian doctrines. Again the celebrated Lazarus Riverius, professor of medicine in the university of Montpellier, publicly defended and taught the circulation of the blood, although he was subsequently summoned by an adherent of the old school to resign his chair. The following year Paul Marquard Slegel of Hambourg produced his commentary on the Motion of the Blood (1650) in which he addresses himself particularly to a refutation of Riolanus, whose pupil he had been, and at the same time shows himself so thoroughly conversant with the general question that he is able to throw additional light on it by new and ingenious arguments and experiments. The victory for the circulation may finally be said to have been won when Plempius of Louvian, the old antagonist of Descartes, retracted all he had formerly written against it, convinced of its truth, as he so candidly informs us, by the very pains he took to satisfy himself of its error and /
and publicly proclaimed his conversion.

Thus, Harvey in his lifetime had the great satisfaction of witnessing his discovery generally received, and inculcated as a canon in most of the medical schools of Europe. He is, therefore, one of the few who lived to see the new doctrines which he had advanced become victorious over opposition and established in public opinion. There is, however, a difference between the general acknowledgment of the factual truth of his experiments and the appreciation of their full significance. It took about fifty years before those best qualified to judge, the anatomists and scientists, realised this and indeed the real significance of Harvey's work in the practice of medicine was not apparent for at least two centuries.

**HARVEY AND THE INTRODUCTION OF THE QUANTITATIVE METHOD.**

Most of Harvey's experiments are quite simple well thought out demonstrations involving ligating or severing blood vessels, and the opening of the cardiac atria and ventricles. The crucial part of his argument, however, is contained in Chapter ix of "De Motu Cordis" in which the quantitative method is used for the first time in physiology. The preceding portion of the book contains introductory sections, four chapters analyzing the motion and function of the heart, two on the pulmonary transit and one, Chapter viii, on his concept of the general circulation. Harvey then proposed to show that the heart pumped the total amount of blood in a relatively brief time, and that the amount of blood going through the pulmonary transit was so great that the ingested food could not possibly supply it as called for by the /
the then current Galenic concept of the origin and motion of the
blood; (ii) that the heart sends blood out through the systemic
arteries in much larger quantities than either the body uses for its
nutrition or, once again, food can supply; and (iii) that the blood
in veins only towards the heart and not also away from it as the
Galenic theory would have it.

Having stated that the proof of these propositions will make it
obvious that blood circulates, Harvey next presented his quantitative
arguments showing that the quantity of blood passing through the
pulmonary transit is so great that it cannot be produced by the in-
gested food. The following translation is essentially that of
Chauncey Leake with a few changes to make it more literal; it is the
only section of Harvey's book that contains specific measurements.

"Let us suppose, by reflection or by experiment, that in the
ventricle of the heart when filled in diastole, contains either two
or three ounces or an ounce and a half. In a cadaver I have found
it holding more than two ounces.

Likewise let us suppose how much less the ventricles contain
when the heart contracts or how much blood it forces into the great
artery with each contraction, for, during systole, everyone will
admit something is always found out as shown in Chapter iii, and
apparent from the structure of the valves. As a reasonable conjecture
suppose a quarter, fifth, sixth or at least an eighth part is forced
into the arteries.

Then we may suppose in man that a single beat would force out
a half ounce, three drams, or even one dram of blood, which because
of/
of the valvular block, could not flow back into the heart.

The heart makes more than a thousand beats in half an hour, in some even two, three or even four thousand. Multiplying by by the drams, there will be in half an hour either three thousand drams, two thousand drams, five hundred drams, or some other such proportionate amount of blood forced into the arteries by the heart, but always a greater quantity than is present in the whole. Likewise in a sheep or a dog, suppose one scruple goes out with each stroke of the heart, then in half an hour one thousand scruples or about three and a half pounds of blood would pass through the heart. But as I have determined in the sheep, the whole body does not contain more than four pounds of blood.

On this assumption on the passage of blood, made as a basis for argument, and from the estimation of the pulse rate, it is apparent that the entire quantity of blood passes from the veins to the arteries through the heart, and likewise through the lungs.

But suppose this would not occur in half an hour, but rather in one hour, or even in a day, it is still clear that more blood continually flows through the heart than can be supplied by the digested food or be held in the veins at any one time.

It cannot be said that the heart in contracting sometimes propels and sometimes does not, or that it propels a mere nothing or something imaginary. This point has been settled previously, and besides, it is contrary to common sense. If the ventricles must be filled with blood in cardiac dilatation, something must always be pushed out in contraction, since the passages are not small nor the contractions few.
few. This quantity expelled is some proportion of the contents of the ventricle, a third, sixth, or an eighth, and an equivalent amount of blood must fill it up in diastole, so that there is a relation between the ventricular capacity in contraction and in dilatation. Since the ventricles in dilating do not become filled with nothing, or something imaginary, so in contracting they never expel nothing or something imaginary, but always blood in an amount proportionate to the contraction. So it may be concluded that if the heart in a single beat in man, sheep or ox sent forth one dram, and there are a thousand beats in a half hour, the total amount transmitted in that time would be ten pounds five ounces; if two drams at a single stroke, then twenty pounds ten ounces; if half an ounce, then forty one pounds eight ounces; if one ounce, then a total of eighty three pounds four ounces, all of which would be transferred from the veins to the arteries in a half hour.

In the first part of this section, Harvey used the contents of the left ventricle to make his basic assumption as to the amount of blood which the right ventricle ejects for passage through the pulmonary transit. He does not explain why he uses the capacity of the left ventricle instead of the right. It may be, however, that since he had already discussed the pulmonary transit in Chapters vi and vii, he used the weight of the contents of the left ventricle as being the quantity of blood which had passed through the transit or, as he would have put it, from the veins to the arteries. This use of the left ventricle has caused confusion amongst some of Harvey's interpreters who would have presented this section as demonstrating the /
the systemic transit, and it is probably the reason for Willis having twice inserted the phrase "into the aorta" in his translation which was the standard English translation until Dr Wale's in 1926.

To make his calculations of the amount of blood flowing through the pulmonary transit, Harvey had to measure the pulse rate and the amount of blood which the heart ejects with each beat; the pulse is easy to measure, but even the most modern procedures for measuring cardiac output give results which vary as much as 25%.

According to Aubrey, Harvey's brief biographer, Harvey while dying gave one of his nephews the minute watch which he had used in his experiments. Although he mentions pulse rate of thirty three, sixty seven, one hundred, and one hundred and thirty three per minute, he used a rate of thirty three in the only calculation in which he specifically mentioned man. It is obvious from this that he did not use his minute watch to make this measurement, and it is apparent from his lumping together "man, sheep, or ox", all with a pulse of thirty three, which is reasonably correct for an ox but only half the correct figure for man or sheep, either that he did not take the trouble to measure their pulse rates, or that he was not particularly concerned about using the correct rate. Of the two alternatives, the latter is the more likely.

When it came to measuring cardiac output, Harvey was obliged to guess at a measurement which has not yet been accurately determined, but he might have been more accurate than he was. The only two specific measurements of the weight of blood that he records are the "more than two ounces" he found in the left ventricle of a cadaver
and the "not more than four pounds", which he obtained exsanguinating a sheep. This figure of four pounds is, of course, low, because by using the rudimentary technique available to him, he could not have drawn off all the blood. His estimate of the stroke volume as being either a quarter, fifth, sixth or eighth of the ventricular content are sheer guesses. Although it would have been impossible for Harvey to arrive at an approximately accurate value of the cardiac output in man, he could have done much better in the case of sheep. If he had severed the aorta of a sheep and had weighed the amount of blood ejected during ten or twenty beats, he could have obtained a fairly accurate figure for the stroke volume. Presumably, he never made this observation or one similar to it, such as Richard Lower's discussed below, because he did not feel that he had to be particularly accurate.

This conclusion is reinforced by an inspection of Table 1, which gives all the possible values for stroke volume in man based on Harvey's assumed value of ventricular capacity and proportion of contents ejected by each contraction. It should be noted that one dram is not one of the possible values, yet Harvey used it in his first and third calculation. Either he did not do the arithmetic in Table 1, or he merely rounded off one and a half drams to one dram. Moreover, he included sheep in his second and third calculation and employed variously a cardiac output of one scruple (1.3g), one dram (3.9g), two drams (7.8g), half ounce (15.6g), and one ounce (31.1g). Certainly Harvey was not concerned with accurate measurement.

Harvey concluded Chapter ix by writing that he would next discuss anastomosis between veins and arteries, "but he doesn't" as Chauncey pointed
Table 1.

Possible Values for Cardiac Volume in Man Based on Harvey's Determinations

<table>
<thead>
<tr>
<th>Estimated Content of Left Heart (L)</th>
<th>Proportion of Content ejected by each contraction (C)</th>
<th>Weight of Blood ejected by each contraction (W)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 L</td>
<td>4/6</td>
<td>1.5 Lg</td>
</tr>
<tr>
<td>1.5 L</td>
<td>4/5</td>
<td>2.0 Lg</td>
</tr>
<tr>
<td>1.5 L</td>
<td>4/4</td>
<td>2.4 Lg</td>
</tr>
<tr>
<td>1.5 L</td>
<td>4/3</td>
<td>3.0 Lg</td>
</tr>
<tr>
<td>1.5 L</td>
<td>4/2</td>
<td>4.0 Lg</td>
</tr>
<tr>
<td>2.0 L</td>
<td>3/8</td>
<td>2.4 Lg</td>
</tr>
<tr>
<td>2.0 L</td>
<td>3/6</td>
<td>2.67 Lg</td>
</tr>
<tr>
<td>2.0 L</td>
<td>3/5</td>
<td>3.2 Lg</td>
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<tr>
<td>2.0 L</td>
<td>3/4</td>
<td>4.0 Lg</td>
</tr>
<tr>
<td>2.0 L</td>
<td>3/3</td>
<td>5.77 Lg</td>
</tr>
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<td>3.0 L</td>
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<td>3.0 L</td>
<td>2/5</td>
<td>4.5 Lg</td>
</tr>
<tr>
<td>3.0 L</td>
<td>2/4</td>
<td>6.0 Lg</td>
</tr>
<tr>
<td>3.0 L</td>
<td>2/3</td>
<td>1.0 Lg</td>
</tr>
</tbody>
</table>
pointed out in a footnote. However, Harvey did write about anastomosis in the first paragraph of Chapter xi so it seems clear that he inserted Chapter x after having written what is now xi to follow ix. Someone had apparently raised an objection to his idea of the circulation by claiming that the blood flowed out of the body in the form of other fluids such as milk from mammals. In the new chapter Harvey answered this criticism by saying that by computation the heart pumps in an hour or less more than all the milk produced in a day, but he did not do any computation.

Chapters xi and xii are devoted to the proof of the second proposition that the "...blood is found by the pulse in the arteries continually and steadily to every part of the body in a much greater amount than is needed for nutrition or than the whole mass of food could supply". Actually, Chapter xi consists almost entirely of descriptions of his well-known experiments using ligatures on limbs to show that blood passes from the arteries to the veins. In a sense most of the chapter deals with anastomosis, but there is no quantitative work in it. One paragraph of Chapter xi, however, does contain quantitative arguments for the systemic transit. Harvey wrote:

"We may very readily compute the amount of blood and come to some conclusion on its circular motion. If, for instance, in phlebotomy, one were to let the blood flow with its usual force and rate for half an hour, there is no doubt but that the greater part of it would drain off, practically emptying not only the arteries but also the great veins, and that fainting and syncope would follow. It is reasonable to assume that as great an amount of blood as is lost in this half hour's time, passed from the great veins through the heart into the/
the aorta. Further, if you figure how many ounces of blood flow through a single arm, or pass under a medium bandage in twenty or thirty heart beats, you will have a basis for estimating how much flows through the other arm at the same time, or through both sides of the neck, or through both legs, and through all the other arteries and veins of the body. Since all these are continually supplied with fresh blood, which must flow through the lungs and ventricles of the heart, from the veins, it must be accomplished in a circuit, since the amount involved is much more than can be furnished from the food consumed, or than is needed for the nourishment of the parts".

Harvey did not make the suggested computation, and the statement hardly seems adequate as a quantitative demonstration of the systemic transit. Although he made measurements, albeit not precise ones, to prove the demonstration of the pulmonary transit, Harvey made no measurements to prove quantitatively the systemic transit.

His third proposition Harvey proved in Chapter xiii by using his excellent demonstration of the valves in the veins and of the derivation of the blood flow in the veins. At the end of the chapter he produced another quantitative argument much like that in Chapter xii. After directing the reader to expel the blood from the section of a vein between two valves, to allow the section to refill and to repeat the procedure "...a thousand times as quickly as possible". By careful reckoning, of course, the quantity of blood forced up beyond the valve by a single compression may be estimated, and this multiplied by a thousand gives so much blood transmitted in this way through a single portion of the veins in a relatively short time, that without doubt /
doubt you will be very easily convinced by the quickness of its passage of the circulation of the blood". But once again he does not make the estimate or the computation, and uses the quantitative argument only by inference, which is hardly what is understood by the phrase "quantitative biology".

These instances of quantitation are the only known examples of Harvey's methods that involve weights. There may have been others in his manuscripts that Civil War rioters destroyed when they ransacked his London house in 1642, or in the eleven now unknown "treatises" to which Charles Goodall (The Royal College of Physicians of London. 1684) referred in 1684 as though they were in existence at that time. Despite these possibilities, there is no evidence of quantitative work by Harvey, other than the aboveexample, that had any influence on subsequent biologists.

The reason why Harvey was not more precise in his measurements was that he did not have to demonstrate his great discovery. Using his lowest estimates for stroke volume and pulse rate which for two or more beats give a cardiac output only one thirty sixth that of the lowest figure accepted today, Harvey could have shown that in ten hours the heart could eject an amount of blood weighing more than the average man. If Harvey had been trained to use instruments of precision to control quantitative methods, he probably would have used an accurate pulse rate, but otherwise it is likely that his calculations would have been the same. Today's more accurate measurement of cardiac output do not change Harvey's conclusion that the blood circulates.
circulates.

The origin of Harvey's quantitative attitude is unknown; it is quite likely that he adopted the well known techniques of measuring with weights and balances as a result of his reasoning. Men had been using weights as a form of measure for at least four thousand five hundred years, and one branch of medicine, pharmacy, had been compounding remedies by using weights for centuries. Apparently, quantitative evidence was not important in leading Harvey to develop the idea of the circulation because there is no quantitation in his Lumleian lecture notes of 1616. Scientists and physicians were just beginning to adopt quantitative methods in investigation, although as Cyril Stanley Smith (1951) has pointed out in the case of assayers, some types of sixteenth century technologists were thoroughly quantitative in their outlook. Galileo was preaching in the university of Padua during the years that Harvey was a student, and it seems almost impossible that Harvey could have completely avoided acquaintance with Galileo's principles of measurement. The Universita Artista, the section in which Galileo taught and which contained the medical school, probably had not more than one or two hundred students enrolled during Harvey's student years. There were fewer than one hundred enrolled in the 1630's, the earliest period for which enrollment records exist. For such a small student body, Harvey surely must have known something of Galileo's work, but there is no direct evidence that he did.

Under Galileo's influence, Sanctorius of Padua (1561 - 1636) was /
was the first to make extensive use of precision instruments to control observations in biology and medicine. He described his pulsilogram for measuring the pulse rate in 1620 and a thermometer for measuring body temperature in 1612. Sanctorius published his celebrated measurements of the insensible perspiration by the use of balances in 1614. Reprinted nearly forty times in the original Latin and in translations during the next one hundred and fifty years, this work ("De Statica Medicina") played a much larger role than Harvey's "De Motu Cordis" in stimulating the use of the balance in biology.

That the Scientific Revolution should have occurred when it did has not been explained, and unfortunately the history of the interrelationships among the technologists, the arts, and the sciences during the latter part of the sixteenth century has not yet been written so that general influences which may have inspired Harvey to use quantitative arguments cannot yet be evaluated. Nevertheless, at Padua quantitation must certainly have been under discussion while Harvey was there, and like experimentation, it was at least in the Paduan air.

In addition to the work of Harvey and Sanctorius, the best known and most important quantitative research in biology in the seventeenth century was that of Jean Baptiste van Helmont (1577 – 1644), Richard Lower (1631 – 1691) and Giovanni Alphonso Bonelli (1608 – 1679). There is every reason to believe that Harvey had no influence on van Helmont's celebrated experiment of weighing a growing tree and the earth in which it was planted, but Harvey's work most certainly had some /
some effect on Lower's experiments. Lower's most important contribution to quantitative investigation of the circulation was the use of the total weight of the blood in the left ventricle as being the amount ejected during systole, instead of some fraction thereof as Harvey had assumed. However, Lower did not arrive at this conclusion by using quantitative methods. Rather he observed that when he cut off the tip of a living heart and inserted his little finger, the ventricle closed so completely during systole that he could not squeeze the walls of the heart more tightly together on the finger. From this observation, he concluded that the entire contents of the left ventricle were ejected with each contraction, but he made no measurements of the stroke volume. He did, however, weigh the contents of the left ventricle removed from cadavers and found it often held much more than two ounces of blood. Nevertheless, in his calculations he used Harvey's measure of two ounces. Lower's method of quantitation was no advance over Harvey's. Bonelli used three ounces as the stroke volume in his remarkable analysis of the dynamics of the circulation, but it is not clear just how he arrived at this figure. Much of Bonelli's book consists of excellent quantitative experiments in which he consistently used the balance and occasionally the thermometer. He not only used precision instruments for control, but also did many geometrical analyses, even of the heart, which are totally lacking in Harvey. Bonelli's work, of course, is completely within the Galilean tradition, and it is most unlikely that Harvey's less sophisticated methods had any important effect on him.

It /
It seems clear from the above analysis that Harvey's elementary quantitation, although adequate for his purposes and influential on a few biological investigations of the seventeenth century, had less effect than is often represented.

THE SIGNIFICANCE OF HARVEY'S WORK.

Although the realisation that the systematic circulation and the pulmonary circulation are but integral parts of one continuous movement was a great discovery and one upon which all physiology is founded, yet it is doubtful if it is the achievement that should be chiefly acclaimed, or rather, that it should be acclaimed in that form. There is little doubt that Harvey's discovery could not long have been delayed. Other workers had come very near to suspecting the fact and with the microscope once introduced it could not have been concealed. How and when the first clear statement would have come, had Harvey remained silent, would be a matter of profitless conjecture. It actually came from Harvey, and we are content to accept that fact. Revolutionary as his discovery was at its time, far reaching in its subsequent development, yet the conclusion was not the best that Harvey gave us. The outstanding quality of Harvey's work lies in his statement of the case, in the lucid nature of his argument, and the finality of his proof. He presents to us a train of methodical and exact observation and experiment, carried forward hand-in-hand with clear and finished reasoning, brilliant for its simplicity and for its power of conviction. His book is a romantic example of scientific exposition, unsurpassed at his time and since his time.

"De Motu Cordis"/
"De Motu Cordis" holds its reader entranced, while each stretch of the path brings a surer promise of the approaching vista; and when the path ends it ends on the hill-top, and there is unfolded to our gaze a land that is ours with certainty, ours for all time. This culmination brings with it a sense of security and accomplishment that fills us with a profound and lasting emotion; and we go forward to hold what he has given us with a great thankfulness to this pioneer, who has not only led us to a new country; but has inspired us and taught us to explore further." 

Thus Harvey not only discovered the circulation of the blood, but he proved the efficiency of the scientific method in medical research; a proof which was to be stated even more clearly by Claude Bernard some two centuries later. The discovery of a principle is always more important than the discovery of a fact, as it leads to further advances. Ehrlich's discovery of chemotherapy out shone his introduction of salvarsan as the remedy for syphilis. Lister's use of the antiseptic method was much more outstanding than was his use of carbolic acid, because this was a new principle, not just a new remedy.

Harvey has been called the Father of Physiology; he was much more than that, he was the founder of Clinical Science, out of which physiology and pathology were afterwards born. Prompted and inspired by clinical observation and by dissection of the dead body, he proceeded further by the method of experiment, using both men and animals, and finally integrated this mass of evidence into one whole. He bequeathed his method to us in his memorial book.

Since /
day than did the millennium before him. His exhortation "to search and study out the secrets of Nature by way of experiment" now has implications he could not have foreseen. Medical research today is the purpose of large organisations with vast budgets at their command, and its guidance and inspiration have outranged our capacity and slipped from our grip.

It is necessary for medicine, still the parent and still largely possessed of guiding authority, to call a check to this subdivision of her estate. It is necessary that steps should be retraced and that territory originally possessed should be reclaimed, so that medicine should not be narrowly confined; it is requisite that medicine should renew its strength to wield its chief weapon, the experimental method. It is to the accomplishment of these ends that the establishment of Clinical Science in its full scope is to be regarded as so important. If this science is to become established it must not be formed into a third unit, which shall presently detach itself and move off to a position of isolation; it must remain firmly within and develop as an integral part of the whole organisation. To secure this most desirable and permanent unity it must establish itself, not as laboratories in our medical schools, but actually within our hospitals, centring upon the wards and out-patient departments, and using laboratories merely as adjuncts for accommodating the necessary equipment. Above all, we must guard against the obsession, which has tended to develop in recent years that useful discoveries are purely the prerogative of laboratories.
Since Harvey's day knowledge has grown apace, and where there was one science there are now many. Clinicians in the age following Harvey became largely absorbed in the descriptions of disease; in the hands of men like Sydenham this fascinating branch of knowledge, derived from observation, rapidly expanded. Though presented sporadically in this country among physicians, Harvey's method fell amongst them into relative disuse until the last century when it was seized upon enthusiastically by a small band of devotees and short ly became the basis of the present science of physiology. The budding off of physiology is almost within living memory, and the process of disruption has continued. First physiology abandoned medicine, and in going took largely from medicine its function of studying the normal processes of the body; it also took something more important, for clinical medicine seemed to relax its claim to use the experimental method, which it had forged and which physiology, its offspring, now chose as its own chief weapon. Pathology has budded or is budding off, assuming for its part the study of the mechanism of disease, human or otherwise, in almost all its aspects. This disruption of medicine, as it was originally constituted and as Harvey knew it, may be the inevitable outcome of its growth, may profit physiology, general pathology, may even profit the medical sciences when viewed as a whole; but it is a process which can be carried too far, when it can and is becoming detrimental to the development of the clinical branches of work.

The world in which we live has seen more change since Harvey's day /
The proper practice of medicine has been built up, and continues to be built up, on a complex basis. The general mass of our knowledge rests upon a tripod, the three limbs of which are each essential to the stability of the superstructure; these limbs are: 1) studies of living man in health and disease; ii) studies of dead men; iii) related experiments on the lower animals.

The full scope of Clinical Science, as the work of Harvey first defined it, embraces all these three. The central and unique studies of Clinical Science, most fundamental of all studies pertaining to the practice of medicine, are these dealing with living men. These cannot be divorced from either anatomy or from experimental work on animals without embarrassing all three, and without seriously weakening the whole edifice.

It is quite necessary to the proper progress of the clinical branches of study that they should be most strongly linked with physiology, with morbid anatomy, and with what has been called experimental pathology. The linkage can be an enduring one only if Clinical Science continues to command opportunities of studying both dead bodies and living animals.

It is essential that those who have held charge of patients and have studied phenomena in the living should themselves, and not through skilled deputies, explore the tissue changes which may underlie disturbed function; for although the skilled deputy may more accurately describe and name the changes in the tissues which are sent to him, he cannot enjoy either full opportunity or the full inspiration to correlate function and structure. It is by those correlations that the...
the meanings of many manifestations during life are explained; it is by correlation rather than by simple study of the cadaver that the meaning of illness and the cause of death are often usually explained.

It is essential that those who in studying human patients perceive opportunities of putting questions to the test of animal experimentation should themselves engage in such work; that correlation should not be left to chance meeting and union of clinical and laboratory studies; that the spirit that moved the original inquiry should live, vitalising and directing the whole work in its progress along a broad path towards a practical goal. To divide or attempt to divide medical research into ward research and laboratory experiment is undesirable on account of limitations so imposed; it is a profound error to believe that there is any essential difference in general method, however different may be the technique.

The physicians and surgeons of our great teaching hospitals become more and more dependent upon technical experts. How easy, as the problems suggest themselves at the bedside, to accept the view that it is fitting that highly trained and fully equipped men should undertake the investigation. But the result so often is that from the first the research is forced into a narrow channel of technicality from which it fails to emerge, and the work ends in one of these reports which, scientific though they may be in their cold logic, unfold no story, and remain uninspiring and lifeless. The fascination and importance of the problem in its wider and practical implications.
implications have been concealed, the inspiration that should have been the compelling force towards its solution has been lost, because the problem is no longer seen in full perspective, a problem primarily concerning the living, in part concerning the dead, and in part deriving from the laboratory. It is just this investigation that is of so much consequence to the vitality of medical research; and this integration is, and always must remain, chiefly within the special province of Clinical Science. Knowledge that is applied usefully to the health of mankind will almost always come by a series of steps, the first of which is the recognition of the human need, the last of which is the application of a test to the human problem. It is therefore in the nature of things, however many steps intervene, that the first and last shall be clinical. He who can see the source of the problem, who can appreciate the satisfaction of its final solution, is uniquely fitted to guide the whole train of thought and inquiry.

Harvey investigated the human body in health and disease, living and dead, and used animal experimentation to supplement his other studies. This is our birthright, derived from him, and we must not depute our tasks. A great need of the medical sciences in the present stage of their development and interrelation is a group of men, primarily clinicians, but fully accustomed by training and daily experience to wrestle with scientific problems; men who, in place of relatively complete and accurate knowledge of some purely laboratory science, hold as the first part of their equipment intimate acquaintance with the relevant diseases as these are seen in living man, who have also acquired/
acquired sufficient knowledge of related physiology and of general pathology, who have the aptitude to acquire quickly and well the necessary technical knowledge and skill, thus to enable them to grapple with the problem both in its detail and its wider aspects, and to drive successfully to the goal.

Such work, it will be clear, requires not only ability, but a man's full energy; it is not the type of work to which those busily employed in practice can give themselves in leisure hours with full prospect of success. Physicians do not live as Harvey did in times of easy clinical activity, but in days of much heavier and complex routine. So if the purpose in mind is to be brought to accomplishment it will be necessary to set free men having the aptitude for the work outlined, to form an advanced guard of trained clinicians who shall bring Clinical Science to a new pitch of scientific efficiency and hold it there. It is to be hoped that the new chair of Surgical Science at Edinburgh University will prove to be instrumental in the achievement of these ideals.

Thus Harvey, inspired by the desire to understand the motion of the heart, set himself to discover its meaning. He did not concentrate upon such of its motions as he might see in his patients; but starting from there, in his wisdom, let his gaze roam. He searched widely, gathering with his own hand and his own brain all such information as he might find pertinent to the furtherance of his studies. It was because he possessed breadth of vision that he brought these studies to a conclusion that has proved fundamental to all medical science. In doing so he gave us an exposition of method of unique force and significance /
significance. He established for us a tradition, a tradition that Clinical Science shall not be confined narrowly or by artificial boundaries, but shall be free to explore how and where it will; a tradition which will not countenance attempts to separate the study of health from that of disease, or the study of animals from that of man, or work at the bedside from that in laboratories. These are among the lessons of "De Motu Cordis" and this is Harvey's leadership.