# THE ADVANCE OF MEDICINE

BY

THE RIGHT HONOURABLE

LORD MOYNIHAN

K.C.M.G., C.B.

President, Royal College of Surgeons
of England

*The Romanes Lecture*

DELIVERED IN THE
SHELDONIAN THEATRE
1 JUNE 1932

OXFORD
AT THE CLARENDON PRESS
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## SUMMARY

I. The advance of Science, including the whole Art and Science of Healing (Ars Medicatrix).

II. Medicine the Mother of all Science. Hippocrates and Observation (Method of Induction). Galen and Experiment (Method of Deduction).

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VI. Parting of the ways. The Physiology of early disease. Need for Hospital research on Man. Training in the experimental method of Galen.

VII. Truancy and Disruption of Physiology. Chemistry, Physics, Bio-Chemistry.

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# THE ADVANCE OF MEDICINE

'Medicine is a Science which hath been more professed than laboured: and yet more laboured than advanced.'

BACON, *Advancement of Learning.*

## I

THE distinguishing feature of the intellectual life of the last half-century has been the revolutionary advance of science. New ideas are to-day expressed in so new a language, new conceptions and changed methods have created so new a vocabulary, that to the scientist of fifty years ago much of the literature of to-day would be unintelligible. In every department of scientific work the advance has indeed been stupendous, almost passing belief. Nor is the wonder of it lessened when we compare or contrast it with all that has happened in other departments of intellectual activity. In painting, in sculpture, in the design or craft of architecture, in literature, we have altered our immediate interests perhaps, and have often changed our tastes, but when we compare our efforts with the ideas and achievements of days gone by we remain in a state of profound and reverent humility. In craftsmanship, as we have learned only in the last few years, perhaps nothing more exquisite has been wrought by men's hands than the finished perfection of works which have been hidden for over 3,000 years in the tomb. The power of man's hand is no greater, its skill neither more subtle nor more cunning, than in days of Tutankhamen. Science, however, has advanced incomparably and in this advance Medicine has at least kept pace.

## II

Medicine may justly claim to be the mother and nurse of all science: for the essential methods by which alone science can advance were brought into being and made perfect by those daily engaged in the practice of medicine. To Hippocrates more than to any other we may attribute the method of induction, the method by which a general law is formulated after observation of a multitude of singular examples. Bacon reminds us of the 'ancient and serious diligence of Hippocrates which used to set down a narrative of the special cases of his patients, and how they proceeded, and how they were judged by recovery or death', an example proper in the father of 'The Art': 'If men intend to observe they shall find much worthy to observe, for many things are new in the manner which are not new in kind.' As observer, collector, correlator, generalizer, the diligence of Hippocrates has in medicine surely never been surpassed. To Galen we owe in medicine the method of deduction by which we pass down the scale rather than up, to exposure of those isolated facts from which generalizations are at last constructed.

## III

Armed with these two indispensable methods the practitioners of medicine were nevertheless for more than 1,000 years almost impotent. This millennium was given over to the reign of incorrigible authority. No Holy Writ was ever so indisputable, never was its sway so tyrannical, its acceptance so complacent, so witheringly destructive of original thought, as were the writings of Hippocrates. His dominance had become established even before the days of Galen, for on occasions when this vain, morose, garrulous man found that experimental results were inconsistent with the teaching of Hippocrates, he held that the experiment was faulty in design or imperfect in execution, and for that sole reason failed to confirm the doctrine of the great master. Authority then was demi-god.

The intellectual supremacy of Hippocrates, the commanding reach and protean influence of his teaching, were in part due to the fact that in his own person he combined a variety of divergent and opposing tendencies. His powers of observation, in range and accuracy never exceeded even by John Hunter himself; his facility for creating general principles where only individual observations had formerly been possible, a mastery never before equally displayed, gave him intellectual authority far surpassing that hitherto conceded to any man. Authority has never been more pernicious. Most cruel of all tyrannies surely are those exercised over the minds of men, denying them both freedom and expression. Tyranny is no force to set in motion the ideas of science; and tyrannous indeed was the control which Hippocrates and Galen exercised for so many centuries. In all that sterile period no new thought is found, no new method, no new experiment. To deny the authority of Hippocrates and Galen or to dissent from their teaching was not merely heterodox, it was heresy, punishable by death itself. So late as the thirteenth century it called for a rare and reckless courage when Henry of Mondeville exclaimed, 'God did not surely exhaust all his wisdom in the creation of Galen'. Nor can we forget that in 1553 unhappy Servetus, discoverer of the pulmonary circulation, was burned as a heretic by Calvin at Geneva.

The teaching of the ancient masters remained therefore supreme: it was kept alive and transmitted by Avicenna and others to the East, where it was treasured until, through the agency of Moors and Arabs, it returned unchanged, at a time when learning and culture in Europe had almost vanished. The Arabian mind was essentially concerned with compiling knowledge from all sources rather than with initiating inquiry; and great and useful work, in this direction, was carried out during the brightest days of the Saracen Empire. The modern world owes much to this careful preservation of knowledge and to the multiplication of copies of standard works on Medicine, before the era of printing; even though the science and art of medicine did not then through such efforts advance one step. In Avicenna we find a mind keen as that of his great predecessors, viewing the human body and its ailments in his own way, although everywhere in his teaching points of resemblance to the works of Galen and Hippocrates are evident. He was not experimenter so much as philosopher, and the power of his mind over so many later centuries is probably to be attributed to his masterly grasp not of medicine and surgery only, but of all sciences. In the art of surgery as far as we can judge by records in the Canon he can hardly have attained the skill of the great founder. In him we do not find all those evidences of mastership in technique which shine so strongly through the writings of Hippocrates. As is characteristic of the Eastern to-day, the knowledge which he possessed and, to judge by the records of his successes, utilized with great practical effect, was of a different order, both intuitive and logical, but intuitive before logical. His skill in dealing with fundamental mathematical problems is hardly surpassed even now, and in this respect he has been almost the only instance of a great mind applying mathematical concepts to medicine and surgery, up till the present era.

Of contemporary and later writers, it is not unfair to say that they all, or almost all, were merely recorders, encyclopaedists it may be, but devoid of any spark of new thought or of wise generalization. They preserved with reverence old tradition and ancient knowledge; they discussed every old device, and, at interminable length, the meaning of every old scripture, 'they lost themselves in the fume of subtile, sublime, or delectable speculations'; they tortured new meanings out of old phrases, they were 'diligent in dressing old words new'; and their ingenuity or infinite prolixity in so doing became the standard of their scholarship. Yet men throughout this period remained fettered and tongue-tied by authority.

## IV

After this long period of intellectual darkness and sterility, the first gleam of light was seen in the University of Bologna, renowned for over a century for its teaching in law and literature, and for its wide scholastic knowledge. Mondinus, the father of anatomy, lectured there from 1315 to 1325; he was the only memorable predecessor of Vesalius, greatest of all anatomists, born in Brussels of Belgian and English parents, a student of Louvain. Vesalius, not content to learn anatomy from the rude dissections of ignorant barbers, asserted 'I had to put my own hand to the business'. His labours resulted in a matchless work, with illustrations of such beauty that many were attributed to Titian or, as Cuvier suggested, to the most distinguished of his pupils. For Vesalius it may also be claimed that he revived the experimental method, that indeed since Galen he was the first of anatomists not only to practise but to teach its value. So he became the forerunner and the inspiration of the great Italians, of Eustachius, of Fallopius who in so few years laboured to such great ends, and of Fabricius, his successor in the Chair of Anatomy and Surgery at Padua. As we in England most gratefully recall, Fabricius was the lodestone attracting our own

William Harvey to Padua, with the result that through his discovery of the circulation of the blood, physiology received a new birth, and the scientific foundation of medicine was for ever truly and firmly laid.

Harvey, a true Aristotelian, said of himself that he 'felt it in some sort criminal to call in question doctrines that had descended through a long succession of ages and carried the authority of the ancients; but he appealed unto Nature that bowed to no antiquity, and was of still higher authority than the ancients'. Many had trembled on the very brink of discovery of the circulation of the blood, and it is hard to understand how the secret eluded them; it does not require Cuvier to tell us that we are often on the edge of discovery without realizing it. A pupil of Vesalius, Realdus Columbus, in 1559 had by inductive reasoning suggested the movement of the blood: but to ingenious speculation the minds of men had long been hardened. It was plain demonstration and undeniable truth for which they sought. They were weary of poetic metaphor in medicine and recalled the reproach of Aristotle to Plato. Harvey's discovery was finally due to his application of the experimental method of Archimedes and Galen to a problem of which many of the factors were already known. In his own words, the circulation of the blood was held to be completely demonstrated by experiment, observation, and ocular inspection against all force and array of argument.

'When I first gave my mind to vivisections, as a means of discovering the motions and uses of the heart, and sought to discover these from actual inspection and not from the writings of others, I found the task so truly arduous, so full of difficulties, that I was almost tempted to think with Fracastorius that the motion of the heart was only to be comprehended by God. . . . At length, and by using greater and daily diligence, having frequent recourse to vivisections, employing a variety of animals for the purpose, and collecting numerous observations, I thought that I had attained to the truth.'

The reception of this discovery was generous at home; tardy and reluctant, or openly hostile, abroad. Riolan, the elder, of Paris, with gallic frugality of recognition denied and derided it: but ample amends were made by his son who became one of Harvey's chief supporters. Everywhere it was eagerly and hotly discussed. Harvey says:

'But scarce an hour has passed since the birthday of the circulation of the blood that I have not heard something for good and for evil said of this my discovery. Some abuse it as a feeble infant, and yet unworthy to have seen the light: others again think the bantling deserves to be cherished and cared for.

These oppose it with much ado, those patronise it with abundant commendation.'

The experimental method revived also by Gilbert, physician to Queen Elizabeth, practised by William Harvey, sanctioned and encouraged by Bacon, was, however, to find no place as yet in the advance of medicine. For over a century great practitioners flourished; were renowned for their powers of observation and for their skill in the salvation of individual sufferers, but neither the science nor the art of medicine made any real advance. With the advent of John Hunter, however, and of John Baptist Morgagni at Padua, the foundations of medicine were strengthened, more deeply, more truly laid, by the creation of the science of pathological anatomy. Gross morbid changes occurring in the bodies of men, structural alterations responsible for symptoms of disease, were for the first time adequately recorded and studied. Symptoms could now with confidence be ascribed to their material causes. The examination of dead bodies for the purpose of revealing organs affected by disease, and of discovering the cause of symptoms had never been regularly practised. To the physician this would have meant humiliation and physical defilement; the barber surgeon was incompetent, and to the anatomists opportunities rarely occurred;

his interest lay in the examination of normal not of morbid anatomy. Bacon tells us:

'And as for the footsteps of disease and their devastations in the inward parts, imposthumations, exulcerations, discontinuations, putrefactions, consumptions, contractions, extensions, convulsions, dislocations, obstructions, repletions, together with all preternatural substances, as stones, carnosities, excrescences, worms, and the like: they ought to have been observed by multitude of anatomies, and the contribution of men's several experiences, and carefully set down, both historically, according to the appearances, and artificially, with a reference to the disease and symptoms which resulted from them, in case where the anatomy is of a defunct patient: whereas now, upon opening the bodies, they are passed over slightly and in silence.'

The tireless industry, unwearying care, and profound sagacity of John Hunter gave to an art that was largely empirical a warrant based upon sound knowledge of morbid processes in all tissues. He was observer, investigator, collector, in each capacity without rival. He was unceasing in his search for truth by way of experiment. 'Don't think, try the experiment', he urged his pupil Jenner. In his own person he did both supremely well. His disregard of the written word was deplorable no doubt, but refreshing after so much barren speculation among his forerunners. 'I am not a reader of books', he said; and again, 'I believe nothing I have not seen and observed myself.' His rebuff to one who accused him of ignorance of the classics is famous: 'Jesse Foot accuses me of not understanding the dead languages, but I could teach him that on the dead body which he never knew in any language, dead or living.' Often he recounts the details of an experiment, but leaves us to draw the conclusion. He changed the whole spirit of practice and placed knowledge on the throne of authority. He changed surgery from crude barbarism to science. The day was gone for ever when pure and dangerous empiricism could be practised; surgery became science and, in its craft, a rational procedure. John Hunter died in 1793 and was buried at St. Martin's-in-the-Fields. When, in 1859, his body was moved to its appropriate resting-place in Westminster Abbey the Royal College of Surgeons recorded on his coffin, 'The Founder of Scientific Surgery'. The museum which he founded and which still bears his name in the Royal College of Surgeons of England is unequalled in all the world, and his own specimens are still to be seen to bear witness to his incomparable services to pathological anatomy. For Morgagni no praise can be too high. His letters, written when he was over 80, may be read to-day with delight. Though his knowledge of disease is, in the modern view, often steeped in medievalism, his long array of facts and of relevant instances, his description of morbid parts, his correlation of conditions found at autopsy with symptoms observed during life, his accurate and searching generalizations, are among the greatest contributions to medical literature in all the ages. He made clinical work rest securely on anatomy and physiology, and set an example splendidly followed by Matthew Baillie and Bichat.

After the lapse of more than twenty centuries since the death of Hippocrates what benefits did the individual patient reap from the work of those I have named, and of a host of others? Almost none! But great changes were impending.

## V

A century ago the atmosphere of the scientific world was strangely calm. The most powerful intellectual excitant in the later years of the eighteenth and the earlier years of the nineteenth century had been the French Revolution, with its mighty consequences. In political life the processes of normal social development were so much impeded or arrested that reform was effected only when long overdue and after agitations of almost disruptive violence. In the intellectual world a similar obduracy and obstruction were encountered. Modes of thought, which time or authority had established, gained universal acceptance and not seldom acquired a rigidity which resisted change or even speculation. Observations were recorded and descriptions accumulated: men's minds became storehouses, and literature a catalogue. The biologist accepted and was moved to wonder at the palaeontological revelations of Cuvier, of Owen of the Royal College of Surgeons, of Mantell of Lewes, Brighton, and London. But speculation as to the meaning of this mass of new knowledge was singularly lacking. The time was one of material curiosity, of inquiry, of capture, rather than of speculative keenness. Intellectual appetites were appeased by acquisition and contemplation of new objects, and rarely sought the more flavoured diet of ideas.

Into this tranquil and complacent atmosphere Darwin threw his hypothesis, in the year 1859, with a resounding detonation. Huxley called it a 'flash of light in the darkness'. This was by far the most considerable event that had ever occurred in the history of biology, a science overburdened with facts and observations, hitherto inexplicable and uncorrelated. The task of enlightenment had happily fallen to a mind of the very first order, strong but gentle, enterprising but wary, imaginative yet severe. The effect of Darwin's work was to give new incentive and fresh energy to the science of life, and biology for a time at least was paramount. To the attainment of this primacy another influence contributed: the discovery of the invisible world of microbes by Pasteur, and the early realization of their significance in the world of medicine by Lister. Darwin's work had essentially been one of orientation. He had found man lonely, isolated, and in relation to his own pretensions slightly ridiculous. He gave him a long legitimate ancestry which included the best blood of the vertebrate kingdom. He showed him to be part and product of his own environment. Yet the environment known to Darwin in regard to the physical and animal worlds was quite incapable of producing the effects ascribed to it. Though Darwin's thesis was indisputably right, we now realize that the knowledge upon which it was based was fundamentally imperfect.

The surroundings of man, whether friendly, indifferent, or hostile, had remained in all essentials unchanged almost from the time of his emergence. To the physical elements he had become inured, by reason of his age-long subjection to them, his conquest over them, or his own inherent, trained, and wide adaptability.

Of his enemies in the animal world he had long since ceased to be afraid; his mastery of their simple wiles no longer brought him terror; they were incapable of inventing or of adapting themselves to new forms of attack, or of meeting him on fresh ground. What enemies then remained for him to encounter? Only his own fratricidal hatred and the accidents of plague, pestilence, and famine. The work of Darwin required the discoveries of Pasteur and of Lister to justify its conclusions, and to vindicate its truth. The world of micro-organisms, existing at all times, in all things, sometimes beneficent, always potentially hostile, was an element in man's environment, far more significant in relation to his survival and evolution than any other. Man had indeed survived and developed and had gained a certain mastery over the physical and animal world known to Darwin, because his own adaptability was not matched by a similar quality in his known adversaries. Victory over his familiar enemies was speedy and simple. But here in this microbic world was a new hostile agency possessed of physical adaptability within a great range, capable of meeting man's versatility in defence, by almost equal versatility in attack. To establish a new defence to strengthen man's arm in attack was Lister's mission.

At the very time when Darwin's observations were accumulating great changes were taking place in the social and industrial world. The 'industrial epoch' had begun; rural life was giving place to urban. Factories and houses for workers were being built with a rapidity never before contemplated, and men, women, and children were living in herds. The threat to the health of the people, in respect, for example, of surgical diseases and their consequences, was grave. Even in the worst pre-antiseptic days surgery was not wholly inadequate for its work when the population with which it had to deal was sparse and scattered. The solitary patient treated in isolation by a prudent surgeon might be able to fight his way through infections which were the scourge of surgery. At the time when Darwin's book was published, the crowding together of the inhabitants of towns, whose populations had so rapidly increased, made treatment in hospital not only more frequently necessary but vastly more dangerous. The hospitals were unprepared for their new responsibilities. Two beds were often placed together and occupied by three patients; over-crowding and ill-ventilation were invariable. The isolated patients in the country had only his own infection (and that of his doctor) with which to contend; the hospital patient was menaced not only by his own, but by other communicated infections, the virulence of which was greatly intensified by passage through the bodies of others in the same bed or even in the same ward. Such diseases as hospital gangrene, erysipelas, pyaemia, rarely or never seen to-day, were then rarely or never absent from hospital wards. John Bell of Edinburgh wrote early in the nineteenth century in his *Principles of Surgery* of hospital gangrene:

'When it rages in a great hospital it is like a plague: few who are seized with it can escape. No operation dare be performed. Every cure stands still. Every wound becomes a sore, and every sore is apt to run into gangrene. It has been named the Hospital Gangrene; and such were its ravages in the Hotel-Dieu of Paris (that great storehouse of corruption and disease) that the surgeons did not dare to call it by its true name: they called the rottenness, foulness, sloughing of the sore. The word hospital gangrene they durst not pronounce, for it sounded like a death-knell; at the hearing of that ominous word the patients gave themselves up for lost.'

The problem of wound infection became therefore the increasingly urgent problem of medicine. To that problem Lister devoted his life. The literature of medicine of the period preceding and coinciding with Lister's early investigations tells poignantly of the disasters which, almost as a matter of course, followed upon surgical procedures, sometimes of the most trivial kind. In Sir Astley Cooper's 'Life' we learn of his intolerable anxiety as to the progress of George IV after the removal of a small sebaceous cyst from the scalp. The older surgeons, Everard Home and Cline, shrank from undertaking so hazardous an operation and were only too happy to surrender the task to the younger hands of Astley Cooper, whose comments upon the matter seem, to-day, amusing in their show of apprehension and anxiety. He feared that the operation 'might by possibility be followed by fatal consequences'; and again, 'I saw that the operation if it were followed by erysipelas would destroy all my happiness and blast my reputation'; and 'I felt giddy at the idea of my fate hanging upon such an event', and he expressed his intention of leaving London if anything happened to the King. John Bell spoke of a hospital as a 'House of Death'; and Lister himself said that hospitals were 'little short of pest-houses'. Innumerable instances of equal significance might be quoted. John Brown's immortal work, *Rab and his Friends*, paints a picture truthful and poignant. Volkmann of Halle, an early apostle of Lister, closed his hospital when the ravages of infection seemed unconquerable.

In the *Life of Pasteur* by Vallery Radot we read:

'During the siege of Paris (1870, 1871) Nélaton in despair at the sight of death of almost every patient after operation declared that he who should conquer purulent infection would deserve a statue made of gold.'

It is now apparent to us all that realization of the full significance of Darwin's work would at once have suggested the reasonable presumption that infective diseases depend upon living causes. The work of Pasteur and of Lister formed the natural, indeed the inevitable, corollary to Darwin's work, and might indeed have been conceived as a simple logical inference from the principles which Darwin established. Of the results of Lister's work it is hardly possible to speak in measured terms. Lister, a true and unfeigned inquisitor of truth, is in my judgement the greatest material benefactor of mankind the world has ever known. Operations which before his time were contemplated with anxiety, and performed with dread, are now so common, and if one may in our work use the word, so trivial, that no slightest doubt is ever felt as to the outcome. Operations which Lister himself neither contemplated nor dared to perform are now to be seen every day in the operation theatre. Lister himself never explored the abdomen of a living patient, yet tens of thousands of such operations are performed every year in this country, to the salvation of life, the assuagement or abolition of suffering, and the restitution of health. Lister indeed opened the gates of mercy to mankind. Operations performed on parts of the body formerly inaccessible permit us now to study almost at leisure morbid processes during the lifetime of the patient. A 'pathology of the living' has been created, and direct research carried out disclosing to us early and still earlier stages in the natural history of disease. Diseases formerly unrecognized from their clinical symptoms are now diagnosed with little or no difficulty by any accomplished practitioner. A close correlation has been established between structural changes now visible during the lifetime of the patient, and the symptoms to which, in these early stages, they give rise. Surgery has indeed been a strong arm of research for medicine, whose therapeutic power has thereby been not so much strengthened perhaps, as newly created. What is possible upon man is possible also upon animals. Direct experiment upon man was soon coupled with collateral experiment upon animals. Without animal experiment and research, our progress would indeed have been slow.

The immediate results of Lister's work were comprised in a series of sustained attacks upon disease of the viscera in the abdomen and chest. The minds of men were soon concerned, therefore, with planning new methods of attack, with devising, modifying, perfecting the technique of surgical procedures; and through this agency, with discovering new diseases, and with revealing earlier stages of familiar disease. The two or three generations that followed Lister were engaged, that is, upon two chief matters, repair or cure of structural changes, with invention of methods and instruments to make this possible; and with fresh adventures, voyages of discovery which gave new knowledge of pathological conditions, and so led to their earlier recognition, alleviation, curtailment, or removal.

## VI

It may safely be claimed that the craft of surgery has in these days almost reached the end of its progress along the lines which so far it has followed. The full fruits of Lister's work have now been garnered. Infection may confidently be denied entrance to any fresh wound in which an infective focus is not opened. Operations are consequently performed by the great masters with a success that leaves little hope of betterment. The gravest, most extensive, most delicate operations are carried out upon every organ in the body including those only recently made accessible, with a success which no one, not Lister himself, could have believed possible. New methods of treatment may no doubt appear in our further development, but so long as cutting operations of the kind now practised have to be applied for relief or cure of disease, it is hardly possible that their success can be improved, except by change in the quality of material submitted, that is, by preliminary preparation of the patient increasing his powers of resistance to attack. If this be true, and I hold it to be indisputable, what further progress is possible, along what lines? The answer is that although in the last fifty years, since Lister's work was accomplished, the methods of surgery have become so finely perfected, the human material submitted for the surgeon's work has changed very little. Can we by following Lister's example do anything to improve that material, or to forestall or prevent disease?

What was the secure foundation underlying Lister's inquiries and practice? It was, assuredly, that Lister was both physiologist and surgeon; perhaps, indeed, greater physiologist than surgeon. His training by Thomas Graham, Sharpey, Wharton Jones, and others in the methods of the laboratory, his saturation with the ideal of unbiased inquiry, his supreme and changeless devotion to truth, his faith in the religion of research, together with his clinical knowledge of surgery, and of those most perplexing and revolting catastrophes which daily resulted from wound infection, gave him both power and incentive for that arduous investigation which culminated in enunciation of the principle that wound infections are due to living particles.

It is, I believe, upon following Lister's example that the advance of medicine now depends. Hitherto we have been engaged, with great success, in discovering methods of dealing with structural diseases by mechanical device. Now we must also concern ourselves with recognition and correlation of those manifold bodily ailments which result from changes in the function of organs. To do this we must make our own inquiries into all relevant physiology, into the physiology of early disease rather than that of normal animals or of normal man. Physiology has so far been ardently and most successfully yet narrowly engaged with study of normal function, chiefly in animals; and physiological experiment has been largely concerned with an endeavour to express in terms of chemistry and physics the isolated vital processes of animals. Normal man, who offers a most promising field for inquiry, had been too much neglected: and in respect of early departures from normal has hardly yet been investigated by physiologists, or by methods of physiology. We need to create a science of para-physiology, and to conduct the most critical investigation of man's functional aberrations at the earliest period of their development. I agree entirely with Professor Samson Wright when he says in the preface to his invaluable work, *Applied Physiology*:

'It seems to me unfortunate that in the teaching of Physiology greater use is not made of the wealth of clinical material present in the wards of the hospitals which could readily be made available. The main facts of the physiology of the nervous system and the ductless glands, at any rate, could thus be clearly demonstrated; and the interest of the student would be aroused when he finds that he is considering in his physiological studies the same patients that he will have to deal with when he is doing his clinical work.'

In medicine we are still engaged with terminal events. Patients seek our aid only, as a rule, when something has gone seriously wrong or is threatening to do so: our hospitals are filled with examples of advanced disease: our opportunities are too often confined to rescues in the last ditch. What would surely advance our knowledge, and perhaps lead on a large scale to prevention of disease, is hospital research on those suffering from slighter ailments. We now lack adequate and leisured opportunity for fullest clinical, chemical, physical, radiological, and other inquiries into inaugural lapses from normal states. The hospital staff would consist of physiologists, or men trained in laboratory methods, who would be not only therapeutists, but chiefly indeed researchers, not coerced by the problem immanent in all our work of bringing relief or cure to a patient, and, perhaps, of fighting against time to do so. They should be afforded facilities for conducting experimental work suggested by their clinical inquiries, side by side with their clinical observations. They would make what Claude Bernard called 'l'observation provoquée'. At present research work and clinical inquiry lie too much apart, are conducted at far distances from each other by men who rarely meet. Experimental work should be more often suggested, and even carried out, by those whose experience in clinical work has shown them exactly where investigation, strictly relevant to the problem in which at the moment they are interested, may become most profitable. Laboratory work is to-day too aloof from clinical necessities. The recent surgical attack upon the sympathetic nervous system, for example, might perhaps have been made a generation ago if Gaskell's and Langley's work had been more accessible to clinicians. Differences between the results of investigations in animals and of operative procedures upon man will, of course, constantly be revealed. The material of the human body is not the same as that of animals nearest to man, nor subject to the same influences; similar functions are not wholly discharged by precisely similar mechanisms; the pressure of environment is not comparable in the two cases; and, above all, the mind of man is infinitely complex in comparison with that of the most intelligent animals. Other reservations are also necessary. In physiological experiments upon living animals the particular process requiring investigation must be isolated from all other processes. That is the essential requirement for accuracy of observation, and for the possibility of bringing to bear upon it those influences whose effect we desire to study. This isolation of one activity from all others is sometimes perfectly achieved, sometimes imperfectly, sometimes not at all. Indeed the necessity for sequestration is not always appreciated, nor is it realized that even if sequestration has been completely secured the process so affected may not behave as it behaves in life when influenced by one or more activities working in harmony with it, contrary to it, or controlled by it.

The changes produced by all such experiments upon normal animals are relatively gross: the changes produced by disease in man, in the stages which should arouse our chief interest, are often minimal, of so fine a texture that we cannot properly compare them with those coarser induced conditions. Care in the selection of animals for experiment in order to afford reasonable accuracy of comparison with man is also extremely important. Nowhere perhaps will discrepancy between man and lower animals in respect of physiological processes be so considerable as in relation to the sympathetic nervous system. There has been a general assumption that discoveries relating to the functions of this system made by experiment upon animals are directly applicable to man. It is already evident that in this respect there are differences between one biological grade and another; and still more certainly does it appear that the actions of sympathetic nerves in man, and the abolition of function resulting from nerve or ganglion removal, are not wholly explicable by any knowledge derived from indirect collateral research. Results of direct hominal research which are already at our disposal do not permit of any final conclusions. We have learned new truths of the anatomy and physiology of the sympathetic nervous system during our work, and it will almost certainly require an extended period of careful observation to appraise correctly the full permanent effects of our operations on man. Once again the methods of the surgeon may prove to be the most trustworthy for inquiry into the physiological problems of man. For our operative procedures in consequence of our slight human experience have already undergone change from those designed to fulfil the purposes which animal physiology had indicated.

However, when fullest allowances are made here and elsewhere, the method of experimental, collateral inquiry remains one of extreme importance, of most fruitful results, of value indeed second in accuracy and relevance only to that of direct hominal research itself, with which, whenever possible, it should be combined. We remember that Bacon says: 'The dissection of beasts alive notwithstanding the dissimilitude of their parts may sufficiently satisfy enquiry.'

Much of the experimental investigation carried out in laboratories throughout the world would have a far higher value in respect of immediate application to human needs if closer brotherhood were created between physiologist and physician. Many of us hoped that a strong bond of union might be forged by the Medical Research Council: but our hopes have not yet been fulfilled.

The suggestions here made, that our clinical work should have closer relation with research and that research workers might find profitable employment in wards and theatres, would involve a change of outlook in the advanced medical student and young practitioner. I feel confident that advance in medicine is dependent upon different training, for some at least of those who are to serve upon hospital staffs in the future. Both physician and surgeon must be steeped in the ideals and bred in the practice of laboratory methods. In the investigation of disease physician and surgeon alike are confronted with a problem sometimes infinitely complex; far more intricate indeed than any submitted to a scientific observer in any other walk of life. Their task is first to investigate the anamnesis, to hear all that the patient has to say with regard to his complaint. Each factor in the story so disclosed is not necessarily a statement of truth. It is a statement no doubt of what the patient believes to be true, but it is modified not only in relation to the patient's general trustworthiness and temperament, but also in regard to what he supposes the physician to require, and it is tainted with inaccuracies which depend upon the patient's mood of the moment, and with a host of other influences. This anamnesis has to pass through the medium of the inquirer's mind, and there again receives colour from a number of influences that hardly need enumeration. In the physical, radiological, chemical, and other relevant examinations there occur more and greater opportunities for error than are to be found in any other of the sciences. Not all cases can at all times be submitted to observation: not all cases display at any one time the same objective features; conditions which present the same physical features, or functional aberrations, or which disclose the same, or approximately the same, sequence of events, do not always affect the bodies of those whose minds are similarly receptive or equally attuned to their disorders. Diseases recognized, let us say, by change of structure, by disturbance of function, or by onset of infection, present a pageant in which innumerable individual phenomena take part. Not every example of a particular disease will bring forward the same evidences of organic or functional change, or elicit the same mental reaction. The complexity inherent in all biological phenomena is seen here also, in extravagant form. In making a decision upon such evidence a quality of 'intuition' may accomplish startling results. An intuitive faculty is doubtless a property of many minds, but vast experience which confers readiness and aptitude may easily be indistinguishable from it.[1] Whatever criticism may be applied to the early training, notoriously defective, of the medical student, it may, I think, be claimed that in all such inquiries the advanced student of medicine is, in some hospitals at least, to-day not inadequately trained. Our failure, especially in regard to the man who is to become teacher, is that instruction rarely goes farther. He is not trained to dissect out from the number of his observations one or two significant items so that these may be submitted by experiment to closer inquiry, and some law attaching to them discovered in isolation. The picture, that is to say, presented to the clinician is infinitely complex, made up of a number of factors not only interrelated, but interacting. To recognize these factors, to appraise their value, to indicate their significance is not enough. Each individual factor must be separated from the result, its qualities studied by appropriately directed experiment, so that the law of nature attaching to it may be learnt while it is unaffected by the

[1] See Appendix I.

influences which other factors in the clinical picture exert upon it. We train the powers of observation in our students; we neglect to teach the value of reason and relevant experiment. We teach the Hippocratic method; we neglect the Galenic. The method of Hippocrates implies the observation of phenomena, of symptoms and signs, in the apparently random condition in which they present themselves, unaffected by any control exerted by the investigator. The Galenic or experimental method relies upon the observation of conditions after specific influence has been directly and consciously exerted upon them by the investigator. Control is the essence of the difference in method. The Hippocratic method must study events in the casual and seemingly haphazard manner in which they present themselves in nature. In surveying a large field it attempts to recognize 'groups of events of which the items are significantly related to each other', to discover similarities, uniformities, or discordances; to make comparisons, and establish classifications, through perception of common attributes, to reason from these, and so to establish general laws. The Galenic method sets up its own inquiries, isolating the events to be investigated, reducing them in each individual example to the simplest terms in order to obtain an unequivocal reply when submitting them to the simplified, precise, and narrow methods of the laboratory. The mental qualities required in the investigator are those which the trained observer in the Hippocratic method possesses; although, owing to the comparative simplicity of the arranged inquiry, the same high demand is not always made upon them after experiment begins. In the devising of apt experiment and in the isolating of the special event calling for inquiry, the highest qualities of imagination find abundant opportunity. In both methods analysis and synthesis are necessary. While in the method of observation analysis predominates, it is by methods of experiment that isolated truths are disclosed which lend themselves at last to synthesis. The act of comparing one observation with another requires analysis in greater degree than synthesis for its effective working.

Lister's incomparable success was due, surely, to the fact that he was master both of the Hippocratic and of the Galenic method, and that in rare degree he combined the physiologist and the clinician; that as surgeon he realized in his daily work where inquiry and experiment were needed, as laboratory worker he was able to put his own hand to the task of elucidation, and as both to make the body of man the temple of his miracles.

## VII

Physiology to-day is unhappily losing the close relationship it formerly had with clinical medicine. Physiology, the science of the function of processes of life, was separated from anatomy, the science of structure, chiefly through the agency of Sharpey, Lister's teacher, counsellor, and friend. The cleavage was all to the advantage of physiology, all to the detriment of clinical medicine. Physiology has wandered away and away upon its own researches, conducted often by men of highest intellectual power, and resulting in immense intellectual triumph, as you in Oxford know well by long personal experience. Its biological inquiries have been conducted almost exclusively upon animals; man has by comparison been neglected. During this time of unhappy divorce the surgeon has gained incalculable victories for clinical medicine. By Lister's aid he has ventured into the innermost sanctuaries of man's being, and there has made astounding discoveries by the aid of technical procedures, himself invented. He has owed little to laboratory workers; has indeed from time to time perhaps been momentarily confused by their teachings based upon animal experiments irrelevantly devised, and found at last to be inapplicable to man. In the future advance of medicine it is beyond dispute essential that physiologist and surgeon shall no longer travel apart, but that they shall join interests and make common attack upon the innumerable mysteries of disease. In application of the methods of Hippocrates and Galen, in accurate observation and critical judgement, in discrimination, followed both by animal experiment and human investigation, and by calling to our aid all that physics and chemistry can so prodigally teach us, we shall most surely and confidently advance along the road of progress. Above all we must connect and transfer the observations and practices of one science to the use of another. We must develop and sustain closer interest in human physiology, in physics and chemistry, in the inaugural symptoms of those changes in function which we call disease, and in the signs which clinical examination or laboratory methods disclose. That is our ideal; and here at least we may suppose that ideals are not only for pursuit but for attainment. In Oxford they have been attained. What greater privilege could any young member of my profession enjoy than opportunity to work here in the laboratory of the greatest of living physiologists and to seek to capture some of his spirit? Therein are being unveiled fundamental truths concerning man's power of feeling and moving. The crumbs which fall from his most bountiful table are gathered by medical men of all countries to the incalculable advancement of their power in the recognition and treatment of obscure disorders.

## VIII

Physiology, the fundamental science upon which medicine stands, is the meeting-ground of physics and chemistry in their application to problems of function, both normal and aberrant, in man and animals. Application of the methods of these sciences to physiology has already increased both its range and complexity. It is more than probable that this science will not long continue whole but will suffer disintegration into a still greater number of subordinate branches. For many reasons this will be regrettable; but it is only by disruptive yet creative processes that such a science as physiology can advance. During recent years realization of the need for physics and chemistry in medicine has grown with astonishing rapidity. 'The progress of science', says Bertrand Russell, 'does not afford any evidence that the behaviour of living matter is governed by any other than laws of physics and chemistry.' At the beginning of the century there was not one Chair of Bio-chemistry in all the universities of this country: now

I suppose no university is without one. The help given to medicine by physics, chemistry, and bio-chemistry has already been invaluable.[1]

In its relation to chemistry and physics medicine feels perhaps a little aggrieved. The enunciation of Darwin's hypothesis in 1859, and the clamour which greeted it, placed biology in the very forefront of the sciences. It has lately fallen from its throne. Physics and chemistry have since that time made such prodigious advances, both in theory and in practice, and the intellectual demands made upon those who work in these subjects have been so stringent, that the ablest and most eager scientists have naturally been attracted to them. Biology, considered a simple and less important subject, has been regarded perhaps with a measure of intellectual disdain. This is greatly to be regretted, for we now realize that in the study of new problems in biology both chemist and physicist may find endless and most exacting opportunities for amplest exercise of their powers.

Biology is no longer concerned merely with minute examination and classification of animals suddenly discovered in newly opened territories; it has in recent years concerned itself with elucidation and explanation, in terms of chemistry, of the processes of life,

[1] See Appendix II.

of the complex reactions, for example, of cell growth and change, of muscular activity, of nerve discharge, and so forth. Such inquiries afford to chemist and to physicist opportunities for exercise of their own methods not inferior to, perhaps even more complex and elusive than, those with which they are customarily engaged. The life of every cell is seen to be, in large measure at least, dependent upon chemical processes in which alternate oxidation and reduction are chief factors: and it appears that these successive changes are set going by enzymes or catalysts, specific in nature. As to the constitution of these enzymes the most recondite research is necessary, for such changes are of incredible rapidity. The substances to be examined have the briefest existence and are to be obtained only in minutest quantities. If difficulty in research is sought, here and in similar problems is enough surely to satisfy the desire of the most ardent. May I quote with warm approval from the Norman Lackyer Lecture delivered last year by one who speaks with high authority, Sir Henry Dale:

'The physicist, even though he be accustomed to observations dealing with sub-atomic dimensions, may find himself repelled by the complexities inherent in the simple mechanism of the living cell, as compared with the artificially simplified conditions which he can make for his experiments on inanimate matter. There was a natural cleavage between the physical and chemical sciences and biology, even when the problems of biology seemed too superficial and too easy: it is of tremendous importance to the future that the cleavage should not unnaturally persist, because the problems which biology is now beginning to handle are becoming too complex and too difficult.'

If it is true, as I believe, that the advance of medicine is impeded by the truancy of physiology and by what we regard as its illicit devotion to problems which, though no doubt highly interesting and important, are nevertheless largely irrelevant to medicine, and if functional biology, of which physiology is now a chief ingredient, is lamenting the indifference or aloofness of chemist and physicist, would it not be to the advantage of all that a closer alliance should be inaugurated, and that each science should try to appreciate its communal no less than its individual value? In his pursuit of knowledge of many of these processes which are a part of life, even the most earnest chemist or physicist may find tasks worthy of highest skill and of infinite patience. We must learn to connect and transfer the observations and practice of one science to the use of another. Without help so given to functional biology, by a conjunction of effort of many workers in many fields, the advance of medicine will be grievously retarded.

Physicist and chemist, we may be interested to observe, showed no eagerness or alacrity to come to work beside the clinician. At first they were a little reluctant to engage in research which did not seem very relevant to their daily work, and they were a little disdainful perhaps of biological problems, looking askance especially at bio-chemistry. Their adventure has, however, not been unrewarded, for the study of the living cell has raised problems which are adding much to the knowledge of pure chemistry. The entry of laboratory methods, and of physicist and chemist, into the domain of medicine has therefore been of incalculable value. Here and there we may observe an acute realization of this truth by those who help us in the laboratories, and who seek to enlarge their own territories and their own authority at the expense of medicine.

## IX

We may also be made aware of the claim for paramountcy of laboratory investigations, of their infallible and unalterable rectitude, whenever discrepancy is found between them and the sober reasoning or intuitive apperceptions of the clinician. We must therefore remind ourselves that though our need is great, and though the aid given by physics, chemistry, physiology is indispensable, these sciences are not medicine but ancillary. Medicine even with the aid of the Hippocratic and Galenic methods cannot live alone, or thrive, or grow. Other sciences nourish and sustain it, reveal new opportunities, strengthen its effort, direct and control its activities, and correct any tendency to error. But medicine is far more than the application to human afflictions of our knowledge of the biological or natural sciences. It may claim to be a science in itself, differing from other sciences only in its greater complexity: to its purely biological qualities it adds others, arising from man's great mental and moral development, which so perplexingly increase its range and activity, and render its problems so intricate, and in these early days of its understanding so bewildering. To the old question, 'Is Medicine Science or Art?' the answer surely will soon be, 'It is both: Science in its methods and inquiries: in its practice Art'.

There is now apparent a danger, of the kind with which our intellectual ancestors were familiar, in our dependence upon other sciences for help in elucidation of our clinical problems. To speak frankly, the danger is that suggestion and contribution to the counsels of medicine may lead to dictation. After all, the material furnished by the laboratory worker is not the whole of the material the clinician must consider. The aid of the laboratory worker is sometimes decisive, sometimes helpful, not seldom negligible. The clinician in his consideration of the problems of diagnosis and of treatment must take heed of all things. The greatest help may sometimes come from study of the anamnesis, sometimes from physical examination of the patient, sometimes from bio-chemist, sometimes from radiologist. The intricate clinical problem must first be resolved into its constituent elements, each one of which may require investigation by, and perhaps receive solution from, co-workers in the laboratory. The aid received from one or more of these inquiries may greatly enlighten, furnishing knowledge without which the clinical problem is insoluble. But synthesis of all answers given from various sides is the work of the clinician, and his alone. He must not surrender his sovereignty, though here and there one meets the clinician who, forgetting that he is artist and humanist, to his infinite debasement, leaves his unhappy patients at the mercy of test-tube or microscope. Clinical manifestations of diseases are not merely combinations of symptoms or signs, not the resultant of a number of forces acting in different manner from the normal. They are not, that is to say, merely aggregations of conditions or qualities each one of which is capable of resolution by physicist, chemist, bacteriologist. The methods of expression in structural change in any organ, or of functional disorder therein, are not always the same; and the same mode of expression may witness changes of varying qualities in different organs. An innumerable host of factors other than the inciting one may play a part in the final clinical revelations of disease, and none but the physician with practised acumen can follow the trail which these symptoms are laying, and discover their starting-point. Medicine must guard against the tendency, not for the first time manifest in its history, to submit to the dictation, rather than to be guided by the discipline, of other sciences. It cannot be imprisoned by the boundaries of any other single science, nor by any combination of sciences. It must never again be beguiled or betrayed, as in days gone by, by such seducers as Borelli in the seventeenth century and the iatro-mathematical school or Francis de la Boë and van Helmont and the iatro-chemists applying chemistry to medicine. The stern discipline of physiologist, physicist, chemist is applicable to their own sciences, and accounts for much of their considerable success, but the form in which it is most profitably used within these sciences is hardly applicable to the problems of the clinician. His judgements and his actions must take into account factors of which he alone is witness, he alone is judge. The claim, not seldom made, that the advance of medicine will come from research in the laboratory, though it contains truth, cannot be fully upheld. 'Nil sine laboratorio vita dedit mortalibus' is no doctrine for my assent. The advance of medicine depends not on clinician alone, nor on laboratory workers alone, but on their happy union in fertile decisive activity.

## X

So far I have considered medicine in its practice and in its dependence upon the science of physiology, itself built upon the sure foundations of chemistry and physics. To those who daily practise it, however, the humanist side is no way inferior to their scientific purpose. Compassion rules their hearts; they seek to assuage pain, to restore health, to turn the hand of death aside. Is it not then remarkable that the greatest of all discoveries in medicine, throughout the ages, have been made by those directly concerned with clinical problems, men whose daily work and a realization of its imperfections were the incentive to those inquiries which brought so great results? We in this country feel special pride in remembering that Harvey by his discovery of the circulation of the blood gave birth to the science of physiology, that Hunter changed surgery from a barbaric practice to a scientific pursuit, that Hillman first gave us anaesthesia, and that Lister not only introduced therapeutic measures of incomparable value but put into our hands the strongest weapon for research in men and in animals. Preventive medicine too owes its origin and much of its earlier development to those engaged day after day in the practice of healing. May we not believe that it was their contact with patients in the time of suffering that both inspired and directed their efforts? The Royal College of Surgeons has realized that, in efforts to advance the cause of surgery, opportunity must be generously afforded the surgeon to undertake, as Lister did, research dictated by his clinical needs, and so to bring therapy and inquiry into closer relation than ever before. The erection of new laboratories, the creation of the Research Farm by the generosity of Sir Buckstone Browne, and the endowment of research workers who are engaged also in the practice of medicine are means taken by my college to fertilize and enrich the minds and direct the practice of those who are to be teachers of surgery. Association of clinical aptitude with propensity for research will by degrees so affect the attitude of practitioners, especially perhaps of surgery, that they will approach their clinical problems not only with the idea of relieving the individual sufferer but, far more strongly than now, with the hope of elucidating fundamental causes, and of preventing similar maladies in others.

If in speaking of the advance of medicine my reference has often been to that branch of it which we call Surgery, it is only because I have devoted my life to that art and have laboured to bring it closer into touch with science. Surgery, however, is more than Science, more than Art, it is a Sacrament. For the surgeon, therefore, no training can be too arduous, no discipline too stern: none of us may measure devotion to our cause. In dealing with menacing realities the surgeon must possess courage and humility; must feel confident in his strength, sincere and tender in its timely application; must work with an exactitude that is piety. For us an operation is an incident in the day's work; for our patient it may be, no doubt it often is, the sternest, most dreaded of all trials, for mysteries of life and death surround it, and it must be faced alone. Those who submit to operation are confronted, it may be after weary days of suffering, with the gravest issues, and far more often than many of us suppose they pass into the valley of the shadow of death, and, in stark dismay, wonder with Beatrice in her aching solitude and panic what will come to pass

> If there should be
> No God, no Heaven, no Earth in the void world,
> The wide, gray, lampless, deep, unpeopled world.

To give courage to those who need it, to restore desire for life to those who have abandoned it, with our skill to heal disease or check its course—this is our great privilege. Ours are not the mild concerns of ordinary life. We who, like the Happy Warrior, are 'doomed to go in company with Pain and Fear and Bloodshed', have a higher mission than other men, and it is for us so to labour that we may prove not unworthy.

# APPENDIX I

The early training of medical students in the methods of observation, correlation, and decision on the one hand, and of experiment on the other, is, I think, seriously defective. Many of the earlier months in the student's career are engaged in acquiring knowledge by neither of these methods, but by the simpler business of memorizing a number of facts apparently unrelated, which he makes haste to forget as soon as the necessary examinations are passed. The student at first hardly realizes that chemistry, physics, physiology, pathology, and their derivatives have any substantial connexion with the clinical inquiries and methods of healing with which, in later years of training, he becomes familiar.

The teachers of earlier and of later years live their lives apart. They rarely pass over that sharp line of demarcation drawn between the early years of scientific preparation for medicine, and the scanty years of clinical experience. There should be an infiltration, made easy by destruction of this line, of scientific work into the wards and theatres: of clinical practice, into the laboratories and museums. Contact with patients should begin in the first session: the methods of the laboratory and of experiment should accompany the student through his clinical work, and stay with him to the end.

Let me illustrate my ideal training for the surgeon of to-day by suggesting the career which I should choose to follow if youth happily returned to me.

Were my days to come again, after leaving examinations behind, I should spend the time necessary to make an adequate knowledge of human anatomy my permanent possession, and then should escape to experimental research, and, in a community of like-minded people, endeavour to train myself for the high destiny of a surgeon, the one man who may engage in direct research. My time would be spent in the laboratory where a youth of plastic mind may learn the methods of approach to new problems or to new extensions of old problems; where old knowledge is merely an impulse to the search for new; where intellectual dissatisfaction is victor over narrow complacencies; where the religion of research inspires him and equips him for his work in days to come. If surgery is to be something more than a wonderful craft, if it is to be the instrument of research which I believe it to have been, and to be destined to be in the future, those who practise it must have their minds shaped and strengthened by conflict with unsettled problems, not cramped and sterilized by monotonous exercise within a narrow province of static knowledge. Their minds must be trained in the laboratory, in collateral research, so that they may be more effectively exercised both in the operation theatre and in the wards upon direct research. The comradeship of laboratory workers and clinicians should be intimate and unbroken. The scientist at work in the laboratory can never reap the full rewards of his lonely researches without close and loyal collaboration with the clinician. Nor can those who serve the same cause in a different atmosphere give their patients the best aid of medicine and surgery without the help of the scientist. The training of the surgeon must not only allow, it must urge, his mind to stray beyond the hard boundaries of old knowledge, over the edge of firm beliefs, into wide territories as yet unexplored and even undivined. In this way only is there escape from the danger which besets the surgeon in the future, the peril of facile automatism in empty dexterities. In this way may the physiologist be brought back from his vagrancies and encouraged to realize that his science best fulfils its destiny when it is applied to the understanding of the functions, normal and aberrant, of the organs of man. It is a delight to me to see that a few of the younger surgeons in this country are taking the path which I should follow were I on the threshold of a surgical career.

## APPENDIX II

HERE let me frankly face criticism that has been directed against the methods of our laboratories, and has resulted in a most lamentable impediment to the advance of medicine. Without experiment on living animals, that advance, already greatly hampered, cannot continue. I recognize and endeavour to understand the motives which animate powerful bodies of noble and highly gifted men and women who are opposed to experimental methods. No right-minded man ever wishes to inflict suffering upon man or animal. That is abhorrent to us all. Opposition to animal research, I firmly believe, is based upon lack of appreciation and understanding; as it is certainly supported by grievous and, I think, unpardonable misstatement. Day by day for many a year it has been my happy duty to operate on men, women, and children who now number a goodly company, in order to save life or bring relief. My heart is full of compassion. I cannot bear to cause or even to hear of suffering. Every one who has experience of laboratory work knows how little pain is inflicted, and what steps are always taken to minimize or abolish it. Yet the slight distress we must occasionally impose in our work upon man is greater in intensity, and far more protracted, than any suffered in our laboratories. It is simply not the truth to say that pain is wantonly, or unavoidably, inflicted there. The experimenter who excites suffering defeats his own aims: for pain changes the issues he seeks to discover. Physiologists and surgeons are the most humane of men. The necessities of their work would impose this quality if it were not already possessed. The whole anti-vivisection campaign, though a great testimony to the tenderness of heart of its supporters, has no slightest foundation in truth, and is a witness to their shut-mindedness and credulity.

## APPENDIX III

### *The Relation of Physics to Medicine*

It is possible that in the relation of physics and chemistry to medicine we stand on the very threshold. The contributions they have made are not only considerable in themselves, they are portent and promise of what we may expect in, perhaps, the very near future. Physics, by its gift to us of the X-ray through Röntgen in 1895, has not only helped in the recognition of many fractures which otherwise might have passed unobserved, but has taught us much of the character of fractures in general, the lines of displacement, the accuracy of reposition, and so forth. It has greatly enlarged our capacity for the discovery of such conditions as gastric ulcer and cancer of the alimentary canal. It has made gall-stones visible, and, with the further help of the 'Graham-Cole' method, we are learning something of the functions of the gall-bladder in health and in disease. It has put into our hands new opportunities for accurate diagnosis of intracranial conditions, which, without its aid, would have remained unrecognized, or would have been misinterpreted. Treatment by deep X-ray of recurrent or unapproachable malignant diseases has given relief, on occasion perhaps even rescue, to many doomed otherwise to acute suffering or death. For these things we are immensely grateful—but more is to come.

Among the most formidable enemies of man are those infinitely minute noxious agents known as 'viruses'. They are the cause of widespread pestilence of highly fatal character in man and in animals. In one year, 1918, influenza, dependent upon a virus, claimed more victims than the World War which lasted four years. They cause not only great suffering but at times financial disaster. The cost of foot-and-mouth disease is a significant example, and the miseries of the common cold are only too familiar. They attack the vegetable no less than the animal world; their power of propagation almost passes belief. Many of them, perhaps, no power of the microscope will ever render visible, even if they are particulate, for one of the few known facts concerning them is that their size may be less than that of the wave-length of light. They cannot be cultivated apart from the living cell, in contact with or within which alone they can really thrive. Though unlikely, it is possible that some of them may be not particulate but unorganized infective toxic material producing effects by compelling the cells attacked to create the agent of their own infection. Some at least of the viruses may, however, be visible. In 1904 Borrel described visible particles in the virus inclusions of fowl-pox, and believed them to be the virus itself. Two years later Paschen observed minute granules in vaccinal material, which have since been described as 'Paschen bodies'. In later investigations he found similar bodies in varicella, and in the variolo, vaccine lesion, and attributed specific qualities to them. There is great difficulty in eliminating artefacts from preparations made for the purpose of studying these 'bodies', and the technical difficulties in their preparation are tedious and considerable. Those who speak with authority have formerly looked askance on much of the work conducted in connexion with these matters; opinion during the last year or two seems, however, to be changing. It was shown in 1929 by Woodruff and Goodpasture (*Amer. Journ. Path.*, 1929, x. 1, and 1930, v. 713) that a

'single Bollinger body—the inclusion body of fowl-pox—when isolated and washed free from any adhering virus is still capable of infecting, and that the contents of the Bollinger body consist of numerous elementary bodies (Borrel bodies) embedded in a gelatinous matrix'.

And the aetiological significance of the Borrel bodies has been further advanced by Ledingham, who recorded in the *Lancet* in September last (*Lancet*, 1931, ii. 525) that by fractional centrifugation he had succeeded in obtaining these bodies in relative purity and in demonstrating their specific agglutination with an anti-fowl-pox serum. Ledingham has also claimed that experiments conducted by himself and Hardy Eagles warrant the conclusion that the cause of vaccinia is the Paschen body. In their last report these distinguished authorities write:

'It is of very great interest that Bedson has been able by very similar means to those employed in this work to secure evidence that the minute bodies found in psittacosis represent in all probability the actual infective agents' (*Lancet*, 1932, iii. 825, 842).

There is hope, however, that the elucidation of the mystery of the viruses and the suppression of their evil sway may come through their examination by the methods of physics. Sir William Bragg's studies of crystals have helped to make him famous throughout the world. The application of his methods by Astbury to the study of the cancer cell by X-ray may lead to an increased knowledge of cell construction and growth, and, taken in conjunction with our increasing knowledge of colloidal states in living cells, may advance our power in attacking at its very heart a dread disease whose frequency is steadily increasing. Physics with its power of action and its magic of conjecture, which have already disclosed not only the constitution of, but also the power of, disintegrating of the atom, may bring indispensable aid in applying exact observation to the physical aspects of cell metabolism which require both analysis and strict measurement.

## *The Relation of Chemistry to Medicine*

The relationship of chemistry to medicine is of long duration. In recent years it has become increasingly intimate and of high importance to the advance of medicine. In the year 1828 occurred one of the most significant events in the history of chemistry, pregnant with influence for both sciences, and destined to lead to an alliance of incalculable importance. Wohler in that year produced urea from ammonium cyanate. Urea had long been recognized as a constituent of certain animals; it was present in the urine of man, and was universally regarded as a typical member of that class of 'organic' substances, obtained directly or indirectly from living animals, which were held to be characteristic and exclusive products of those activities we call 'life', of a 'vital force'. Ammonium cyanate, on the other hand, belonged to the class of 'inorganic' or mineral substances. The distinction between 'organic' and 'inorganic' substances had long been regarded by the chemist as fundamental. Wohler's discovery first disproved this supposition, first demonstrated that there was no intrinsic difference between the two groups, and that the same chemical laws and methods of chemistry could therefore be henceforth regarded as capable of successful application to study of the structure, properties, modes of production, changes, relationships of substances taking part in all processes concerned with the work of the body during life, whether in health or in disease. In Wohler's discovery chemists found impulse and incentive to that research which, immense though its achievements already are, maybe is only at the beginning of further impending changes in our power to recognize, treat, and prevent disease.

The contributions already made are of several degrees of importance: they refer to therapeutics; to more penetrating study of that department of physiology we know as bio-chemistry upon which many exceedingly important advances have been based; to examination of changes taking place in disease, knowledge which leads to easier and earlier recognition of morbid processes, and to enhanced power of control over them. They are not separate, unrelated studies but are still parts of one corpus of inquiry.

In treatment of disease many substances of natural origin, such as plants, have for centuries been used empirically. In respect of the proportion of active ingredients present in such medicament there was great variation; consequently the physiological dosage was a matter of uncertainty, and administration of the drug for that reason was not free from danger. The chemist has in many cases discovered the active agent of such plants, has isolated it, recognized its chemical constitution, constructed it from inorganic substances, and enabled us to administer the therapeutic dose. Alkaloids extracted directly from plants have been of great value; we need name only morphine (from poppy), digitalin (from fox-glove), atropine (from belladonna) to realize how much we owe to the chemist. In certain cases inherent defects of the natural alkaloid have been eliminated in the drug fashioned by the chemist; novocain and other allied substances now replace the original natural alkaloid cocaine. The chemist has even gone beyond this merely imitative construction of new drugs; he has created synthetic drugs, such as barbituric acid (by Finck, 1864), salvarsan, tryparsamide, Beyer 205, and others, and has built up a whole series of powerful bactericides of even greater potency than any extracted from natural products. Many such antiseptics are derived from dyestuffs. The whole practice of 'chemotherapy' is based upon the work of chemists; a reference to the Reports of the Medical Research Council will show what interest and importance this subject has now attained. All life-processes are essentially built up of chemical reactions. Food, owing to the changes occurring after ingestion, builds up the energy and creates the heat of the body, tissues being changed and repaired, and normal growth steadily maintained. Our knowledge of dietetics is based largely upon careful investigation by the chemist: men like Emil Fischer who did so much to elucidate the nature of proteins and sugars, and set up landmarks both in chemistry and in medicine. To the more recent work on 'vitamins' discovered by Gowland Hopkins, the chemist has largely contributed. That such food factors existed was made probable by early observation of those gross effects of their absence, scurvy and beri-beri. The discovery by Mellanby that rickets was a 'deficiency disease', a disease, that is, dependent upon the absence, and relieved or cured by the administration, of a food factor now known as Vitamin D, was of the highest importance not only in relation to this age-long disease, but as incentive and direct encouragement to further investigation by both chemist and clinician. The belief that cholesterol was the parent substance from which this essential vitamin could be produced by irradiation was soon replaced by the knowledge that a substance closely related to cholesterol, and by ordinary means inseparable from it, ergosterol, held this relationship. The story of the exceedingly complex work, embracing the activities of physicist, chemist, biologist, which has resulted in the discovery of what is believed to be the pure form of the antirachitic Vitamin D (calciferol) is one of the most marvellous records of research in recent years. It illustrates the imperative necessity for close co-operation of many individuals each highly trained in his own department, of those skilled in matters of hand, in building of new instruments, no less than of those gifted with versatility of mind, and with patience that can never be subdued. The past Report of the Medical Research Council tells us that:

'The crystalline calciferol has astonishingly intense biological activity. Weight for weight it has 40,000,000 times the value of a good sample of cod-liver oil, in preventing or curing rickets. A certain daily ration of Vitamin D is needed for the proper development and growth of every child. Lacking this, though it has otherwise abundant food, the child becomes stunted, deformed, and enfeebled. A single ounce of calciferol, dissolved in suitable liquid, could produce the necessary daily ration for more than a million children.

'It seems almost incredible that a particular addition to the food so infinitesimal in amount, taken into the child's body for distribution to every part of it, should be so potent in its deep-seated activity as to make all the difference between crippling and disease on the one hand, and healthy life and development on the other. Similar instances of the significance in nutrition of "infinitely little" are provided of course by other vitamins. We now have for the first time the description of a vitamin, or at least a very close approximation to it, in terms of known chemical and physical characters. This is a notable advance, and high credit should be given to the ingenuity, skill, and perseverance that have led to this new stage of knowledge.'

The work of Mrs. Mellanby on the value, indeed the necessity, of Vitamin D for the growth of teeth and their resistance to decay is happily being applied in practice. May I quote again from the Report of the Medical Research Council of this year:

'Four years ago the Council thought it well, on the advice of their Dental Committee, to make a large-scale trial of the effects of giving Vitamin D to groups of children living under urban conditions and supplied with diet believed to be fully adequate. The results collected after unbroken observation for two years were so significant as to call for an interim publication made in September last. The children, all living under similar institutional conditions, were divided into groups of from 65 to 86 in each group. Each group received a specific addition to the standard diet. All the children were regularly examined and progress of dental decay in the permanent teeth recorded. It was found that there was a striking difference in the rate of increase of decay between the groups receiving Vitamin D either in the form of cod-liver oil or of artificially manufactured Vitamin D given as "radiostol", on the one hand, and those, on the other hand, not receiving additional Vitamin D, but only receiving either treacle or olive oil for purpose of comparison. As between the first inspection of the teeth and the final inspection after two years, the percentage increase in decay for the olive oil or the treacle group was close to 46 per cent. That for the cod-liver oil (natural Vitamin D) group or the radiostol (artificial Vitamin D) group was in each group close to 10 per cent.

Corresponding results had been previously obtained in a more limited trial undertaken at Sheffield by Mrs. Mellanby and by Dr. Lee Pattison.'

These results apply only to teeth already formed when the trial began. When the Vitamin is given at a still earlier stage even more decisive results may confidently be anticipated. It is interesting to observe that similar effects are not seen after the administration of Vitamin D to animals. The Report of the Zoological Society for 1931 says (p. 23):

'Experience has shown that certain animals—civets, genets, and others—very susceptible to rickets, cannot be cured by the usual antirachite treatment. It seems likely, therefore, that man and wild animals differ widely in their vitamin and mineral requirements and that such diseases as rickets and osteomalacia in man and in wild animals may not be aetiologically identical.'

In regard to every organ in the body it is no exaggeration to say that a large part of our knowledge of its function depends upon the application of chemistry; and that any further increases in our knowledge will be similarly derived. The liver, for example, may be regarded as a laboratory in which a multitude of processes of chemical analysis and sythesis simultaneously occur. So also the activities of the stomach in health and in disease, the vagaries of the chemical constitution of its secretions, the effect of these upon pathological processes attacking not only the stomach but other parts, have been elucidated by chemical inquiries. Our knowledge of the various aspects of renal function is almost wholly the gift of chemistry, and our insight into the gigantic influence of the secretions of ductless glands depends too in large measure upon chemical work. The discoveries of Banting and the isolation of insulin, with their immense and eternal benefits to mankind, though prompted by clinical knowledge, were accomplished through the agency of chemistry. The results so far obtained in Vitamin research are not only extremely important in themselves, and of incalculable value to the community in respect of the prevention and alleviation of disease, but they are suggestive of still greater impending advances in our knowledge of the chemistry of all processes and of the influences mutually exerted by parts of the body which act in harmony with, or are corollary to, each other.

The studies of normal function and disordered function have not always or often held a logical relationship to each other. A multitude of observations regarding certain diseases have been accumulated while the normal function of the affected organ or organs has still remained obscure. Since the year 1775 we have known that sugar is present in the urine in each case of diabetes, though our knowledge of some of the functions of the pancreas has only recently been created. Perhaps the oldest application of chemistry to medicine concerns tests for recognition of diseases. Examination of blood, urine, cerebrospinal fluid may enable us to recognize the presence of diseases when other evidences are slight, indefinite, or even, as yet, absent. So that a well-equipped laboratory enabling such tests to be made is now a necessary equipment at every important hospital, and should be more available to general practitioners.

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