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THE PULMONARY CIRCULATION—BEFORE AND AFTER HARVEY*

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"What a zigzag path, how unlike a straight line is man's progress in search of Truth."—MICHAEL FOSTER.

The Views of an Arabian Teacher

The history of the discovery of the pulmonary circulation has been the subject of much controversy, and it is a strange paradox that, though it was the part of the vascular system in which the idea of a forward motion and not an ebb and flow of the blood stream was first conceived, it was the last to be studied systematically. The Greek philosophers were handicapped by the religious and sentimental objections to human dissection. Wiberg suggests that the early Greeks knew of the circulation, and quotes a passage from one of the Hippocratic writings which would bear that interpretation. It was in Alexandria, under the Ptolemies in the third century B.C., that a flourishing though short-lived school of medicine was established where the study of dead human bodies was permitted and even encouraged, with the result that real advances were made in anatomy; and here Herophilus first gave the name of *artery-like vein* to the pulmonary artery and *vein-like artery* to the pulmonary vein, and these descriptions persisted until Harvey's time. Erasistratus (about 290 B.C.) came very near to discovering the circulation, but unfortunately he thought the arteries contained air.

Galen, whom Harvey described as "a divine man, father of physicians," was the most original and profound of all the ancient medical and biological philosophers. He proved that the arteries contained blood, but thought that the passage of the blood to the tissues, including the lungs, was by ebb and flow, and that there was a communication between the two ventricles through invisible pores. He chafed at his inability to study human anatomy, and advised his students to collect exposed bones from graveyards if opportunity offered.

There is grim irony in the fact that the same embargo on human dissection later enforced by the great religions—the Christian and Mohammedan—hindered progress for centuries. Bayon (1938, 1939a, 1939b) in his exhaustive and profound studies entitled *William Harvey, Physician and Biologist: His Precursors, Opponents, and Successors*, to which I am most deeply indebted, as I have no doubt will be all future students of Harvey's work, writes, "It is also remarkable that while in the Middle Ages life was cheap, and there was little compunction in burning, quartering, or torturing the living, there was a definite horror about dissecting the dead."

It has been generally supposed that Servetus was the first to describe and publish the conception of the pulmonary passage, but it appears he was anticipated by an Arabian teacher by no less than three centuries. The history of this dramatic historical discovery is worth noting.

In 1924 an Egyptian medical student, Mohyi-el-Din-el-Tatawi, from Tanta in Egypt, presented as his thesis for the degree of Doctor of Medicine at the Albert Ludwig University of Freiburg-in-Breisgau an account of the views of an Arab physician, Al Qurishi (generally known as Ibn-an-Nafis). About two years previously he had found among the MSS. of the Prussian State Library in Berlin a copy of Ibn-an-Nafis's commentary on the Canon of Avicenna. This College is fortunate in having had as a recent benefactor the late Professor Dobbin, for he has given us a copy (modern but none the less of great value) of the Arabian MSS. of Ibn-an-Nafis, and also some special literature relating to this interesting and notable page in the history of medicine, together with other gifts which will enrich our College Library.

Although at present we know but little of Ibn-an-Nafis, it is clear that he was a man of remarkable ability. There is a most striking parallelism between him and Servetus. He is said to have been not only a great physician but also an authority on language, philosophy, Moslem canon law, and traditions. Michael Foster described Servetus as "in turn jurist, astronomer, meteorologist, and doctor, but above all things a theologian." Like Servetus, Ibn-an-Nafis was a heretic, and like him would now be called a Unitarian. An interesting study of Ibn-an-Nafis and his views has been published by Haddad and Khairallah (1936). They give a translation into English of the passages relating to the pulmonary circulation as follows:

"And we say, and God is the All-knowing, whereas, one of the functions of the heart is the creation of the spirit from very thin blood strongly miscible with air, and air, so it is necessary to make in the heart, very thin blood to make possible the creation of the spirit from that mixture. The place where the spirit is created is in the left cavity of the two cavities of the heart. Therefore, it is necessary in the heart of man and his like—of those who have lungs—to have another cavity where the blood is thinned to become fit for mixing with the air. For if the air is mixed with the blood while it is still thick, it would not make a homogeneous mixture. This cavity (where the blood is thinned) is the right cavity of the two cavities of the heart. If the blood is thinned in this cavity it must of necessity pass to the left

* The Harveian Oration (abridged), delivered to the Royal College of Physicians of London on December 15, 1939.

cavity where the spirit is created. But between these two cavities there is no passage as that part of the heart is closed and has no apparent openings as some believed and no non-apparent opening fit for the passage of this blood as Galen believed. The pores of the heart there are obliterated and its body is thick, and there is no doubt that the blood when thinned passes in the vena arteriosa to reach the left cavity of the two cavities of the heart; having mixed with the air and become fit for the creation of the spirit. What is left of this mixture, less attenuated, the lung uses for its own nourishment. This is the reason why the vena arteriosa is made of thick walls and of two coats, so that what passes through its pores be very thin, and the arteria venosa thin and of one coat."

"The need of the lung for the vena arteriosa is to transport to it the blood which has been thinned and warmed in the heart, so that what seeps through the pores of the branches of this vessel into the alveoli of the lung may mix with what there is of air therein and combine with it, the resultant composite becoming fit to be spirit when this mixing takes place in the left cavity of the heart. The mixture is carried to the left cavity by the arteria venosa."

It should again be remembered that dissection was forbidden, so that Arabian philosophers, while making great advances in the physical, chemical, and mathematical sciences, contributed little to anatomy, physiology, or pathology. This makes the original conception of Ibn-an-Nafis all the more notable. At the same time he gives covert hints that he has performed dissection, though he states that he has *not* done so because of the authority of the law and an inherent compassion. He avers that he has relied on the words of those who had preceded him, especially the honourable Galen. Sarton (1931) in referring to Ibn-an-Nafis states that:

"In five different places does he state in unmistakable terms that the blood cannot pass from the right to the left ventricle through invisible pores in the septum, but must pass through the 'veinous artery' to the lungs, be mingled there with air, pass through the arterious vein into the left ventricle, and there form the 'vital spirit.'"

It is remarkable that these views of Ibn-an-Nafis were neglected and forgotten, but this is probably due to their heretical and original character.

The debt of Western medicine to the Arabian conquest of Southern Europe in the eighth century is nowadays almost forgotten. The Arabs endeavoured to acquire and adapt the scientific and philosophical knowledge of the Greeks and, to a less extent, that of the Romans. Until the revival of learning by the humanists the views of Plato, Aristotle, and Galen were only studied through translations, often garbled and inaccurate, from the Arabic versions. We can understand the avidity with which the scholars welcomed the originals after the shadows their predecessors had had to be content with. The part played by Linacre and Caius in the return to the original Greek texts and their accurate translation into Latin has been eloquently stressed by two previous Harveian orators, the late Dr. J. F. Payne and Dr. Arnold Chaplin.

Servetus on the Pulmonary Circulation

So far as is at present known no further conceptions of the pulmonary circulation appear until Servetus's well-known description in the *Christianismi Restitutio*. The history of Servetus is one of almost undiluted tragedy, save for the few years in which he practised medicine. Hunted and wandering in his early life, condemned to a cruel death, traduced, and even forgotten until one of the three surviving copies of his banned book was studied by W. Wotton in 1694, he has even been belittled and neglected by many modern writers. He was a fellow student at Paris with Vesalius, whom he succeeded as

prosecutor. In 1539 Guinther wrote of him that he was distinguished for his general culture and his skill in dissection, and described him as scarcely second to any in his knowledge of Galenical doctrine.

In 1545, or at latest early in 1546, he sent a manuscript copy of his theological opinions to Calvin, and stated that he wished to visit Geneva. It is assumed that this contained the note on the "pulmonal passage." A manuscript in Paris, which may be the original or a genuine copy, is stated to include this (Mackall). Servetus had his book secretly printed in Vienne early in 1553, and it is known that 1,000 copies were pulled. No name is printed on the title-page, but at the end the initials M. S. V. appear. So far as is known only two complete copies have survived.

Servetus's description of the pulmonary circulation is given in Book V of *Christianismi Restitutio*, dealing with the Trinity. I may here quote Michael Foster's (1901) translation of the essential passages:

"In order, however, that we may understand how the blood is the very life, we must first learn the generation in substance of the vital spirit itself which is composed and nourished out of the inspired air and very subtle blood. The vital spirit has its origin in the left ventricle of the heart, the lungs especially helping towards its perfection; it is a thin spirit, elaborated by the power of heat, of a yellow (light) colour, of a fiery potency so that it is as it were a vapour shining out of the purer blood containing the substance of water, of air, and of fire. It is generated through the commingling which is effected in the lungs of the inspired air with the elaborated subtle blood communicated from the right ventricle to the left. That communication does not, however, as is generally believed, take place through the median wall (septum) of the heart, but by a signal artifice the subtle blood is driven by a long passage through the lungs. It is prepared by the lungs, is rendered yellow (light) and from the artery-like vein is poured into the vein-like artery. Then in the vein-like artery it is mixed with the inspired air, and by expiration is cleansed from its fumes. And so at length it is drawn in, a complete mixture, by the left ventricle through the Diastole, stuff fit to become the vital spirit."

"That the communication and preparation does take place in this way through the lungs is shown by the manifold conjunction and communication of the artery-like vein with the vein-like artery."

"This view is confirmed by the conspicuous size of the artery-like vein, which would not have been made so large and so stout, and would not discharge from the heart itself such a power of very pure blood into the lungs for the mere purpose of nourishing these organs. Nor would the heart serve the lungs in this manner, especially since, at an earlier date in the embryo on account of the little membranes of the heart, the lungs themselves are up to the hour of birth nourished from other sources, as Galen teaches."

We do not know by what means Servetus arrived at these remarkable conclusions. It has even been suggested that he knew Arabic, and that he revived the views of Ibn-an-Nafis. A translation was published in Venice in 1547 by Alpago, who was afterwards professor of medicine at Padua. Other detractors of Servetus have suggested that he derived his opinions from Realdus Columbus. I can see no reason to minimize Servetus's position as a genuine and notable precursor of Harvey. There can be little doubt that Harvey was not aware of his opinions, though he knew of those of Columbus. Servetus was no doubt an arch-heretic in the times in which he lived, but should now be accepted as a pioneer and a martyr.

Stepping-stones to "De Motu"

Bayon emphasizes the fact that the anatomical researches of the sixteenth century, particularly those of Vesalius and Columbus, paved the way or provided the "stepping-stones" for Harvey's demonstration of the circulation.

Leonardo da Vinci, who with others of the great Italian artists gave impetus to the study of anatomy, proved by experiment that the heart was muscular and was not passive. He also demonstrated the efficiency of the tricuspid valve. He described the moderator band and attempted to estimate the output of the heart. The pioneer of anatomical study is, however, Vesalius, whose life history and achievements form one of the most fascinating stories in the history of medicine. In view of the destruction of his notes it must always be a matter of speculation why it was that, having disproved the Galenic views on the structure of the heart, he did not advance to overthrow Galen's theories as to its function. The immediate successor of Vesalius for a brief period was his pupil and assistant Realduus Columbus. There is no doubt that Columbus had a clear conception of the pulmonary circulation and that he brought forward evidence, clinical and experimental as well as anatomical, in support of his views. He pointed out, sixty-nine years before Harvey's *De Motu* was published, that blood coughed up in disease was "spirituous" or arterial, and that the pulmonary vein in animals contained red arterial blood and not fuliginous or sooty matter as some supposed. He actually described its contents as blood mixed with air from the lungs. His statement of his views is characteristically egotistical and bombastic; but it is clear and concise, and I now quote Michael Foster's translation:

"Two cavities, that is two ventricles, are present in the heart, not three as Aristotle thought. Of these one is on the right side, the other on the left. The right is much larger than the left. The right contains the natural blood, but the left the vital blood. It is very interesting to observe that the substance of the heart surrounding the right ventricle is very thin, but that on the left side very thick; and this is so arranged on the one hand in order to keep up the balance and on the other to prevent the vital blood which is exceedingly thin from transuding out of the heart. Between these ventricles there is placed the septum through which almost all authors think there is a way open from the right to the left ventricle; and according to them the blood is in the transit rendered thin by the generation of the vital spirits in order that the passage may take place more easily. But these make a great mistake; for the blood is carried by the artery-like vein to the lung and being there made thin is brought back thence together with air by the vein-like artery to the left ventricle of the heart. This fact no one has hitherto observed or recorded in writing; yet it may be most readily observed by anyone."

He was the first to recognize that cardiac systole and arterial expansion were synchronous.

Cesalpinus, another anatomist and a man of wide culture, also seems to have recognized the pulmonary circulation and even to have conceived the possibility of a systemic movement of the blood in a sense different from that of Galen. He has even been acclaimed by some as the actual discoverer of the circulation, a claim that was disproved by Sir Edward Sieveking in his *Harveian Oration* of 1877. Recently Bayon has also dealt destructively with claims put forward as to the priority of Cesalpinus. In 1571 he published his *Peripatetic Questions*, in which he notes the pumping character of the heart's action in forcing the contents of the left ventricle into the aorta and that of the right into the pulmonary artery. In his second work, *Medical Questions*, published in 1593, he reaffirms this and writes: "Thus there is a sort of perpetual movement from the vena cava through the heart and lungs into the aorta artery—as I have explained in my *Peripatetic Questions*." Unfortunately the view of Cesalpinus attracted little notice, and he is not mentioned by Harvey.

But it is still more to be wondered at that Fabricius ab Aquapendente, the greatest anatomist of his time, should have returned, if not to the anatomy of Galen in regard to the heart, certainly to his physiology of the heart and lungs. Harvey used with some modification one of the illustrations from the great work on the valves in the veins *De Venarum Ostiis*, which was published in 1603, as the only illustration to the *De Motu Cordis*. He refers to Fabricius several times, and affectionately describes him as "a most skilful anatomist and venerable old man." Fabricius wrote a book, *De Respiratione et eius instrumentis*, dealing with the general and muscular mechanisms of respiration. He still applied the name of rough artery to the trachea, but believed that the vein-like artery (pulmonary vein) exists to convey air to the heart.

Harvey : Pioneer of the Experimental Method

Such, then, was the confused state of opinion in regard to the functions of the heart and lungs when Harvey returned to England in 1602, after his wander-years at Padua. It is established that the work of Fabricius influenced Harvey towards his great discovery, as the well-known statement of Robert Boyle in 1688 proves. The reason he will always be revered as one of the greatest of men of science is that he pioneered the experimental method in medicine. He progressed from the study of the static art of anatomy to the kinetics of function, and left as his testament the advice "to search and study out the secrets of Nature by experiment."

There can be no doubt that Harvey was puzzled at the implications of his great discovery, especially as to the reason why the same amount of blood should be sent to the lungs at each systole as was sent to the whole of the rest of the body. It is so obviously much greater than the nutritional needs of the lung texture itself; and let us note that Harvey did not know of the additional supply from the bronchial arteries, which were first demonstrated by Ruysch in 1665 by injection methods.

Harvey dissected and studied more than eighty different kinds of animals, and he mentions twice that animals without lungs have no right ventricle, and on the second occasion he states: "It may be said that the right ventricle is made for the sake of the lungs, and for the transmission of blood through them, not for their nutrition."

Function of the Lungs : Harvey's Speculations

The problems of respiration and the changes induced by it in the blood obviously were of great interest to him, and on two occasions he promises to return to these subjects and to investigate them. In *De Motu* he writes that he has made a vast number of observations to explain the functions of the lung: "It must be either because the larger and more perfect animals are warmer and when adult their heat greater—ignited, as I might say, and requiring to be damped or mitigated; therefore it may be that the blood is sent through the lungs, that it may be tempered by the air that is inspired, and prevented from boiling up, and so becoming extinguished, or something else of the sort." This is only very slightly modified Galen physiology, and in the same chapter he adds: "I shall leave such topics till I can more conveniently set them forth in a treatise apart." In his *Praelectiones* he says: "Life and respiration are convertible terms, for there is no life without breathing, and no breathing without life." One of his illuminating marginal notes reads: "Why and how air is needed by animals

which breathe, and also air is necessary to a candle and to fire—see W. H.”

It would seem that Harvey had come near to the real explanation, for which science had to wait till the chemists, whom Harvey is said by Aubrey to have had in small esteem, had discovered oxygen. It is clear that as late as 1651 he was still working at this problem, for in an essay on parturition he states:

“Whoso shall attend carefully to these things and consider more closely the nature of air will, I think, readily grant that air is given to animals neither for cooling nor as nutriment. Thus much merely by the way, on the subject of respiration. Perhaps I shall treat of it more fully in its proper place. Surely a more knotty subject could hardly be found, as the arguments on both sides are evenly balanced.”

Another matter which exercised the logical and inquiring mind of Harvey was the nature of the communication between the arteries and veins. One of the most interesting of his letters is that which he sent to P. M. Slegel dated March 26, 1651, describing his perfusion experiments on the heart and lungs of a man who had been hanged, conclusively demonstrating that the blood from the pulmonary artery reached the left ventricle, and that there was no direct communication between the two ventricles. He adds almost exultingly: “You may try this experiment as often as you please; the result you will find to be as I have stated it.”

Malpighi's Demonstration

Ten years after these speculations of Harvey were written, and but four years after his death, the capillaries were discovered and the actual movements of the blood seen in those of the lungs by Malpighi, who was born in the year that *De Motu* was published. His discoveries and his views on the functions of the lungs are propounded in his work *De Pulmonibus*, which is in the form of two long letters written to his teacher Borelli, and dated Bologna, 1661. There is an almost naïve sense of wonder and exaltation as he describes the blood flowing in different directions in the arteries and the veins of the lung of a frog, as seen through a compound microscope. He adds: “so that the circulation of the blood is clearly exposed.” He proceeds to describe the network of capillaries, and then explains: “It is clear to sense that the blood flows away through the tortuous vessels, that it is not poured into spaces, but always works through tubules, and is dispersed by the multiplex winding of the vessels.” In regard to the lungs he writes:

“Concerning the use of the lungs I know that many views are held from the ancients onwards, and about them there is very much dispute—especially about the cooling which is taken to be the principal purpose when it strives with the imagined excessive heat of the heart, which may require evaporation; wherefore these things have made me diligently inquisitive in the investigation of another purpose, and from these things which I subjoin I can believe that the lungs are made by Nature for mixing the mass of blood.”

The more these two letters are studied the more the genius of Malpighi becomes apparent. In writing of the foetus he suggests that in pregnant women the placenta acts vicariously for the lungs. He also suggests that “the lungs are made by Nature as if for a storehouse of blood, so that it may constantly in turns give forth blood to the heart, which thence driven into the whole body by continual circulation, may impart life and motion to everything.” This seems to be the first suggestion of “blood depots” in the literature.

What must give to most of us a pang of regret is that Harvey was so near to the ocular demonstration of the

link between the arteries and the veins. Microscopes of primitive form were available in his actual lifetime.

In 1674 Leeuwenhoek described the red corpuscles, and noted that they were circular in mammals but oval in birds, frogs, and fish. He also pointed out that the red colour of blood was due to these corpuscles. It is now known that they had actually been observed by another Dutchman, Johannes Swammerdam of Amsterdam, in 1658, one year after Harvey's death.

Light from the Physico-chemical Side

The most important researches in regard to the functions of the lungs and the objects of the pulmonary circulation came from the physico-chemical side, and stand largely to the credit of British observers. Boyle by his air-pump experiments in 1666 showed that air was essential to life. In the next year Hooke proved that it was the supply of air to the blood which was the main object of respiration. Lower, in 1669, demonstrated that the difference between arterial and venous blood was the change of colour, that this was due to the air in the lungs, and that the change occurred in the lungs and not in the heart. In 1668 Mayow recognized that only part of the air, his “spiritus nitro-aereus,” was necessary to life. Black in 1757 rediscovered the “gas Sylvestre” of van Helmont, which he called “fixed air,” now known as carbon dioxide. Priestley, another persecuted Unitarian, in 1774 rediscovered oxygen, which he called “dephlogisticated air.”

The position was eventually clarified by the tragic Lavoisier, himself another martyr of science, guillotined by the French Convention in 1794. He recognized the true nature of Priestley's “dephlogisticated air” in 1777, and called it “acidifying principle or oxygen.” He demonstrated for the first time that in the process of respiration the air breathed lost oxygen and gained “fixed air” of Black, and, further, that the latter was a compound of carbon and oxygen. It was left to Spallanzani to discover tissue respiration and to Magnus to confirm and establish its nature.

The study of the physics of the circulation languished after Borelli until Stephen Hales (1733), the indefatigable clergyman-physiologist of Teddington, published his researches. In volume ii of *Statical Essays* he records dramatically his experiments upon the blood pressure in the horse, sheep, and dog. He measured the rate of flow in the capillaries of the lungs of a frog by direct observation. He suggested that the blood must traverse the lungs with “vastly greater rapidity than through other parts of the body.” Although he was not able to measure pulmonary blood pressure directly, he deduced that the thinner walls of the right ventricle indicated that that ventricle had less work to do to force the blood through the lungs than the left ventricle had to maintain the systemic circulation.

There was little advance till J. Hope (1839), from 1828 to 1838, studied the physics of the failing heart, and described the symptoms and signs of cardiac insufficiency. He differentiated the effects of failure of the right ventricle from those of the left. His descriptions have recently been shown to be remarkably accurate, and, though long neglected, his work is now one of the landmarks in the study of the physics of the circulation.

A great advance was made when Poiseuille in 1828 introduced the U-shaped mercurial manometer, and thus simplified the observation of blood pressure. In 1847 Ludwig, one of the greatest, most stimulating, and most modest of teachers and investigators, added the float, and made the blood record its pressure. He harnessed living

processes to write their own story and taught his pupils how to interpret the records. His work laid the foundations of modern methods of experimental study of the problems of the circulation.

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(To be concluded)

BACTERIAL ENDOCARDITIS: POSSIBILITY OF CURE BY SULPHONAMIDES

WITH REPORT OF A CASE

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The endocardium is one of the latest territories to be assailed in the chemotherapeutic advance of the last few years. It was inevitable, however, that drugs which had been used with such marked success in bacterial invasion of other tissues should be applied to the treatment of the corresponding infection of the endocardium. The reports so far available are on the whole encouraging (Ellis, 1938; Whitby, 1938a, 1938b; Manson-Bahr, 1938; Major and Leger, 1938).

In attempting to assess the possible value of any chemical agent in the treatment of this malady certain factors have to be constantly borne in mind. (1) The difficulty that exists in certain cases in establishing the diagnosis. (2) The possibility of spontaneous recovery. (3) The anatomical peculiarities of the site of infection and of the lesion, which render the organisms difficult to reach by therapeutic agents.

The Diagnostic Difficulty

The cardinal signs of bacterial endocarditis are usually given under four heads (Horder, 1920, 1926): (a) multiple arterial embolism; (b) evidence of existence of endocarditis; (c) presence of bacteria in the blood stream; (d) fever. It is safe to say, however, that the majority of cases run their course without providing the evidence mentioned under all of these four heads, and even when present that evidence may be scanty or intermittent. Thus arterial embolism may manifest itself only by the presence of a few petechiae in the region of the clavicle or a few red blood cells in the urine at irregular intervals; or in those not infrequent cases in which the right side of the heart alone is involved the case may proceed to a fatal issue with no evidence of embolism at all. Signs of endocarditis may be scanty or completely absent when, as in one of my cases, the vegetations are implanted on the mural endocardium. All observers now agree that many cases in which repeated attempts to culture organisms from the blood are unsuccessful proceed to a fatal termination (Cotton, 1920; Lewis and Grant, 1923; Grant, 1924; Libman, 1913, 1920). This is especially true of the type known as endocarditis lenta, in which the organism responsible is a non-haemolytic streptococcus.

And, finally, in many cases fever is a late symptom (Starling, 1920), and apyrexial periods of several weeks' duration may complicate the clinical picture even at a late stage of the illness (Libman, 1913, 1920).

It is clear, then, that the diagnosis often presents difficulties, and, in fact, in some cases in which recovery has been claimed the diagnosis has not been established beyond doubt. The greatest difficulty arises in those cases in which the blood culture is persistently negative and in consequence the identity of the invading organism must be largely a matter of surmise. This I consider an important point, as it seems to me that these are just the cases which give most promise of success in treatment. Further reference is made to it below.

Spontaneous Recovery

Although such a termination is extremely rare there would appear to be no doubt that recovery has occasionally taken place. Most cases recorded are cases of endocarditis lenta, and this is not to be wondered at when it is remembered that non-haemolytic streptococci are found as normal inhabitants of the alimentary and upper respiratory tracts. Indeed, one of the problems of this disease is to know why this relatively harmless organism should assume a virulent form at all. In a search of the literature we have found records of five cases reported to have recovered from bacterial endocarditis before the advent of the sulphonamide group of drugs. Some details of these are appended in a table (see next page) together with four cases given sulphonamide therapy. One case in which surgical intervention was successful is also recorded.

A glance at the table shows one striking feature in both groups—namely, the rarity of a positive blood culture. This is true not only of the cases in which there might be some doubt as to the diagnosis but also in cases such as that now recorded, in which the evidence is practically such as to establish the diagnosis with certainty. In only two cases was a positive blood culture obtained. That of Davidson (1934)—a case of *B. coli* endocarditis—must be regarded as a rarity; while the case in the second group—that of Major and Leger (1938)—ended in death three weeks after the temperature had settled to normal, and the wisdom of its inclusion in the list is doubtful.

Anatomical Peculiarities of the Lesion

One of the problems in the pathology of bacterial endocarditis is the means by which the organisms obtain a foothold on the endocardium. On the one hand it has been held that they gain access to the tissues by being arrested in the coronary capillaries (Wadsworth, 1919), and on the other that they implant themselves directly on the surface of the valve (Keefer, 1937; Swift and Kinsella, 1917; Miller and Branch, 1923; Leary, 1932). This latter view presupposes the formation of small platelet thrombi on a previously damaged valve, such thrombi offering passing organisms a foothold and nidus for their establishment (Grant, Wood, and Jones, 1927-9). In either case the resulting vegetation is found to contain organisms aggregated in quite large masses near the periphery of the vegetations (Wright, 1925). The therapeutic problem would appear to be not simply that of controlling the septicaemia but that of reaching the depth of these foci.

The absence of bacteria from the blood in many cases of bacterial endocarditis has led to the further observation that the antibody titre is often at a high level, even in the septicaemic cases (Wright, 1925; Kinsella and Garcia, 1925-6). Wright mentions a case with septicaemia of fifty