THE GOULSTONIAN LECTURES

ON

PHARMACOLOGY AND ITS RELATION TO THERAPEUTICS.

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LECTURE I.

IN the course of these lectures, I purpose to consider Pharmacology and its Relations to Therapeutics, or, in other words, the relations between the action of drugs on the healthy body and their uses in the cure of disease. In dealing with this subject, I shall divide it into four sections:

1. The reasons why therapeutics has made such slow progress in the past, as shown by the history of medicine.
2. The methods by which it is at present advancing.
3. Some of the most important results obtained by the use of these methods.
4. The prospects of therapeutics in the future.

Although few persons possessing any knowledge of the history of medicine will deny that therapeutics has made some progress during the last thousand years, yet it is impossible to read the writings of the ancients without feeling that, not to mention such men as Hippocrates and Galen, if some of the old Egyptian physicians were to arise from their graves and commence practice, we would have but little cause to sneer at their treatment, although we have the advantage of possessing the medical knowledge accumulated during the two or three thousand years which have elapsed since they flourished. For those old Egyptians seem to have been acquainted with the use of emetics, enemas, and purgatives, those potent agents which are, perhaps, more used and more useful than any others in our own armamentarium. They paid attention to the diet of their patients. For the cure of dropsies, they used squills and iron.* In addition to drastics,† squill, broom,‡ and balsams,§ an ancient Greek would have tapped the abdomen when the distension became great, and would have taken every precaution to prevent syncope from the operation. These are the very methods of the modern physician; and, although he might give digitalis and blue pill along with the squills, and suggest nitrous ether and juniper, yet his reasons for this would be the same as those of the Egyptian or Greek—viz., that he had seen the remedies prescribed do good before, and expected them to prove beneficial again. As to the *modus operandi* of these remedies, or the reason why they should succeed in one case and fail in another, the ancient and the modern would be almost equally in the dark; for medicine with both would be an art, not a science.

If we turn to other branches of knowledge—astronomy, chemistry, or physics—the case is widely different. Not that the ancients were entirely ignorant of these subjects—far from it. The Egyptians had a fair knowledge of chemistry as an art, for they made glass mosaics such as Venetian manufacturers have only of recent years been able to fabricate.¶ They produced imitations of precious stones such as moderns can hardly surpass.¶ They mixed metals into a bronze almost equal in toughness and elasticity to steel.** They used metallic oxides so as to give their porcelain most beautiful colours. They knew how to fashion patterns in cloth by the use of acids, in much the same way as our own Manchester manufacturers.†† Their technical knowledge was deep and varied. Modern skill has striven in vain to equal or surpass many of their achievements. But here their triumphs end; for in modern times—we may say in the preceding century—science has taught us that wonderful affinity in nature which enables us almost to rival nature in the beauty and perfection of our work; to discern the relationships of the elements; to pull a compound to pieces; to tear down and build up; to create the most complex

products of vegetable life—dyes of brilliant and enduring lustre,* and poisons of deadly power.†

The same is the case with astronomy and physics. Thales might predict eclipses,‡ and Hipparchos could calculate them with accuracy; but they had no conception of the laws which regulate the movements of the heavenly bodies—laws which enable us to calculate the position of the planets at any given moment for centuries backwards or forwards, to determine their masses, to measure their distances from the sun, to ascertain the rate at which they roll along their orbits, and foretell the existence of unseen bodies which disturb the regularity of their motions. Archimedes was acquainted with the reflection of the solar ray, and may have used his knowledge to destroy the ships of an enemy; but he was utterly ignorant of those wonderful properties of light which have enabled us within the last few years to accomplish the apparent impossibility of analysing the composition of the sun and stars, millions of miles removed from us, almost as readily as that of a meteorite which has fallen to the earth; to ascertain that an apparently motionless star is receding from us with enormous rapidity, and to affirm that a great conflagration is going on in another star with as much confidence as that a chimney has caught fire in a neighbouring street.

While the ancients had an isolated knowledge of facts, we know them in their relations. This difference is as great as the difference between our knowledge of a man from a casual meeting in the street, and a thorough acquaintance with his early training, his circumstances, his associations, his life-long conduct. You can tell what the former will do in circumstances in which, to your knowledge, he has already been; you can foretell what the latter will do under conditions in which he has never been. Your knowledge of the former is empirical; of the latter, scientific. You can tell that your casual acquaintance will salute you in passing, or that he will leave town by his daily train, because you know that he has done these things regularly for weeks, months, or years back; but you do not know whether he would prove a true man or a knave if you were to entrust him with an important commission. In the case of your life-long acquaintance, on the other hand, you could predict the result of such a trial, although you had never made it; and from your knowledge of him you could make certain that, according to his character and circumstances, he would wilfully break his pledge, like the faithless friend of the unfortunate Essex; or would, like Regulus, fulfil his engagements, though torture and death should be the result. It is such an intimate acquaintance as this with the properties of light that enables us to predict that, under certain conditions, one beam will extinguish another, so that, contrary to all our usual experience, two lights make a dark; and to understand the reason of our partial failure if we produce mere dimness instead of complete darkness in our endeavours to demonstrate the fact experimentally. An intimate knowledge of the chemical nature and relations of bodies enables us not merely to say that certain substances—for example, members of the alcohol series—may exist, but to foretell their properties, and, by using certain processes, to make them, although they had previously never been known, and probably had never even existed in a separate state. Unfortunately, we do not know medicine as we do chemistry and physics. We have medical sciences; for physiology, pathology, and pharmacology, are justly beginning to lay claim to the title; but medicine itself—the recognition and cure of disease—is still an art, and not a science. The truth of this becomes evident if we consider the case of ague, the disease in which the power of medicine, both as regards prophylaxis and treatment, is most marked.

We know that if a man pass through certain districts, and more especially if he sleep in them, he is likely to be attacked with a fit of shivering, which, after lasting some time, will be succeeded by a burning fever and then by profuse sweating, after which he will feel comparatively well until the next day, when another shivering fit will come on at the same hour, and run the same course as the first. We know that, by warning the man against the dangerous locality, or by making him adopt certain precautions, take cinchona alkaloids, if he cannot avoid the place, we may be able to prevent the disease; by administering one large dose of quinine before a paroxysm we may stop its approach, and by continuing the remedy we may prevent its recurrence altogether. But we are ignorant of the nature of malaria, as we term the cause of these paroxysms, whatever it may be. We do not know how it acts upon the bodily mechanism so as to cause them. We have no notion of the manner in which quinine counteracts the malarial effects, or why quinine should sometimes fail and arsenic prove

* Pauw, *Recherches Philosophiques sur les Egyptiens et les Chinois*. Berlin, 1773; tom. i. p. 134.

† *Paulus Aegineta*, by Adams, Sydenham Society, p. 570.

‡ *Op. cit.*, p. 575.

§ *Op. cit.*, p. 571. Compare H. Thompson, *Lancet*, Nov. 29th, 1869, p. 742.

¶ Wilkinson's *Popular Account of the Ancient Egyptians*. London, 1854, vol. ii, p. 61.

¶ Wilkinson, *op. cit.*, p. 63.

** *Op. cit.*, p. 159.

†† *Op. cit.*, p. 66.

* Graebe and Liebermann, *Jahresber. für Chemie für 1869*, pp. 494 and 1160.

† Conia made synthetically by Hugo Schiff, *Bericht der Deutsch. Chem. Gesellschaft*, December 26th, 1870, p. 946; and Muscarin by Schmiedeberg and Harnack, *Centralblatt für die Med. Wiss.*, 1875, p. 598.

‡ Herodotus, i, 74.

efficacious.* We foretell the occurrence of an ague-fit after exposure in a certain locality, and its prevention by quinine, in the same way that an astronomer of ancient Babylon could predict the recurrence of an eclipse.† He saw that one was followed after a certain interval by another; and we have observed that exposure is followed by ague, and the administration of quinine by the diminution or absence of the paroxysm. Having seen the same sequence of phenomena before, he reasoned that it would come again, even as we reason now. But he had no idea of the cause of the eclipses. He did not know what was going on in the eighteen years' interval between them, nor could he account for any irregularity in their occurrence. We may say that the immediate cause of the ague-fit is probably intense irritation of the vaso-motor centre in the medulla oblongata, but we have no idea of the nature of the irritant, and we cannot even guess why the irritation should occur at regular intervals. We do not know the changes in the nervous system and tissues which occur during the intermissions, and we are utterly at a loss to explain why a man should come from a malarious district in India and die in England of jungle-fever, although he had never had it while abroad, and it is never seen in residents at home. We have no such accurate and comprehensive knowledge of the relations between the organism, malaria, and quinine as astronomers have at the present day of the relations between this globe of ours, its attendant satellite, and the solar and stellar systems, a knowledge which enables them to fix, years before, the precise spot on the earth's surface at which an eclipse may be seen, although totally invisible for thousands of miles around their home, and to make preparations for observing it accordingly.

If we inquire why medicine is so far behind astronomy, we shall find two reasons. The first is, that medicine is much more complicated and difficult than astronomy. For, instead of depending on mathematics and physics, it rests upon pathology and pharmacology, which in their turn depend upon physiology, while physiology depends on chemistry and physics. Some one has compared the advance of the sciences to a game at leap-frog, one jumping over the backs of the others. There is much truth in the comparison. Physics helps chemistry, chemistry helps physics, and both help physiology. Indeed, it is only through them that physiology can advance; for, without chemistry, the processes of respiration and digestion would be incomprehensible, and without physics a knowledge of the properties of the nervous system would be unattainable. Until chemistry and physics had made a certain amount of progress, physiology was obliged to stand still, and consequently pathology, pharmacology, and therapeutics could not advance.

The second reason for the slow progress of medicine is, that during many centuries it has been studied by wrong methods. In reading its history, I have found it by no means easy to understand the various phases through which it has passed, for I could not enter into a manner of thought so different from our own as that of Paracelsus until I remembered a trifling incident which occurred when I was a child. As others may have had the same difficulties as myself, and as this incident may help them as it has helped me, I shall not scruple to relate it. One day, when playing with a box, I "made believe" that the lock was out of order; and again "making believe" that I could mend it by the proceeding, I picked off a piece of the ivory with which the box was inlaid, and drove it into the keyhole, thus ruining the lock and seriously injuring the box. Every one here, I may even say every one in the world, has had some similar experience, for the habit of "making believe" is universal, and some of the oldest relics of nations past and gone are children's toys.‡ The little boy "makes believe" that a walking-stick is a horse, and feeds it with hay and corn. The little girl "makes believe" that her doll is good, and she pets it; naughty, and she punishes it; or sick, and she nurses it. As these children grow up, they throw aside their rocking-horses and dolls, but

they do not altogether throw aside their practice of "making believe". In early ages it did, and amongst rude peoples it still does, remain as a lifelong habit. Nor is it entirely destroyed, although it is of course lessened, by an advanced civilisation. We daily see around us illustrations of the proverb that the wish is father to the thought, the person who wishes "making believe" that facts correspond to his desire. It is evident, therefore, that this practice of "making believe" is not a mere childish folly, unworthy of a moment's consideration, but the outcome of a deeply rooted tendency of the human mind, and therefore deserving of most serious attention. Its nature is evident enough, for a few moments' thought will suffice to show that, in "making believe", we form a conception in our own mind, and proceed to act upon it, as if it were true, when there may be not the slightest accordance between it and things as they really are.

Indeed, the name we give to the power is sufficiently descriptive—imagination; *i. e.*, the forming of images, or, as the Germans term it, *Einbildung*, the painting of pictures in our brains, which may be perfectly unlike the real things they are intended to represent. We probably have all heard of the story of the camel, the parts played by the different nationalities varying according to the country in which it is told. An Englishman, a Frenchman, and a German were asked to describe and figure a camel. The Englishman went to Egypt, where he could see it in its home. The Frenchman went to the Jardin des Plantes, where he could see it without trouble. The German went to his study and evolved it of his moral consciousness. We laugh at the idea of the ludicrous discrepancies there would be between the picture of the camel drawn by the student from his imagination and the actual portrait of the animal, and yet every day we make a similar blunder. We form mental pictures of persons, of scenery, of occurrences, but how rarely do these coincide with the reality. How seldom does any celebrated person, for example, resemble the ideal of the imagination. Even after we have seen him, our mental portrait is still an ideal, for we picture him to ourselves either with qualities which he does not possess, or without qualities which he does possess. It is only by frequent intercourse, by repeatedly comparing our ideal with the reality, that we come to know the truth. In medicine, we find the same thing. Two physicians stand by the bedside of a patient who has a high temperature, rising at night and falling in the morning, a doubtful spot or two on the skin, tenderness over the abdomen, slight diarrhoea, moist râles in the chest, and a very indefinite and unsatisfactory history. One says the patient is suffering from typhoid fever with bronchitis, and immediately pictures to himself ulcers in the intestines and congestion of the bronchi. Both of these, he thinks, may get well, and he looks for the recovery of the patient. The other says tuberculosis, and pictures to himself the lungs studded throughout with white nodules, and the serous membranes strewed over with pearly granules. Instead of recovery, he looks for exacerbation of the symptoms, and predicts a fatal issue to the illness. The late Dr. Hughes Bennett, in his clinical teaching, used to insist strongly on the difference between ideas and facts. A student would be called to auscultate a patient, and was then asked by the professor what he had heard; "I think I heard a murmur," he would say. "Think," said Bennett, "I don't want to hear what you think; I want facts; there either is, or there is not, a murmur; and I want to know which." Of course, it is impossible for any one to communicate to another anything more than his idea, but he may take much trouble to make it coincide with facts; and the importance of insisting upon this in teaching, as Dr. Bennett did, cannot be overestimated. It is the agreement or non-agreement of the idea in the physician's mind with objective facts that makes his diagnosis right or wrong, and his treatment a success or failure. It is the practice of acting as if the creations of the physician's imagination were realities, without ascertaining whether they were so or not, that has proved so fatal to the progress of medicine; and it is only through the diligent comparison of ideas and facts that we can hope for its advance.

We may divide the modes of studying medicine into three.

1. Where the disease has been attributed to unseen powers, gods, or spirits, and means have been sought to influence them;
2. Where disease has been attributed to some disturbance of the mechanism of the body, but where the physician's ideas regarding that mechanism, as well as regarding the action of his curative measures upon it, have been erroneous;
3. Where disease has been attributed to some disturbance in the mechanism of the body, and where the physician's ideas regarding that mechanism, as well as the action of his curative measures upon it, have been rendered more or less correct by means of experiment.

I have already dwelt much upon the practice of "making believe", and have preferred this childish expression to the usual term of imagination, because childhood's follies present us with an exaggerated

* The recent researches of Lanzi and Terrigi render it highly probable that malaria is of a vegetable nature; but this cannot yet be considered as perfectly proven. Lanzi was able to produce a zoogloeal-like vegetation by cultivation of the pigment granules found in the livers of persons who had suffered from malaria. These granules he considers to be identical with the granules found in withered algae; and Terrigi found them in animals which had breathed for some time the air from a swamp. *Centralblatt d. Med. Wiss.*, 1875, p. 713.

† Whewell's *History of the Inductive Sciences*, 3rd ed. London, 1857, vol. i, page 121.

‡ When at Larnica in Cyprus, several years ago, I saw some relics obtained from excavations made in the neighbourhood. Underneath an old Greek town, and about fourteen feet below its level the explorers came to the ruins of a Phœnician town. As the Greek town had been destroyed about the Christian era, and the depth at which the Phœnician ruins lay below it showed that it had been demolished many years before the Greek town, we are probably within the mark in estimating the age of the Phœnician relics at three thousand years. Amongst the most interesting objects discovered was a wooden horse, the plaything of some Phœnician boy. Wooden dolls, found in Egyptian tombs, are also figured by Sir J. Gardner Wilkinson, *Popular Account of the Ancient Egyptians*. London, 1854, vol. i, p. 196.

picture of our own, and enable us clearly to see things to which we might otherwise have been blind. For this reason, I shall ask you again to turn to the trivial incident which I have already mentioned, and consider what a child finding a box locked is likely to do. He may believe that some spirit, good or evil, prevents him from opening the lid, may consider his failure as a punishment for breaking his mother's china vase, and endeavour to appease the spirit by weeping over the fragments; he may try to propitiate it by burning his sister's best doll as a peace-offering, or may attempt to drive it away by putting snuff into the keyhole. Or, without believing in a spirit, he may fancy the lid held down by some occult indefinite power—bewitched, in fact—and may pull hairs out of the cat's tail to remove the enchantment. If we replace the words child, open, and lid, by physician, cure, and patient, we shall have a tolerably fair example of medicine in one of its phases.

Perhaps no better illustration can be given of one form of "making believe" than that which I now quote from the book of Isaiah. Speaking of an idolator the prophet says: "He planteth an ash and the rain doth nourish it. Then shall it be for a man to burn; for he will take thereof and warm himself; yea, he kindleth it and baketh bread; yea, he maketh a god and worshippeth it; he maketh a graven image and falleth down thereto. He burneth part thereof in the fire, with part thereof he eateth flesh, he roasteth roast, and is satisfied, yea he warmeth himself, and saith, Aha! I am warm, I have seen the fire; and the residue thereof he maketh a god, even his graven image, he falleth down unto it and worshippeth it, and prayeth unto it, and saith, Deliver me, for thou art my god. And none considereth in his heart; neither is there knowledge nor understanding to say, I have burned part thereof in the fire; yea, also, I have baked bread upon the coals thereof; I have roasted flesh and eaten it, and shall I make the residue thereof an abomination; shall I fall down to the stock of a tree?" Should such a devotee as this be stricken by plague, pestilence, or famine, he will believe it due to the wrath of his block of wood, and will offer gifts to appease it. He may attribute his calamity to the anger of a lump of stone, and call upon his block of wood for deliverance. In the Friendly Islands,* for example, the natives believed that when a chief was sick he might appease the Deity and recover by strangling his relations. In Tahiti,† the priests pronounced certain words over the sick man, and tied cocoa-nut leaves to his fingers and toes. "In Madagascar,‡ when any person is sick, the nearest relations apply to the *ombiasse* or priest, who goes by night to the *amounque* or sepulchre of the father, or, if the father be still living, of the grandfather of the afflicted person; then making a hole in the monument, he places a kind of cap upon the aperture, and begins his incantations with many grimaces, invoking the spirit of the deceased to take pity on the person disordered, and restore his helpless progeny to health and vigour. If the patient recover, the *ombiasse* receives great applause and is loaded with presents; but, if he die, the *ombiasse* imputes it to the evil demons, or to fate (for the Madagascerians are great predestinarians), but never to any fault in himself or his incantations."

In ancient Greece, the medical art was almost entirely exercised by the priesthood, and especially by the priests of Æsculapius, to whose temple patients were brought in order to be cured. The remedies consisted partly in prayers and offerings, and partly in remedies applied to the body, and intended to act upon it.§ As time rolled on, the secrets of the priests became known to the laity, and their practical traditions became modified by the speculations of the philosophers. Alexandria, as it rose to eminence amongst the schools of learning, attracted the Greek philosophers and physicians who there met with the sages of the East, and learned from them the wild fancies of the Jewish Kabbalah.¶ While some rejected these new doctrines, and strove by eager examination of nature to advance their art, others gave themselves fully up to the influence of fancy, and developed a complete system in which the Deity, good spirits, and evil spirits, all played a part. Good spirits were coerced by prayers, evil ones by oaths (contracts) and offerings. The latter could be exorcised by means of certain magical words, and these were written up above the doors to prevent disease from entering. The early Christian fathers, Origen, Tertullian, and others, adopted this doctrine; it became the creed of the church, and, during the dark period of the middle ages, the influence of evil spirits or of undefined powers, included under the terms witchcraft and magic, were generally regarded as a common cause of disease. Amulets, relics, prayers to saints, and

visits to holy places, were the chief means of cure employed by the monks in whose hands medicine almost entirely lay, and the church pursued with unrelenting severity all those who were so unfortunate as to incur the suspicion of witchcraft. Luther ascribed most diseases to the direct agency of the devil; according to Robert Fludd, the exponent and apologist of the Rosicrucians, they were consequences of sin, and caused by four fallen angels. The celebrated Hoffmann attributed nervous diseases to diabolical agency, and it is little more than half a century ago that Windischmann, professor in Bonn, declared that a physician ignorant of exorcism lacked one of the most powerful agents of his art.

Besides the direct influence of demons, various undefined sympathies, relations, and powers, were supposed to exist between man and the stars, lower animals, plants, and metals. A man's fortune in life depended on the star under which he was born. The result of an undertaking could be foretold from the position of the planets. It was most important that medicines should be prepared and administered exactly at the time of particular planetary conjunction. By making an image in wax, repeating certain incantations, and performing certain ceremonies, it was supposed that one might establish such a relation between the image and a person whom he hated, that on pricking it with pins his enemy would be racked with pains in every part of the body, and would fall dead when it was pierced through and through. A sympathy was also supposed to exist between a wound and the sword, or other weapon with which it had been inflicted; so that by applying a salve to the sword, and carefully leaving the wound alone, it would heal. But if an enemy became possessed of the weapon, he could so treat the weapon as to cause the wounded man to suffer intolerable pain. A similar belief is not quite extinct even yet, for many persons still think that if a dog go mad after it has bitten a man he runs a risk of getting hydrophobia, and they, therefore, kill it to avert the danger. It is not much more than a year ago, that a man in the Midland Counties killed a poor woman by whom he thought himself bewitched. Nay, more, we daily use in our prescriptions a sign which, although now intended for recipe, was formerly the sign of the planet Jupiter, the cross in its tail bearing witness to its origin.

The doctrine of relations received a new impetus from Paracelsus, who, in particular, gave prominence to the imaginary virtues of magnets, and applied them to the body as a means of cure. He supposed that the body itself also possessed a kind of magnetic power by which the sick could infect the healthy. His follower, Van Helmont, also believed in a magnetic power of the body, capable of such external action, that he himself was often able by his mere presence to cure the sick and to impart peculiar virtues to medicines by his will. These ideas were adopted by various authors, but received their full development at the hands of Mesmer and Hahnemann. The former, by the application of magnets, afterwards by passes of the hands, and, latterly, by mere contact through a rod, was able to produce many extraordinary effects upon his patients, which he attributed to magnetism, but which we now ascribe simply to suggestion. The latter propounded the doctrine that diseases may be cured by small doses of those drugs which, in the healthy man, produce symptoms similar to those of his disease.

This principle, *similia similibus curantur*, is recognised by Hippocrates, who remarks that, under certain circumstances, purgatives will bind the bowels, astringents will loosen them, and substances which cause cough and strangury will also cure them.* But the Father of Medicine also admitted the other doctrine, *contraria contrariis curantur*, and Hahnemann not merely rejected this, but launched out into the wildest vagaries. He was not content with making his doses so small as to obviate the slightest risk of producing symptoms like those they were intended to cure, but reduced them to an infinitesimal amount; imagining, however, that what he lost in quantity he gained in quality, by imparting to the drugs through repeated trituration a mysterious potency which Van Helmont had fancied he could do by the simple exercise of his will.

[To be continued.]

* Works of Hippocrates, Sydenham Society's edition, p. 77.

DEATH FROM LAUDANUM.—Mr. John Cecil Wayett, son of the rector of St. Stephen's, Bristol, a medical student in Bristol Infirmary, some days ago, while suffering severely from neuralgia, rubbed his gums with laudanum to deaden the pain. The effect was to create thirst and stupor, and, while in this state, Mr. Wayett drained the laudanum-bottle of its contents. The stomach-pump, emetics, and all known remedies, were tried, but the unfortunate gentleman died from the effects of the poison, after remaining insensible for four hours.

* Cooke's *Universal Geography*, vol. i, page 90.

† Cooke, *op. cit.*, p. 35.

‡ Cooke, *op. cit.*, p. 814.

§ Works of Hippocrates, Sydenham Soc. edition, vol. i, p. 6; Sprengel, *Histoire*

pragmatique de la Médecine, traduit par Geiger, vol. i, sec. iii, p. 43.

¶ Ennemoser, *History of Magic*, translated by Howitt, Bohn's ed., vol. i, p. 443.