THE
SCIENCE & ART OF MEDICINE

IN HIS excellent history of the Cambridge Medical School the late Sir Humphry Rolleston states that 'The office of Regius Professor of Physic was founded in 1540, nearly at the same time as the dissolution of the monasteries by Henry VIII, who has been described as "that munificent donor of other people's property". The original stipend was £40 a year, in those days a generous figure', and, in the letters patent which I, the 22nd holder of the office, have received, the figure of £34. 18*s.* 0*d.*—£40. 0*s.* 0*d.*, less fees—of 'good and lawful money' is named as the emolument of the ancient office. This, in fact, is the amount which the crown still contributes to the salary of the Regius Professor. Fortunately, it is supplemented, indeed swamped, by the amount contributed from other sources.

All my predecessors have been distinguished in the art of medicine. Some, such as Winterton and Ward, were pre-eminently scholars; some, such as Glisson, whose name is perpetuated in Glisson's capsule and who was a scientist far in advance of his time, were original investigators. Three—Glisson, Paget and Allbutt—

were Fellows of the Royal Society. The remainder were physicians distinguished mainly for their learning, their wisdom and their skill in practising the art of medicine. From 1540 to 1892 the physician selected for the post was almost always a local resident. Many regarded the Chair as a sinecure and a comfortable addition to the emoluments and dignity of their private practices. The appointment of Sir Clifford Allbutt in 1892 broke the local tradition and, perhaps not unnaturally, was not well received by the practising Cambridge physicians. In consequence, this great man had to endure many humiliations at the hands of his Cambridge colleagues, who denied him access to beds in Addenbrooke's Hospital for eight long years—years which gave Allbutt an opportunity to write his classic *System of Medicine*. He came eventually to be a very great figure in Cambridge medicine, a classical scholar, a prolific writer of easy-flowing and beautifully phrased English, an original observer with an instinctive power for evaluating new methods, and an experienced physician with an international reputation for his skill in the art of medicine.

Even as the appointment of Sir Clifford Allbutt broke a centuries-old tradition, so has my own done likewise. This is the first occasion on which a man has been appointed whose practice, tastes, training and original work have been in the scientific, rather than in the clinical, field. It may well be an instinctive recognition of the importance of the scientific aspects of medicine, not forgetting that science is not all factual and itself contains much art. The welding of art and science will make for good medicine, the field of which is now so large that no one man can hope to till more than a small corner of it.

One has often heard it said that medicine is an art and not a science. In my own experience, this platitude has usually been a cloak to cover ignorance of some modern scientific procedure. The simple facts are that medicine is both a science and an art. It is true that medicine will never be an exact science, because the normal variations in individuals have such a wide range that automatic and mechanical treatment is prohibited, whilst every patient requires a different method of approach according to his psychology. This, the frequently ridiculed bedside manner, which secures the confidence of the patient, is of fundamental importance in practice; it is an art which is inborn and not acquired. Nevertheless, even the most confirmed artist cannot now neglect to keep up to date with the facts and findings of science upon which his diagnosis and treatment must be based. Nor will the artistic claim be very sympathetically received by a court of law, should the claimant have neglected the scientific aspect. But one of the attractions of the profession is the personal and individual character of its practice: the latitude with which a qualified doctor may exercise his own judgement, express his own opinions and practice his own art. This, indeed, is one of the strongest objections to nationalization and standardization. If the profession

Cambridge University Press
978-1-107-67355-7 - The Science and Art of Medicine: An Inaugural Lecture
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of medicine be robbed of its scope for individuality, the soul will go out of it.

And so to inaugurate myself as Regius Professor of Physic in my own University, I have thought that a brief exposition of one aspect of scientific medicine might show that scientists are also artists and that their science has been and can always be readily welded into the art of bedside medicine.

Medicine has been practised for countless ages. But in order to grasp the daily increasing significance of the scientific aspect, one has to look no further back than the middle of the last century. The fundamental requirement for curing the diseased body is to eliminate the cause of the disease. From the middle of the nineteenth century onwards, many causes have been brilliantly revealed with the work of Pasteur, Koch and others in the bacterial world, of Ross, Bruce and Leishman in the parasitic world, of Mellanby, Gowland Hopkins and others in the field of vitamins, of Harington, Banting, Best, Dodds and others with internal secretions. In parallel, there has grown up an immense accumulation of knowledge on the habits and mode of life of parasites, as well as the complex science of immunology, which has elucidated some of the mechanisms by which the body eliminates an infection, some of the methods by which the protective powers of the body can be increased and some of the means by which organisms or parasites exert their pathogenic action.

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These facts were beginning to alter the picture of medical science in the closing years of the last century and the opening years of this one. Before that time, drugs and treatments had been used with much success, with much art, and with much skill for the alleviation of symptoms, but with little or no knowledge as to the action of the drugs (if any) on the primary cause. In principle, the physician could relieve symptoms, but the cure was in the hands of nature. The physician was an artist in diagnosis and in the writing of neatly balanced prescriptions, often containing ten or more compatible ingredients, many of which had literally no action and many of which were survivals from the dark ages of medievalism and even witchcraft. It was true, and it is still true to-day, that certain drugs were beneficial in their own limited sphere, such as morphia, cocaine, digitalis, iron, bromides or anaesthetics. It is also true that centuries of empirical experimentation on the human subject had led to the discovery of quinine for malaria, of ipecacuanha for dysentery, of fresh fruits and vegetables for scurvy, and of mercury and iodides for the treatment of syphilis. But these discoveries preceded the finding of the cause of the disease, and the real action of the remedies was quite unknown. To-day we do not tend to produce physicians as shrewd and as skilled in diagnosis as those who were forced to rely entirely on their personal observations and experience. Undoubtedly, in the old days, many wrong diagnoses were buried in the grave, but the modern student, with so many exact scientific checks at his command, would do well to imitate his forbears more closely by carefully orientating his cases before demanding wholesale laboratory work.

From 1890 onwards there began to be developed the treatment of disease in relation to cause rather than symptoms. Beginning in the immunological field with diphtheria anti-toxin, there followed, through the period of my own lifetime, the perfection of numerous specific anti-toxins and sera, the practice of actively immunizing against certain infectious diseases, the exploitation of the internal secretions (such as thyroid and insulin), the conquest of some of the vitamin-deficiency diseases, the development of liver for the treatment of pernicious anaemia, and the realization of Paul Ehrlich's dream of safe and potent specific chemotherapeutic agents.

In the science of immunology, the world of medicine owes much to the imaginative genius of Paul Ehrlich, whose picturesque theories of immunity are familiar to every medical student. Though Ehrlich's views have had to be substantially modified in the light of modern experience, their fundamental insistence on specificity holds true to this day, and Ehrlich's stubbornness on this one important point (though it taxed his ingenuity to change the detail of his theory with each new discovery) undoubtedly saved the science of immunology from becoming chaotic during the earlier stages of development. It was Ehrlich's immunological studies which revealed to him that though demonstrable immunity is a feature of many bacterial diseases, none is developed in the protozoal diseases such as malaria. It was clear that these last would have to be attacked in an entirely different manner. He realized, too, that although quinine was known to have an action in malaria, its effect on the parasite itself was quite unknown, nor could its action be properly demonstrated without a susceptible animal or a means of cultivating the organism. Paul Ehrlich is rightly considered to be the father of modern chemotherapy. His dogmatic and picturesque views on the mechanism of immunity greatly coloured his manner of approach to the problems. His dream was an armamentarium of 'magic bullets'—many of you may have seen the film depicting Ehrlich's life, which is titled 'The Magic Bullet'. These 'bullets', or specific remedies, when introduced into the body would, ideally, speed straight to the target, the particular infecting organism, and obliterate it, at the same time leaving the tissues of the host unharmed. This last proviso is, of course, an axiom. We know many agents which will destroy bacteria or parasites. But the metabolism and susceptibility of these primitive organisms are not greatly different from those of our own complex make-up, and there is little advantage in eliminating the parasite, and, at the same time, terminating the existence of the host.

Great discoveries commonly originate from the fact that a man suddenly grasps the significance of a simple observation or some variation of it, that has perhaps been known for many years. 'Imagination bodies forth the form of things unknown.' So it was with Ehrlich. The beginning of the science of chemotherapy dates from the day on which his mind connected two well-known facts—first, that methylene blue stained the malaria parasite intensely and, secondly, that methylene blue was harmless to the human body. In human beings, however, though there was a hint of success, methylene blue was obviously very inferior to quinine. Yet it is of extreme interest to find that years after Ehrlich's death, when biological experiments with bird malaria made the testing of synthetic human remedies possible, it was the structural analogy with methylene blue, rather than quinine, which led to the development of *mepacrine* and *pamaquin*. These two modern synthetic drugs more than filled the gap when the world supplies of quinine were denied to us during the war. It is no exaggeration to say that they have been more important to us for the successful prosecution of our Far Eastern campaigns than many of the modern lethal weapons. In Burma, at one time, our casualties from sickness were more than ten times those caused by Japanese bullets. In the last year of the war, mainly due to mepacrine and good anti-malaria discipline, the balance was approaching equality. Ehrlich's first real success was with dyes in the treatment of trypanosomiasis, a protozoal disease which could be easily studied in mice, the most convenient and prolific of all experimental animals. In these animals, the parasite causes an acute and fatal disease, so that it is possible to get a rapid and a clear-cut biological result on the survival rate. Ehrlich's *trypan red* was effective in mice, but ineffective in human beings, yet later it provided the starting point for the colourless but active modern analogue known as *Bayer* 205. Far more important than the partial success of these synthetic remedies was the contribution they made to the understanding of mode of action. Ehrlich's views were coloured by his magic bullet theory. Probably no chemotherapeutic agent conforms to this view, though penicillin comes remarkably near it. In the mouse, it was easy to observe the staining of the trypanosome, as well as its motility and liveliness in a mere drop of blood. Ehrlich noticed that though the parasites were stained, they were not killed; they swam quite merrily in a drop of blood. Yet when this infected blood was injected into other mice, no infection occurred. This was interpreted to mean that though the dye had not killed the trypanosomes, nevertheless the parasites were incapable of reproducing themselves. At that time there could be no crucial test of this because no method of artificial culture was then available. But since that time, and with other substances, the explanation has been shown to be correct. For example, *emetine*, used in the treatment of amoebic dysentery, is almost inactive against the amoeba *in vitro*, in a concentration which the human body can tolerate, but *in vivo* the drug is highly active.

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Unable to reproduce itself, the parasite dies out and the infection subsides. In strong contrast is an allied substance, *demethoxyemetine*, which is very lethal to the amoeba *in vitro*, but which is almost inactive in the human host *in vivo*. The more subtle form of attack, the interference with reproduction, is therefore more effective than a direct amoebicide. This is a good example of art and imagination in the scientific world.

Ehrlich will always be remembered for his work on the arsenicals in the treatment of syphilis. Here again, the point of departure was from an arsenical known as *atoxyl*, which was found to have an action on trypanosomes. Ehrlich showed that atoxyl was quite inactive *in vitro*, but that the arsenoxide which was produced by reduction when the material was put into the living body, was rapidly lethal to the parasites. He extended the scope of his work and, in 1910, announced the synthesis of *salvarsan*, often called *606*, this being the schedule number in his records. Salvarsan is an example of curative action due, not to the substance injected, but to the oxidation product, arsenoxide, which is slowly and continuously liberated in a concentration sufficient to kill the spirochaete of syphilis. The continuity of the action is of fundamental importance for ensuring total elimination of the parasite. This could not be achieved by the direct administration of arsenoxide unless the administration were to be continuous over a very long period—an impracticable proposition. The medical student of to-day