An Address
ON
THE PLACE OF BIOCHEMISTRY IN MEDICINE.

DELIVERED AT THE OPENING OF THE COURTAULD INSTITUTE OF BIOCHEMISTRY AT THE MIDDLESEX HOSPITAL ON JUNE 14TH,

BY

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FOR more than a century past every medical man has had, in his consulting room or near it, a shelf with a few bottles of reagents, a spirit lamp, and some test tubes, with which to carry out certain simple chemical investigations which form part of clinical routine. That shelf is the prototype of this great institute, with which the munificence of Mr. Samuel Courtauld has enriched the Middlesex Hospital; and the contrast between prototype and achievement is no greater than that between the medical chemistry of a hundred years ago and the biochemistry of to-day.

Indeed, the year 1828 marked an epoch, for in it the German chemist Wöhler, afterwards the fellow worker with Liebig, obtained that most abundant product of animal chemistry, urea, as a result of a reaction in the laboratory, and so began the removal of the barrier which was believed to separate organic from inorganic compounds—the chemistry of living things from the chemistry of the rocks.

Early Association of Chemistry with Medicine.

But the association of chemistry with medicine dates back much further. Even the alchemists tried to prepare the elixir of life. In the early part of the sixteenth century lived that eccentric genius who called himself Paracelsus, who looked upon medicine from the standpoint of chemistry; and in the sixteenth century was born van Helmont, who has been called the father of chemical physiology, of both of whose contributions you may read in Michael Foster's *Lectures on the History of Physiology.* In the seventeenth century our countryman Thomas Willis discovered glycosuria. Many of the pioneers of chemistry were medical men, some of whom occupied chairs both of medicine and of chemistry; and so medicine has played an important part in the building up of this, as of other branches of pure science, and often provided the early chemist with a means of gaining his livelihood. In return chemistry has rendered immense services to the advancement of medicine.

Wherever a medical school was founded a professor of chemistry was appointed, and in Edinburgh, at the end of the eighteenth century, there was a remarkable group of chemist-physicians, which included Cullen, Joseph Black, the discoverer of latent heat, and Daniel Rutherford. In those days numbers of future physicians, and amongst them not a few graduates of Oxford and Cambridge, went to Edinburgh for their clinical training, and some of these, returning to London, brought with them the current teachings of the school. Amongst these was Alexander Marcet, a native of Geneva, and afterwards physician to Guy's Hospital, who made some valuable contributions to pure chemistry as well as to chemical pathology. A slightly older contemporary was William Hyde Wollaston, a Cambridge man, the discoverer of the ductility of platinum, a property of far-reaching value to chemists and physicists. Wollaston, who abandoned medical practice after failure to be elected to the staff of St. George's Hospital, devoted himself to pure science, and gained distinction in physiology, pathology, mineralogy, optics, and botany. He was the first to make a scientific study of the composition of calculi. A junior contemporary of these, and like Marcet an Edinburgh graduate, was William Prout, who is entitled to a very high place among the founders of chemical physiology, for he was the discoverer of hydrochloric acid in the gastric juice—a vital finding in connexion with the physiology and pathology of digestion. He won fame as a chemist also; for his celebrated hypothesis that the atomic weights of other elements are multiples of that of hydrogen and that from hydrogen all other elements are derived has ever since set chemists thinking, and has proved a powerful stimulus to research.

The generation which succeeded these men in London produced another group of chemist-physicians, whose work was carried out in the middle years of the last century. Among them Henry Bence Jones may claim a prominent place. He was a pupil of Thomas Graham, who first investigated the colloid state, and of Liebig, and a friend and the biographer of Faraday. His best remembered contribution to medical chemistry was the discovery in urine of the peculiar protein substance which bears his name. Among his contemporaries, and also a pupil of Thomas Graham, was my father—not to refer to him in this connexion would be the outcome of a false modesty. He, in 1848, by means of a test of extreme simplicity, but which calls for some skill to carry it out, demonstrated the presence of uric acid in the blood of gouty subjects, and estimated approximately its amounts. Thus was chemical examination of the blood of living persons first made available as a means of diagnosis; and the developments of such methods, in the hands of Bang, Folin, and others, are familiar to students at the present day. These modern methods yield, with small quantities of blood, drawn from a vein or even from the lobe of the ear, results of great accuracy and diagnostic value. Somewhat younger contemporaries were Thudichum, whose work is now better appreciated than formerly, and Frederick William Pavy, who devoted much time throughout a long working life to the study of diabetes, but did not live to see the discovery of insulin. He it was, also, who first described cyclic albuminuria. It is told that one of his colleagues at Guy's Hospital, himself a great physician, expressed surprise that Pavy should devote all his best energies to the study of an incurable malady; but granting that even now we cannot cure diabetes, the advance made towards that goal shows that the time and energy of those who have worked at the subject have not been wasted.

Meanwhile, in a wider sense, and in a far wider field, the study of animal chemistry was advancing steadily. Much of the advance was due to the teaching, influence, and opportunities of research provided by Justus von Liebig in his laboratories at Giessen, and later in Berlin; and there come to mind the names of other great biochemists of the nineteenth century, among them those of Pasteur, Wurtz, Hoppe-Seyler, Karl Schmidt, Emil Fischer, Huppert, and Arthur Gamgee, to mention only a few.

Nowadays very different conditions prevail. A considerable number of those who obtain medical degrees or qualifications turn aside from the path of practice and devote themselves to laboratory work in the medical sciences, as pathologists, physiologists, biochemists, or pharmacologists. For these men it has been necessary to provide adequate accommodation. The Institute of Physiology no longer houses both biophysics and biochemistry; pathology has split into several branches—namely, bacteriology, morbid anatomy, and pathological chemistry. In biochemistry far more work is being done, and those who pursue it are almost all able to devote their whole time to it. The names of living biochemists who have done or have surpassed such work as that of our forefathers referred to, form a very long list, in which our own countrymen occupy a place of which we may be proud. Centres of biochemical teaching and research, such as that over which Sir Frederick Hopkins presides at Cambridge, are now being formed in various universities in this country, and we are met together for the inauguration of the latest of these to-day.

Bacteriology and Chemical Pathology.

It must not be forgotten that the aims and methods of the several branches which are included under the collective name of pathology differ considerably; and this is specially true of bacteriology and chemical pathology, although in the field of immunity they overlap and must collaborate. The bacteriologist studies the actual agents of disease, the stone which, as it falls into the pool, ruffles its surface, whereas the biochemist studies the ripples which spread outwards in increasing circles, from the point of impact of the stone—in other words, the disturbances of the metabolic processes which result from the bacterial invasion.

Of recent years, under the spell of the advances of bacteriology and protozoology, we have tended to lay all the stress upon the invading malady and to pay too little attention to the reaction of the organism invaded, but there are signs that the pendulum is returning from the limit of its swing, and in its modern dress the revived doctrine of diathesis will rest largely upon a chemical basis.

The newer biochemistry does not restrict itself any longer to the older problems of chemical constitution and the products and methods of metabolism. The physico-chemical aspects of the subject are receiving more and more attention. We may hope that, important as those aspects are, they will not so engross attention that the older problems will be neglected.

Not only does the modern pathological chemistry embrace a far larger field, but the simple methods of our predecessors no longer suffice for its requirements. Examinations of greater and greater delicacy are called for; apparatus is needed which requires ample laboratory space, and which is itself often costly. No wonder that the cost of hospital equipment and upkeep has increased greatly. Fortunately donors are beginning to realize that by providing a great hospital with such an institute as this they are rendering as much, or more, aid to the sick and suffering around us as by the addition of so many more beds. The value of a hospital depends not only upon the number of patients treated, but also upon the quality of the relief given, and, as I shall hope to convince you, the value of such a hospital as this, and the good which it does, is not limited to the area in which it is situated, nor even to its wider clientele; but, so far as it is a place in which knowledge is increased, its influence extends to wherever medicine is taught, and those who are trained here diffuse its teachings all over the world.

The Importance of Biochemistry in the Diagnosis, Prognosis, and Treatment of Disease.

Let me try, then, to set before you wherein the importance of biochemistry to medicine consists, and why such departments as that which has been opened here to-day are desirable, or even essential, parts of the equipment of such a hospital as this. Let me speak first of the more strictly practical aspects of my subject, of the aid which biochemistry affords in the diagnosis, prognosis, and treatment of disease.

There are a few maladies the diagnosis of which rests upon chemical evidence, or in which a derangement of the chemical processes is usually the earliest sign. This is often the case with diabetes, which is not infrequently first detected on examination of the patient for life insurance, and the earlier the recognition of the malady the better is the prospect of treatment. Indeed, all through the course of diabetes chemical tests are of value, as indicators of relapse or of response to treatment, as well as of the imminence of danger from acetonaemia. The estimation of glucose in a few drops of blood is of special value, especially in distinguishing between true diabetes and varieties of glycosuria which are apparently harmless, which call for no restrictions of diet, and in which such restrictions may be undesirable. From such examinations also the effects of dietetic and insulin treatment can be determined. Again, the reducing power of the urine may be due to sugars which are not glucose, and have quite different significance, and these can be recognized by various chemical tests.

The modern methods employed in these examinations of glycosuric patients demand technical skill in the examiner, and a variety of manipulations which are best carried out in a laboratory.

Another disease which has always been classed as a disorder of metabolism is gout. It looms less largely on the popular, as well as on the medical, horizon than was the case twenty or thirty years ago. Two factors combine to bring this about. First, a large number of conditions formerly classed as gouty are now referred to other categories—oral sepsis or what not; and secondly, owing presumably to change of habits and modes of life, true gout, the podagra of the ancients, is much less common in London than it used to be. How rarely do we now see the chalk-stones upon the hands, with which our forebears were falsely reported to have been able to score upon the cloth of the card-table. Now that we can measure with accuracy the amount of uric acid in small quantities of blood we can exclude the cases which do not fall into the strict category, and include others the goutiness of which is apt to cause surprise.

There are various rare conditions for the recognition of which testing of the excreta is essential; and by such chemical tests it is often possible to detect a drug which has been administered. Some poisons also are found by examination of certain tissues, such as arsenic in hair.

Chemical tests may afford most important evidence as to the functional efficiency or otherwise of certain organs, and these tests have been multiplied and greatly elaborated in recent years.

In most cases a diagnosis consists of two parts—namely, the nature and the seat of the disease—and it is with the seat that we are at this moment concerned. The detection of albumin in the urine is one of the oldest means of detecting damage to the kidneys, but, as with glycosuria, not all albuminuria is of evil omen. In more recent years the tests of renal efficiency have been greatly multiplied, and have become more delicate: by the administration of urea by the mouth and the study of its excretion we may measure the efficiency of the renal apparatus; by the administration of certain other substances we may obtain information as to which part of the renal apparatus is chiefly at fault. Moreover, by estimation of urea in the blood or cerebro-spinal fluid we can learn about the efficiency of the kidneys from the other side, so to speak, and gain information as to accumulation in the blood and tissues of substances which it is the function of the kidneys to get rid of. So we can estimate the risk of uraemia in a patient whose kidneys are diseased, although urea is not the cause of uraemia, and we do not yet know what is its cause.

Tests on somewhat similar lines, such as administration of levulose by the mouth, and estimation of the tolerance of that sugar, which is more readily excreted in the urine when the liver is diseased, or by the determination of the sugar curve in the blood after its administration, afford valuable evidence as to the functional efficiency of the liver.

One of the most important, and at the same time most elusive, of our organs is the pancreas. Deeply seated as it is, it is almost out of reach of direct clinical examination; only in comparatively recent times was the part played by this gland in connexion with carbohydrate metabolism discovered by von Mehring and Minkowski. Yet, by putting two and two together, by the cumulative evidence of a series of tests, it is often possible to reach a correct diagnosis in cases of pancreatic disease. These tests are for the most part chemical, and the determination of the nature and amounts of the fatty substances discharged from the intestine is the most important of them.

To Prout's discovery of hydrochloric acid in the gastric juice I have already referred, and in recent years methods of increasing delicacy and efficiency have been devised, and are in common use, for the chemical examination of the gastric or duodenal juice obtained after a test meal or by passage of a duodenal sound.

The metabolic processes at work in the living organism are of almost infinite variety; special enzymes are entrusted with each small metabolic task, and if one fails, or is lacking, more or less conspicuous derangements result. We can no longer regard the body as a simple furnace in which the food supplied is burned without discrimination. Nevertheless it is sometimes useful to determine the sum total of the chemical activities of which the body is the seat, and this may be carried out without much difficulty. For example, the metabolic fires burn up, or burn low, according as the thyroid gland is functionally overactive or supplies too little of its hormone; and so by determining the amount of oxygen utilized we may estimate the well-being or otherwise of the thyroid gland.

It is true that these tests can seldom be carried out by a doctor in busy practice; but it is one of the chief uses of such a department as this to help the practitioner as well as the hospital staff, by reporting upon material submitted to it. In this way the benefits of the biochemical department reach a much wider circle than the staff and patients of the hospital to which it is attached. It may be objected that the more elaborate investigations must needs take time, whereas medicine is always in a hurry, and cannot wait. Grave disease often strikes quickly, and it may be necessary to act before a report can be received. This is true in some cases, but in the majority there is no such urgent haste; and modern diagnostic methods would prove a curse rather than a blessing if the practitioner, trusting to them, neglected to acquire a thorough knowledge of the older methods of diagnosis, which rely upon the use of hands, eyes, ears, and nose. These instruments he has with him always, and, when properly used, they serve him well.

I might go on to speak of the use of chemical tests in prognosis, which is perhaps the most difficult province of medicine. This is well seen in connexion with diabetes. In the domain of treatment, also, biochemistry plays an important part. A better knowledge of the constituents of diet, their utilization, and needful proportions, together with the discovery of vitamins, is revolutionizing the science of dietetics, or rather is creating such a science.

Functions of Biochemical Laboratories.

I trust that I have said enough to make it clear that the practical applications of biochemistry are of great use for the solution of the problems which confront us at the bedside; that they help in the diagnosis, prognosis, and treatment of disease. That in itself is enough to justify the establishment of biochemical laboratories in connexion with all hospitals. But if that were all we should feel much satisfaction, but not the enthusiasm which is experienced to-day by all who have the welfare of this hospital and its medical school at heart, on the occasion of the opening of this splendid institute.

There are two much greater functions which the institute will perform. In it generations of students will learn from competent teachers biochemical methods, and how to carry out the various tests which are so helpful in clinical work. It is true that many of them may not, in after-life, have the opportunity of performing these tests for themselves; but it is hardly necessary to insist on the point that he who acts on the result of a test should know how it is carried out. If he has himself learned how to do it he is better able to judge of its value and significance.

The students of the London schools distribute themselves over the world, and carry the teaching which they have received into remote parts of the earth. Obviously teaching is one of the chief functions of this institute.

To speak now of the third, and to my mind its most important, function. It is now recognized that, in addition to its teaching, every university and place of advanced study has as one of its duties the furtherance of original research, and that the advanced teacher will do his work better if he has himself advanced knowledge of the subject which he teaches.

Medicine may be looked upon from several distinct standpoints, but, in importance, the chemical standpoint is second to none, as is becoming more clearly recognized from year to year. Biochemistry is not merely a useful preliminary subject of study for the medical man, but is part of the very essence of his science, and, through his science, of his art.

We know that members of different genera and species of animals and plants differ from each other in chemical structure and chemical life, and evidence is accumulating that no two individuals of a species are any more identical in chemistry than in form. It would seem that there is a chemical basis for those departures from type which are styled mutations, and I for one believe that the liabilities of certain individuals to, or their immunity from, certain maladies—what may be called their diatheses—have chemical origins. Undoubtedly the mechanisms by which the body protects itself against bacterial invasions or poisons introduced are, for the most part, chemical; and it is not necessary to point out the importance of the parts played in the animal economy by such chemical substances as hormones and vitamins. If all this be true it is obvious that a chemical outlook is needful for the comprehension of morbid processes, and that there are unlimited openings for research in biochemistry.

Here young investigators will be guided and instructed in the methods of research by the professor and other experienced teachers, who will encourage and help them to pursue promising lines, and will extract them from the blind alleys down which they are so apt, in their inexperience, to wander.

Let us wish, then, to all who work within these walls, whether as teachers, learners, or investigators, good success. Let us wish, too, that the numbers of those who shall engage in biochemical research may be as large as the accommodation provided admits, for so will knowledge and wisdom be increased; and in the book of Wisdom it is written that "the multitude of the wise is the welfare of the world."

ACUTE NECROSIS OF THE PANCREAS.

REPORT OF A SERIES OF CASES.

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ACUTE pancreatitis, although one of the rarer causes of the acute abdomen, in some of its less acute and dramatic manifestations is possibly more common than is generally realized. In reading records of reported cases it is obvious that it is frequently diagnosed prior to operation as intestinal obstruction, perforation of a viscus, etc., by competent surgeons.

It has happened that in the past two years six cases of this condition have come under my personal observation—two in private and four under my care in the Cardiff Royal Infirmary. Prior to this period I had only come across or recognized one undoubted case, and in the above period, after a careful search, I have only been able to find records of five other cases in charge of the other surgeons of the hospital. By their courtesy I am permitted to include these in the following series. As several of these cases present some one or other feature of interest, and as the diagnosis is always difficult and early diagnosis is of vital importance, I have thought them of sufficient interest to record.

In Zachary Cope's *Early Diagnosis of the Acute Abdomen*[1] it is stated that "pancreatitis is a rare condition seldom diagnosed correctly before operation, occurs most commonly in men, and for the most part is only met with in those over middle age." In the following series of twelve cases no fewer than ten occurred in women, and in seven of these their ages ranged from 20 to 33.

A brief analysis of these cases shows: Males, 2 cases; ages 55 and 69. Females, 10 cases; ages 20, 22, 25, 26, 29, 32, 33, 54, 72, and 63. It is seen that whilst the age of the males is in agreement with that usually stated, that of the females shows a striking proportion of very young women, and in 3 cases where the sexual history is given parturition had taken place one month, six weeks, and three months respectively prior to the onset of the attack, and in the last case symptoms of gall-bladder trouble dated immediately from childbirth.

In 10 cases stones were found in the gall-bladder, and in 2 of these in the common duct, and of the latter one was found impacted in the ampulla of Vater, the common duct being greatly distended. In this case the patient died as the abdomen was opened.

At operation fat necrosis was found in 10 cases, haemorrhagic fluid in the abdomen in 2 cases, "beef broth" fluid in 2, and straw-coloured serous fluid in 2 cases. Brocq[2] states: "des deux phénomènes qui la caractérisent, l'hémorrhagie et la nécrose graisseuse, seul le premier est constant." In my series fat necrosis was the almost constant sign, whilst haemorrhagic fluid free in the abdomen was found on only two occasions, and beef broth fluid on two other occasions.

In 2 cases suppurative cholangitis was found. In one of these (No. 4) small stones were present in the common