KARL ERNST VON BAER.

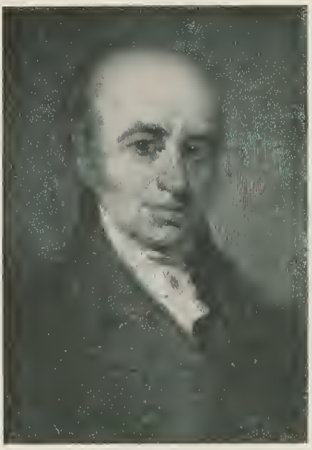
THE CENTURY'S PROGRESS IN ANATOMY AND PHYSIOLOGY.

BY HENRY SMITH WILLIAMS, M.D.

I.

THE focal points of the physiological world toward the close of the eighteenth century were Italy and England, but when Spallanzani and Hunter passed away, the scene shifted to France. The time was peculiarly propitious, as the recent advances in many lines of science had brought fresh data for the student of animal life which were in need of classification, and as several minds capable of such a task were in the field, it was natural that great generalizations should have come to be quite the fashion. Thus it was that Cuvier came forward with a brand-new classification of the animal kingdom, establishing four great types of being, which he called vertebrates, molluscs, articulates, and radiates. Lamarck had shortly before established the broad distinction between animals with and those without a backbone; Cuvier's classification divided the latter—the invertebrates—into three minor groups. And this division, familiar ever since to all students of zoology, has only in very recent years been supplanted, and then not by revolution, but by a further division, which the elaborate recent studies of lower forms of life seemed to make desirable.

In the course of those studies of comparative anatomy which led to his new



WILLIAM HYDE WOLLASTON.

MATTHIAS JAKOB SCHLEIDEN.

classification, Cuvier's attention was called constantly to the peculiar co-ordination of parts in each individual organism. Thus an animal with sharp talons for catching living prey—as a member of the cat tribe—has also sharp teeth, adapted for tearing up the flesh of its victim, and a particular type of stomach, quite different from that of herbivorous creatures. This adaptation of all the parts of the animal to one another extends to the most diverse parts of the organism, and enables the skilled anatomist, from the observation of a single typical part, to draw inferences as to the structure of the entire animal—a fact which was of vast aid to Cuvier in his studies of paleontology. It did not enable Cuvier, nor does it enable any one else, to reconstruct fully the extinct animal from observation of a single bone, as has sometimes been asserted, but what it really does establish, in the hands of an expert, is sufficiently astonishing.

Of course this entire principle, in its broad outlines, is something with which every student of anatomy had been familiar from the time when anatomy was first studied, but the full expression of the "law of co-ordination," as Cuvier called it, had never been explicitly made before; and notwithstanding its seeming obviousness, the exposition which Cuvier made of it in the introduction to his classical work on comparative anatomy, which was published during the first decade of the century, ranks as a great discovery. It is one of those generalizations which serve as guide-posts to other discoveries.

Much the same thing may be said of another generalization regarding the animal body, which the brilliant young French physician Marie François Bichat made in calling attention to the fact that each vertebrate organism, including man, has really two quite different sets of organs—one set under volitional control, and serving the end of locomotion, the other removed from volitional control, and serving the ends of the "vital processes" of digestion, assimilation, and the like. He called these sets of organs the animal system and the organic system, respectively. The division thus pointed out was not quite new, for Grimaud, professor of physiology in the university of Montpellier, had earlier made what was substantially the same classification of the functions into "internal or digestive and external or locomotive"; but it was Bichat's exposition that gave currency to the idea.

Far more important, however, was another classification which Bichat put forward in his work on anatomy, published just at the beginning of the century. This was the division of all animal structures into what Bichat called tissues, and the pointing out that there are really only a few kinds of these in the body, making up all the diverse organs. Thus muscular organs form one system ; membranous organs another; glandular organs a third; the vascular mechanism a fourth, and so on. The distinction is so obvious that it seems rather difficult to conceive that it could have been overlooked by the earliest anatomists; but, in point of fact, it is only obvious because now it has been familiarly taught for almost a century. It had never been given explicit expression before the time of Bichat, though it is said that Bichat himself was somewhat indebted for it to his master, the famous alienist, Pinel.

However that may be, it is certain that all subsequent anatomists have found Bichat's classification of the tissues of the utmost value in their studies of the animal functions. Subsequent advances were to show that the distinction between the various tissues is not really so fundamental as Bichat supposed, but that takes nothing from the practical value of the famous classification.

II.

At the same time when these broad microscopical distinctions were being drawn there were other workers who were striving to go even deeper into the intricacies of the animal mechanism with the aid of the microscope. This undertaking, however, was beset with very great optical difficulties, and for a long time little advance was made upon the work of preceding generations. Two great optical barriers, known technically as spherical and chromatic aberration—the one due to a failure of the rays of light to fall all in one plane when focalized through a lens, the other due to the dispersive action of the lens in breaking the white light into prismatic colors—confronted the makers of microscopic lenses, and seemed all but insuperable. The making of achromatic lenses for telescopes had been accomplished, it is true, by Dolland in the previous century, by the union of lenses of crown glass with those of flint glass, these two materials having different indices of refraction and dispersion. But, aside from the mechanical difficulties which arise when the lens is of the minute dimensions required for use with the microscope, other perplexities are introduced by the fact that the use of a wide pencil of light is a desideratum, in order to gain sufficient illumination when large magnification is to be secured.

In the attempt to overcome these difficulties, the foremost physical philosophers of the time came to the aid of the best opticians. Very early in the century, Dr. (afterward Sir David) Brewster, the renowned Scotch physicist, suggested that certain advantages might accrue from the use of such gems as have high refractive and low dispersive indices, in place of lenses made of glass. Accordingly lenses were made of diamond, of sapphire, and so on, and with some measure of success. But in 1812 a much more important innovation was introduced by Dr. William Hyde Wollaston, one of the greatest and most versatile, and since the death of Cavendish by far the most eccentric, of English natural philosophers. This was the suggestion to use two plano-convex lenses, placed at a prescribed distance apart, in lieu of the single double convex lens generally used. This combination largely overcame the spherical aberration, and it gained immediate fame as the "Wollaston doublet."

MARIE FRANÇOIS XAVIER BICHAT.
From the medallion by David d'Angers.

To obviate loss of light in such a doublet from increase of reflecting surfaces, Dr. Brewster suggested filling the interspace between the two lenses with a cement having the same index of refraction as the lenses themselves—an improvement of manifest advantage. An improvement yet more important was made by Dr. Wollaston himself, in the introduction of the diaphragm to limit the field of vision between the lenses, instead of in front of the anterior lens. A pair of lenses thus equipped, Dr. Wollaston called the periscopic microscope. Dr. Brewster suggested that in such a lens the same object might be attained with greater ease by grinding an equatorial groove about a thick or globular lens and filling the groove with an opaque cement. This arrangement found much favor, and came subsequently to be known as a Coddington lens, though Mr. Coddington laid no claim to being its inventor.

Sir John Herschel, another of the very great physicists of the time, also gave attention to the problem of improving the microscope, and in 1821 he introduced what was called an aplanatic combination of lenses, in which, as the name implies, the spherical aberration was largely done away with. It was thought that the use of this Herschel aplanatic combination as an eye-piece, combined with the Wollaston doublet for the objective, came as near perfection as the compound microscope was likely soon to come. But in reality the instrument thus constructed, though doubtless superior to any predecessor, was so defective that for practical purposes the simple microscope, such as the doublet or the Coddington, was preferable to the more complicated one.

Many opticians, indeed, quite despaired of ever being able to make a satisfactory refracting compound microscope, and some of them had taken up anew Sir Isaac Newton's suggestion in reference to a reflecting microscope. In particular, Professor Giovanni Battista Amici, a very famous mathematician and practical optician of Modena, succeeded in constructing a reflecting microscope which was said to be superior to any compound microscope of the time, though the events of the ensuing years were destined to rob it of all but historical value. For there were others, fortunately, who did not despair of the possibilities of the refracting microscope, and their efforts were destined before long to be crowned with a degree of success not even dreamed of by any preceding generation.

The man to whom chief credit is due for directing those final steps that made the compound microscope a practical implement instead of a scientific toy was the English amateur optician Joseph Jackson Lister. Combining mathematical knowledge with mechanical ingenuity, and having the practical aid of the celebrated optician Tulley, he devised formulæ for the combination of lenses of crown glass with others of flint glass, so adjusted that the refractive errors of one were corrected or compensated by the other, with the result of producing lenses of hitherto unequalled powers of definition; lenses capable of showing an image highly magnified, yet relatively free from those distortions and fringes of color that had heretofore been so disastrous to true interpretation of magnified structures.

Lister had begun his studies of the lens in 1824, but it was not until 1830 that he contributed to the Royal Society the famous paper detailing his theories and experiments. Soon after this various Continental opticians who had long been working along similar lines took the matter up, and their expositions, in particular that of Amici, introduced the improved compound microscope to the attention of microscopists everywhere. And it required but the most casual trial to convince the experienced observers that a new implement of scientific research had been placed in their hands which carried them a long step nearer the observation of the intimate physical processes which lie at the foundation of vital phenomena. For the physiologist, this perfection of the compound microscope had the same significance that the discovery of America had for the fifteenth-century geographers—it promised a veritable world of utterly novel revelations. Nor was the fulfilment of that promise long delayed.

III.

Indeed, so numerous and so important were the discoveries now made in the realm of minute anatomy that the rise of histology to the rank of an independent science may be said to date from this period. Hitherto, ever since the discovery of magnifying-glasses, there had been here and there a man, such as Leuwenhoek or Malpighi, gifted with exceptional vision, and perhaps unusually happy in his conjectures, who made important contributions to the knowledge of the minute structure of organic tissues; but now of a sudden it became possible for the veriest tyro to confirm or refute the laborious observations of these pioneers, while the skilled observer could step easily beyond the barriers of vision hitherto quite impassable. And so, naturally enough, the physiologists of the fourth decade of our century rushed as eagerly into the new realm of the microscope as, for example, their successors of to-day are exploring the realm of the X ray.

Lister himself, who had become an eager interrogator of the instrument he had perfected, made many important discoveries, the most notable being his final settlement of the long-mooted question as to the true form of the red corpuscles of the human blood. In reality, as everybody knows nowadays, these are biconcave disks, but owing to their peculiar figure it is easily possible to misinterpret the appearances they present when seen through a poor lens, and though Dr. Thomas Young and various other observers had come very near the truth regarding them, unanimity of opinion was possible only after the verdict of the perfected microscope was given.

These blood corpuscles are so infinitesimal in size that something like five millions of them are found in each cubic millimetre of the blood, yet they are isolated particles, each having, so to speak, its own personality. This, of course, had been known to microscopists since the days of the earliest lenses. It had been noticed, too, by here and there an observer, that certain of the solid tissues seemed to present something of a granular texture, as if they too, in their ultimate constitution, were made up of particles. And now, as better and better lenses were constructed, this idea gained ground constantly, though for a time no one saw its full significance. In the case of vegetable tissues, indeed, the fact that little particles encased in a membranous covering, and called cells, are the ultimate visible units of structure had long been known. But it was supposed that animal tissues differed radically from this construction. The elementary particles of vegetables "were regarded to a certain extent as individuals which composed the entire plant, whilst, on the other hand, no such view was taken of the elementary parts of animals."

In the year 1833 a further insight into the nature of the ultimate particles of plants was gained through the observation of the English microscopist Robert Brown, who, in the course of his microscopic studies of the epidermis of orchids, discovered in the cells "an opaque spot," which he named the nucleus. Doubtless the same "spot" had been seen often enough before by other observers, but Brown was the first to recognize it as a component part of the vegetable cell, and to give it a name. That this newly recognized structure must be important in the economy of the cell was recognized by Brown himself, and by the celebrated German Meyen, who dealt with it in his work on vegetable physiology,

JEAN BAPTISTE DUMAS.

CLAUDE BERNARD.

WILLIAM BENJAMIN CARPENTER.
Photograph by Elliott and Fry, London.

HUGO VON MOHL.

published not long afterwards; but it remained for another German, the professor of botany in the university of Jena, Dr. M. J. Schleiden, to bring the nucleus to popular attention, and to assert its all-importance in the economy of the cell.

Schleiden freely acknowledged his indebtedness to Brown for first knowledge of the nucleus, but he soon carried his studies of that structure far beyond those of its discoverer. He came to believe that the nucleus is really the most important portion of the cell, in that it is the original structure from which the remainder of the cell is developed. Hence he named it the cytoblast. He outlined his views in an epochal paper published in Müller's *Archives* in 1838, under title of "Beitrage zur Phytogenesis." This paper is in itself of value, yet the most important outgrowth of Schleiden's observations of the nucleus did not spring from his own labors, but from those of a friend to whom he mentioned his discoveries the year previous to their publication. This friend was Dr. Theodor Schwann, professor of physiology in the university of Louvain.

At the moment when these observations were communicated to him Schwann was puzzling over certain details of animal histology which he could not clearly explain. His great teacher, Johannes Müller, had called attention to the strange resemblance to vegetable cells shown by certain cells of the chorda dorsalis (the embryonic cord from which the spinal column is developed), and Schwann himself had discovered a corresponding similarity in the branchial cartilage of a tadpole. Then, too, the researches of Friedrich Henle had shown that the particles that make up the epidermis of animals are very cell-like in appearance. Indeed, the cell-like character of certain animal tissues had come to be matter of common note among students of minute anatomy. Schwann felt that this similarity could not be mere coincidence, but he had gained no clew to further insight until Schleiden called his attention to the nucleus. Then at once he reasoned that if there really is the correspondence between vegetable and animal tissues that he suspected, and if the nucleus is so important in the vegetable cell as Schleiden believed, the nucleus should also be found in the ultimate particles of animal tissues.

Schwann's researches soon showed the entire correctness of this assumption. A closer study of animal tissues under the microscope showed, particularly in the case of embryonic tissues, that "opaque spots" such as Schleiden described are really to be found there in abundance—forming, indeed, a most characteristic phase of the structure. The location of these nuclei at comparatively regular intervals suggested that they are found in definite compartments of the tissue, as Schleiden had shown to be the case with vegetables; indeed, the walls that separated such cell-like compartments one from another were in some cases visible. Particularly was this found to be the case with embryonic tissues, and the study of these soon convinced Schwann that his original surmise had been correct, and that all animal tissues are in their incipiency composed of particles not unlike the ultimate particles of vegetables—in short, of what the botanists termed cells. Adopting this name, Schwann propounded what soon became famous as his cell theory, under title of *Mikroskopische Untersuchungen über die Uebereinstimmung in der Structur und dem Wachsthum der*

Thiere und Pflanzen. So expeditious had been his work, that this book was published early in 1839, only a few months after the appearance of Schleiden's paper.

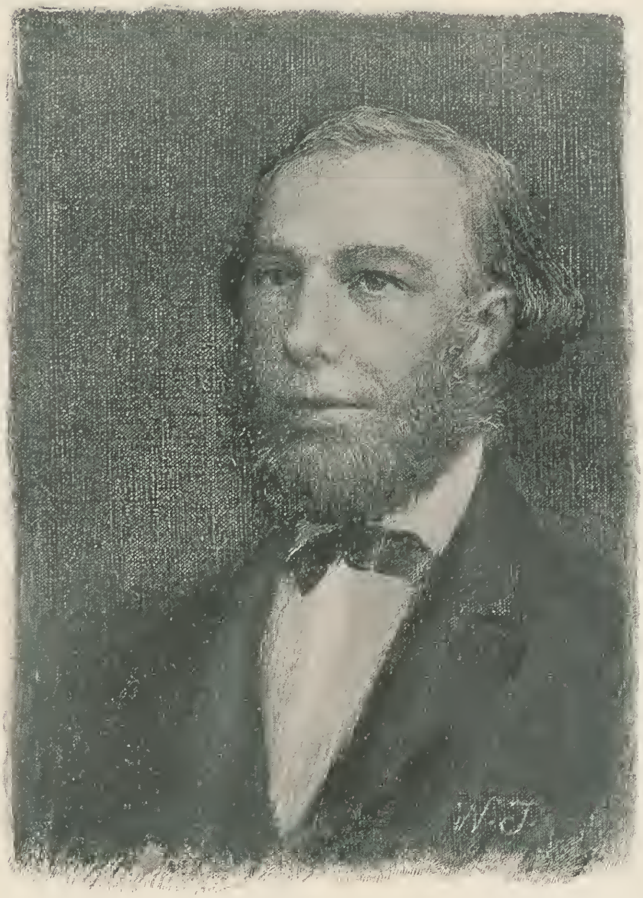
As the title suggests, the main idea that actuated Schwann was to unify vegetable and animal tissues. Accepting cell-structure as the basis of all vegetable tissues, he sought to show that the same is true of animal tissues, all the seeming diversities of fibre being but the alteration and development of what were originally simple cells. And by cell Schwann meant, as did Schleiden also, what the word ordinarily implies—a cavity walled in on all sides. He conceived that the ultimate constituents of all tissues were really such minute cavities, the most important part of which was the cell wall, with its associated nucleus. He knew, indeed, that the cell might be filled with fluid contents, but he regarded these as relatively subordinate in importance to the wall itself. This, however, did not apply to the nucleus, which was supposed to lie against the cell wall, and in the beginning to generate it. Subsequently the wall might grow so rapidly as to dissociate itself from its contents, thus becoming a hollow bubble or true cell; but the nucleus, as long as it lasted, was supposed to continue in contact with the cell wall. Schleiden had even supposed the nucleus to be a constituent part of the wall, sometimes lying enclosed between two layers of its substance, and Schwann quoted this view with seeming approval. Schwann believed, however, that in the mature cell the nucleus ceased to be functional, and disappeared.

The main thesis as to the similarity of development of vegetable and animal tissues, and the cellular nature of the ultimate constitution of both, was supported by a mass of carefully gathered evidence which a multitude of microscopists at once confirmed, so Schwann's work became a classic almost from the moment of its publication. Of course various other workers at once disputed Schwann's claim to priority of discovery, in particular the English microscopist Valentin, who asserted, not without some show of justice, that he was working closely along the same lines. But so, for that matter, were numerous others, as Henle, Turpin, Dumortier, Purkinje, and Müller, all of whom Schwann himself had quoted. Moreover, there were various physiologists who earlier than any of these had foreshadowed the cell theory; notably Kaspar Friedrich Wolff toward the close of the previous century, and Treviranus about 1807. But, as we have seen in so many other departments of science, it is one thing to foreshadow a discovery, it is quite another to give it full expression and make it germinal of other discoveries. And when Schwann put forward the explicit claim that "there is one universal principle of development for the elementary parts of organisms, however different, and this principle is the formation of cells," he enunciated a doctrine which was for all practical purposes absolutely new, and opened up a novel field for the microscopists to enter. A most important era in physiology dates from the publication of his book in 1839.

JOHANNES MÜLLER.

IV.

That Schwann should have gone to embryonic tissues for the establishment of his ideas was no doubt due very largely to the influence of the great Russian Karl Ernst von Baer, who about ten



MAX SCHULTZE.

years earlier had published the first part of his celebrated work on embryology, and whose ideas were rapidly gaining ground, thanks largely to the advocacy of a few men, notably Johannes Müller in Germany, and William B. Carpenter in England, and to the fact that the improved microscope had made minute anatomy popular. Schwann's researches made it plain that the best field for the study of the animal cell is here, and a host of explorers entered the field. The result of their observations was, in the main, to confirm the claims of Schwann as to the universal prevalence of the cell. The long-current idea that animal tissues grow only as a sort of deposit from the blood-vessels was now discarded, and the fact of so-called plantlike growth of animal cells, for which Schwann contended, was universally accepted. Yet the full measure of the affinity between the two classes of cells was not for some time generally apprehended.

Indeed, since the substance that composes the cell walls of plants is manifestly very different from the limiting membrane of the animal cell, it was natural, so long as the wall was considered the most essential part of the structure, that the divergence between the two classes of cells should seem very pronounced. And for a time this was the conception of the matter that was uniformly accepted. But as time went on many observers had their attention called to the peculiar characteristics of the contents of the cell, and were led to ask themselves whether these might not be more important than had been supposed. In particular Dr. Hugo von Mohl, professor of botany in the university of Tübingen, in the course of his exhaustive studies of the vegetable cell, was impressed with the peculiar and characteristic appearance of the cell contents. He observed universally within the cell "an opaque, viscid fluid, having granules intermingled in it," which made up the main substance of the cell, and which particularly impressed him because under certain conditions it could be seen to be actively in motion, its parts separated into filamentous streams.

Von Mohl called attention to the fact that this motion of the cell contents had been observed as long ago as 1774 by Bonaventura Corti, and rediscovered in 1807 by Treviranus, and that these observers had described the phenomenon under the "most unsuitable name of 'rotation of the cell sap.'" Von Mohl recognized that the streaming substance was something quite different from sap. He asserted that the nucleus of the cell lies within this substance, and not attached to the cell wall as Schleiden had contended. He saw, too, that the chlorophyl granules, and all other of the cell contents, are incorporated with the "opaque, viscid fluid," and in 1846 he had become so impressed with the importance of this universal cell substance that he gave it the name of protoplasm. Yet in so doing he had no intention of subordinating the cell wall. The fact that Payen, in 1844, had demonstrated that the cell walls of all vegetables, high or low, are composed largely of one substance, cellulose, tended to strengthen the position of the cell wall as the really essential structure, of which the protoplasmic contents were only subsidiary products.

Meantime, however, the students of animal histology were more and more impressed with the seeming preponderance of cell contents over cell walls in the tissues they studied. They too found the cell to be filled with a viscid, slimy fluid, capable of motion. To this Dujardin gave the name of sarcode. Presently it came to be known, through the labors of Kölliker, Nägeli, Bischoff, and various others, that there are numerous lower forms of animal life which seem to be composed of this sarcode, without any cell wall whatever. The same thing seemed to be true of certain cells of higher organisms, as the blood corpuscles. Particularly in the case of cells that change their shape markedly, moving about in consequence of the streaming of their sarcode, did it seem certain that no cell wall is present; or that, if present, its rôle must be insignificant.

And so histologists came to question whether, after all, the cell contents rather than the enclosing wall must not be the really essential structure, and the weight of increasing observations finally left no escape from the conclusion that such is really the case. But attention being thus focalized on the cell contents, it was at once apparent that there is a far closer similarity between the ultimate particles of vegetables and those of animals than had been supposed. Cellulose and animal membrane being now regarded as mere by-products, the way was clear for the recognition of the fact that vegetable protoplasm and animal sarcode are marvellously similar in appearance and general properties. The closer the observation the more striking seemed this similarity; and finally, about 1860, it was demonstrated by Heinrich de Bary and by Max Schultze that the two are to all intents and purposes identical. Even earlier, Remak had reached a similar conclusion, and applied von Mohl's word protoplasm to animal cell contents, and now this application soon became universal. Thenceforth this protoplasm was to assume the utmost importance in the physiological world, being recognized as the universal "physical basis of life," vegetable and animal alike. This amounted to the logical extension and culmination of Schwann's doctrine as to the similarity of development of the two animate kingdoms. Yet at the same time it was in effect the banishment of the cell that Schwann had defined. The word cell was retained, it is true, but it no longer signified a minute cavity. It now implied, as Schultze defined it, "a small mass of protoplasm endowed with the attributes of life." This definition was destined presently to meet with yet another modification, as we shall see; but the conception of the protoplasmic mass as the essential ultimate structure, which might or might not surround itself with a protective covering, was a permanent addition to physiological knowledge. The earlier idea had, in effect, declared the shell the most important part of the egg; this developed view assigned to the yolk its true position.

In one other important regard the theory of Schleiden and Schwann now became modified. This referred to the origin of the cell. Schwann had regarded cell growth as a kind of crystallization, beginning with the deposit of a nucleus about a granule in the intercellular substance — the cytoblastema, as Schleiden called it. But von Mohl, as early as 1835, had called attention to the formation of new vegetable cells through the division of a pre-existing cell. Ehrenberg, another high authority of the time, contended that no such division occurs, and the matter was still in dispute when Schleiden came forward with his discovery of so-called free cell formation within the parent cell, and this for a long time diverted attention from the process of division which von Mohl had described. All manner of schemes of cell formation were put forward during the ensuing years by a multitude of observers, and gained currency notwithstanding von Mohl's reiterated contention that there are really but two ways in which the formation of new cells takes place, namely, "first, through division of older cells; secondly, through the formation of secondary cells lying free in the cavity of a cell."

But gradually the researches of such accurate observers as Unger, Nägeli, Kölliker, Reichart, and Remak tended to confirm the opinion of von Mohl that cells spring only from cells, and finally Rudolf Virchow brought the matter to demonstration about 1860. His *Omnis cellula e cellula* became from that time one of the accepted data of physiology. This was supplemented a little later by Fleming's *Omnis nucleus e nucleo*, when still more refined methods of observation had shown that the part of the cell which always first undergoes change preparatory to new cell formation is the all-essential nucleus. Thus the nucleus was restored to the important position which Schwann and Schleiden had given it, but with greatly altered significance. Instead of being a structure generated *de novo* from non-cellular substance, and disappearing as soon as its function of cell-formation was accomplished, the nucleus was now known as the central and permanent feature of every cell, indestructible while the cell lives; itself the division-product of a pre-existing nucleus, and the parent, by division of its substance, of other generations of nuclei. The word cell received a final definition as "a small mass of protoplasm supplied with a nucleus."

In this widened and culminating general view of the cell theory it became clear that every animate organism, animal or vegetable, is but a cluster of nucleated cells, all of which, in each individual case, are the direct descendants of a single primordial cell of the ovum. In the developed individuals of higher organisms the successive generations of cells become marvellously diversified in form and in specific functions; there is a wonderful division of labor, special functions being chiefly relegated to definite groups of cells; but from first to last there is no function developed that is not present, in a primitive way, in every cell, however isolated; nor does the developed cell, however specialized, ever forget altogether any one of its primordial functions or capacities. All physiology, then, properly interpreted, becomes merely a study of cellular activities; and the development of the cell theory takes its place as the great central generalization in physiology of our century. Something of the later developments of this theory we shall see in another connection.

V.

Just at the time when the microscope was opening up the paths that were to lead to the wonderful cell theory, another novel line of interrogation of the living organism was being put forward by a different set of observers. Two great schools of physiological chemistry had arisen—one under guidance of Liebig and Wöhler in Germany, the other dominated by the great French master Jean Baptiste Dumas. Liebig had at one time contemplated the study of medicine, and Dumas had achieved distinction in connection with Prevost at Geneva in the field of pure physiology before he turned his attention especially to chemistry. Both these masters, therefore, and Wöhler as well, found absorbing interest in those phases of chemistry that have to do with the functions of living tissues; and it was largely through their efforts and the labors of their followers that the prevalent idea that vital processes are dominated by unique laws was discarded and physiology was brought within the recognized province of the chemist. So at about the time when the microscope had taught that the cell is the really essential structure of the living organism, the chemists had come to understand that every function of the organism is really the expression of a chemical change—that each cell is, in short, a miniature chemical laboratory. And it was this combined point of view of anatomist and chemist, this union of hitherto dissociated forces, that made possible the inroads into the unexplored fields of physiology that were effected toward the middle of our century.

One of the first subjects reinvestigated and brought to proximal solution was the long-mooted question of the digestion of foods. Spallanzani and Hunter had shown in the previous century that digestion is in some sort a solution of foods; but little advance was made upon their work until 1824, when Prout detected the pres-

Quoted by Beaumont

ence of hydrochloric acid in the gastric juice. A decade later Sprott and Boyd detected the existence of peculiar glands in the gastric mucous membrane; and Cagniard la Tour and Schwann independently discovered that the really active principle of the gastric juice is a substance which was named pepsin, and which was shown by Schwann to be active in the presence of hydrochloric acid.

Almost coincidently, in 1836, it was discovered by Purkinje and Pappenheim that another organ than the stomach—the pancreas, namely—has a share in digestion, and in the course of the ensuing decade it came to be known, through the efforts of Eberle, Valentin, and Claude Bernard, that this organ is all-important in the digestion of starchy and fatty foods. It was found, too, that the liver and the intestinal glands have each an important share in the work of preparing foods for absorption, as also has the saliva—that, in short, a coalition of forces is necessary for the digestion of all ordinary foods taken into the stomach.

And the chemists soon discovered that in each one of the essential digestive juices there is at least one substance having certain resemblances to pepsin, though acting on different kinds of food. The point of resemblance between all these essential digestive agents is that each has the remarkable property of acting on relatively enormous quantities of the substance which it can digest without itself being destroyed or apparently even altered. In virtue of this strange property, pepsin and the allied substances were spoken of as ferments, but more recently it is customary to distinguish them from such organized ferments as yeast by designating them enzymes. The isolation of these enzymes, and an appreciation of their mode of action, mark a long step toward the solution of the riddle of digestion, but it must be added that we are still quite in the dark as to the real ultimate nature of their strange activity.

In a comprehensive view, the digestive organs, taken as a whole, are a gateway between the outside world and the more intimate cells of the organism. Another equally important gateway is furnished by the lungs, and here also there was much obscurity about the exact method of functioning at the time of the revival of physiological chemistry. That oxygen is consumed and carbonic acid given off during respiration the chemists of the age of Priestley and Lavoisier had indeed made clear, but the mistaken notion prevailed that it was in the lungs themselves that the important burning of fuel occurs, of which carbonic acid is a chief product. But now that attention had been called to the importance of the ultimate cell, this misconception could not long hold its ground, and as early as 1842, Liebig, in the course of his studies of animal heat, became convinced that it is not in the lungs, but in the ultimate tissues to which they are tributary, that the true consumption of fuel takes place. Reviving Lavoisier's idea, with modifications and additions, Liebig contended, and in the face of opposition finally demonstrated, that the source of animal heat is really the consumption of the fuel taken in through the stomach and the lungs. He showed that all the activities of life are really the product of energy liberated solely through destructive processes, amounting, broadly speaking, to combustion occurring in the ultimate cells of the organism.

Further researches showed that the carriers of oxygen, from the time of its absorption in the lungs till its liberation in the ultimate tissues, are the red corpuscles, whose function had been supposed to be the mechanical one of mixing of the blood. It transpired that the red corpuscles are composed chiefly of a substance which Kühne first isolated in crystalline form in 1865, and which was named hæmoglobin—a substance which has a marvellous affinity for oxygen, seizing on it eagerly at the lungs, yet giving it up with equal readiness when coursing among the remote cells of the body. When freighted with oxygen it becomes oxyhæmoglobin, and is red in color; when freed from its oxygen it takes a purple hue; hence the widely different appearance of arterial and venous blood, which so puzzled the early physiologists.

This proof of the vitally important rôle played by the red blood corpuscles led, naturally, to renewed studies of these infinitesimal bodies. It was found that they may vary greatly in number at different periods in the life of the same individual, proving that they may be both developed and destroyed in the adult organism. Indeed, extended observations left no reason to doubt that the process of corpuscle formation and destruction may be a perfectly normal one; that, in short, every red blood corpuscle runs its course and dies like any more elaborate organism. They are formed constantly in the red marrow of bones, and are destroyed in the liver, where they contribute to the formation of the coloring matter of the bile. Whether there are other seats of such manufacture and destruction of the corpuscles is not yet fully determined. Nor are histologists agreed as to whether the red blood corpuscles themselves are to be regarded as true cells, or merely as fragments of cells budded out from a true cell for a special purpose; but, in either case, there is not the slightest doubt that the chief function of the red corpuscle is to carry oxygen.

If the oxygen is taken to the ultimate cells before combining with the combustibles it is to consume, it goes without saying that these combustibles themselves must be carried there also. Nor could it be in doubt that the chiefest of these ultimate tissues, as regards quantity of fuel required, are the muscles. A general and comprehensive view of the organism includes, then, digestive apparatus and lungs as the channels of fuel-supply; blood and lymph channels as the transportation system; and muscle cells, united into muscle fibres, as the consumption furnaces, where fuel is burned and energy transformed and rendered available for the purposes of the organism, supplemented by a set of excretory organs, through which the waste products—the ashes—are eliminated from the system.

But there remain, broadly speaking, two other sets of organs whose size demonstrates their importance in the economy of the organism, yet whose functions are not accounted for in this synopsis. These are those glandlike organs, such as the spleen, which have no duct and produce no visible secretions; and the nervous mechanism, whose central organs are the brain and spinal cord. What offices do these sets of organs perform in the great labor-specializing aggregation of cells which we call a living organism?

As regards the ductless glands, the first clew to their function was given when the great Frenchman Claude Bernard (the man of whom his admirers loved to say, "he is not a physiologist merely; he is physiology itself") discovered what is spoken of as the glycogenic function of the liver. The liver itself, indeed, is not a ductless organ, but the quantity of its biliary output seems utterly disproportionate to its enormous size, particularly when it is considered that in the case of the human species the liver contains normally about one-fifth of all the blood in the entire body. Bernard discovered that the blood undergoes a change of composition in passing through the liver. The liver cells (the peculiar forms of which had been described by Purkinje, Henle, and Dutrochet about 1838) have the power to convert certain of the substances that come to them into a starchlike compound called glycogen, and to store this substance away till it is needed by the organism. This capacity of the liver cells is quite independent of the bile-making power of the same cells; hence the discovery of this glycogenic function showed that an organ may have more than one pronounced and important specific function. But its chief importance was in giving a clew to those intermediate processes between digestion and final assimilation that are now known to be of such vital significance in the economy of the organism.

In the forty-odd years that have elapsed since this pioneer observation of Bernard, numerous facts have come to light showing the extreme importance of such intermediate alterations of food-supplies in the blood as that performed by the liver. It has been shown that the pancreas, the spleen, the thyroid gland, the suprarenal capsules, each in its own way, are absolutely essential to the health of the organism, through metabolic changes which they alone seem capable of performing; and it is suspected that various other tissues, including even the muscles themselves, have somewhat similar metabolic capacities in addition to their recognized functions. But so extremely intricate is the chemistry of the substances involved that in no single case has the exact nature of the metabolisms wrought by these organs been fully made out. Each is in its way a chemical laboratory indispensable to the right conduct of the organism, but the precise nature of its operations remains inscrutable. The vast importance of the operations of these intermediate organs is unquestioned.

A consideration of the functions of that other set of organs known collectively as the nervous system is reserved for a later paper.

HARPER'S
NEW
MONTHLY
MAGAZINE

No. 574.
MARCH, 1898.
35 Cents.

HARPER & BROTHERS, Publishers,
NEW YORK AND LONDON.
