

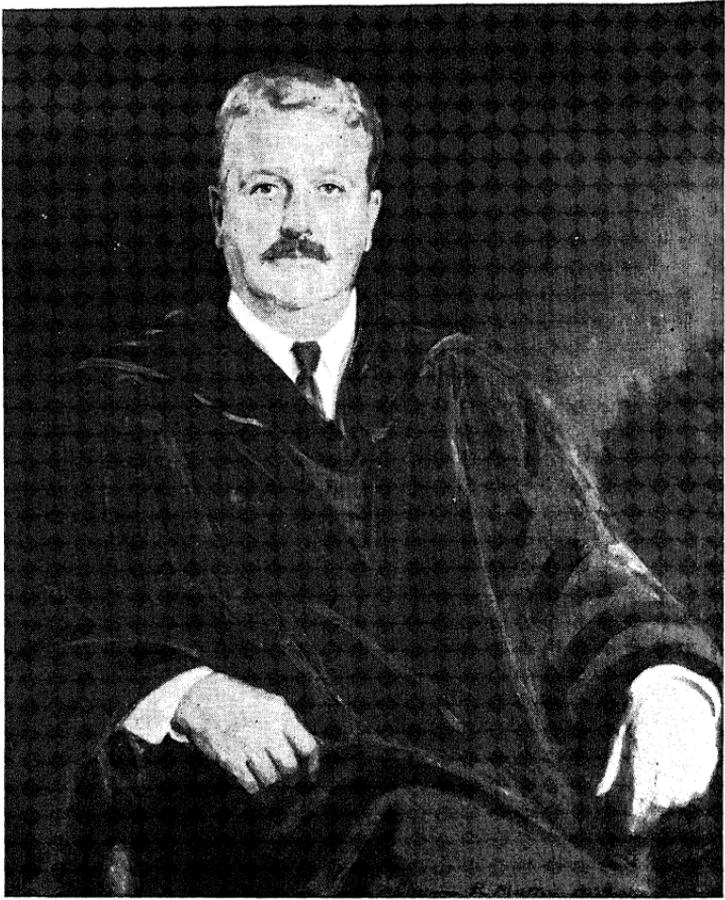
Logan Clendening Lectures on the
History and Philosophy of
Medicine

First Series

by

John Farquhar Fulton

Logan Clendening Lectures on the
History and Philosophy of
Medicine
First Series



Logan Clendening
(1884-1945)

Logan Clendening Lectures on the History and
Philosophy of Medicine

First Series:

I

Vesalius Four Centuries
Later

II

Medicine in the Eighteenth
Century

by

John Farquhar Fulton

*Sterling Professor of Physiology and Keeper of Medical
History Collections, Yale University*

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Prefatory Note

In 1949 Mrs. Logan Clendening presented to the School of Medicine of the University of Kansas a sum of money to establish a lectureship on the history and philosophy of medicine in memory of her husband, the late Dr. Logan Clendening.

The initial series of lectures was given on November 15, 1949, by Dr. John Farquhar Fulton, M.D., Ph.D., D.Sc., LL.D., Sterling Professor of Physiology and Keeper of Medical History Collections in Yale University.

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I
Vesalius Four Centuries
Later

Vesalius Four Centuries Later*

I deem it a great honor to be invited to inaugurate the Logan Clendening Lectureship on the History and Philosophy of Medicine established in memory of Dr. Clendening, for he was an old and a valued friend and, as a book collector, an energetic and, I might add, most devastating rival. His knowledge of the great figures of medical history was vast, his memory for dates and places unailing; and the extensive collection which he and Mrs. Clendening gathered together and have given to this University stands as an enduring monument to his fame.

There are not many such collections in the country, and of those that do exist, few are made freely available to medical students. Those of us who love books realize that there is no greater privilege than to be able to browse in a well-stocked library. This was how William Osler developed his taste for literature and his wide knowledge of the historical backgrounds of the profession, and it was in gratitude for the stimulus he had received from living with Dr. James Bovell and having free access to his library as a first-year medical student that he ultimately came to give his important collection to McGill. The Osler Library at McGill opened its doors just twenty years ago,

*Delivered at Lawrence, Kansas, on 15 November 1949 at eleven a.m.

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and a generation of students has now received the stimulus that comes of being able personally to examine the books which have made medicine what it is today. Some of you may not know that Harvey Cushing was inspired to follow in Osler's footsteps after he had paid a visit to the Osler Library in 1934 and had seen what the collection meant to the student body. The result was that in 1941 we were able to open the doors of a medical-historical library at Yale.

As with Dr. Cushing's, the Clendening Library has great strength in certain special areas of medical history. Dr. Clendening was deeply interested, for example, in the history of anesthesia and at the time of his death he had one of the most important collections in private possession. He was also an ardent follower of Edward Jenner and the literature of vaccination. When pursuing a particular theme, he was indefatigable. He would follow his hero to his native town and photograph whatever landmarks of his life still remained and any monuments raised after his death. It wouldn't do for someone to take the photographs on his behalf—this would be beneath the dignity of a real collector. When interested in Crawford Long, Dr. and Mrs. Clendening made the long trip to Jefferson, Georgia, themselves to photograph his statue. Finding that the corner grocery store where Long obtained his provender was still standing, they photographed that, too, for good measure.

Dr. Clendening visited similar medical shrines in Eu-

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rope, Africa, Central and South America. He traced Laennec through the villages of his beloved Brittany, and of course went to Louvain to see where Vesalius had made off, one dark night, with the body of a criminal from the city gibbet; by nightfall the body had been so well picked by the vultures that only the skeleton remained. These and a hundred other places of medical interest were subjects for Dr. Clendening's camera. He had intended to make the material he had so laboriously obtained available in the form of an illustrated medical gazetteer, but most unhappily he did not live to see this remarkable book through the press. Unfortunately also, the number of illustrations he planned to incorporate has caused every publisher who has so far been approached to run quickly in the other direction, but it is hoped that one day Dr. Clendening's trustees may find one sufficiently venturesome, so that we may all have the benefit of what he had hoped to give us.

Dr. Clendening was especially proud of his copy of the first edition of Harvey's *De motu cordis* and one time when I had abused him for never having given me a photograph of himself, he relented and sent an excellent likeness taken while holding his precious Harvey. Beneath was an amusing inscription to the effect that on rare occasions he was actually seen in good company. Dr. Clendening was likewise deeply interested in the early anatomists, having acquired among other things the rare *Anatomie universelle* (1561) of Ambroise Paré; and with Dr.

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Cushing he also shared an abiding interest in Andreas Vesalius. In his *Source Book of Medical History* there is a long section which he had had translated from his copy of the first edition of the *Fabrica*. He regretted that neither the *Fabrica*, Vesalius' great masterpiece, nor the companion volume, generally known as the *Epitome*, had ever been translated into English. For this reason, Dr. Clendening was heartily enthusiastic when Professor Lind, Dr. Tracy, and Dr. Asling came to him with the proposal that the *Epitome* be put in English dress. As you know, the attractive rendering has just been published and we were especially proud at Yale to have the book appear as a volume in the series of monographs from the Historical Library. Mrs. Clendening carried forward her husband's interest in the project and it was her generosity that made publication possible. For us it has meant a continuance of the happy relationship between Kansas and Yale.

Now why has this man Vesalius engaged the interest of both medical men and artists for over four hundred years? In April of 1900 a young American surgeon, who was then scarcely more than a medical student, stood in the courtyard of the University of Bologna lost in wonderment and delight at its beauty, because, as he wrote, "There can be few spots in the world which have for a medical man associations of greater historic interest than this old university building But should this courtyard fail to excite more than curiosity, what will call forth excla-

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mations of joy is the old Teatro Anatomico into which one enters from the upper tier of arcades. A room finished simply in wood to which time has given the richness of color that no learned artificial process can accomplish—a room which, were it not from an artistic standpoint beautiful and unusual, would still make us stand bareheaded as though before a shrine, for here Vesalius reawakened the study of anatomy which since Galen had had a long, unquestioned period of rest.”

Andreas Vesalius is one of the most colorful figures in all medical history—not only was he a man much talked of in his own time, but through the centuries he has been the subject of many studies which have attempted to interpret the relatively few facts known about his brief life and to shed further light on his extraordinary career. Since publication of Dr. Cushing's *Bio-bibliography* in 1943 (commemorating the four-hundredth anniversary of the *Fabrica*), some eighty additional publications have appeared, the two most extensive among the recent ones being Singer and Rabin's monograph on the six anatomical tables issued in England and Dr. Lind's translation of the *Epitome*, which I have just mentioned.

Vesalius was born in the last hour of the year 1514 in the town of Brussels in Belgium. It was not unusual for a boy who had four generations of physicians behind him to show an interest in dissecting rats and moles in his early years, but his grandfather as personal physician to the Emperor Maximilian and his father as apothecary to the im-

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perial household of Charles V had not set an example for the activities which later caused him to leave his native Belgium hurriedly and to seek the more enlightened climate of Italy. The first tendency to stray from the conservative and conventional pattern of his upbringing appeared in Paris, where in 1533 he had gone to study medicine.

Some idea of student life in Paris in those days can be gleaned from a lucid passage in Sherrington's engaging biography of the great French scholar-physician, Jean Fernel, who was lecturing in medicine at this time:

We were up at 4, and, having said our prayer, went to 5 o'clock lecture, our huge books tucked under one arm, writing-case and candle-stick in our hands. Lectures lasted until 10. Then, after half-an-hour for correcting our notes, we went in to dinner. From one o'clock onward we attended lectures again, and at five o'clock got back to our lodgings, went through our notes and looked up references. Supper at 6 o'clock.*

Vesalius plunged into his medical studies with impetuous enthusiasm—an enthusiasm that later brought him into conflict with his conservative teachers, the eminent anatomists Jacobus Sylvius and Winter von Andernach, and particularly with Sylvius, a confirmed Galenist. Little attempt, prior to this time, was ever made to compare the written word with observations on the dissected body—the texts were read by the professor seated on the platform

*C. S. Sherrington, *The Endeavour of Jean Fernel*, Cambridge, 1946, p. 60.

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while the barbers carried out the dissection. This method of instruction did not content Vesalius—he wanted to wield the scalpel himself. He let it be known that he had had some experience in dissection and persuaded his teachers to let him take the place of the barbers. He began as an ardent follower of Galen; he was familiar with the Galenical anatomical texts which at that time had just begun to appear from the presses of Paris and Lyon. Little by little, however, it became apparent to him that Galen was describing, not the human body, but the anatomy of pigs and monkeys, and he was forced to exclaim: “I acknowledge no authority save the witness of mine own eyes—I must have the liberty to compare the dicta of Galen with the observed facts of bodily structure.” Now, four centuries later, it is difficult to appreciate the extent of his heresy, but Galen’s writings had been adopted by the early fathers of the Christian church as official canon and anyone who deviated one hairsbreadth from the Galenical text was as guilty of heresy as if he had questioned the doctrine of the Trinity.

Within a year of his arrival in Paris, Vesalius was, as Streeter has said, “galvanized into action. He plotted to end those traffickings with the seven types of lower animals which Galen allowed as substitutes and to humanize the study material. At the risk of his own life he made forays to the gibbets of Montfauçon and the graves of the Cemetery of the Innocents.”* Sylvius was outraged by

*E. C. Streeter, “Vesalius at the University of Paris,” *Yale Journal of Biology and Medicine*, 1946, 16, p. 122.

his nonconformity, and Vesalius seems to have devoted his final year at Paris to working with Andernach, with whom he managed to remain on relatively good terms; at least Andernach in his small textbook of anatomy mentions that he had two highly skillful assistants, one, Andreas Vesalius, and the other, the ill-fated scholar-physician, Michael Servetus. He stated in his Preface: "With the aid of these two, who attended my lectures on Galen, I have examined in the bodies themselves all the muscles, veins, arteries, and nerves to the limbs and of the other external parts." But we have it from Vesalius that Andernach himself never soiled his hands with a scalpel.

Early in 1535, just before he would have been examined for his medical degree, the Holy Roman Emperor, Charles the Fifth, in whose court Vesalius' father served, elected to march down the valley of the Marne in the hope of taking Paris. Vesalius in consequence had to leave Paris in great haste to join his father, and it was no doubt during this period that he had his first taste of military surgery.

Unfortunately there is no documentary evidence as to his activities during the two years that followed beyond the fact that he translated the Ninth Book of Rhazes, which was apparently submitted to the authorities at Louvain as a thesis; but there was no record in the Louvain archives in 1900 that he was actually given a medical degree, and there is no reference in any of his writings to his having received one although he styled himself on the title-

page of the translation as "*Medicinae candidato.*" Since the Louvain Library has been twice destroyed and since such of the archives as were saved in the first World War were lost in the German bombardment in 1940, this part of Vesalius' career will probably never be known.

The Rhazes was published at Louvain in February of 1537 and a second edition was brought out not long thereafter in Basel, where Vesalius had gone en route to the more friendly atmosphere of northern Italy. We next hear of him on 5 December 1537, when he was made a reader in surgery at the University of Padua at the age of twenty-two. It was an extraordinary appointment for a man so young—and a foreigner at that—but it reflects the liberality of the Italian universities in those days, a liberality which gave Vesalius just the opportunity that he needed, for the only responsibilities of his lectureship were to give public dissections several times each year.

The other details of Vesalius' life can be summarized briefly and I shall then take up his three major anatomical publications. Within four months of his appointment at Padua he issued, with the aid of the artist, Jan van Calcar, a fellow Belgian, the now celebrated *Tabulae sex*, the six anatomical tables. He then plunged into the preparation for a large work over which he slaved feverishly for the next five years. In 1543, when he was but twenty-eight years of age, his monumental volume, *De humani corporis fabrica*, made its appearance from the press of Oporinus of Basel. It was followed in two months' time by an

Epitome, summarizing the chief disclosures which had been described at much greater length in the *Fabrica*.

The outcry against Vesalius from fellow anatomists was so intense that in a fit of rage and disappointment he burned all his manuscripts, left Padua, and took haven in Madrid as a court physician. He brought out a second edition of the *Fabrica* in 1555, also a second edition of the *Epitome*, but there is no evidence that he ever dissected after 1543, although he conducted occasional autopsy examinations. Legend has it that during one such autopsy, which he carried out in Madrid in 1563, someone watching the procedure thought he saw the heart beat and rumor quickly got about that Vesalius had conducted an anatomy on a living human being. Shortly after this Vesalius left Madrid on a pilgrimage to the Holy Land—some say to do penance, others that he was bored with the court and wanted an excuse to leave that would not offend his royal patron, Philip II, others that he longed to get back to Italy. On his return journey he was shipwrecked on the Island of Zante, where he died in 1564 in his fiftieth year. The most reliable account of his death is contained in an unpublished letter of 1565 from a citizen of Cologne named Metellus to one Arnold Birkman, a letter translated for the Historical Library by Dr. C. D. O'Malley. The rendering runs thus:

A certain man of Nuremberg relates that in October of last year Andreas Vesalius died while returning from Jerusalem. It happened as follows: since Vesalius, inflamed by

a greed for wealth, had provided too little money, although upon his return he was to receive much from many persons with whom he had entered into an agreement that he would undertake the journey thither [i.e., to Jerusalem]. Through too great avarice he entrusted himself to a pilgrims' ship, not to the Venetian fleet, where he had a letter of recommendation from Philip [II] and might have received money on credit; also through avarice he provided too slightly for himself in regard to shipboard fare. On the return he fell in with this man of Nuremberg who was considering his return from Egypt to Venice, whom he induced to leave his ship and join him as a companion. The man of Nuremberg willingly did it because of their common tongue. Again Vesalius provided too poorly for himself. [The ship] driven for full forty days by storms, and when unable to reach land, with several [of the passengers] sick, partly through lack of biscuit and partly overwhelmed by the water [which had been shipped], and when all the dead had been cast into the sea, [Vesalius] with his mind so consumed by this matter, so that he fell sick first through anxiety and then through fear, asked that if he should die he might not, as with the others, become food for the fishes. Finally, the ship reached Zante, after being tumbled about in the sea and Vesalius so soon as possible leapt down from it and made his way to the gate of the city, where he fell to the earth dead. That companion from Nuremberg placed a stone for him as a sepulchre. That same person told these things in the presence of me and of Echtius. Therefore consider how the death of that very famous man will serve you and me and will be an example for many. Farewell, etc.

The Tabulae sex

In 1538 Vesalius issued six anatomical tables for the benefit of his students and also for artists interested in human anatomy. He drafted the first three and van Calcar the last three showing the human skeleton in different poses. The first group portray the portal circulation with a five-lobed liver, the venous system, and the arterial system. They have no trace of originality; indeed, they represent slavish adherence to Galenic physiology, the vessels being inaccurately portrayed and the liver that of a pig rather than a man. The last three tables, however, represent a great advance in anatomical knowledge and while also inaccurate in certain details, the mistakes are more of draftsmanship than of original observation. Vesalius in introducing them remarks: "I have sent these drawings to the press [the first three]. To them we have annexed others comprising three representations of the skeleton which I have set up for the gratification of the students, rendered from three standard aspects by the distinguished contemporary artist, Jan Stephan [van Calcar]."

The *Tabulae sex* has been a source of conjecture and controversy for many years. Only two complete sets are known to have survived—one at the San Marco in Venice, the other that of Sir William Stirling-Maxwell now in the Hunterian Library at Glasgow. The Stirling-Maxwell figures have been reproduced in the recent Singer and Rabin monograph. They refer to the *Tabulae* as "essentially

and brilliantly modern—modern in appearance, modern in outlook, modern in method, modern in its art and in its technique. It is a startling apparition in the very midst of that imitative world of the revival of classical learning which still pervades its language.”* The survival of the *Tabulae sex* is most fortunate, since a comparison of these tables with the *Fabrica* reveals the extraordinary evolution which had occurred in Vesalius’ thinking during the five years between 1538 and 1543 when the *Fabrica* was published.

The Fabrica

The frontispiece of the *Fabrica* has served to tell us almost as much about Vesalius as can be found in the known facts of his life. In the place of the conventional figure of the professor seated on a throne directing underlings in the conduct of an anatomy, we find Vesalius, having swept the barbers aside, himself demonstrating the abdominal viscera of a cadaver. A skeleton stands at the head of the dissecting table. Eager onlookers crowd the benches, and at the foot of the table, the barbers sit ignominiously sharpening instruments for the master. Among those on the bench is a student with a notebook bearing the initials “S.C.”—a fact which has been taken as evidence, otherwise unsubstantiated, that Stephen van Calcar was the artist. Preliminary sketches signed by him and executed

*Charles Singer and C. Rabin, *A Prelude to Modern Science*, Cambridge, 1946, p. iii.

in ink identical with that used for the original have been looked upon as further proof that Calcar was responsible for the frontispiece. But there is no indication as to who executed the illustrations in the text, nor did Vesalius make any acknowledgment to an artist as he did in the *Tabulae sex*. The only hint is contained in a reference in the Blood-letting Epistle, issued by Vesalius in 1539, in which he stated that if Calcar would co-operate, he would proceed with his plan for the larger work.

Not only are the plates themselves masterpieces of artistic design, but they represent the greatest single advance in the history of anatomy. There are two series of muscle men arranged on a continuous landscape so that, when they are placed side by side, one beholds a rural scene which has been identified as the Euganean Hills outside Padua. The woodblocks from which these beautiful figures were made survived until the bombing of Munich in World War II. In 1935 they were reprinted by the Bremer Press in Munich under the auspices of the New York Academy of Medicine. A contemporary Vesalian scholar, Max H. Fisch, has given us a picture of Vesalius and his book which I should like to quote:

Even the skeletal figures seem miraculously alive. The spirit of the Lord had set the prophet of old in the valley of dry bones and asked, "Son of man, can these bones live?" There was an earthquake, and the bones came together, bone to bone; and lo, there were sinews upon them, and flesh came up, and skin covered them above;

and breath came into them, and they lived, and stood upon their feet. So wherever Vesalius taught, he articulated a skeleton, set it up above or beside the corpse that lay on the table, and invited his students to take the muddy vesture of decay which he anatomized before them, reknit its parts, made clean and sweet again, project it in imagination on to those dry bones, and breathe again into its nostrils the breath of life. But it must have been a rare student, even in the Renaissance, for whom the miracle came to pass at the master's word. What the word could not evoke, the craft of artist, engraver and printer enacted in the *Fabrica*.*

Although beautifully proportioned, these figures are not perfect from an anatomical standpoint. In 1943, at the time of the four-hundredth anniversary of the *Fabrica*, we had a contest among the students to see who could discover the greatest number of errors in the muscle plates. Two students tied for the prize, each having found twenty-one inaccuracies, the most glaring being in the delineation of the rectus abdominis muscles which Vesalius represented as taking their origin near the clavicle (as in the monkey) and in the portrayal of the clavicle itself. But these inaccuracies are unimportant beside the fact that this book marked the first significant break with classical authority, and popularized once again the experimental method. Those who doubted Vesalius' findings were prompted to go to the dissecting table to discover the truth

*M. H. Fisch, "Vesalius and His Book," *Bulletin of the Medical Library Association*, 1943, 31, pp. 220-21.

for themselves, and thus was knowledge advanced. Dr. George Corner has said of the *Fabrica*:

Its chief anatomical contributions are now commonplace: an exact description of the skeleton and the muscles, and careful tracing of the nervous system and the blood vessels, greatly excelling all predecessors and illustrated with brilliant skill. Through these details the enthusiasm of Vesalius runs like a flood, turning even minor descriptive passages into records of his own intellectual struggle, until the book becomes an embodiment of his energy, his precision, and his independence. Its main contribution is thus intellectual, it is not too much to say spiritual, for the work became at once and has always remained a symbol of intellectual freedom and an inspiration to pioneers in every field of thought.*

It was something of this inspiration that had filled the young Harvey Cushing as he stood in 1900 in the anatomical amphitheatre at Bologna "bareheaded as though before a shrine."

The Epitome

The great plates of the *Fabrica* were designed and originally drawn, it has been thought, in the studio of Titian. Some have believed that Titian himself was responsible for the original planning, and it is probable that students working with him, such as Calcar, took over responsibility for their execution. There is ample evidence, moreover, that artists as well as anatomists were interested in

*G. W. Corner, *Clio Medica Series, Anatomy*, New York, 1930, p. 26.

the figures (as indeed they have been ever since), but because they were not especially concerned with the wordy text of the *Fabrica*, Vesalius sought to make his principal anatomical disclosures available in abbreviated form. So it came about that almost immediately after the appearance of the *Fabrica*, i.e., in June 1543, he issued an *Epitome* in which the chief anatomical relations of the human body were summarized. Medical students also used the *Epitome* since many of them could not afford the huge original work. Although it was intended for artists and impecunious students, Vesalius had another reason for issuing the *Epitome*, a reason which comes out in an amusing passage in his dedicatory letter to Philip II. I give you the passage, which has a great deal of relevance for today, in Professor Lind's excellent rendering:

While I strive to be useful to them [physicians] yet at the same time I am anxious to snatch opportunity from the hands of certain rascally printers who may later seize in possession upon the labors of another to reduce them ineptly into small space and publish them under their own names (creatures born for the destruction of letters!). . . . For no one is ignorant how much is lost in all sciences by the use of compendiums. Though indeed they seem to provide a certain way and systematic approach to the perfect and complete knowledge of things and seem to contain in short and in sum that which is set down elsewhere with more space and prolixity and are for this reason considered in the light of an index on the very abode of memory, in which matters written down at length are fitly

reduced to their proper place, nevertheless, compendiums do signal injury and wreak a great havoc upon literature; for, given to the use of compendiums alone, we read scarcely anything else through to the end these days. This is true even for those who have delivered themselves completely to learning, to this degree aspiring only to the shadow and superstructure of science, digging little or not at all beneath the surface.*

Of the nine woodblocks chosen from the *Fabrica* for the *Epitome*, the seven skeletal figures are identical but appear in the *Epitome* some six centimeters taller. The idea has been advanced that Vesalius had them drawn for the *Fabrica*, but that they proved too large for convenient handling. The two blocks containing the drawings of organs designed to be cut out and superimposed on the skeletal figures he for some reason retained in the larger size and they had to be folded in the *Fabrica*. In addition, there were two completely new drawings for the *Epitome*, the famous "Adam and Eve" plates. The frontispiece title-page is identical with that in the *Fabrica*. Since it was of course smaller, Vesalius, in the space at the bottom, placed twelve lines of directions to the reader about how to use the text and figures.

The format of the *Epitome* was so large that in all of the copies I have seen, traces of a horizontal folding are still apparent, suggesting that the printer had to bend them so that they would fit into the saddlebags of the

*L. R. Lind, tr., *The Epitome of Andreas Vesalius*, New York, 1949, p. xxxiv.

mule teams which carried them over the Alpine passes. In those days it was impossible to send things over the mountain passes in carts because even the Simplon, the widest of the passes, had long stretches that were scarcely two feet in width. The *Fabrica* just fitted into the saddlebags, but its weight and the configuration of the mules' backs caused the books to arrive in a warped condition and in many of the vellum-bound copies signs of the original misshapeness are still visible.

Vesalius brought out the second edition of the *Fabrica* in 1555, and to many it has seemed odd that another *Epitome* was not issued at the same time. Some years ago Dr. Erik Waller, the eminent Swedish collector, announced that he had found a copy of the *Epitome* dated 1555, which had originally belonged to the distinguished Italian surgeon, Antonio Scarpa. It is identical with the 1543 *Epitome* except that the date had been changed on the final page from MDXLIII *Mense Junio* to MDLV *Mense Aprili*. Dr. Waller was at first skeptical of the authenticity, fearing that it might be a cleverly planned fake, but careful study of the watermarks of the final sheet M showed the paper to be identical with that used in the 1555 version of the *Fabrica*, whereas the other sheets were on paper with 1543 watermarks. Hence the 1555 version must have been issued from remainders of the 1543 edition with the final sheet altered.

Andreas Vesalius, whose driving energy and daring brought him to great achievement at the early age of

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twenty-eight, has served as an inspiration to students of medicine for more than four hundred years. His work illustrates the importance of an open mind and a healthy skepticism about anything set down in books as scientific truth. As the late Sir Thomas Lewis so trenchantly put it—in the science of medicine no doctrine is sufficiently supported if yet another serious argument may be urged in its favor. The challenge Vesalius throws out to you in the well-known drawing in the *Epitome* which shows him demonstrating the muscles of the arm is to believe nothing anyone tells you—even if it is Dr. Major—until you yourself have proved the correctness of the dictum to your own satisfaction. Only in this way can you travel securely on the road to truth.

II
Medicine in the Eighteenth
Century

Medicine in the Eighteenth Century*

I welcomed the opportunity to inaugurate the Clendenning Lectureship on the History and Philosophy of Medicine because I feel strongly that anything which serves to keep alive the spirit and advance the work of such men as Logan Clendenning is both a privilege and a duty. In this age when the need for humanism in science is so great in order that we may maintain our cultural traditions, Logan Clendenning's approach to medicine demands re-emphasis. He had the rare gift of making history come alive, of making its study meaningful and useful to the physician of today both as a pleasurable pastime and as a means through which the rich heritage of our profession might enrich and broaden our lives. Let me quote from the preface of one of Dr. Clendenning's well-known books:

Behind the doctor—so many centuries, so many stories, so many people. I see them crowding around him—a great throng of old ghosts as he walks into the room. When he takes out his stethoscope to listen to your heart, there is thin, consumptive Dr. Laennec, of Paris, peering over his shoulder. When he taps your chest, another ghost—jolly, music-loving Dr. Leopold Auenbrugger, of Vienna, smiles in appreciation of his discovery living through the years. When the urine is examined, there is

*Delivered at Kansas City, Kansas, on 15 November 1949 at four p.m.

Dr. Richard Bright, of London, rattling his seals and ordering his carriage to take him to Russell Square to treat the great British merchants. . . .

Many other ghosts, too! . . . There is the stout figure of Benjamin Jesty among his cows, and scornful Lady Mary Montagu and her scapegrace son wearing his turban and sitting crosslegged on the floor of the British Embassy in Venice, . . . and Andreas Vesalius, the Belgian, slinking through the dusky streets of Paris with a skeleton in his wheelbarrow. . . All these and thousands of others are behind the doctor. Vivid people in their day, full of hopes and interests and queer notions.

This morning at Lawrence I spoke about Vesalius because Dr. Clendening was an ardent student of Vesalian anatomy and because he sponsored the distinguished translation by Professor Lind of the *Epitome* of Vesalius' monumental work, *De humani corporis fabrica*. This afternoon I have chosen as a subject another theme which was close to Dr. Clendening's heart, namely, the advance of medicine in eighteenth-century England. And in his wide collecting he concentrated on one of the greatest triumphs of that century—the discovery that vaccination with cowpox conferred permanent immunity to the dreaded scourge of smallpox. In his quest for the landmarks of medicine Dr. Clendening sought out the birthplace of Edward Jenner and he also collected photographs connected with his work. In 1938 he had an amusing letter from Dr. Cushing, who was also a Jenner enthusiast, in appreciation of a Jenner item he had sent as a gift.

MEDICINE IN THE EIGHTEENTH CENTURY

Dear Sir Logan: Thanks for the portrait of Jenner's cow. Unappetizing as it appears, I regard it as a most generous quid-quod or cud for the Jones volume I sent you. I shall add it to my Jenneriana with gratitude.

With greetings to your long-suffering Lady, I am,
Sincerely yours, Harvey Cushing.

But the development of vaccination was only one of the advances for which the eighteenth century is notable. Scientific inquiry, given strong impetus by the Royal Society, had progressed to the point where it was no longer in the hands of amateurs, and in medicine there was material progress in three spheres, namely, the physiology of respiration, morbid pathology, and the recognition of clinical syndromes. I propose in this lecture to summarize the more important developments in these three fields.

I. PHYSIOLOGY

By the end of the seventeenth century, William Harvey's doctrine of the circulation of the blood was generally accepted, but its clinical application was not yet widespread. Malpighi and Leeuwenhoek had meanwhile discovered the capillaries and this important disclosure furthered the establishment of the concept of the circulation. The next contribution came from Richard Lower, who had observed that venous blood turns red on exposure to the air and had concluded that the passage of blood through the lungs was designed to transform venous blood into arterial and that a particular "quality" of the air was absorbed in the process.

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The air itself had been intensively studied by Robert Boyle and it was he—along with his pupils, Richard Lower, Robert Hooke, and John Mayow—who concluded that the air was made up of particles of different affinities and that one group of particles in particular was essential to life and was responsible for converting venous blood into arterial. The chemical entity to which we now refer as oxygen was not actually isolated by Boyle and his followers, but its existence was clearly proclaimed. Boyle, in fact, stated in no uncertain terms that the quality in the air which was essential for the burning of a candle was the same quality that maintained the life of a mouse or a sparrow. The disappearance of this property in the air in his low-pressure chamber caused the flame of the candle and the life of the sparrow to be simultaneously snuffed out. From the point of view of the history of science this was a highly important deduction, as was his concept of the molecular structure of the air. Shortly before he died Boyle wrote:

Only I shall here intimate that though the Elastical Air seem to continue such, rather upon the score of its Structure than any external Agitation; yet Heat, that is a kind of Motion, may make the agitated Particles strive to recede further and further from the Centers of their Motions, and to beat off those, that would hinder the freedom of their Gyration, and so very much add to the endeavour of such Air to expand it self. And I will allow you to suspect, that there may be sometimes mingled with the Particles that are Springy, upon the newly mentioned

Account, some others, that owe their Elasticity, not so much to their Structure, as their Motion, which, variously brandishing them and whirling them about, may make them beat off the neighbouring Particles, and thereby promote an expansive Endeavour in the Air, whereof they are Parts.*

The seventeenth century can also claim one of the greatest minds in the history of scientific progress. In the year 1687 Isaac Newton published his epic book, the *Principia*, and thereafter Newtonian mechanics became the order of the day. Those who sought to understand the functions of the human body began to think in the terms that Newton had laid down. And thus the stage was set for the most able physiologist of the eighteenth century, the Vicar of the parish of Teddington on Thames—Stephen Hales.

Stephen Hales

In the year 1691 (which witnessed the death of Robert Boyle), Stephen Hales matriculated at Corpus Christi College in Cambridge. At this time Isaac Newton's influence was at its height and Hales, profiting thereby, received sound instruction in mathematics and the physical sciences, although he was planning ultimately to enter the church. He took his B.A. in 1699 and four years later was admitted a Fellow of Corpus Christi and was also ordained a Deacon. But circumstances now conspired to

*R. Boyle, *The General History of the Air*, London, 1692, p. 6.

influence Hales in another direction. At the turn of the century Richard Bentley became Master of Trinity College and since Newton had now left Cambridge to become Governor of the Mint, Bentley sought to carry on with the scientific tradition which Newton had established, and bent his energies toward the development of a school of natural science. As a tutor of the University, Hales was brought into close contact with Bentley and between 1700 and 1709 he carried on experimental work and tutored a number of young men who were studying in the sciences. In 1709, however, having been ordained priest, he left Cambridge to become the "Perpetual Curate" of the Parish of Teddington and there for the next fifty years he remained "passing rich on eighty pounds a year."*

An unusual parish priest was Hales, for his interest in science did not subside after leaving Cambridge and he occupied himself between sermons with experiments that covered a wide range in the sciences, including the physiology of plants, the chemical constitution of the air, studies on reflex action, and, above all, his celebrated experiments on arterial and venous pressures in warm-blooded animals. Hales was slow to publish and it was not until 1727 that he issued the first volume of his *Statical Essays*, the so-called *Vegetable Staticks*, and six years later that he published the second volume, which he designated the *Haemastaticks*.

*William Doolin, *Wayfarers in Medicine*, London, 1947, p. 124.

Hales is important in the history of physiology for three significant experiments. The first had to do with respiration. In 1674 John Mayow had observed that when an animal breathed within a glass container sealed by water, the water was gradually sucked up into the container, indicating that the animal absorbed a measurable volume of air in the process of breathing. Here, then, was visual proof of Boyle's deduction that the lungs absorb a particular quality of the air in the course of respiration. Hales cited Mayow's observation and proceeded to confirm it on himself by breathing in and out of a bag. He found that when the volume of air in the bag had diminished by twelve to thirteen per cent, he became giddy. "Toward the end of the minute the bladder was become so flaccid," he wrote, "that I could not blow it above half full with the greatest expiration I could make . . . whence it is plain that a considerable quantity of the elasticity of the air contained in my lung and the bladder was destroyed."

Not only did Hales find that part of the air was absorbed when he breathed in and out of the bag, but he suspected that the failure of the remaining air to support respiration stemmed not only from the absorption of a particular quality but from the contamination of the remaining air by toxic vapors. He accordingly developed an expiratory valve (similar to those used in oxygen masks) which he moistened with "sal tartar" and in these circumstances it was possible to rebreath in and out of the bag

for from five to eight minutes. He then found that the sal tartar valve increased in weight more than could be accounted for by the absorption of water vapour. Thus Hales defined oxygen, as had Boyle and Mayow, as the substance in air which is absorbed during respiration. He likewise described carbon dioxide even though he never isolated it in pure state except as it appeared as a carbonate on his respiratory valve.

Had one sauntered into the churchyard of Teddington Parish in December 1731 one would have beheld the handsome Vicar engaged in even more curious activities than breathing in and out of a bag. He had cast a white mare to the ground, lashing her to a farm gate. The horse was weary and old in service, and the parson had secured her for the purpose of performing a terminal experiment. After tying the animal securely, he laid open the jugular vein and inserted in that part which comes from the head a glass tube some four feet in length. The rest of the story should be told in Hales' own words:

3. The Blood rose in it, in three or four Seconds of Time, about a Foot, and then was stationary for two or three Seconds; then in three or four Seconds more, it rose sometimes gradually, and sometimes with an unequally accelerated Motion nine Inches more, on small strainings of the Mare: Then upon greater Strainings it rose about a Yard, and would subside five or six Inches: Then upon a larger Strain or Struggle of the Mare, it rose so high, as to flow a little out at the Top of the Tube; so that had

the Tube been a few Inches higher, it would have risen probably to that Height.

4. When the Mare ceased to strain and struggle, the Blood subsided about eighteen or twenty Inches; so the Return of the Blood into the Vein was not hindered by the Valves; which I have also observed in other Parts where there are Valves, tho' sometimes they absolutely hinder the Return of any Fluid.

5. The Diameter of the Brass Pipe and Tube which were fixed to the Vein, were nearly one seventh of an Inch: The Diameter of the Jugular Vein about half an Inch.

6. Then laying bare the left Carotid Artery, I fixed to it towards the Heart the Brass Pipe, and to that the Wind-Pipe of a Goose; to the other End of which a Glass Tube was fixed, which was twelve Feet nine Inches long. The Design of using the Wind-Pipe was by its Pliancy to prevent the Inconveniencies that might happen when the Mare struggled; if the Tube had been immediately fixed to the Artery, without the Intervention of this pliant Pipe.

7. There had been lost before the Tube was fixed to the Artery, about seventy cubick Inches of Blood. The Blood rose in the Tube in the same manner as in the Case of the two former Horses, till it reached to nine Feet six Inches Height. I then took away the Tube from the Artery and let out by Measure sixty cubick Inches of Blood, and then immediately replaced the Tube to see how high the Blood would rise in it after each Evacuation; this was repeated several times, till the Mare expired. . . .

8. We may observe, that these three Horses all expired, when the perpendicular Height of the Blood in the Tube was about two Feet.*

*Stephen Hales, *Statical Essays: Containing Haemastatics*, London, 1733, pp. 14-16.

This direct determination of the systolic pressure in a horse caused widespread comment. It was significant not only because of the pressures which Hales recorded but because of his secondary observation—that on continuous withdrawal of blood the systolic pressure remained nearly constant until almost a third of the total volume of blood had been removed. He was thus led to postulate the existence of a compensatory mechanism for closing the peripheral vessels in order to maintain arterial pressure.

Hales may also be given credit for the fundamental experiment in the history of reflex action, for he found that a frog would continue to hop about after it had been decapitated, that its hind limbs would be withdrawn when a nocuous stimulus was applied, but that all such reactions vanished when the spinal cord itself was destroyed. Hales did not publish the experiment but described it in a letter to Robert Whytt of Edinburgh, who was the first to apply the concept of reflex action to the problems of clinical neurology. In Whytt's celebrated book, *On Certain Vital and Other Involuntary Movements of Animals*, he describes the reflex response of the pupils to light and determined the pathways involved in the reaction. He also introduced our modern terminology of stimulus and response.

Priestley and Lavoisier

Joseph Priestley, another eighteenth-century divine, attacked the chemistry of the gases, taking up where Hales had left off. He had become interested in the "mephitic

air," as he called it, which emanates from fermenting beer vats. He discovered that this particular air was freely soluble in water and that it could be kept in solution if placed under pressure—and so emerged Priestley's great benefaction to the human race, charged water. Believing that it would be useful to the Royal Navy, he addressed the tract describing its discovery to the First Sea Lord, the Earl of Sandwich. But this was only the beginning.

In March 1772 he issued a paper "On Different Kinds of Air" in which he recorded the isolation of nitric acid and hydrochloric acid. The discovery of other gases followed, and on the first of August 1774 he caused a gas to be evolved by heating the red calx of mercury with a burning glass. "A candle burned in this air with a remarkably vigorous flame and the gas supported respiration of small animals five times as long as an equivalent amount of ordinary air." But Priestley, although he had isolated oxygen, failed to place the proper interpretation upon what he had discovered and concluded that the new air supported a flame better than ordinary air because it had been "dephlogisticated." At this distance the idea may seem quaint. But Priestley did not yet know about nitrogen, and if one substitutes nitrogen for phlogiston in Priestley's writings, the interpretation does not seem unreasonable.

The remainder of the story is too well known to require repetition. Priestley told Lavoisier about his new air and Lavoisier quickly grasped its significance and established to his own satisfaction that it was in fact the prin-

principle which combines with metals during their "calcination." For a time Lavoisier referred to it as "the principle which combines with metals," but realizing that a shorter term was desirable and believing that the gas was present in all acids, he adopted the phrase "the acidifying principle." But since his "*principe acidifiant*" was also awkward, he turned to his Greek roots and combined "*oxus*" meaning "acid," and "-gen" (the root of *gennaos*, "I beget") into a single word, "*oxygène*." Thus was the new gas born and christened.

Lavoisier was quick to study the new gas both in respect to its power of combining with metals and its function in respiration. With Laplace he found that during muscular work oxygen is consumed in increasing amounts and carbon dioxide output likewise is increased, but that the nitrogen-hydrogen content of inspired air was not altered by exercise. And so with the recognition of oxygen as a separate element, and with the simultaneous recognition of CO_2 as a noxious vapor given off by the lungs during respiration, biochemistry and physiology entered upon a wholly new era, for this was indeed the greatest milestone in the history of physiology after the discovery of the circulation of the blood. When the French Revolution descended, Lavoisier, a man scarcely turned fifty, was deeply involved in these studies. Despite his generous public service, his wealth and position were used against him and he was arrested, given a farcical trial, and sent to the guillotine on May 8, 1794. The following day someone

commented: "Only a moment to cut off that head, but a hundred years may elapse before France will produce another like it."

In this century there were a number of other contributions to physiology which had far-reaching applications. The physiology of digestion was notably advanced by Réaumur in France, who studied the effects of gastric secretion on various foodstuffs *in vitro* and *in vivo*. These studies were made upon his pet kite, a bird which has the obliging habit of regurgitating undigested matter. Spallanzani, an Italian priest, carried out similar studies on himself and established that human gastric juice was capable of digesting various foodstuffs outside of the body provided body temperature was maintained. In England the physiology of the lymphatic vessels was studied by John Hunter and his gifted pupil, William Hewson, and in Italy by Mascagni.

The invention of the Leyden jar in 1746 had an immediate influence on the course of physiological thought, for it made possible artificial stimulation of nerves and muscles. Albrecht von Haller, Boerhaave's pupil who dominated physiology in the mid-eighteenth century, immediately took up the study of neuro-muscular physiology and published four impressive volumes on irritability which led to the great controversy between him and Robert Whytt of Edinburgh. The problem of the relation of electricity to the nerve impulse was under continuous discussion until 1791, when Galvani published his memor-

able book on animal electricity. His compatriot, Alessandro Volta, did not believe that Galvani had established the existence of animal electricity and that the frogs' legs in his experiments had been stimulated through potentials that had resulted from contact of dissimilar metals. Galvani retorted with his rheoscopic nerve-muscle preparation in which the nerve of one muscle was allowed to lie on the surface of another muscle, causing the first to contract whenever the second was stimulated. Volta accepted this as proof of animal electricity, but just as the century was drawing to a close he discovered that a *continuous* potential could be obtained if dissimilar metals were arranged one on top of another in a pile. He had in short discovered the electric battery.

II. PATHOLOGY

Progress in the field of pathology during the eighteenth century was almost as significant as that in physiology, largely due to the efforts of one man, Giovanni Battista Morgagni, whose monumental folio, *De sedibus et causis morborum*, marks the great turning point in the history of pathology. Prior to Morgagni's time, very few physicians had had the hardihood of soul to study post-mortem findings with the end in view of correlating them with disease processes seen during the life of a patient. There was one notable exception to this in the work of another Italian, Antonio Beneveni, which was published by his brother in 1507 five years after Beneveni's death. In the

small book 111 cases are described with autopsy findings. Among these one finds cases of gallstone, mesenteric abscesses, mesenteric thrombosis, and several cases having abnormal arteries. Benevieni's book apparently caused little stir in its time and others failed to emulate his example for more than two hundred years.

Giovanni Morgagni

Morgagni was a conscientious general practitioner and professor at Padua who had studied at Bologna. Over the years he had made a careful practice of carrying out post-mortems upon any patient under his care who chanced to die. Several of his younger colleagues prevailed upon him when an old man to record his experience in correlating post-mortem findings with disease processes, and he proceeded to present his cases in a series of informal letters which were ultimately published in a huge folio issued at Venice in 1761. In the section devoted to the heart and arteries, one finds cases of diseased pericardium, abnormalities of the valves, ruptured dilation and hypertrophy of the heart itself, also calcification of the aorta. Osler believes that he gave the first recognizable description of angina pectoris. Thus:

A lady forty-two years of age, who for a long time, had been a valetudinarian, within the same period when exercising, was subject to attacks of violent anguish in the upper part of the chest on the left side, accompanied with a difficulty of breathing, and numbness of the left arm;

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but these paroxysms soon subsided when she ceased from exertion. In these circumstances, but with cheerfulness of mind, she undertook a journey from Venice, purposing to travel along the continent, when she was seized with a paroxysm, and died on the spot. I examined the body on the following day. . . . The aorta was considerably dilated at its curvature; and, in places, through its whole tract, the inner surface was unequal and ossified. These appearances were propagated into the arteria innominata. The aortic valves were indurated. . . .*

Morgagni's influence proved to be enormous. Medicine at that time was infested by systems, schisms, and isms: iatromechanics, iatrochemistry, animism, vitalism, and the predecessors of homeopathy, but his clear, deliberate voice sounded above all this, and from his teachings came the solid foundation upon which modern clinical medicine was erected—the foundation of morbid anatomy. Morgagni had followers in many countries—the meteoric Bichat in France, Matthew Baillie and John Hunter in England, Cullen in Scotland, and Benjamin Rush in America, who carried the deadhouse tradition to Philadelphia, where it flourished throughout the nineteenth century.

III. INTERNAL MEDICINE

In the sphere of clinical medicine the eighteenth century was able to profit by the experience of the greatest of seventeenth-century clinicians, namely, Thomas Syden-

*W. Osler, *The Evolution of Modern Medicine*, New Haven, 1921, p. 188 (quoted from Cooke's *Morgagni*, I, 417-418).

ham. He was not particularly interested in morbid anatomy as such, yet he studied disease processes with a keen and discerning eye and was led by this circumstance not only to describe many new disease entities but to foster a number of new therapeutic agents, one of them the Peruvian bark, which at that time had just been brought to Europe from Brazil by the Jesuits.

Educated at Oxford and Montpellier, Sydenham had settled down to practise in London in 1656. Among his friends was the Honourable Robert Boyle, who suggested to Sydenham that he publish his observations on fevers and smallpox. This small octavo volume of 156 pages, Sydenham's first publication, was issued in the author's forty-second year. It was well received both in England and abroad, and in 1668 a second edition was called for, to which a chapter was added on the plague that had ravaged London three years earlier. The second edition also contained a laudatory Latin poem by John Locke—an earnest of the lifelong friendship of these two colorful figures. Sydenham's philosophy is well stated in this book on fevers. He was a disciple of intensive clinical study, paying little heed to tradition except perhaps to that of Hippocrates; it has been said by Newman* that "the scientific method of observation and induction, laid down by Sydenham as the foundation of sound medical practice, will endure forever."

*G. L. Newman, *Thomas Sydenham Reformer of English Medicine*, London, 1924, p. 19.

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Sydenham's study of fevers and the plague led him to believe that contagious diseases occur in cycles, that they are influenced by climate and atmospheric conditions, and that the character of any given epidemic would depend upon a concatenation of cosmic circumstances. His studies on the relation of geography and meteorology to epidemic disease indeed entitle him to be regarded as one of the founders of epidemiology. In addition to this, he described the malarial fevers of his time and gave, shortly before his death, a classical description of the gout (from which he himself suffered). He can also be credited with clear-cut accounts of scarlatina, measles, broncho-pneumonia, lobar pneumonia, dysentery, chorea, and hysteria. From the point of view of his influence on medicine in the eighteenth century, a booklet published posthumously in 1692 entitled *Processus integri* proved to be the *vade mecum* of the English practitioner for the next hundred years. He had prepared the booklet for his son to help him in his practice and in it he named seriatim sixty-one morbid conditions and set down the best prescriptions and methods of treatment for each one. Practitioners learned the book by heart and to medical students it became a bible. Largely because of this booklet Sydenham's influence continued until the time of Rokitansky and the rise of the Vienna school.

Hermann Boerhaave

The first commanding clinical figure of the eighteenth century was Hermann Boerhaave of Leyden. An ardent

disciple of Sydenham, he came to occupy a position of even greater eminence in European medicine than his distinguished English predecessor. Students flocked to him from all over Europe and his reputation in Scotland was so great that for a time nearly every medical student at Edinburgh was advised to spend part of his time in Leyden.

Boerhaave's importance lay in the fact that he insisted upon applying the newer developments in chemistry, physics, and biology to clinical problems. He felt that his students had insufficient background in what we should now designate the preclinical sciences and at the turn of the century he began to give special courses of lectures in medical chemistry and in the principles of physiology. In 1708 he issued these lectures in book form under the title *Institutiones medicae*—"The Institutes of Medicine." In 1726 a chair of the Institutes of Medicine was founded in Edinburgh and for the next hundred and seventy-five years chairs of physiology in all Scottish universities and in those of the Dominions were designated chairs of the Institutes of Medicine. Sir William Osler, for example, occupied such a post for a time at McGill. It may be said, therefore, that Boerhaave was the founder of the academic discipline of physiology. Historically this is of considerable significance, for it means that physiology came into the academic curriculum in response to the needs of the clinic, a fact that must not be forgotten although it is now a subject in its own right.

It would be impossible in a brief survey such as this

to mention all who contributed significantly to the advancement of medicine in the eighteenth century. One thinks of John Fothergill's classic description of epidemic sore throat, which we now know to have been diphtheria, of Lind's account of scurvy at sea and of diseases peculiar to tropical climates, of Baker's description of lead poisoning.

During this century new methods of clinical investigation were developed, the most notable being Floyer's pulse-watch (1707) with which the pulse was for the first time actually counted, and Auenbrugger's introduction of the art of percussion (1761), so ably applied by Rozière de la Chassagne and later by Laennec. But from the therapeutic standpoint, the crowning discoveries of the century were those of William Withering and Edward Jenner.

William Withering

The story of how William Withering discovered the therapeutic action of foxglove is best put in his own words.

In the year 1775, my opinion was asked concerning a family receipt for the cure of the dropsy. I was told that it had long been kept a secret by an old woman in Shropshire, who had sometimes made cures after the more regular practitioners had failed. I was informed also, that the effects produced more violent vomiting and purging; for the diuretic effects seemed to have been overlooked. This medicine was composed of twenty or more different herbs; but it was not very difficult for one conversant in

these subjects, to perceive, that the active herb could be no other than the Foxglove.*

Although Withering began to use the decoction of foxglove in 1775, he did not publish an account of his experience until ten years later. He was then forced into doing so by the fact that Erasmus Darwin had rushed into print the year before with a wholly unsatisfactory account of the action of digitalis as seen in a number of cases which Darwin and Withering had seen together in consultation. Withering was restrained in his references to Darwin and his book as a whole, *An Account of the Foxglove*, is a model of concise, clinical description and will stand as one of the principal landmarks in the history of therapeutics.

Edward Jenner and Vaccination

The work of Edward Jenner on vaccination represented the culmination of a great revival of interest in smallpox which began in 1721 when the disease appeared in epidemic form on both sides of the Atlantic. The origin of the practice of inoculation (or, better, "variolation"), as opposed to vaccination, is shrouded in the dim mists of historical uncertainty. Marius, the Bishop of Avenches, is said to have made reference to smallpox inoculation in his sixth-century Chronicle. A tenth-century verse in the School of Salerno *Regimen* has been translated by Klebs

*W. Withering, *An Account of the Foxglove and Some of its Medical Uses*, Birmingham, 1785, p. 2.

to read: "In order that variola may not produce death among tender babes, put into their veins a favorable variola."* In ancient China and in India the pustule was said to have been dried and blown into the nostrils for purposes of protection. None of these early reports, however, had much effect in Western Europe until the practice had reached a higher stage of development. In 1717 Lady Mary Wortley Montagu, wife of the British Ambassador to Turkey, wrote enthusiastically to a friend in England after seeing inoculations performed in Constantinople. So impressed had she been that in 1714 she had had her three-year-old son Edward inoculated, and others in the diplomatic corps in Turkey had followed her example. Before her letter arrived there had already been some agitation in England. An Oxford-trained Greek physician, Emanuel Timoni, published a tract on variolation at Constantinople in 1713 which was summarized in the *Philosophical Transactions* of the Royal Society the following year (Volume 29), as was Pylarini's tract issued at Venice in 1715.

In the spring of 1721 the smallpox appeared in England in epidemic form. By this time Lady Mary had returned and in April she had her four-year-old daughter, the future Lady Bute, inoculated. The next month, Dr. Keith, a member of the College of Physicians, inoculated his six-year-old son. The Court by this time had become uneasy

*A. C. Klebs, *The Historic Evolution of Variolation*, *Johns Hopkins Hospital Bulletin*, 1913, 24, p. 70.

about the smallpox and after the King had had the procedure tried on six condemned criminals without adverse results, he ordered that his grandchildren be inoculated.

Similar tentative trials were being made at the same time in America. The smallpox appeared in Boston on 15 April 1721, and Cotton Mather, who had read the Timoni and Pylarini papers in the *Philosophical Transactions*, induced a prominent physician, Zabdiel Boylston, to attempt some inoculations. The uproar which followed placed Boylston's and Mather's lives in danger. Abusive attacks were made on the innovators, a hand grenade was thrown into Mather's study, and a war of pamphlets was launched, constituting the earliest substantial block of medical writing to be issued on this side of the Atlantic—a literature, be it said, which has never been thoroughly studied and which would well repay analysis.

In the years that followed, the inoculators accumulated impressive evidence concerning the value of the procedure in persons who survived the inoculation. Now and again, however, disfiguring and sometimes fatal cases of smallpox were transmitted by inoculation, so that when Edward Jenner came forth with the thesis that cowpox, which in man is a far less serious disease than smallpox, conferred immunity against the latter disease, laymen and physicians alike were prepared to listen. Jenner obtained his idea, as had William Withering, from talking with country folk—farmers in Gloucestershire who had noted that the dairymaids who had contracted cowpox from milking infected

cows never succumbed to smallpox. Being of an experimental turn of mind, Jenner in May 1796 scratched into the skin of James Phipps, a boy of eight, lymph of a cowpox pustule from the hand of Sarah Nelmes, a dairymaid. The boy developed cowpox and recovered. On July 1, Jenner inoculated him with smallpox and it failed to take. This was all that Jenner needed—it clearly completed his argument and he proceeded to vaccinate others with cowpox lymph, finding that his subjects were subsequently resistant to smallpox inoculation. By June of 1798 he had assembled his evidence and his report on twenty-three cases was published in the form of a thin quarto of seventy-five pages entitled *An Inquiry into the Causes and Effects of the Variolae Vaccinae, a Disease Discovered in Some of the Western Counties of England, Particularly Gloucestershire, and Known by the Name of the Cow Pox*. As with Withering on the foxglove, Jenner's "Inquiry" will always be ranked as one of the great medical classics—a monument to his wisdom and perseverance. Like all innovators, Jenner met stern and often highly emotional opposition. He replied several times to his critics and then retired to Gloucestershire, where he continued happily in a rural practice, collecting fossils and pursuing his hobby of ornithology.

These were the advances in scientific medicine in the eighteenth century—they served as the foundation for others, even more important, in the next century in the sphere of metabolism, in cellular pathology, and in clinical fields.

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In closing, may I express again my pleasure in being here on this occasion. In giving life to the men and women of medical history, Dr. Clendening created a kind of immortality for himself, and it is not hard to imagine him moving among them in the Elysian Fields, a familiar and jolly figure in that company behind the doctor—"vivid people . . . full of hopes and interests and queer notions" out of which the medicine of today has been created.

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