

The Evolution of the Concept of the Circulation

by LEON CUDKOWICZ, M.D., M.R.C.P.

The evolution of the concept of the circulation is a provocative subject because of its links to the history of the evolution of man between the Euphrates and Atlantic. As a part of the history of our civilization it shares to the fullest the tedium, fury, indifference, fanaticisms, exaltations and shame which attaches to the often macabre practices of this particular nursery of humanity.

By inviting you to join me in a brief escapade into the past, I am aware that we shall be rolling back 2,000 years or more, glancing only at the antics, agony, and serenity of a few men caught up in the bustle of time, without pausing, of course, to feel the quality of their experience. We shall witness the remarkable dichotomy of art and science through the ages, the former dominated by personality, the latter searching for the open mind.

Plato denied man's right to priorities in ideas. He conceived ideas as eternally existing patterns of which individual examples are imperfect copies. Absolute reality exists externally only in the substance of God, and not in the gaze of man, and clearly invalidate man's claim to priorities even in the organization of matter.

Thus, all ideas of God are locked in the bosom of the Universe, of which man can, at best, conceive but an imperfect image. In a way this was implied by Michelangelo¹¹ when he stated that all perfect sculpture slumbers in rock. The sculptor in accordance with his skill, liberates but a few layers which always continue to conceal the ultimately perfect. As a concept the circulation never seems to have existed a priori in the mind of man. It was and remains an idea almost of platonic remoteness awaiting patiently the chisel of man's mind. It clearly existed outside man's consciousness and we are concerned with the many imperfect and clumsy strokes directed against the rock of concealment of the circulation in the 2,000 years preceding Harvey.

HIPPOCRATES.

The dawn of recognition of the rock holding the mystery of the circulation broke with Hippocrates in the 4th Century B.C. He found that the pulmonary artery contained venous or dark blood, whereas red blood percolated in the pulmonary veins. At this time respiration and cardiac action became interwoven and it was assumed that expiration cooled the body and eliminated the heat produced by cardiac contraction. The cooled inspired air was conveyed to the lungs and entered the pulmonary veins.

ERASISTRATUS.

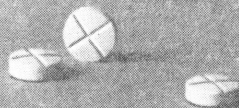
One hundred years later and soon after the decline of the golden age of Athens, Erasistratus, the father of experimental medicine, began a number of experiments in Alexandria. He was first an anatomist whose description of the heart and brain evinced a knowledge of detail not to be reached again until the days of Vesalius. Unfortunately, all his works were destroyed when the great Library of Alexandria was burnt down. What we know of his experiments is derived from Galen and this is probably biased because of his bitter criticism of Erasistratus. Erasistratus conceived air being drawn into the lungs by negative pressure within the thorax during inspiration. He assumed that cardiac diastole was an active movement and that similar negative pressure extended into the heart during diastole. However, the left ventricle in diastole was thought to draw in air, instead of blood, via the pulmonary veins, and this air was then forced into the arteries. Thus, he reached the conclusion that in health the arteries contain air, not blood. Blood, he maintained, was conveyed in the veins and right ventricle alone, and that in disease only did it leak over through the peripheral anastomoses into the arteries, where it gave rise to the heat, swelling and pain of inflammation. These concepts of Erasistratus appear to have en-

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dured for 400 years, because Galen in the second century A.D. set out deliberately to refute his results.

Before leaving Greek antiquity we have this brief comment by Erasistratus concerning research.⁶ "Those who are altogether unaccustomed to research are, at the first exercise of their intelligence befogged and blinded, and quickly desist owing to the fatigue and failure of intellectual power, like those without training who attempt a race. But one who is accustomed to investigation, worming his way through and turning in all directions does not give up the search his whole life long. He will not rest, but will turn his attention to one thing after another which he considers relevant to the subject under investigation until he solves his problem."

With Erasistratus departed academic experiment. Greece was on the march. Soldiers displaced philosophers. The fortunes of soldiers determined the pattern of life. Not until the Roman Empire reached the zenith of its power and splendour under the Emperor Marcus Aurelius, in the second century A.D. could our rock engage the interest of another outstanding mind.

GALEN.

Claudius Galen, born in 130 A.D. in Pergamum, Asia Minor, found his way to Rome in the year 164. He became the friend and physician of Marcus Aurelius who, like him, was a stoic philosopher and ardent Hellenist. Galen's knowledge of anatomy from personal dissection of animals was vast. Man was the animal of which he had least direct knowledge. He reports vivisection of pigs, goats, sheep, horses, mules, asses, cows, stags, bears, mice, birds, and at least one elephant. His physiology was based on the principle of ablation. He cut, tied and severed. The exposure of the beating heart and lungs in living animals he found too difficult, because of deaths from pneumothorax. By removing the sternum, Galen observed the beating heart of pigs. But he could no more analyze this in the quick moving heart than Harvey 1500 years later. "It is impossible to ligate the pulmonary vein", he lamented, "it can be done around the base of the heart, but the animal dies at once." He is balked. He reached the limit of his technical skill and so he failed to break Erasistratus' idea of active cardiac diastole. He did, however, establish that arteries contain blood in life.

Armed with this fact he proceeded to enunciate one of the most formidable misconceptions ever to have dominated human thought. A misconception which ruled supreme until the 16th century, and became the official doctrine of the Church.

Galen, having found the arteries filled with blood, realized that connections must exist between veins and arteries. Ignoring the peripheral anastomoses between veins and arteries postulated by Erasistratus, he sought for some other communication between them, and found it in the "invisible pores" which, he insisted, communicated between the right and left ventricles through the septum of the heart, whereby in diastole blood was sucked from the venous into the arterial tree.



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Galen's concept of blood flow was that of ebb and flow. Hepatic blood reaches the right ventricle, he said, whence it enters the pulmonary artery and lungs. This blood carries soot which leaves the lung in expiration. Inspiration cools the blood and provides "pneuma" to the pulmonary venous blood. With diastole the two types of blood return to their respective ventricles. The left ventricle contains the "spiritual" blood which is distributed to the arteries and also to some extent to the right ventricle by being forced through the invisible septal pores to add some nutritive properties also to venous blood. The heart thus became a furnace emitting soot and being cooled by "pneuma".⁴ Darkness descended upon Europe and Asia Minor, and Galen's porous furnace became dogma. Life was cheap in the Middle Ages. Men were quartered, speared, broken on the wheel or burnt for heresy, yet dissection of the dead was forbidden, by both the Christian and Mohammedan Churches.

IBN-AN-NAFIS

The scene of interest shifts from Medieval Europe to the Middle East. The guardians of the faith spread the Gospel with the sword and the elite of European youth perished in the great Crusades against Islam. Nevertheless, in this age of spiritual darkness a light was glowing in the early 13th Century in the person of Ibn-an-Nafis. This great physician, jurist, philologist, philosopher and theologian, born in Damascus, maintained a bridge with ancient learning, yet was suspect amongst his contemporaries and obviously suppressed. Not until 1924 did it become known. The Egyptian Medical Student, Moleyi-el-Din-el Tatawi, studying in Freiburg University, for the purpose of his thesis, went to the Prussian State Library in Berlin. There one day he came across an early manuscript written in Arabic. The author, Ibn-an-Nafis, had written a commentary to the canon of Avicenna, the Galen of Arabian medicine. In five separate places he unmistakably mentions that blood from the right ventricle cannot pass through septal pores, but reaches the left ventricle via the lungs by way of the

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Plate 1

— PORTRAIT OF LEONARDO —

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pulmonary veins. He wrote, "But there is no opening as some thought there was between these two cavities, for the septum of the heart is watertight without any apparent fenestrations in it. How, as held by Galen, would an invisible opening be suitable for the passage of this blood, for the pores of the heart there are not patent and its septum is thick." He regarded the content of the pulmonary vein as a mixture of air and blood saying, "But the view that the function of the pulmonary vein is to transport nourishment from the heart to the lungs has been shown to be unfounded, since the function of this vessel is to transport the air already mixed with rarified blood from the lungs to the left ventricle."²²

Who had shown this? We shall probably never know. This beacon became extinguished and almost 200 years elapsed before Europe awoke from its long and inconceivable slumber of 1400 years.

The Renaissance brought the printing press, and with it that catalyst of knowledge, Leonardo da Vinci.

LEONARDO DA VINCI.

Born an illegitimate child in the small hill town of Vinci in 1452, he received a very poor education and appeared to be able to read but not write Latin. He was extremely attached to his mother in early childhood but completely lacked paternal guidance. He had no guidance. Soon after the age of 16 in Verocchio's Studio, he left his mark as a painter of unique individuality and brilliance. The angel painted by him on a canvas by Verocchio almost extinguished the art of the teacher. He was alone, and he had the unique ability of knowing this. "One has risen before dawn and my companions are still asleep." Elsewhere: "Whoever refers to authorities in disputing ideas, works with his memory rather than with his reason."¹⁰ So vast were the interests of this genius that we must pause for a moment. A universe existed and he set out without guide or compass to make it comprehensible to himself, relying entirely on his own observations and own judgment.

Leonardo da Vinci questioned all he had read and disregarded most established forms of knowledge, except geometry. His contributions in the Arts of painting and sculpture are well known and cannot be considered here, except perhaps for the fact that he did so many things at the same time that even his greatest paintings like the Mona Lisa and the Last Supper remain incomplete. His observations in the sciences are too well known to be elaborated here. What is by no means fully established concerns our scholarship of Leonardo's knowledge of Anatomy and Physiology. Detailed accounts of the fate of Leonardo's Anatomical note books, probably the most beautiful of their kind ever compiled by man, exist and are conflicting.⁸

Before I venture to summarize da Vinci's observations, I must mention that he dissected over 30 human cadavers almost alone, in Italy, at an age that knew not



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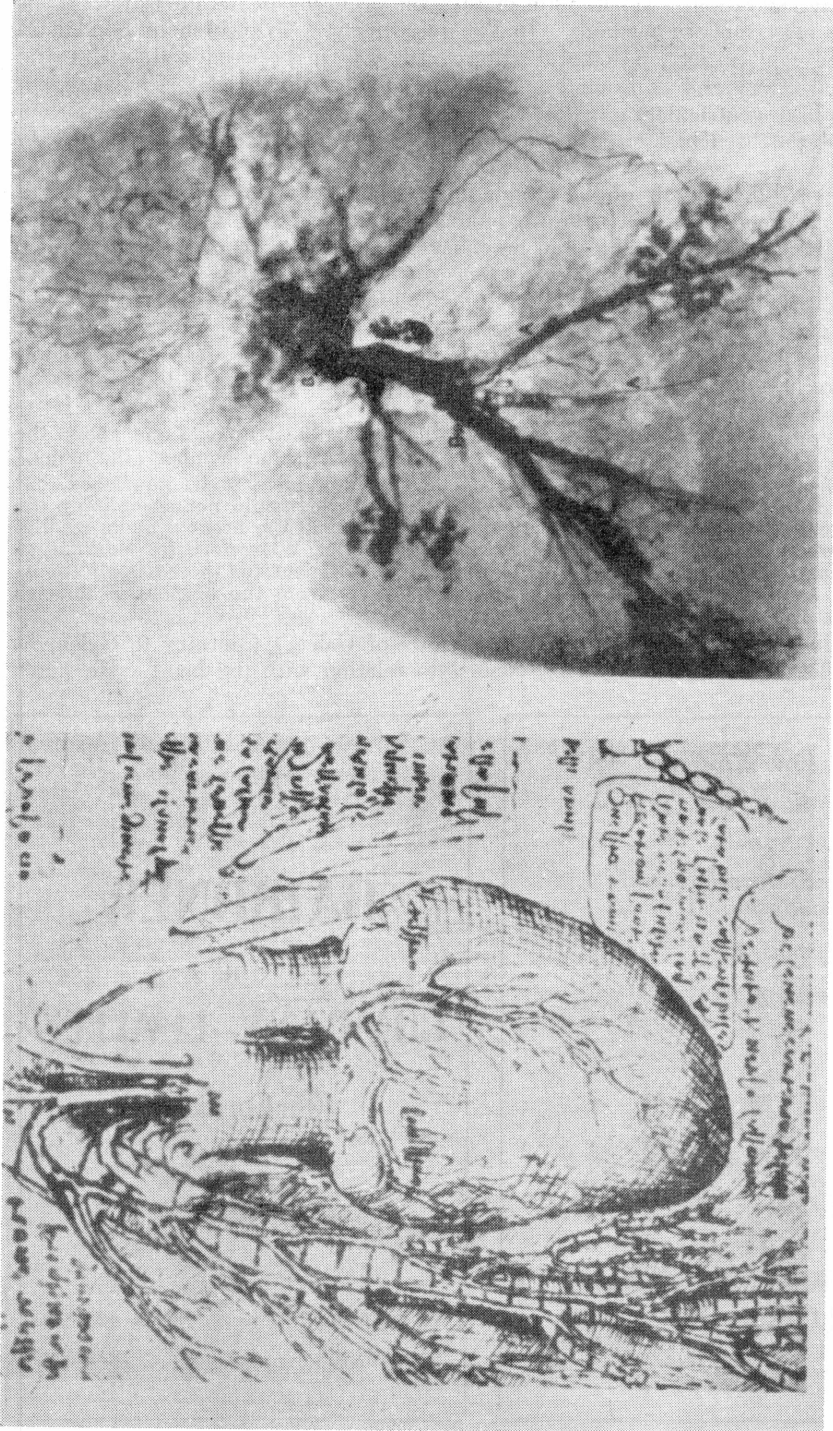


Fig. 1—Drawing by Leonardo da Vinci of the heart, aorta and left bronchial arteries is depicted as well as their course along the bronchial tree. (This is a mirror image drawing, therefore showing the apex of the heart and the aorta on the right hand side.)

Fig. 2—Lateral Radiograph of a left lung. The bronchial arteries and the bronchial tree have been injected with a contrast medium.
(A) Bronchial arteries.
(B) Bronchial tree.

formalin or refrigeration. Yet in spite of this, the accuracy of his dissections rivals those by the most modern methods. In the quincenary exhibition in London in 1951 at the Royal Society, a femoral arteriogram was juxtaposed with a drawing of the femoral artery and its branches. The similarity was complete. The same applied to cerebral ventriculography and the antrum of Highmore. A post mortem angiogram of the bronchial circulation and that of his drawings is here for you to compare.

What then did he know of the circulation? da Vinci's endless thirst for detail enabled him to depict the heart, lungs, pulmonary arteries and veins, heart valves, aorta and aortic valves, bronchial and coronary circulation with unrivaled accuracy. To this must be added nearly all other systems of the human frame. He studied these systems as separate phenomena and not as a co-ordinated whole. In so doing he failed, as far as we know, to grasp the secret of the circulation. And yet, how are we to interpret such extra-ordinary statements as that concerning the bronchial circulation, where he for the first time in our knowledge enunciates the need of an arterial blood supply for the nutrition of an organ.³

"Why nature duplicated artery and vein in such an instrument, one above the other, finding themselves for the nourishment of one and the same member (the lung)."

"You may say that the bronchial tree and the lung have to be nourished, but if you had to do with a single large pulmonary artery, this could not accompany the bronchi without great interference with the movement which the bronchi make in dilatation and contraction as well as in length and thickness. Wherefore for this nature gave a vein and artery to the bronchi which would be sufficient for their life and nourishment and somewhat removed the other large vessels from the bronchi to nourish the substance of the lung with greater convenience."³

Leonardo was the first to question the views of Galen. Contrary to Galen, he demonstrated that the bronchi do not come into relation with the heart. He stated

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that after branching and diminishing in size they finally end blindly. He inflated the lungs with air and found that none could be driven from the bronchi into the heart and that the pulmonary veins could not, therefore, convey air, but conveyed blood. His intense interest in hydrodynamics brought him to investigate the movement of blood. He proved that the pulmonary and aortic valves allowed blood to move only in one direction. The aortic valve received most of his attention. Its cusps were drawn in situ, open and closed. He made a cast of the base of the aorta out of wax and over this a hollow cast of gypsum. This he lined by a sheet of blown glass. To this he attached a triangular pipe and allowed water, containing a few millet seeds to emerge through the valve. He found that three vortices are formed. This returning circular flow closed the valves by a lateral and not a vertical force, pushing them against one another like three bellying sails.⁷ Did he know more than just unidirectional flow?

This mysterious genius died in exile in France in 1519 with an overwhelming treasure of knowledge, most of it hidden forever from our eyes.

Our rock has clearly been struck by the most powerful chisel thus far, but the dust settled upon it rapidly by Leonardo's death. We now come to the most martyred of giants. A man who almost tore the last remaining veil of stone from this stubborn rock, but who was finally thwarted by man's uncompromising fanaticism.

MICHAEL SERVETUS.

Michael Servetus was born in 1511 in the province of Navarre, Spain, to parents of minor nobility. The spirit of his country, indulging in an orgy of self-righteous faith, appalled him.

In 1537 we find him in Paris studying Medicine under Fernel, and Anatomy with none other than Vesalius. While in Paris he wrote on syrups and astrology



MICHAEL SERVETUS

and fought extensively with the Dean of Medicine. Some peace came at last to this restless man in Lyon, where he managed to practice Medicine for 12 years.

He went to Italy in 1529 as a secretary to a court preacher and watched the coronation of Charles V by Pope Clement VII and accompanied the Royal train back to Augsburg for the opening of the Diet in June, 1530. His first hand experience of the papacy in Italy affected him in much the same way as the young Luther. While engaged in practice he secretly wrote the Book "Christianismi Restitutio", which made his name immortal, but also became the cause of his final arrest and betrayal.

This astonishing book, which has no author's name, starts on a remarkable note. "The whole apostolic church is summoned to the threshold." Wedged between a ferocious theological tour de force we read in Chapter V, p. 170 the following, "the vital spirit is then transfused from the left ventricle of the heart into the arteries of the whole body." "The passage of the blood from the right to the left ventricle does not take place through the median partition of the ventricle as is generally supposed; but by an elaborate device the refined blood is driven from the right ventricle of the heart over a long course through the lungs, where it is prepared and made yellow and thence passes from the arterial vein (pulmonary artery) into the venous artery (pulmonary vein)."

"In order to understand how this communication takes place through the lungs, we must learn the connections, the multitude of unions of the pulmonary artery with the pulmonary veins in these lungs. This view of the manner of communication is confirmed by the caliber of the Arterial Vein (pulmonary artery) which would not be so large nor carry such an amount of blood to the lung if nutrition alone was to be provided for, especially since in the embryo the lung is nourished through other channels, and this blood does not reach it. It must then be for another purpose that

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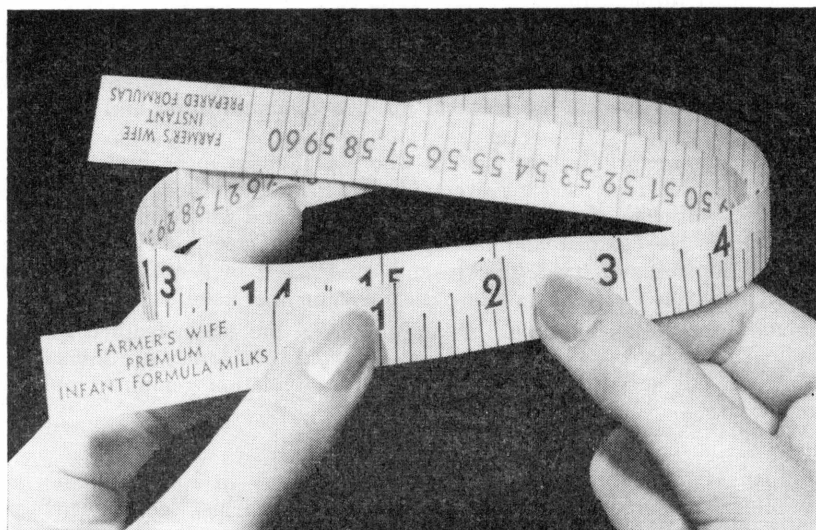
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the blood is sent in such abundance from the heart to the lungs immediately after birth; moreover, it is not simply air, but air mixed with blood which is sent from the lungs to the heart through the pulmonary vein, so that the mixture takes place in the lungs. The yellow color is given to the spirituous (arterial) blood by the lungs and not by the heart. In the left ventricle, there is no place large enough for so copious a mixture, nor is that elaboration sufficient for the bright tint. Moreover, the middle wall, since it lacks orifice, is not suitable for this communication and elaboration."⁹ This amidst theology.

A copy was sent to Calvin of Geneva who was thought to be sympathetic to this rebellious spirit. No reply was received. Calvin placed the book at the disposal of the inquisition. Michael Servetus was tracked down and imprisoned by the inquisition in France. He escaped and managed to get to Geneva. He was recognized and promptly imprisoned, tried quickly and condemned to death. On October 27, 1555 at Champel, on Lake Geneva he was burnt on the stake.

Servetus on the stake uttered, "Because I loved the truth, loathed lies, I must die in exile." His book was burnt and only about five volumes are known to have escaped. Thus, his discovery of the pulmonary circulation remained unknown to his contemporaries.

VESALIUS.

Vesalius, became professor of Anatomy and Surgery in 1537 at Padua and restarted public dissections. Within five years he published his, "de Humani Corporis Fabrica", the basis of all modern Anatomy.

Vesalius' ideas concerning circulatory physiology are of considerable interest. In the "Fabrica" he subscribed to the teachings of Galen but there was one point about which he was uncertain: the permeability of the inter-ventricular septum. In the first edition of his book he wondered at the handiwork of the Almighty who permitted the blood to sweat through the openings which were invisible to the human eye, but he nevertheless agreed with Galen that "blood soaks plentifully through the septum from the right ventricle to the left."

Two young men by the name Realdo Columbus of Cremona and his friend Valverde worked with Vesalius at that time. They began to cast doubt on the observations of Galen which Vesalius was at first perpetuating in his book.¹² Occasionally Columbo substituted for Vesalius in public dissections. As a result of this, jealousy entered into their relationship. So much so that in 1546 Vesalius spoke of Columbo as follows, "an uneducated man, a half-knower who learned something from me about anatomy, has seen me several times search in vain for this duct in public dissections and has had my preparations before his eyes. During one dissection which took place in my absence, he postulated that a vein unknown to me could be demonstrated"¹¹ This was a vein between the stomach and spleen, which is not of importance to the present discussion. However, the atmosphere at Padua became unhealthy. Vesalius left Padua and Columbo and Valverde became demonstrators in anatomy.

VALVERDE.

Valverde was probably the shrewdest of observers, as well as the most outspoken. He said, "the partition, like the rest of the substance of the heart which the left ventricle forms is hard, thick and strong. No blood passes from one ventricle to the other as Vesalius appears to have written of it until now."¹¹ He was even more outspoken in respect of the teachings of Galen and this is what he said: "Concerning Galen of Pergamum who has been until now the most learned and most eloquent man in his art, Galen, desirous of teaching everyone, and believing there was very little difference between the fashion of man and that of the ape, wrote an anatomy of our body, using as an example, the ape. And because there were in that age few men

who had written about this, and they of little reputations, and because he was most excellent in other fields of Medicine, everyone readily believed him, no-one being able to prove the contrary since dissection of man was forbidden. Galen's reputation endured until our time. No-one having ever dared to contradict him in anything until Andreas Vesalius began to open the eyes of many showing that one ought not to lend faith to all that which is found in books as do many who wish to appear wiser than they really are Furthermore, since all the books in ancient times were written by hand, besides the fact that many errors were made in copying them, it often happened that someone reading the book noted something in the margin and from then on those who were copying not knowing that they were annotations, presented the marginal notes as the works of the author. In this and in many other ways, as each one can consider for himself, I believe that the books of the ancients are incorrect in such a way that no man of good sense can nor should give much credence to them without first investigating facts which lazy teachers pass on to him. They should not seek to defend their ignorance with the authority of this or that author, especially in those things in which one can touch the contrary with one's own hand. If we were to consider anatomy of which we now speak, we shall readily find many things therein which demonstrate clearly that those who wish to defend Galen, saying that he wrote the anatomy of man, do that author a great injustice, making him a liar at every turn and further show that they have never seen any man dissected."¹

REALDO COLUMBUS

Columbo went to Pisa, and there described quite clearly the pulmonary circulation. He stated, "that most observers have been in great error, for the blood is carried through the pulmonary artery to the lung and is there attenuated and thence carried

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WILLIAM HARVEY

along with air through the pulmonary vein to the left ventricle of the heart." "Hitherto no-one has noticed this or left it in writing"¹. This is, of course, untrue as we know from the work of Ibn-an-Nafis and Michael Servetus. There is some evidence to suggest that the writings of Ibn-an-Nafis might have been known in the areas adjacent to Venice. According to the thesis of a Yale student, ¹ Padua might have known something of Ibn-an-Nafis.

WILLIAM HARVEY.

Into this atmosphere of doubt and speculation at Padua steps the serene and gifted William Harvey. I do not wish here to evaluate the contributions which Harvey has made in the final discovery of the circulation. His writings are well known and every student of physiology has seen the demonstrations which he gave concerning the structure of the veins, position of their valves in relation to blood flow and his careful analysis of cardiac systole in the snake.

Harvey almost uncovered the total secret of the circulation but remained in ignorance as to the terminal branches of capillaries both in the lungs and periphery. This, of course, required the microscope and with its invention Marcello Malpighi finally closed our circle. Not until Antoine Laurent Lavoisier, however, was it understood that the "vital spirit" which came into contact with the blood in the pulmonary capillaries was not "phlogiston, pneuma", or some other mystical substance, but oxygen. Lavoisier demonstrated this clearly. In May 1777 Lavoisier communicated to the Academy of Sciences the results of accurate and convincing observations which demonstrated the complete analogy between respiration in animals and chemical combustion. He wrote, "the eminently respirable air is absorbed during inspiration, and the lung gives off the chalky aeriform acid, in equal volume." In the same report he suggested that the red color of the blood was due to the combination of oxygen with "animal liquor". Unfortunately, his brilliant life of incomparable scientific output was cut short by the French Revolution. At the age of 50, Coufinhal, the president of a Revolutionary Tribunal, sent him to his death on the guillotine stating that "the Republic had no need for scientists".²

The secret of the rock appears to be revealed, but according to Plato the challenge is still there. Although each man has left his mark, let us close with Harvey:

"from hence the way being thus pervious, others trusting to more pregnant wits, may take occasion to do better and search further".⁵

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