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THE CONSUMMATION OF WILLIAM HARVEY*

BY

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"When I finally reckon up the number of questions that can be settled, doubts resolved, and obscure places made clear, given this illuminating truth, in every part of medicine . . . I find a field of such vast extent that, if I explored it fully in all directions, not only would this treatise of mine turn, contrary to my plan, into a full-sized book but the rest of my life would perhaps not suffice for my writing of it."¹ The quotation is from Kenneth Franklin's translation of *De motu cordis*, and I take this opportunity to add to the tributes he has already received the simple statement that by his work Franklin has left this College for ever in his debt.

As examples of questions that Harvey considered might be settled if his belief in the circulation of the blood proved to be well founded he chose some common problems of clinical practice—the things with which all physicians were familiar in contagion, poisoned wounds, the bites of serpents, and in venereal disease. In venereal disease he pointed out that the genitals were at times unharmed and that the first symptoms might be headache or pain in the shoulders or manifestations in other parts of the body. After the bite of a mad dog he had known fever and other dread symptoms to occur when the wound had healed. If the idea of the circulation of the blood were accepted was it not probable that the contamination first imprinted on a part reached the heart in the returning blood and thereafter polluted the whole body? And did not the same idea provide a satisfactory explanation of the observed fact that some medicaments applied to the skin had effects similar to those following their administration by the mouth? Surely it was not unreasonable to suppose that some of the substances placed on the surface were absorbed by the veins, carried in the blood to the heart, and so distributed throughout the body.

A Seventeenth-century Riddle

And yet, as our Harveian Librarian observed in his Linacre Lecture last year,² it remains a riddle of the seventeenth century why so seminal a discovery as the circulation of the blood remained fruitless for so long a time. As Sir Charles Dodds said, even Harvey in clinical methods and treatment reflected nothing unorthodox from the Galenical point of view, and this seems particularly strange when we remember that he invoked the circulation of the blood to explain the clinical phenomena I have just mentioned. If the fetters of traditional belief with no basis but speculation were

too strong for so acute a mind it is not surprising that many others did not escape them in succeeding generations.

My purpose on this occasion is to recall the slow and faltering progress during the two centuries that followed the publication of *De motu cordis* until, in the nineteenth century, the consummation of William Harvey is reached, the true value of his work recognized, and the measure of achievement assessed.

In his oration of 1935 Sir Henry Dale³ reminded us that in addition to *De motu* and *De generatione* Harvey contemplated a treatise on "The causes, uses and organs of respiration." Whether he ever wrote it we shall never know, for on the outbreak of civil war in 1642 his rooms in Whitehall were looted and many of his papers were destroyed. In the seventeenth century accepted doctrine about respiration derived from Aristotle, who believed its primary function, like that of pulsation, was to mitigate heat engendered in the heart. In his introduction to *De motu* Harvey quotes a passage from a new book by Fabrizio d'Acquapendente which runs, "since the pulsation of the heart and arteries is inadequate for the fanning and cooling of the blood nature has fashioned the lungs round the heart," but he is mainly concerned at this stage to make the point that what the earlier authors had written about systole and diastole of the heart and arteries had been penned with an eye upon the lungs.

Harvey returns to the problem later when he asserts that "larger animals . . . can reasonably be described as overheated and hard put to it to get rid of the excess. So the hot blood is carried to and through the lungs to be tempered by the inspired air and to be freed from bubbling to excess." To those who pointed out that anatomical studies had revealed no path by which the blood could pass through the lungs he replied that the liver was a much denser structure than the lung and no one doubted that large quantities of fluid from the alimentary tract could pass through it. He suggested also that judging by their naked-eye appearance lungs might well act as sponges sucking in the blood when they expanded with inspiration and squeezing it out as they contracted, and he drew an analogy between the formation of streams and springs in porous earth and the collection of blood in the pulmonary vein after it had passed through the porosities of the lungs.

Although he could not trace the precise path of the pulmonary circulation and, as he wrote to Jean Riolan, he had "expended not a little of both time and effort in anastomosis exploring but never succeeded in finding vessels namely arteries with veins mutually connecting

*Harveian Oration before the Royal College of Physicians of London on October 18, 1961.

by inosculation,"⁴ Harvey remained convinced that the blood must pass through the lungs from the right ventricle to the left.

The Work of Servetus

He was not the first to express that opinion. Many years earlier—in 1543—Servetus had come to the same conclusion. In his book *Christianismi Restitutio*⁵ there is this remarkable passage: "It [the vital spirit] is generated through the commingling which is effected in the lungs of the inspired air with the . . . 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 . . . the blood is driven by a long passage through the lungs." Unhappily Servetus, after a dispute with Calvin about what my friend Lancelot Hogben has termed a matter of celestial arithmetic, was burned at the stake, and little evidence remains for final judgment on the claims put forward on his behalf as the precursor of Harvey in the problem of the circulation. Those claims do not appear to me to be well founded. In the first place Servetus never referred to the possibility of a systemic circulation, and his contention was that "vital spirit" could only be engendered in the left ventricle if the blood within it had first been "commingled" with inspired air in the lungs. His reason for that belief was the statement in Genesis ii, 7, that "The Lord God formed man of the dust of the ground, and breathed into his nostrils the breath of life; and man became a living soul."

His brilliant intelligence enabled Servetus to work in theology and law, to lecture in Ptolemaic geography and astrology, to qualify in medicine at the University of Paris after sharing a prosectorship in anatomy with no less a person than Andreas Vesalius,⁶ and he was concerned to show that the structure of the human body was so ordered that man might continue to absorb the breath of life (in theological language "the immanent, animating force in the universe—the very being of God")⁷ from the air around him to be fashioned into vital spirit in the heart, carried to the brain, and there converted to the anima or soul. His assertion that the blood passed through the lungs was based on theological conviction fortified by anatomical observation of the size of the pulmonary vessels and the impermeability of the "median wall" of the heart. For this he deserves great credit, but it was a very limited contribution to the problem of the circulation as a whole. The reconciliation of theology with his work in natural science is in Servetus's chapter on the doctrine of the Trinity and for heresy in this regard he suffered martyrdom.

Malpighi's Observations

The path of the blood through the lungs was not revealed by the microscope until four years after Harvey's death, when Marcello Malpighi, professor of medicine at Bologna, published *De pulmonibus* in 1661.⁸ This book is in the form of two letters to Borelli, the remarkable mathematical physicist with whom he had worked for three years at Pisa. In the first Malpighi described the vesicular structure of the lungs and showed how the divisions of the trachea ended in air sacs. The second letter—under the heading "I see with my own eyes a certain great thing"—records observations on the lung of a living frog. "While the heart is still beating . . . the circulation of the blood is clearly laid

bare; and indeed the same may be even more happily recognized in the mesentery." He goes on, "By this impulse [the heart-beat] the blood is showered down in minute streams through the arteries after the fashion of a flood . . . and . . . is poured out on all sides until it approaches the walls and angles and the absorbing branches of the veins. The power of the eye could not be carried further . . . hence I might have believed that the blood escaped into an empty space and was gathered up again by a gaping vessel." But "by the help of our more perfect microscope" it was clear that it was not so and the blood "remained in" vessels joining together in a ring-like fashion "which formed a network connecting the arteries and veins."

That great man, van Leeuwenhoek,⁹ the attractive draper of Delft and janitor of the City Hall, confirmed Malpighi's work, and for anatomical reasons there could no longer be any rational objection to the idea of the circulation. Even so, its influence on medical thought and practice remained slight; and perhaps not surprisingly. Medicine was dominated by the doctrines of humoral pathology. There were four humours—blood, phlegm, black and yellow bile—based on the Greek conception of four elements or principles of matter—earth, air, fire, and water. Corresponding with these elements were four qualities—hot, cold, dry, and moist. When later Galenic and Arabian speculation attributed degrees and varying proportions to these qualities the whole humoral system became so elastic that it could be used, in a manner convenient for pedantic display, to explain all sorts of observed phenomena, and the question whether the blood circulated or not seemed of comparatively slight importance. Some "obscure places" were, however, made clearer as Harvey hoped. In the seventeenth century little was known of the function of "glands," a term which then embraced the brain and nearly all the viscera with the exception of the heart and alimentary canal. Until it was proved that blood circulated through all the organs it was believed that it was carried to and from them by the veins and there was no clue to the way in which the secretions of the glands were formed.

In 1643 Wirsung¹⁰ had described the pancreatic duct, and in a treatise based on lectures given to this College in 1652 Thomas Wharton gave an account of the duct of the submaxillary gland, but, while not denying that arterial blood provided material for the gland, he attributed its secretion to transfer of fluid from the nerves that entered it.

Aware of these discoveries and of the work of Borelli on the kidney, of Glisson on the liver, and of Stensen on the conglomerate glands, Malpighi, by demonstrating the close relation of the capillaries with the tissues of these glands, made possible a much clearer and more accurate conception of the way in which their functions were discharged.¹¹ To him belongs the credit for the first fruitful extension of Harvey's work. Unfortunately the great Italian made no progress in the problem of respiration and believed to the end that its purpose was thorough mixing of the blood.

Experimental Work

Six years after the publication of Malpighi's book on the lungs Robert Hooke¹² demonstrated an experiment to the Royal Society. He showed that a dog could be kept alive without any respiratory movement. With the

thorax opened and after pricking the surface of the lungs to prevent distension it was only necessary to blow air continuously with bellows down the trachea. At the end of the experiment he asked "whether suffering the blood to circulate through a vessel so that it may be openly exposed to the fresh air may not suffice (instead of lungs and breathing) for the life of the animal"? Mixing of the blood could no longer be deemed the essential function of respiratory movement: what was needed was fresh air in the lungs, and normally this was supplied by the bellows action of the thorax.

Richard Lower, who performed the first blood transfusion and in 1669 wrote a book on the heart which gave a more accurate account of its structure and nerve supply than any previously published, used Hooke's experiment to prove that dark venous blood became bright red as it passed through the lungs so long as the flow of air down the trachea was maintained.¹³ He drew the right conclusion that the change in colour was due to the blood "deriving some quality from the air." But what was the "quality" so absorbed?

There has been much dispute about the contribution of John Mayow to this problem. He asserted that atmospheric air contained "a vital, fiery and in the highest degree fermentative spirit"¹⁴—the spiritus-nitro-aereus—and that it was this that was necessary for the burning of flames and the life of animals. In his lecture on the English Physiological School of the seventeenth century Sir Michael Foster wrote a panegyric of Mayow in 1901 and claimed that his spiritus-nitro-aereus was what we now call oxygen and that he ranks with the great scientists of the world. Professor Patterson¹⁵ examined the matter again 30 years later and records a totally different judgment. In his opinion Mayow was never an independent investigator; he had merely reflected the thoughts and speculations of his contemporaries, and there had been "an astonishing tendency, one might almost say a conspiracy . . . enormously to exaggerate the resemblance of Mayow's views to our own; to read into his statements ideas that were by no means in his mind and to credit him with the discoveries and views of others." Whatever the truth about Mayow his work had little influence; Foster's generous eulogy lacks firm foundation and is like the fantastic claim made for the Epicurean, Lucretius, that he forestalled Pasteur in bacteriology because in his description of the plague in Athens he explained the nature of epidemics by the presence of countless atoms flying about that were poisonous and pestiferous.¹⁶

A Blow to a Doctrine

Further progress waited on the development of chemistry. In the first half of the seventeenth century chemistry was very much what it had been in Alexandria before the dawn of our era. The doctrine of the four elements was accepted and the Alexandrian chemists believed that all substances were convertible or transmutable by suitable adjustments of their proportions. Their belief was fostered by several simple observations. Water when evaporated to dryness invariably left a powdery sediment, and this was taken to be an indication of the conversion of one element, water, into another, earth, under the influence of fire and heat. No account was taken of the possibility that the water might have contained earthy matter in solution or that the sediment might come from the vessel in which it was boiled. The continuous growth of plants when regularly watered in

a small amount of earth pointed in the same direction; the water had been converted into the matter of the plant. Similarly when galena, a submetallic mineral lead sulphide, was roasted in air apparently pure lead was recovered, and this when further heated in a cupel (a porous dish made of bone ash) yielded a small button of silver, traces of which, as we now know, are frequently present in lead ores.¹⁷ From this came the stimulating thought that if he were clever enough a chemist might transmute base materials to gold, and alchemy for centuries absorbed the attention of too many able minds.

It is questionable whether van Helmont (1577–1644), the mystical Belgian friar who took to medicine, should be credited with the first blow to the doctrine of the four elements. Boyle thought highly of him as "an author more considerable for his experiments than many learned men are pleased to think him," and he certainly invented the word gas to denote the carbon dioxide produced by fermentation (he called it gas sylvestre). He failed, however, to distinguish CO₂ from a poisonous gas found in coal mines or in charcoal-burning; to him the three seemed identical because they all failed to support combustion.¹⁸ Nevertheless the original notion that air was not an element may have come from van Helmont.

Boyle's Pursuit of Truth

However that may be, there is no doubt that Robert Boyle was the first to attack the accepted doctrines effectively and to demonstrate their fallacies. This remarkable son of the Earl of Cork devoted wealth and energy throughout his life to the pursuit of truth, confident that "the goods of mankind may be much increased by the naturalist's insight into trades," among which, presumably, he included the practice of medicine. Boyle was tall of stature but slender, and his countenance pale and emaciated; "his constitution was so delicate that he had divers sorts of cloaks to put on and in this he governed himself by his thermometer." His diet was simple and austere; in youth he declined marriage on grounds of policy and in later life for philosophical reasons. Devoted as he was to the reformed religion, he refused to take orders because his influence on others would be greater if it were known that he was not paid to exercise it. In addition to his scientific activities he had the four Gospels and the Acts of the Apostles translated into the Malayan language, and he was a First Governor of the "Corporation for propagating the Gospel in New England and parts adjacent in America," whose charter with great propriety was granted by Charles II.¹⁹

The Sceptical Chymist or Chemical and Physical Doubts and Paradoxes touching the Experiments whereby Vulgar Spagyristes are wont to evince their Salt, Sulphur and Mercury to be the true Principles of Things—to give it its full title—was published in London (1661) soon after Harvey's death. Obviously it was designed as a direct attack on the disciples of "Paracelsus and some few sooty Empiricks" who . . . "having their eyes darkened and their brains troubled by the smoke of their own furnaces began to rail at the Peripatetick doctrine which they were too illiterate to understand and to tell the credulous world that they could see but three ingredients in mixed bodies."²⁰

But you do not read far in Boyle's famous book before you discover that the Peripateticks with their

four elements are as much under fire as the Paracelsians with three. In the first dialogue Boyle defines his position. "I am of so diffident or dull a nature as to think that if neither of them can bring more cogent arguments to evince the truth of their assertion than are wont to be brought, a man may rationally enough retain some doubts concerning the very number of those material ingredients of mixed bodies which some would have us call elements and others principles." The Peripatetic case for the four elements is put by Themistius: "For if you but consider a piece of green wood burning in a chimney you will readily discern in the disbanded parts of it the four elements of which we teach it and other mixt bodies to be composed. The fire discovers itself in the flame by its own light; the smoke by ascending to the top of the chimney and there readily vanishing into air, like a river losing itself in the sea, sufficiently manifests to what element it belongs and gladly returns; the water in its own form boiling and hissing at the ends of the burning wood betrays itself to more than one of our senses; and the ashes by their weight, their fieriness and their dryness put it past doubt that they belong to the element earth." A complete review of the theoretical arguments and experimental facts which Boyle marshals to demolish the accepted doctrine is beyond the scope of this address, but I mention a few.

Why was it assumed that fire is "the genuine and universal resolver of mixt bodies" when we already know that other reagents such as aqua fortis can resolve them? Why was it believed that all the distinct substances obtained from a mixed body by fire were pre-existent in it in the forms in which they were separated from it?

Let it be conceded that substances separated from mixed bodies were their ingredients; yet the number of such substances is not always the same and some of them are resolvable into simpler substances. And the application of fire to a mixed body produced results which varied according to the manner in which the influence of the fire reached it; if guaiacum or blood were distilled, for example, the results differed from those obtained by burning.

Finally, "having thus finished his discourse against the received doctrine of the elements" he concludes "that the experiments brought to demonstrate its truth do not evince what they are alleged to prove, and it may as yet be doubted whether or no there be any determinate number of elements or, if you please, whether or no all compound bodies do consist of the same number of elementary ingredients or material principles."

A New Conception

Boyle did for chemistry what Harvey had done for physiology. He challenged accepted doctrine and substituted for it a new conception which later proved to be true. But despite his many contributions to knowledge after the publications of the *Sceptical Chymist* it seems doubtful whether he completely freed himself from the stranglehold of the four elements. He knew, for instance, that the calx formed when lead was heated in air weighed more than the original metal from which it came, but to the end he believed that the increase of weight was due to absorption of material from the fire. Although Boyle devised a successful method for collecting various forms of gas and studied their properties he always thought of them as different sorts

of air. To him in the laboratory air and fire continued to be important elemental substances just as the Galenic hypotheses were the basis of Harvey's clinical practice.

Progress was slow, and slower than it might have been had not another speculative idea been introduced to explain observed phenomena.

Conceived by Johann Becher in 1669 and expounded by his pupil C. E. Stahl,²¹ the phlogiston theory dominated philosophical thought for a century. All combustible bodies contained this mysterious principle, phlogiston; when they burned phlogiston escaped, and the more of it they contained the smaller the residue. The process was deemed to be reversible. Thus when a metallic calx was heated with charcoal the phlogiston left the charcoal and was transferred to the calx to restore the metal to its original purity. The awkward fact that the metal then weighed less than the calx was dealt with by the assumption that phlogiston had a negative weight. The theory presented to chemists the same difficulty that Galenic natural and vital spirits presented to physicians when Harvey wrote *De motu*.

The Prelude to Modern Chemistry

The "first gleam of understanding in this prevailing darkness"—to quote Dr. E. Ashworth Underwood²²—came from Edinburgh in 1756, when Joseph Black wrote his M.D. thesis entitled "Experiments upon magnesia alba, quicklime and some other alkaline substances."

A student of William Cullen, Black was faced with the clinical problem that caustic alkalis had harmful effects when used in practice as solvents for stone, and he turned to magnesia alba as a possible substitute. He showed that when heated its weight diminished owing to loss of "fixed air" (carbon dioxide) and that the difference between mild and caustic alkalis was due not to the presence of fire matter (phlogiston) but to the fixed air which he also found in the gas produced by fermentation and in air expired from the lungs. One of his large-scale experiments is worth notice. In the roof of a church sheltering a congregation of 1,500 people he placed rugs moistened with caustic soda. At the end of a long service he proved that the caustic soda had become mild alkali, and he was eventually satisfied that air was not an element but a mixture of different gases. I mention this experiment not only as a tribute to his ingenuity but also to the piety of Scottish congregations which sustained services lasting 10 hours, in an obviously ill-ventilated church.²³

Henry Cavendish

The stage was now set for the last scene of the drama which forms the prelude to modern chemistry. The principal actors were three—Henry Cavendish (1731–1810), Joseph Priestley (1733–1804), and Antoine Lavoisier (1743–94)—and they played their parts against the background I have sketched. Cavendish, who made the next step, was the grandson of the second Duke of Devonshire.²⁴ His father, Lord Charles, was a scientist who earned the respect of Benjamin Franklin, and in the paternal laboratory Henry Cavendish began his career. Whatever his merits as a scientist, Lord Charles, by modern standards, was distinctly peculiar as a parent. At the age of 29 Henry became a Fellow of the Royal Society, but he had no independent income or allowance of his own and was compelled to ask his

father for the cost of every society dinner—and never received more than five shillings, the exact price of the meal.

His mother had died while he was an infant and Henry grew up to be a recluse. Tall and thin, with a squeaky voice, he wore the oddest clothes and was terrified of women. In middle life he inherited an enormous fortune and died one of the richest men in England. Changed circumstances did not affect his way of life; his three houses were dedicated to scientific work and he dined invariably on a leg of mutton and usually alone. It is said that after a chance meeting with a housemaid he promptly had another staircase built in order that so unseemly an event should not recur. His published work established him in the first rank of scientists, and when he died in 1810 Sir Humphry Davy said that England had suffered no greater loss since the death of Newton. Cavendish's contribution to Harveian fulfilment lay in his isolation of hydrogen (which he called inflammable air) in 1766 and in the later experiments by which he proved that when "423 measures of inflammable air . . . exploded with 1,000 measures of common air, almost all the inflammable air and about one-fifth part of the common air are condensed into the dew which lines the glass." The accuracy in the circumstances is astonishing; he found the composition of "the dew" to be in the proportion of 2.03 parts of hydrogen to one of that part of the common air we know as oxygen.

Joseph Priestley

Joseph Priestley was born in 1733 near Leeds.²⁵ From Batley Grammar School he went to the Dissenting Academy at Daventry to be trained for the Ministry. After a period of pastoral work in Suffolk he became a school-teacher, and in 1761 joined the staff of Warrington Academy as a tutor in languages. Work in the humanities did not conflict with his scientific interests, and each year he spent a month in London to meet other scientists, who were so impressed by his *History of Electricity* that they elected him to the Fellowship of the Royal Society in 1766. Theology, however, was always his main pursuit, and he recorded the opinion that it is "only a small part of their leisure that most men can be justified in giving to science." In 1767 he was appointed minister of Mill Hill Chapel, Leeds, and there in the course of the next six years he did a great deal of work in chemistry. His first interest was in the "fixed air" of Joseph Black. Priestley impregnated water with it, and the "exceeding pleasant sparkling water" that resulted had in its early days an interesting history. It was known that fresh vegetables prevented scurvy in sailors and it was assumed that the medicinal value of the vegetables was due to the production of fixed air in the course of their fermentation in the digestive tract. Both this College and the Royal Society recommended the Admiralty to use fixed air as an antiscorbutic, and two battleships were fitted with apparatus to make what we now know as soda-water.²⁶

On leaving Leeds, Priestley was librarian to Lord Shelburne for some years before he went to Birmingham as a dissenting minister in 1779. Twelve years later his house was burned by a riotous mob whose fury had been excited by the welcome he and his friends had given to the dawn of the French Revolution. In 1794

he emigrated to America, where he died. It is pleasant to recall that during his last years in Pennsylvania he enjoyed the friendship of Thomas Jefferson, who became President of the Republic in 1801.

In chemistry Priestley was mainly concerned with different types of air. When he began three were known: common air, the fixed air of Joseph Black, and the inflammable air of Henry Cavendish. To these he added seven new ones by devising an improved technique for collecting gases. The experiment with which his name will ever be connected he described in 1774. After directing the heat of the sun through a lens to a sample of mercuric oxide in a closed glass vessel over mercury he noticed "air was expelled from it very readily. Having got 3 or 4 times the bulk of my materials I admitted water to it and found that it was not imbibed by it. But what surprised me more than I can well express was that a candle burned in this air with a remarkably vigorous flame," and although he knew candles burned in a similar way in "nitrous air" which he had isolated two years earlier, he goes on, "I was utterly at a loss to account for it," for he knew no nitrous acid had been used in the preparation of the mercury calx. In a similar experiment Priestley got the same sort of air from red lead, and in the following year tested its value in respiration.

A mouse in a confined space survived longer in the new air than in common air, and he called it "dephlogisticated" because it appeared to absorb more phlogiston from the burning candle and from the mouse than common air. The fact that the new air was "eminently respirable" and capable of prolonging the survival time of a mouse in a closed space led to its use in clinical medicine. A book, *Medicinal Use of Factitious Airs*, by Dr. Thomas Beddoes and James Watt, the great engineer, was published in Bristol in 1794. Its price was half a crown; it is bound in leather and there are 700 pages with beautiful illustrations. In the first part Beddoes reports clinical observations. Watt's contribution deals with the design of machinery to produce the airs in quantity and the apparatus for their administration to patients. The engineer had a keen personal interest in the matter, for his son had pulmonary tuberculosis and he hoped factitious airs might help the boy. Thomas Beddoes, I remind you, discovered Humphry Davy, who, while employed as his assistant, discovered the anaesthetic properties of another factitious air—nitrous oxide—but unfortunately did not realize its importance.

Priestley has been severely criticized for his failure to emancipate himself from the phlogiston theory and to draw the conclusion that his dephlogisticated air was an integral ingredient of mercuric oxide. Sir Oliver Lodge, the first principal of my university, said of him "in theory he had no instinct for guessing right such as the great men of science have had—an intuitive feeling for the right end; he may almost be said to have had a predilection for the wrong end"; and Huxley thought "he had no deeper comprehension of his own work." In a critical paper, Sir Philip Hartog²⁷ has come to Priestley's defence and has shown conclusively that, whatever his deficiency in guessing may have been, Priestley's attitude to scientific method was beyond reproach. Sir Philip reminds us of Priestley's statement, "nature exhibits nothing but particulars; all general propositions as well as general terms are artificial things . . . for the convenience of our conception and

memory," and of his warning of "the danger of considering a hypothesis too soon a fact." In 1774 Priestley spent a month in France with Lord Shelburne. He did not find Paris congenial; there were so many agnostics who did not hesitate to tell him that he was the only intelligent man they had met who professed to believe in Christianity.²⁵ His reaction to these uneasy contacts is recorded in his *Letters to a Philosophical Unbeliever*. But in Paris he met Antoine Lavoisier, the man who was to find the key to these mysteries.

Lavoisier

Like Priestley, Lavoisier¹⁸ was a spare-time scientist, but his conception of spare time was liberal; he worked in his laboratory from 6 to 9 in the morning and from 7 to 10 at night. Professionally he was a sort of civil servant. Unhappily, as events proved, Lavoisier had purchased a share in the Ferme Générale, which paid an agreed sum to the Government for the right to collect taxes. The hatred that the Ferme inspired, and the personal enmity of Marat, whose scientific papers he had subjected to caustic criticism, led to Lavoisier's execution during the Terror.

When he met Priestley Lavoisier's reputation as a scientist was established; he had been elected a member of the French Academy six years earlier and his interests were wide. He had already exposed the fallacies of the theory of the transmutability of matter based on the recovery of earthy sediments when water was evaporated to dryness, and he had suggested the right solution of the problem of plant growth. In a memorandum of 1773 he had written of the "processes by which one can succeed in fixing air, vegetation, the respiration of animals, combustion, in some conditions calcination; also some chemical changes," and it was his meeting with Priestley and the account of dephlogisticated air that gave him the clue to the nature of combustion and the true explanation of the formation of water when Cavendish's inflammable air was exploded in common air.

During the next 20 years Lavoisier's work laid the foundation of modern chemistry, and his attack on the phlogiston theory was decisive. Chemists, he wrote, had made it a vague principle, sometimes with weight, sometimes without; never had it been precisely defined, and in consequence it might be adapted to explain any problem they wished. For phlogiston he substituted a clear conception of combustion. It never occurred save in the presence of oxygen (the name he gave to Priestley's dephlogisticated air in the mistaken belief that it was essential to the formation of acids). Always, he added, there was, in combustion, absorption of this air, and the increase in weight of the total products of combustion was equal to the weight of the air absorbed; heat and light were generated in the process.

Of supreme importance to the consummation of Harvey's work was Lavoisier's conclusion that respiration was a slow form of combustion and that it was true "that the flame of life was lit when a child draws its first breath." At the end of the eighteenth century the source of animal heat was thought to be the friction of the blood as it coursed through the vessels and the heart. For this Lavoisier correctly substituted the idea of slow combustion, but he went astray in fixing its site in the lungs. He thought that pure air in the lung suffered a decomposition like that which took place

in the burning of charcoal and that the heat set free was carried by the blood throughout the body. The wheel had come full circle. The lungs did not disperse heat engendered in the heart, as Harvey thought, but actually warmed the blood by a process of combustion prior to its circulation.

Consummation of Harvey's Work

And there, after the death of Lavoisier, the matter rested for well-nigh 40 years. In 1812 Berzelius,²⁸ Professor of Chemistry at the University of Stockholm, while investigating the composition of animal fluids noted the presence of considerable amounts of iron in the blood and suggested that it might be associated with the absorption of oxygen from the inspired air, but it was not until another 25 years had passed that Gustav Magnus²⁹ faced effectively the problem of the presence of carbon dioxide in the breath expired in respiration. Was this gas really formed in the lungs (as Lavoisier and Seguin had thought) or did the venous blood already contain it when it reached the lungs and there set it free? He proved that there was more carbon dioxide and less oxygen in venous than in arterial blood but was puzzled by the fact that the two types of blood contained both gases. His final conclusion was tinged with admirable scientific caution. It was "very probable that inspired oxygen is absorbed in the lungs and carried away by the circulating blood in such a way that it permits an oxidation in the capillaries with the formation of carbon dioxide. I say probably because we can not be sure that the expired carbon dioxide is replaced by an exactly equal volume of oxygen and therefore it is still possible that some may be formed in the lungs."

In 1872 E. F. W. Pflüger,³⁰ Professor of Physiology at Bonn, finally proved that nearly all oxidation occurred in the tissues and not in the blood-stream, and there it seems to me we reach the full consummation of William Harvey's work—more than 250 years after his statement in a Lumleian Lecture to this College "that the movement of the blood is constantly in a circle and is brought about by the beat of the heart." At long last the chief purpose and significance of the circulation had been revealed.

You may feel, "excellent doctors" (for so Harvey addressed your predecessors when he described his new concept "of the heart's movement and function of the blood's passage round the body"), that I have placed too much emphasis on the contribution of the chemists to the completion of the structure of which he laid the foundation. It is true, of course, that in the two and a half centuries that separate Harvey from Pflüger many other "obscure places" had been made clearer by studies remote from chemistry and in the field of medicine. In his oration of 1928 Sir Humphry Rolleston gave an admirable summary of the progress made in normal and morbid anatomy and by clinical observation.

The first treatise on diseases of the heart was published by J. B. de Senac in 1749; even earlier Albertini, of Bologna, had associated palpitation and dyspnoea with cardiac disorder. In 1728 Lancisi's book *On the Motion of the Heart and Aneurysms* was published, but incontestably the greatest contribution came from Giovanni Battista Morgagni (1682–1771), Professor of Anatomy at Padua,³¹ where William Harvey had learned from Fabricius of the valves in the veins a hundred years

before. *De sedibus et causis morborum* (1761) was published in Latin when he was 79, and he lived to see several reprintings before he died in his ninetieth year. There are five books in this great work descriptive of "Disorders of the Head, the Thorax, the Belly, the Chirurgical and Universal Disorders and, finally, of such things as may be added to the former books." The whole is made up of a series of letters to an intimate friend in which Morgagni records over 700 necropsies he had either conducted himself or witnessed. What was entirely new was his careful and elaborate clinical history of each patient and his endeavour to relate symptoms and signs to the pathological changes found after death. Not unnaturally he made mistakes, but he paved the way for the rapid progress that followed.

Morgagni realized more clearly than others had done before him that although a morbid process might be established principally in a particular organ its effects might also be widely diffused through the body. In his preface there is this notable passage: "As there are very few diseases especially if of any long continuance to which some other disorder is not joined . . . for this reason every observation of such a disease after having been given under the head whereunto it particularly belongs ought without doubt to be made mention of under other heads to which it likewise relates in some measure." For humoral pathology he substituted the idea of the location of diseases in organs. I have browsed in the English translation by Benjamin Alexander, M.D., which was printed in London in 1769 and found in it a pleasure akin to that I felt on first reading Pepys's diary.

Not only do Morgagni's letters record daily activity of much interest but they also reveal curious facets of his personal attitude and character. He was a patrician and something of a snob. His satisfaction in describing the subjects of his necropsies as "potentates of distinction" or "bishops of eminence" is obvious, but when he found a curious abnormality in the chest of a woman and tells us that he inquired whether her relatives were similarly affected he is careful to point out that he did not often undertake work of that kind in the case of common people. His influence in England is to be seen in the careful note-taking of Heberden's *Commentaries* (1802) and his description of angina as a disorder of the heart. At about the same time Pitcairn and Jenner recognized the association of rheumatic infection with valvular disease. A little earlier Withering had introduced the foxglove as a remedy for dropsy. Although he did not distinguish dropsy due to cardiac failure from other types, Withering knew that his new drug was most effective when it was used in cases with the irregular pulse we now attribute to auricular fibrillation.

Important as these things were, and others like them, they do not transcend in significance the elucidation of the problems that Harvey faced when he became convinced that the heart and circulation were the basis of life, and it was the chemists who proved the truth of his inspired vision when they showed that the cells of the organs and tissues depend on an adequate capillary circulation for all their vital activity.

Conclusion

In telling in broad outline the story of the discoveries that led in the course of 250 years to the consummation

of Harvey's work I am conscious of a slight feeling of unease, for in childhood I learned from a stern Calvinistic governess that all stories should have a moral. In the one I have set before you to-day there may be two. First, that the only sound basis for medicine is natural science and the scientific method and, although we are compelled at times by ignorance or necessity to determine our course by empirical experience, we must never permit ourselves to attribute overmuch importance to it. The second is the danger of unquestioning belief in accepted doctrine. The four elements, the humours, and the phlogiston theory, based on nothing more than speculation, impeded progress in the development of Harvey's work and in natural science as a whole. This danger is probably not as great as once it was. One of the disconcerting experiences that physicians of my generation have suffered is the lapse of authority. When I was young senior members of a hospital staff spoke with the voice of God in the manner of the House of Lords interpreting the law. Now we know that our judgments may at any moment be set aside by a scientist working in a laboratory. That has proved a wholesome discipline, and we must see that it is applied in all fields of our activity. In most I think it is, but there are still some in which a battle of creeds usurps the place of the scientific method which Harvey first established in medicine.

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