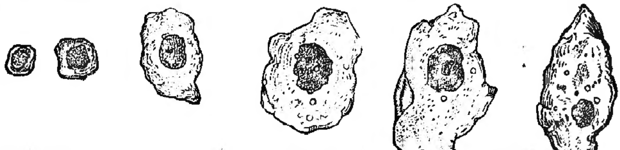
THE CELL DOCTRINE.

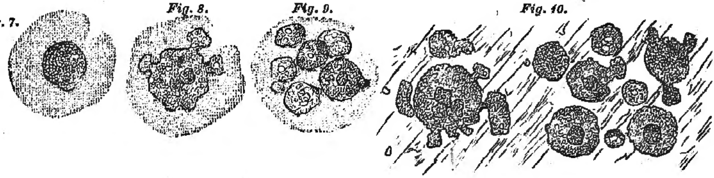
Fig. 1. *Fig. 2.* *Fig. 3.* *Fig. 4.* *Fig. 5.* *Fig. 6.*



Youngest layer. Middle layer. Oldest layer.

Production of formed material from germinal matter in Epithelial cells, from section through layer of Epithelium covering papillæ of the tongue. ×700.

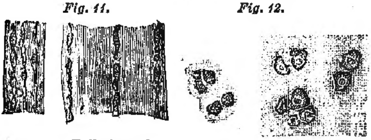
Fig. 7. *Fig. 8.* *Fig. 9.* *Fig. 10.*



FORMATION OF PUS.

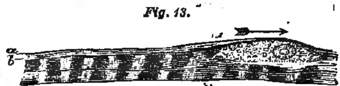
To illustrate the change in germinal matter of an Epithelial cell, resulting from increased nutrition, showing the manner in which the germinal matter of a normal cell, if supplied freely with pabulum, may give rise to pus.

Fig. 11. *Fig. 12.*



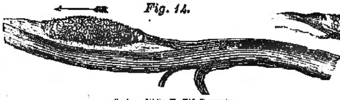
Young. Fully formed. Young. Fully formed.
TENDON. CARTILAGE.

Fig. 13.



a, Sarcolemma. *b*, Contractile matter.
MUSCLE.

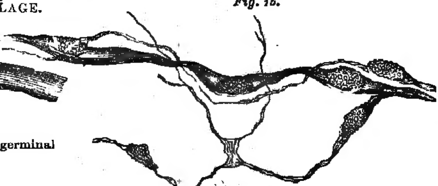
Fig. 14.



ELASTIC TISSUE.

The arrow shows the direction in which germinal matter is supposed to be moving.

Fig. 15.



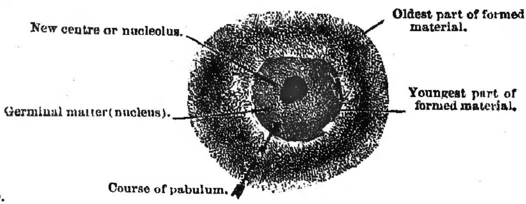
NERVE.

Development of young, dark-bordered nerve fibres, at an early period, showing germinal matter and formed material of elementary parts. ×1800.

Fig. 16.

AMŒBA.
Pure germinal matter. ×5000.

Fig. 17.



H. Sebald, Sc.

PLATE ILLUSTRATING DR. BEALE'S VIEWS.

THE CELL DOCTRINE:

ITS HISTORY AND PRESENT STATE.

FOR THE USE OF

STUDENTS IN MEDICINE AND DENTISTRY.

ALSO,

A COPIOUS BIBLIOGRAPHY OF THE SUBJECT.

BY JAMES TYSON, M.D.,

PROFESSOR OF GENERAL PATHOLOGY AND MORBID ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA; ONE OF THE VICE-PRESIDENTS OF THE PATHOLOGICAL SOCIETY OF PHILADELPHIA;
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ETC., ETC., ETC.

SECOND EDITION,

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ILLUSTRATED.

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1878.

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TO

THE MEDICAL CLASS

OF

THE UNIVERSITY OF PENNSYLVANIA,

This Little Volume

IS RESPECTFULLY INSCRIBED,

BY

THE AUTHOR.

PREFACE

TO THE SECOND EDITION.

THE highly favorable and quite unexpected reception accorded the first edition of this book has stimulated my interest in the subject, and in preparing a second, I have sought to improve it as much as possible. In doing so, many of the original sources of my information have been re-examined, and from them some additions made and inaccuracies corrected. The section on *the Present State of the Cell Doctrine*, incorporating my own views, has been entirely rewritten, as was necessitated by the very important and numerous contributions to the subject since the first edition appeared.

The bibliography has been increased by the addition of over three hundred and fifty new references, mostly to papers contributed directly on the subject since the first edition was issued. To make room for these, many of the references included in the bibliography of the first edition have been omitted where there did not seem to be a sufficiently close bearing on the subject.

The suggestion of one of the reviewers of the first edition, that the bibliography should be chronologically instead of alphabetically arranged was carefully considered, and at one time I had concluded to adopt it, but when I attempted to do so, I found that the inconvenience resulting from the wide separation of several papers by a single author, more than offset the advantages of a chronological arrangement. I therefore adhered to the original plan.

For valuable assistance in collecting references and examination of papers I am greatly indebted to my assistant, Dr. H. F. Formad.

1506 Spruce Street,
October 1st, 1878.

PREFACE

TO THE FIRST EDITION.

THE author has become convinced, by several years' intimate intercourse with students of medicine, that their acquaintance with the subjects he has endeavored to include in this little volume would be facilitated, if the views, which are now taught and scattered throughout the often expensive works of their authors, were collected in a convenient form for study and reference. Taking it for granted that a knowledge of this subject is of fundamental importance in its bearing upon the study of physiology and pathology, and stimulated by the frequent inquiries of students for an appropriate source of information, he has prepared what he now submits to them.

He has sought to obtain a continuous history of the evolution of the "cell doctrine" up to its present state, without embarrassing his pages with a large number of isolated facts. He has attempted, however, to secure a completeness, and to make the work useful to physicians and others engaged in research, by careful references, and the addition of a bibliography, which he has sought to make accurate and extended. Some authors may have been overlooked; such the writer cordially invites to send him references to their own papers, or to those of others they believe to have a bearing upon the subject.

ILLUSTRATIONS.

THE CELL DOCTRINE.

The idea that animals and plants, however complex their organization, are really composed of a limited variety of elementary parts, constantly recurring, was appreciated by Aristotle, who was born 384 years before Christ, while it appears to have been little more clearly conceived by the acknowledged father of medical science, Galen, who lived 400 years later. Aristotle distinguished as "partes similares," those structures, such as bone, cartilage, fat, flesh, blood, lymph, nerve, ligament, tendon, membrane, vessels, nails, hairs, and skin, which were not confined to one part of the body, but distributed throughout it generally. He applied the term "partes dissimilares" to the regions of the head, neck, trunk, and extremities. Fallopius of Modena, 1523–1562, to whom we are indebted for our knowledge of the conceptions of Galen in regard to these "partes similares" or "simplices," has further developed the subject of general anatomy in his "Lectiones de Partibus Similaribus Humani Corporis." These, however, plainly do not correspond with the "elementary parts" or "cells" of the present day. As Prof. Huxley says in his valuable essay on "The Cell Theory," they were ultimate to Fallopius, because he could go no further, "though it is, of course, a very different matter whether we are stopped by the imperfection of our instruments of analysis, as these older observers were, or by having really arrived at parts no longer analyzable."* These "partes similares" really correspond to the "tissues" of the present day, which are *collections of elementary parts.* The conceptions of these older writers with regard to the "vital endowment" or "independent vitality" of their similar parts or tissues, were singularly correct, and correspond almost identically with those held by the majority of physiologists of the present day.

Further than this, however, the anatomists of the period of Fallopius could not go—not because, as we now well know, they had arrived at parts no longer analyzable, but because of their imperfect means of analysis.

It is probable that the magnifying properties of lenses were known to the Egyptians, as well as the Greeks and Romans, over 2000 years ago; since a table of refractive powers is introduced into his "Optics" by Ptolemy, since Aristophanes, the Athenian poet (B.C. 500), speaks of "burning spheres" of glass as sold in the grocers' shops of Athens, and since both Pliny and Seneca refer to lenses and their magnifying properties; while lenses themselves have been found in the ruins of Nineveh,

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* The Cell Theory—a Review, by T. H. Huxley; Br. and Foreign Med. Chir. Rev. for October 1853, No. xxiv.

Herculaneum, and Pompeii. But it is quite certain, also, that they did not become available as compound microscopes until about 1590, when the Jansens, father and son, of Holland, are said to have invented the compound microscope. Fontana, in 1646, writes that he had invented the microscope in 1618. Galileo, as early as 1612, is said to have sent a microscope to King Sigismund of Poland, though whether it was his own invention, or made after the pattern of another, is not easily determined. In 1685, Stelluti published a description of the parts of a bee he had examined with the microscope, and although George Hufnagle is said to have published in Frankfort, in 1592, a work upon insects, illustrated by fifty copper plates, it is highly probable that these, as well as very many most important observations made after the invention of the compound microscope, were made with the simple instrument.*

It is impossible to estimate the assistance the microscope has been to us in opening up the minute structure of animals and vegetables, and in thus affording a reliable basis on which to build a doctrine of organization. Prof. Huxley further says, "The influence of this mighty instrument of research upon biology, can only be compared to that of the galvanic battery, in the hands of Davy, upon chemistry. It has enabled *proximate* analysis to be *ultimate*."† But it is more than this. Since, as he correctly states, it

* For an interesting and exhaustive history of the invention of the compound microscope, see Das Mikroskop, Theorie, Gebrauch, Geschichte und gegenwärtiger Zustand desselben. Von P. Harting. In drei Bänden. Braunschweig, 1866. Dritter Band, ss. 1–35.

† Huxley, loc. citat., p. 290.

has enabled *proximate* physical analysis to become ultimate, it corresponds, not to the galvanic battery alone, but to all the appliances made use of in ultimate chemical analysis.

The time prior to the invention of the compound microscope may be considered as the *first period* in *histology;* that between this date and that of the observations of Schleiden and Schwann (1838), inclusive, the *second period;* while the time subsequent to these observations becomes appropriately the *third period.* Notwithstanding the imperfect state of instruments during quite two hundred years after the invention of the compound microscope, a flood of facts was added to our knowledge of the minute structure of living things.

Borellus, of Pisa, seems first to have used the microscope in the examination of the higher animal structures, about the year 1656, but his observations were grossly misinterpreted in his attempt to adapt them to the prevailing idea of the day, that diseases were caused by animalculæ in the blood and tissues. As a result, he describes pus-corpuscles as animalcules, and even says he has seen them delivering their eggs.

According to Boerhaave, Swammerdam had recognized the blood-corpuscle in the frog in 1658.

Malpighi,* between 1661 and 1665, had seen the blood-corpuscle in the hedge-hog, had witnessed the circulation of the blood, and had published observations upon the minute structure of the lungs, which he had even compared to a racemose gland,† of the

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* Malpighi, Opera Omnia. London, 1686.

† Fort, Anatomie et Physiologie du Poumon, considere comme

kidneys, spleen, liver, and membranes of the brain, and with some of these structures his name has become inseparably associated. In 1667, Robert Hooke* pointed out the *cellular* structure of plants, and Malpighi† further elaborated the same subject with considerable accuracy in his "Anatome Plantarum," in 1670. He showed that the walls of the "cells" or "vesicles," were separable, that they could be isolated, and gave to each the name "*utriculus*," believing also the "cell," or "utriculus," to be an independent entity. The latter observer‡ also recognized the blood-corpuscle. Leeuwenhoek, in 1673,§ described these corpuscles with considerable accuracy, not only in man, but also in the lower animals. He also demonstrated the capillaries, examined most of the tissues, and made the discovery of the spermatozoids, which he conceived to be spermatozoa or sperm animals, and of different sexes.

Theory of Haller, 1757.—No attempt, however, seems to have been intelligently made at building up the tissues by an ultimate physical element, to correspond with the "atom" of the inorganic chemist, prior to that of Haller. He resolved the solid parts of animals and vegetables into the "*fibre*" (*fibra*),

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un organe de Secretion. Paris, 1867, Preface; or a notice of Dr. Fort's book, by the writer, in American Journal of Medical Sciences, October, 1869.

* Hooke, Rob., Micrographia. London, 1667.

† Malpighi, Anatome Plantarum. London, 1670.

‡ Malpighi, Opera Posthuma. London, 1697.

§ Leeuwenhoek, Opera Omnia seu Arcana Naturæ detecta. Tom. ii, p 421. Leyden, 1687. Vel Opera Omnia, etc., Lugd. Batav., 1722.

and an "*organized concrete.*" To the former he assigns the most important position, asserting that it is to the physiologist what the line is to the geometrician; that a "fibre," in general, may be considered as resembling a line made up of points, having a moderate breadth, or rather as a slender cylinder.*

The second elementary substance of the human body according to Haller, the "organized concrete," must not be lost sight of, as appears to have been the case with many eminent authorities who have attempted to give his views. This, he says, is a mere glue, evasated and concreted, not within the fibres, but in the spaces betwixt them, in illustration of which it is stated, that cartilages seem to be scarcely anything else besides this glue concreted. But these views of Haller were clearly not based upon microscopic observation, though the microscope had been for some time in use. For Haller himself tells us that the fibre is invisible, and to be distinguished only by the "mind's eye,"—*invisibilis est ea fibra, solâ mentis acie distinguimus.*† No allusion to the cell beyond the imperfect description of the blood-

* Haller, Elementa Physiologiæ, vol. i, lib. i, sec. i. Lausan., Helvet., 1757.

† A singular discrepancy exists between these words of Haller and those found in both the Latin and English editions of the "elegant compend" of Haller's works printed in Edinburgh, the former in 1766, and the latter (an edition in the possession of the writer), in 1779, under the inspection of William Cullen, M.D. In the latter, we have the following: "The solid parts of animals and vegetables have this fabric in common, that their elements, or

corpuscles and spermatozoids appears to have been made by Haller.

Theory of Wolff, 1759–74.—Better founded, in being based upon observation, was the theory of Wolff, and it contained many of the elements of truth. For an available exposition of these views, physiologists are much indebted to Prof. Huxley, who in the able review already cited, has presented them as agreeing partially, also, with his own. The doctrine of Wolff, as given by Prof. Huxley, is as follows: "Every organ is composed, at first, of a mass of clear viscous, nutritive fluid, which possesses no organization of any kind, but is at most composed of globules. In this semifluid mass, cavities (Blaschen, Zellen) are now developed; these, if they remain rounded or polygonal, become the subsequent cells, if they elongate, the vessels; and the process is identically the same, whether it is examined in the vegetating point of a plant, or in the young budding organs of an animal. Both cells and vessels may subsequently be thickened by deposits from the 'solidescible' nutritive fluid. In the plant, the cells at first communicate, but subsequently become separated from one another; in the animal, they always remain in communication. In *each case they are mere cavities and not independent entities; organization is not effected by them, but they are the visible results of the action of the organizing power inherent in*

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the smallest parts we can see *by the finest microscope*, are either fibres or an organized concrete."[1]

[1] First Lines of Physiology. By the celebrated Baron Albertus Haller, M.D. Translated from the correct Latin edition, and printed under the inspection of William Cullen, M.D. Edinburgh, 1779.

the living mass, or what Wolff calls the *vis essentialis*. For him, however, this *vis essentialis* is no *Archæus*, but simply a convenient name for two facts which he takes a great deal of trouble to demonstrate; the first, the existence in living tissues (before any passages are developed in them), of currents of the nutritious fluid determined to particular parts by some power which is independent of all external influence; and the second, the peculiar changes of form and composition, which take place in the same manner."*
Two points are here particularly to be observed as cardinal,—first, the non-independence of cells, either anatomically or physiologically; that they are effects, *passive results*, and *not causes* of a vitalizing or organizing force; second, that organization takes place from the "differentiation" of the homogeneous living mass in these parts, through the agency of the vis essentialis or inherent vital force. The radical difference between these principles of development and those generally held at the present day, will be better appreciated when these latter have been worked out. An acknowledged error may, however, be pointed out,—the probable result of the inferiority of the instruments of that day—that of supposing the cells of plants and animals in all instances to communicate when in their youngest state, and in the latter to continue thus in communication throughout life. It will be observed, also, that this theory involved the *spontaneous* origin of the cell, that is, independent of any previously existing cell.

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* Huxley, loc. citat., p. 293–4. Wolff, C. F., Theoria Generationis, 1759. Ed. Nova, Halae, 1774.

The theory of Wolff, however, full as it was of original conception, and based on actual observation, seemed to claim little attention, and would have been still less known but for the labors of Prof. Huxley. The "fibre" theory of Haller was still further expanded, and that fibres were the groundwork of nearly all the tissues, continued the prevailing view, until the latter part of the eighteenth century, and there are few of the older Physiologies even of a later date, which do not contain an account of it. Naturally, it maintained itself longest in the case of the fibrous tissues, since the appearances of these tissues, when examined by the highest powers, are those of structures apparently composed of fibres.

Oken, 1808.—The first clear expression with regard to the cellular or vesicular composition of *animal* organisms as well as vegetable, comes from the physical school in the language of Oken, who, as early as 1805, in his work on "Generation," refers to elementary parts as "vesicles;" and who says in his "Programm über das Universum" in 1808, "The first transition of the inorganic to the organic is the conversion into a vesicle (Blaschen), which I, in my theory of generation, have called infusorium. *Animals and plants are throughout nothing else than manifoldly divided or repeating vesicles*, as I shall prove anatomically at the proper time." This most explicit statement seems also to have been overlooked.

The Globular Theory, 1779–1842.—The reaction which took place at the date referred to against the "fibre" theory, culminated in the "globular" theory, due less to speculation than erroneous methods of observation and imperfect instruments. Leeuwenhoek* (1687) early announced the "globular" structure of the primitive tissues of the body, but the "globule" apparently attracted little notice until this period of reaction against the "fibre," when it claimed the attention of Prochaska† (1779), Fontana‡ (1778), the brothers Wenzel§ (1812), Treviranus‖ (1816), Bauer¶ (1818 and 1823), Heusinger** (1822), MM. Prevost and Dumas,†† Milne-Edwards‡‡ (1823), Hodgkin§§ (1829), Baumgartner‖‖ (1830–42), Frederick

* Leeuwenhoek, op. citat.

† Prochaska, De Structura Nervorum. Vind., 1779. Opera min., Pars i.

‡ Fontana, Sur les Poisons, 1787, ii, 18; Abhandlung über das Viperngift, das Amerikanische Gift, u. s. w. Aus dem Italien. Berlin, 1787.

§ Wenzel, Joseph and Charles. De structura cerebri. Tubing., 1812.

‖ Treviranus, Vermischte Schriften, Anatom. und Physiolog. Inhalts Bd. i. Gottingen, 1816.

¶ Bauer, Philosoph. Transac. for 1818, and Sir E. Home's Lectures on Comparative Anatomy, vol. iii, Lect. iii. London, 1823.

** Heusinger, System der Histologie. Thl. i Eisenach, 1822–4

†† MM. Prevost and Dumas, Bibliothèque Universelle des Sciences et Arts, T. xvii.

‡‡ Milne-Edwards, Mémoire sur la Structure Elémentaire des Principaux Tissues Organiques des Animaux. Paris, 1823. Also, Recherches Microscopiques sur la Structure Intime des Tissues Organiques des Animaux, in Ann. des Sci. Nat. December, 1826.

§§ Hodgkin, in Grainger's Elements of General Anatomy. London, 1829. Also Hodgkin and Fisher's translation of M. Edwards "Sur les Agens Physiques." London, 1832. Hodgkin's Lectures on the Morbid Anatomy of the Serous and Mucous Membranes. London, 1836, p. 26. Am. Ed., Philadelphia, 1838, vol. i, pp. 17–18.

‖‖ Baumgärtner, K. H., Beobachtungen über die Nerven und das Blut in ihrem gesunden und Krankhatten Zustande, February, Arnold* (1836), Dutrochet† (1837), Raspail‡ (1839); all except Hodgkin admitting in greater or less degree the importance of the globule as an ultimate physical element; while it is evident, also, that there was much confusion in the use of terms, the words *globule*, *granule*, and *molecule*,§ being often indiscriminately used, and the word *globule* sometimes used to indicate what is now clearly recognized as the "cell."

1830. His views are further elaborated in his Beiträge zur Physiologie und Anatomie. Aus der Lehre von der Gegensazen in den Kraften in lebenden thierschen Körper, ein Grundriss zur Physiologie und zur allgemeinen Pathologie und Therapie, 2te Auflage, besonders abgedruckt. Stuttgart, 1842.

* Arnold, Friedreich, Lehrbuch der Physiologie des Menschen. Erst. Theil, Zurich, 1836.

† Dutrochet, Mémoires pour servir a l'Histoire Anatomique et Physiologique des Végétaux et des Animaux, t. ii, Atlas. Paris, 1837.

‡ Raspail, Recherch. sur la struct. et le developm. de la feuille et du tronc, et sur la struct., et devel. des tissus Animale, Paris, 1837.

§ The German authors of this period, and even more recent times (Henle, 1841, Virchow, 1858), at least in speaking of the development of histology, seem to use indiscriminately the terms *granule* or *molecule* and *globule*, whereas they are morphologically something distinct. A *globule* is usually held to be a body which, under the microscope, is more or less spherical in form, possessing a *bright* centre, and *dark* outline,—the width of this outline being directly as the difference between the refracting power of the globule itself and that of the menstruum in which it floats. Thus, the dark outline of a globule of oil floating in water is wider than that of the same globule floating in glycerin. A *granule* or *molecule*, on the other hand, is *indeterminate* in size and shape, and appears as a mere dot under the highest powers of the microscope. It is true that what appears as a granule under a low power, may appear as a globule under a higher.

Prochaska,* in 1779, described the brain as made up of globules eight times smaller than blood-globules. In the year 1801, the philosophic mind of Bichat elaborated his excellent classification, but he seems to have made no original investigations in minute structure, or to have adopted any special theory of an ultimate physical element. The brothers, Joseph and Charles Wenzel,† in 1812, described the brain as composed of globules of small size. Among the earliest histologists worthy of mention, is Treviranus,‡ whose elements, according to Henle, were first, a homogeneous, formless matter; second, fibres; third, globules (kügelchen). Mr. Bauer,§ quoted as a most experienced microscopic observer by Sir Everard Home, in 1818, and again in 1823, described the ultimate globules of the brain and of muscular fibre as of the size of a globule of blood when deprived of its coloring matter, or about $\frac{1}{2000}$ of an inch in diameter. The fibre was excluded as an ultimate element of organization by Heusinger‖ in 1822–4, who started all tissues from the *globule*, still, however, retaining the formless material of Haller and Treviranus. Heusinger formed the fibre by the linear apposition of his globular elementary parts, and even explained how canals and vessels were formed by a similar arrangement of *vesicles* which had originated from the globules. The account given by Henle¶ of the method in which Heu-

* Proschaska, Opera Minora, Part I, p. 342

† Wenzel, op. citat., p. 24.

‡ Treviranus, op. citat.

§ Bauer, op. citat.

‖ Heusinger, op. citat., p. 112.

¶ Henle, Allgemeine Anatomie. Leipzig, 1841, p. 128.

singer built up his fibres and vessels is interesting and important, since there is in these views an approximation to the truth. "As the result of an equal contest between contraction and expansion, there arises the *globule*, of which all organisms, all organic parts, are originally composed. By a stronger exercise (Spannung, tension) of power, there originates from the often more homogeneous globule, the *vesicle*. Where in an organism *globules* and a *formless mass* are present, the *globules* arrange themselves according to chemical(?) laws and form *fibres*. Where vesicles arrange themselves, there arise *canals* and *vessels*." In the latter sentence one cannot fail to note a close approximation to the truth, though the facts upon which the theory was based are partly false and partly misinterpreted.

But the observations and writings of Milne Edwards* may be looked upon as having given, more than those of any other author, position and popularity to the "globular theory." He examined all the principal tissues, and announced that the fibres of the then so-called cellular (fibrous) tissues, membranes composed of these fibres, muscle and nerve, were composed of globules of about the same size, from $\frac{1}{8000}$ to $\frac{1}{7500}$ of an inch in diameter; whence he concluded that these spherical corpuscles, by their aggregation, constituted all organic textures, vegetable or animal, and whatsoever their properties or functions. There is little doubt but that many of these so-called globules described by Edwards were

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* Edwards, loc. citat.

really cells, seen with indifferent instruments, and further distorted by the glare of direct sunlight.

Similar, as regards the element of organization, were the views of Baumgärtner* and Arnold,† who were joint observers.

They considered‡ the fundamental elements of organization to be the *formative globule* (Bildungskugel), and the *molecular granule* (Molecular-kugelchen). The first is primarily formed by a simple aggregation of smaller granules first represented by the granules of the yolk united by a formless material. The "molecular granule" arises from a breaking up of the "formative globule." A modification of the "formative globule" out of an aggregation of which the entire embryo is first formed, is the hæmatoid body (Hämatoidkörper). This is a nucleated discoid body with a distinct ring-like border (geringtes Körperkern mit einem Ringe).

Further, "Out of these two kinds of globules and out of formless material," says Baumgärtner, "all tissues are formed, namely, the tissue-fibres (threads) out of the molecular granules, and the hæmatoid bodies out of the formative globules and newly-formed tissue-fibres. The molecular form is not everywhere equally expressed, which is owing in the first place to the fact that often the molecular gran-

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* Baumgärtner, loc. citat.; also, Virchow, Cellular Pathology, Am. Ed. of Chance's Translation. Philadelphia, 1863, p. 53.

† Arnold, loc. citat.; also, Virchow, Cellular Pathology, Am. Ed. of Chance's Translation. Philadelphia, 1863, p. 53.

‡ Baumgärtner, Beiträge zur Physiologie und Anatomie, 1842, p. 36.

ules more or less fuse together, and second, that formless material surrounds the molecular granules and makes their outline indistinct. The theory here brought forward of the fundamental form of organization in animals may well be called the *globular theory*." P. 83.

It is evident that the "formative globule," or at least the modification of it called the *Hæmatoidkörper*, is nothing more nor less than the nucleated cell, which, however, Baumgärtner did not admit, contending as late as 1842 against the cell doctrine; asserting also (p. 40, *op. citat.*) that in the development of tissues the formative globule never divides to form two, in other words, that there is no such thing as cell division.*

Arnold also says that† all fluid and solid parts of the human body are resolvable first into a fluid or half fluid material of no determinate form, and second, into granules which are more or less completely spherical, and in all solid structures appear for the most part as minute globules. The granules, which are the second more important element, occur not only in all fluids and solid parts of the completely formed human organism, but they are also the original and essential constituents of the human embryo. Out of these by their aggregation are formed the most complex tissues of the organism.

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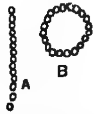
* To the student desiring to pursue further this very interesting subject, with the argument against the cell theory by Baumgärtner, I would recommend the perusal of the very interesting "Beiträge zur Anatomie und Physiologie" alluded to.

† Lehrbuch der Physiologie des Menschen, 1836, p. 82.

The error of these and other observers seems to have been clearly pointed out by Dr. Hodgkin,* though much importance was still attached to the

FIG. 1.



Illustrating the Globular Theory.

A, Fibre, composed of elementary granules (molecular granules), drawn up in a line. B, Cell, with spherically arranged granules. (After Virchow, slightly modified.)

globule as an element of organization (but perhaps from this time forward, more in the stricter sense of the term granule), which has continued, in this latter sense, to the present day.

It should be mentioned that in 1828 Döllinger† announced that the tissues of the body are built up of blood-corpuscles, which move in wall-less (wandlos) channels in these tissues.

From the foregoing facts it is evident that for some time prior to the year 1838, the cell had come to be quite universally recognized as a constantly recurring element in vegetable and animal tissues, though as yet little importance had been attached to it as an element of organization, nor had its characters been clearly determined. As stages in its growing importance may be mentioned, the demonstration of the cellular structure of plants by Robert Hooke,

* Hodgkin, loc. citat.

† Dollinger, Ignaz, Vom Kreislaufe des Blutes, 1828.

in 1667, the further elaboration of this subject by Malpighi, and his statement that each "utriculus" was an independent entity, the very clear statement of Oken in 1808 with regard to the cellular composition of animals and vegetables, the description of Heusinger, in 1822, of the mode of formation of vessels by the apposition of *vesicles*, already referred to, and the announcement, though erroneous, of Döllinger, in 1828, that the body is built up of blood-corpuscles which move in wall-less (wandlos) channels in the tissues.

Raspail, 1837.—Singularly near the truth did Raspail* approach, in 1837, when he tells us that in the condition of development there are *vesicles* or *cells*, endowed with life and the property, almost unlimited, of producing out of themselves other cells of the same structure and similar endowments, of spherical form, and capable of taking up oxygen when exposed to the atmosphere; that the cell membrane in its fresh state is structureless. Yet he considers the organic cell as made up of granules or atoms, spirally arranged about an ideal axis, comparing the cell with the crystal, and speaks of organization as crystallization in vesicles (*crystallization vesiculaire*).

Dutrochet, 1837.—Similar was the view of Dutrochet,† who divided the component parts of the body into *solids* and *fluid*. The *solids* were formed by the aggregation of cells of a certain degree of firmness; the *liquids*, as the blood, are also made up of cells, which, however, float freely among each other, and there are also tissues in which the cells are so feebly

* Raspail, op. citat.

† Dutrochet, op. citat.

united, that one can scarcely tell in what class to place them. The contents of the cell may be more or less solid, but the highest degree of vitality is only compatible with liquid cell contents. *Muscular fibres, and the remaining animal fibres, are cells much elongated. And he considers the same general plan to prevail in the animal and vegetable.* The approach of both of these observers to the truth is striking. Both, however, either failed to detect the nucleus or to attach any importance to it. They failed also to lay down a law of organic development, and their views were soon forgotten.

Discovery of the Nucleus, 1833.—A most important contribution to the anatomy of the cell was made before this, however, in the discovery of the "nucleus," by Dr. Robert Brown, of Edinburgh, whose paper, "Organs and Mode of Fecundation in Orchideæ and Asclepiadeæ," appeared in the Transactions of the Linnean Society of London, in 1833. He failed, however, to appreciate its importance, though its discovery was another fact added to those necessary to complete the data on which has been founded the so-called "cell theory."

Meyen, 1836.—Meyen* sought to establish the opinion that the cell is formed of spiral fibres which lie closely upon one another, founding his view upon his own observation.

Since the discovery of the nucleus, by Dr. Robert Brown, in the vegetable cell, it had been recognized by many observers in various pathological, as well as

* Meyen, Pflanzenphysiologie, Bd. i, 1836.

healthy animal cells, and in the germ cell or ovule of birds, as early as in 1825, by Purkinje;* while Purkinje,† Valentin,‡ and Turpin,§ had actually called attention to the relations of the animal and vegetable cell to each other.

The pre-existence of the nucleus, and the gradual development of the cell about it, Valentin had attempted to demonstrate in the case of pigment cells, C. H. Schultz‖ in the blood-corpuscle, Rudolph Wagner in the egg, and Henle in epithelium, all before the work of Schleiden had appeared. Müller had also insisted on the analogy between the cells of the chorda dorsalis and vegetable cells.¶ Valentin, too, had said, when describing the nucleus of epidermic cells, which he was the first to point out, that they reminded him of the nucleus of the cells of vegetable tissues.** Not only this, but Armand de Quatrefages†† and Dumortier‡‡ had actually observed the origin of young cells from the full grown, in the

* Purkinje, J., Ev. Symbolæ ad ovi avium historiam ante incubationem, cum duobus lithographis. Vratis., 1825.

† Purkinje and Raschkow, Meletemata circa Mammalium Dentium Evolutionem. Diss. Inaug. Vratis., 1835, p. 12.

‡ Valentin, Ueber den Verlauf und die Enden der Nerven, aus den Nov. Act. Nat. Curios., vol. xvii; besonders abgedruckt. Bonn, 1836.

§ Turpin, Ann. d. Sci. Nat., 2 ser. vii, 207.

‖ Schultz, C. H., Müller's Archiv für Anatomie, Physiologie und Wissenschaft. Med., p. cvii, 1837.

¶ Stricker, Manual of Human and Comparative Histology, New. Syd. Soc. Translat., 1870, p. 1.

** Valentin, Nov. Act., N. C. xvii, pt. I, p. 96.

†† Quatrefages, Annales des Sci. Nat., 2 ser. ii, p. 114.

‡‡ Dumortier, Annales des Sci. Nat., 2 ser. vii, p. 129.

embryo of the freshwater snail, while Valentin had furnished examples of the development of fibres out of cells in the muscular fibres, and in the substance of the crystalline lens. In fact, as stated by Dr. Waldo J. Burnett, in his admirable paper,* Valentin "perceived the true physiological relations of cells as far as he well could without apprehending the grand fact that the nucleated cell is the fundamental expression of organic forms."

Virchow had also compared the whole organism to a free state containing individuals endowed with equal privileges if not with equal powers.†

SCHLEIDEN AND SCHWANN, 1838.

It was reserved for Schwann to accomplish this masterstroke in observation and generalization, through the intermediate results of Schleiden, without whose observations on vegetable structures, the true position of the cell would probably have remained undetected for some time longer. Schleiden, in 1838, clearly pointed out the formation of cells in vegetable structures, according to a single and uniform method, and elaborated the theory of development of which the cell was the unit, and which Schwann immediately extended to animal tissues.

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* Burnett, W. J., The Cell; its Physiology, Pathology, and Philosophy, as deduced from original investigations. To which is added its History and Criticism. A prize essay, read before the American Medical Association, and published in vol. vi of its Transactions. Philadelphia, 1853.

† Stricker, op. citat., p. 2.

A formidable obstacle for some time in the way of a law of development, applicable to animal and vegetable tissues, was the opinion, long entertained, that the growth of animals, whose tissues are furnished with vessels, is essentially different from that of plants; an independent vitality being ascribed to the elementary particles of vegetables growing without vessels. So firmly was this believed, that the ovum, which exhibited undoubted evidences of an actual vitality at one period of its growth, was said by all physiologists to have had a plant-like growth. This obstacle was removed in 1837, by Henle,* who showed that an actual growth of the elementary parts of epithelium took place without vessels.

Taking up the nucleus as discovered by Robert Brown, Schleiden,† in reference to its function, applies the name cytoblast (κυτος, a cell, βλαστος, a bud or sprout), or "cell bud," and in a careful study of its anatomy, discovers that "in very large and beautifully developed cytoblasts, there is observed a small, sharply defined body, which, judging from the shadow which it casts, appears to represent a thick ring, or thick-walled hollow globule."‡ One, two, three, and even four of these may be present. Without further present comment than that these characters, as

* Henle, Symbolæ ad Anatomiam vill. intest. Berol., 1837.

† Schleiden, Beiträge zur Phytogenesis, Müller's Archiv, 1838, p. ii; Contributions to Phytogenesis, Sydenham Soc. Transl., p. 233.

‡ The term nucleolus or nucleus-corpuscle (Kernkörperchen), seems to have been first applied by Schwann. (See Introduction to Schwann's Researches, Syd. Society's Translation.)

given by Schleiden, are by no means constant, it is plain that what is commonly known as the *nucleolus* is here intended, to the discovery of which we are therefore indebted to him, though Valentin also claims its discovery at an earlier period.* He further states that the observations he has made upon all plants, lead him to the conclusion that these small bodies are found earlier than the cytoblasts.

According to Schleiden, when starch, which is superfluous nutritive material deposited for future use, is to be employed in new formations, it becomes dissolved into sugar or gum, which are convertible into one another. The sugar appears as a perfectly transparent fluid, not rendered turbid by alcohol, and receiving from tincture of iodine only so much color as corresponds to the strength of the solution. The gum is somewhat yellowish, more consistent, less transparent, and coagulated into granules by tincture of iodine, assuming a pale yellow color, which is permanent. In further progress of organization, in which the gum is always the last immediately preceding fluid, a quantity of exceedingly minute granules appears in it, most of which, from their exceeding minuteness, appearing as black points. It is in this mass that organization takes place, though the *youngest* structures are composed of another distinct, homogeneous, perfectly transparent substance—so transparent as to be invisible when

* Valentin, "Outline of the Development of Animal Tissues," in Wagner's Elements of Physiology, translated by Dr. Willis. London, 1844, p. 214; Leipzig, 1839; where he refers to Valentin's Repertorium, vol. i, p. 143.

not surrounded by opaque or colored bodies,—and continuing thus after pressure. This substance, which frequently occurs in plants, Schleiden calls vegetable gelatin, and considers as slight modifications, pectin, the basis of gum tragacanth, and many of the substances usually enumerated under the term vegetable mucus. It is this gelatin which is ultimately, through the agency of the nucleus, converted into the actual cell-wall, or structures which consist of it in a thickened state, and into the matter of vegetable fibre.

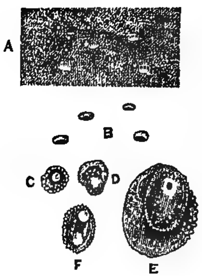
There are two situations in the plant in which new organization may be observed most easily and clearly, in consequence of there being cavities closed by a simple membrane, 1st, in the large cell, which subsequently contains the albumen of the seed, the *embryonal sac*, and 2d, in the extremity of the *pollen tube*, from which the embryo itself is developed. The embryonal sac never contains starch originally, but probably in most instances the saccharine solution or gum. The *pollen* always contains starch, or representing it, a semi-granulous substance identical with the small granules in the gum above alluded to, which Schleiden calls *mucus*.

In both of these situations the above-mentioned minute *mucus*-granules are very soon developed in the gum, upon which the solution, previously homogeneous, becomes clouded and more or less opaque.

Single, larger, more sharply defined granules next become apparent, A, Fig. 2, constituting the *nucleoli*, and soon after the cytoblasts or *nuclei*, B, appear, looking like granulous coagulations about the granules.

The cytoblasts then grow considerably in the free state, C, but so soon as they have attained their full size, a delicate transparent vesicle rises upon their surface, assuming the relation of the watch-crystal to a watch, D, E. This is the young cell, which at first

FIG. 2.



Cellular Tissue, from the embryo sac of Chamædorea Schiedeana, in the act of formation.

A, Formative substance, gum, mucus-granules, nuclei of cytoblasts (nucleoli).

B, Cytoblasts.

C, Single and free cytoblast, more highly magnified.

D, Cytoblast with cell forming in it.

E, Same, more highly magnified.

F, Cytoblast isolated after destruction of cell.

From Schleiden's "Beiträge zur Phytogenesis."

represents a very flat segment of a sphere, the plane side of which is formed by the cytoblast, and the convex side by the young cell, which is placed upon it somewhat like a watch-glass of a watch. In a natural medium it is distinguished almost by this circumstance alone, that the space between its convexity and the cytoblast is perfectly clear and transparent, and probably filled with a watery fluid, and is bounded by the surrounding mucus-granules, which have been aggregated at its first formation, and are pressed back by its expansion, as shown in D, E. But if these young cells be isolated, the mucus-granules may be almost entirely removed by shaking the stage. They cannot, however, be absent for any length of time, for in a few minutes they become completely dissolved in distilled water, leaving only the cytoblasts behind. The vesicle gradually expands and becomes more consistent, and with the exception of the cytoblast, which always forms a portion of it, the wall now consists of gelatin. The entire cell then increases beyond the margin of the cytoblast, and quickly becomes so large that the latter at least merely appears as a small body inclosed in one of the side-walls in such a manner that the wall of the cell splits into two laminæ, one of which passes exterior and the other interior to the cytoblast. That upon the inner side is generally the more delicate, and in most instances only gelatinous, and is also absorbed simultaneously with the cytoblast. Within these cells, again, new cytoblasts arise, grow, and form young cells, which grow and fill up the mother cells, and finally cause the latter to disappear. This is *endogenous cell formation*, while the formation of cells external to other cells constitutes *exogenous cell formation.* But according to Schleiden "the entire *growth* of the plant consists only of a formation of cells within cells."* No other method of formation of new cells seems to have been conceived by him. For although the multiplication of cells, by fissiparous division of previously existing cells, had been demonstrated by Mirbel,† and confirmed by Von Mohl,‡ and the seg-

* Loc. citat., p. 257.

† Mirbel, Recherches sur la Marchantia, 1833. Schleiden, however, says distinctly (op. cit. p. 232), "Mirbel does not make any allusion to the process of cell formation."

‡ Von Mohl, Entwicklung und Bau der Sporen der Kryptogam. Gew., Flor., 1833.

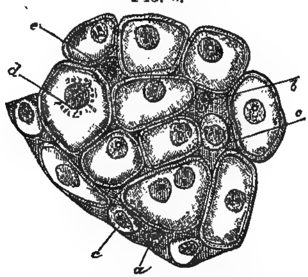
mentation of the egg had been observed even earlier (1824) by Prevost and Dumas, all before the investigations of Schleiden had been made, the latter author considered the apparent growing across of the partition walls an illusion, and that the young cells escape observation in consequence of their transparency, until, at a late stage, their line of contact is regarded as the partition wall of the parent cell; while even Schwann states somewhat hesitatingly what is now so generally admitted.* This is the cell theory of Schleiden, which he assumes to be the universal law for the formation of vegetable cellular tissue in the phanerogamia. At that time the cryptogamia had not been examined, and Schleiden had not then expressed his views in reference to the cambium.

The merit of Schwann consisted in applying this theory to animal tissues, his conclusions being based upon the study of the formation of the chorda dorsalis and cartilage, and a comparison of their cells with those of vegetable tissues. Thus, in a cytoblastema, either structureless or minutely granulous, "a nucleolus is first formed; around this a stratum of substance is deposited, usually minutely granulous, but not yet sharply defined on the outside. As new molecules are constantly being deposited in this stratum between those already present, and as this takes place within a precise distance of the nucleolus only, the stratum becomes defined externally, and a cell nucleus, having a more or less sharp contour, is formed. The nucleus grows by a continuous deposition of new

* Schwann, op. citat, Introduction, p. 4.

molecules between those already existing, that is by intussusception. (See Fig. 3, *e.*) If this go on equally throughout the entire thickness of the stratum, the

FIG. 3.



From the point of a Branchial Cartilage of Rana esculenta. (From Schwann.)

nucleus may remain solid ; but if it go on more vigorously in the external part, the latter will become more dense, and may become hardened into a membrane, and such are the hollow nuclei."*

When the nucleus has reached a certain stage of development, the cell is formed around it. The following is the process by which this takes place: "A stratum of substance, *which differs from the cytoblastema*, is deposited upon the exterior of the nucleus. (See Fig. 3, *d.*) In the first instance, this stratum is not sharply defined externally, but becomes so in consequence of the progressive deposition of new molecules. The stratum is more or less thick, sometimes homogeneous, sometimes granulous: the latter is most frequently the case in the thick strata which occur in the formation of the majority of ani-

* Schwann, op. citat., p. 175.

mal cells. We cannot, at this period, distinguish a cell cavity and cell wall. The deposition of new molecules, between those already existing, proceeds, however, and is so effected that when the stratum is thin, the entire layer, and when it is thick, only the external portion, becomes gradually consolidated into a membrane. The external portion of the layer may become consolidated soon after it is defined on the outside; but, generally, the membrane does not become perceptible until a later period, when it is thicker and more defined internally; many cells, however, do not exhibit any appearance of the formation of a cell membrane, but they seem to be solid, and all that can be remarked is that the external portion of the layer is somewhat more compact.*

"Immediately that the cell membrane has become consolidated, its expansion proceeds as the result of the progressive reception of new molecules between the existing ones; that is to say, by virtue of a growth by intussusception, while at the same time it becomes separated from the cell nucleus. . . . . . The interspace between the cell membrane and the cell nucleus is at the same time filled with fluid, and this constitutes the *cell contents.* During this expansion the nucleus remains attached to a spot on the internal surface of the cell membrane." Though, according to Schwann, in animal cells the nucleus is never covered by a lamella passing over its inner surface, as is the case with the vegetable cell according to Schleiden.

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* Schwann, op. citat., p. 176. Stricker also informs us (Sydenham Soc. translation, p. 5) that the corpuscles of mucus and pus, even in the eyes of Schwann, had no cell-wall.

Thus is formed the animal cell according to Schwann, and although its method is very similar to that of Schleiden, both as to endogenous and exogenous cell formation (for Schwann did not restrict cell genesis to endogenous cell formation), we have quoted his own paper because he is plainly fuller and more precise in his descriptions. The object of each observer was, however, the same with regard to the tissues studied; the additional object of Schwann being to show that *all organisms*, whether *animal or vegetable*, are formed on a *common principle*, and that this principle is *origin from cells*,—that the various tissues of the plant and animal, however simple or complicated, are all combinations of these cells, modified in adaptation to the special peculiarities of tissues.

The *conception* of Schleiden was truly original, though its *application* was less difficult in consequence of the simplicity of vegetable tissues. The conception of Schwann was easier, in being the reflection of that of Schleiden, while its application was more difficult, in consequence of the great diversity of animal tissues; so difficult that he acknowledged that "there are some exceptions, or at least differences, which are as yet unexplained." This need not surprise us when we recollect that one of the ablest modern exponents of the cell theory admits the difficulty of its application to some of the so-called higher tissues.* Indeed, the careful reader of Schwann's

* Virchow, Cellular Pathology, Chance's Translation. Am. Edit., Philadelphia, 1863, p. 78.

researches cannot but be surprised at the accuracy of the observations of this histologist, nor can he fail to realize how comparatively few have been the changes necessitated in his descriptions, or the method of application of his theory to the formation of the different tissues; while the portion of the theory of Schleiden and Schwann which does not accord with the latest expression of the cell doctrine, is not so much that which pertains to the formation of tissues from existing cells as that which relates to the method in which they supposed the cells to originate; which, it will be recollected, was by a species of *spontaneous generation* of the essential parts of the cell, in a homogeneous cytoblastema.

A difference in the anatomy of the cell as given by Schwann and physiologists of the present day, is seen in the location of the nucleus by the former, who places it not merely *eccentrically*, but actually "separated from the surface only by the thickness of the assumed cell-wall."* At the present day, the situation of the nucleus, though usually central, is known to be not unvarying. Again, the primary and absolutely essential presence of the *nucleolus*, as well as the universal presence of the *cell-wall*, may be considered characteristics of Schleiden and Schwann's idea of the cell, which are now no longer insisted upon.

As already stated (p. 38), Schwann would seem to have admitted also, the formation of cells by division, though with some hesitation. Thus he writes:†

* Schwann, op. citat., p. 37, a. f.

† Schwann, op. citat., Introduction, p. 4.

"A mode of formation of new cells, different from the above described, is exhibited in the multiplication of cells by division of the existing ones; in this case, partition walls grow across the old cell, if, as Schleiden supposes, this be not an illusion, inasmuch as the young cells might escape observation in consequence of their transparency, and at a later stage, their line of contact would be regarded as the partition wall of the parent cell."

Schwann believed that the cell-wall was the most active constituent of the cell, that it possessed the power not only of producing physical and chemical changes in its own substance and the cell contents, but of secreting materials from the surrounding substance, and depositing them in its interior, explaining in this manner the secretions of glands, the formation of fat in some cells, pigment in others, etc.

It would be easy to point out other defects in the theory of Schleiden and Schwann, when it is tested by comparison with the more accurate observation of the last twenty-five years, none of which should be permitted to detract from the credit which attaches to the originators of this conception. It must not be forgotten, that it is no less true of science than of art, that great and important truths in their entirety are gradually developed, and that no single mind is capable of elaborating them from their incipiency to their complete expression. And as many clever people had daily noticed the rising of steam from the boiling kettle without thinking of utilizing its principles of expansion, so also, many careful observers had time and again witnessed the cellular or vesicular composition of plants, and yet failed to appreciate the importance of the nucleated cell, and to deduce from it a law of development applicable to all organic forms. Again, as the engine of Watt was far different from the beautiful and powerful creation of the mechanic of the present day, so the cell theory, as developed by Schleiden and Schwann, has been further evolved by later histologists. We may therefore truthfully reiterate, with Prof. Huxley, that "whatever cavillers may say, it is certain that histology before 1838, and histology since then, are two different sciences—in scope, in purpose, and in dignity—and the eminent men to whom we allude, may safely answer all detraction by a proud '*circumspice.*'"*

According to these observers, then, a perfectly formed cell would be defined as a *closed vesicle*, with certain contents, among which were *essentially* a *nucleolus* and *nucleus.*

HENLE, BERGMANN, REICHERT, AND OTHERS, 1840–46.

It is not consistent with our object to include all of the numerous observations which were multiplied after this period, incited by the researches of Schleiden and Schwann. It is simply to point out the salient features of those results which point towards and have culminated in accepted views. It has been stated that previous to Schleiden's researches, in 1838, the formation of cells by *division* had been asserted as one mode of origin, that Schleiden had declared this an error of observation, and that Schwann

* Huxley, op. citat., p. 290.

had hesitatingly, if at all, accepted it as a rare method of cell formation.

Henle,* who, in general, adopted the view of Schwann as to the *primary origin* of cells, though he made exception to its universality of application, says that cells *multiply* in three ways:

1. By *budding* (durch Sprossen), as in certain lower plants.

2. By *endogenous* cell development (durch endogene Zeugung), where the cell contents of the mother cell become the cytoblastema of the daughter cells, as originally given by Schleiden and Schwann.

3. By *division* or *segmentation* (durch Theilung), of which he says, however, no examples are found among animals; though he also states in the paragraph† immediately following, "We would, with Schwann, consider cell formation in the yolk, by 'furrowing,' an analogous process, if we may consider the yolk as a simple cell." He then proceeds to describe how, by a constriction of the surface, the yolk is divided into two equal parts, these into four, and so on until the entire yolk becomes a *mulberry mass*, made up of little round bodies. This segmentation of the ovum already observed in the yolks of frogs, fish, molluscs, and medusæ, Henle says at this time (1841), has perhaps merely escaped notice‡ in the case of the higher animals, as plausibly suspected by Bergmann,§ a suspicion which we need

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* Henle, Allgemeine Anatomie. Leipzig, 1841, p. 172 *et seq.*

† Henle, op. cit., p. 176. ‡ Henle, op. cit., p. 177.

§ Bergmann, Müller's Archiv, 1841. Bergmann also in this paper objected to the existence of a cell membrane, and correctly scarcely say was amply confirmed a little later. But Henle also states, in the same connection, that certain cases arise in which perfect cells are developed in a cytoblastema, in a manner which is inexplicable, and that from these cells tissues are finally developed.* Whence the undetermined state of the question at that time may be easily inferred. Nor is mention here made by Henle of the nucleus of the cell as the primary seat of the segmentation. The surface of the cell is said to be "constricted" or "furrowed," deeper and deeper, until the division takes place. This description is still adhered to by many physiologists of the present day, who consider that there is a simple disappearance of the germinal vesicle or nucleus of the ovum after fecundation, rather than a division of it into two, and substitution of these for the original one. While endeavoring to trace out the steps by which the present most generally accepted views with regard to the origin of cells were arrived at, it must not be forgotten that other dissenting views were also advanced, though tending differently from those incorporated in the text, where it is desired more particularly to trace those culminating in existing doctrines. Thus did Reichert† early (1840), dissent from Schwann, since he failed to find the nucleus universally present in the yolk, and he was the first to defend the view

maintained that the spheres of segmentation are cells which are at first destitute of a cell membrane, though they become invested by one at a subsequent period.

* Henle, op. cit., p. 177.

† Reichert, Das Entwickelungsleben im Wirbelthierreich. Berlin, 1840, pp. 6, 93.

that the segments into which the egg breaks up are cells. Karsten* (1843), published a dissertation upon the cell, in which he stated that cells originate without a pre-existing nucleus, and by the expansion of amorphous granules of organic matter; and more recently (1863), the same author practically reiterates this view, since he says that all "cells of vegetables originate as minute *free vesicles* in the fluid contents of previously existing cells," and regards the nucleus as a "small tertiary cell, retarded in its development."† Again, "when the nucleus is present, the origin of new cells is quite independent of it."‡ In addition to the statement already given, Henle also (1843), alleged that some of the so-called fibrous tissues were "formed by the aggregation of granules in a certain way without the intervention of true nucleated cells."§ Kölliker,‖ one of the foremost exponents of the cell doctrine of the present day, in 1844 expressed his dissent from the idea of unity in the mode of cell formation, and states that if there is a single method of cell formation which is invariable, it remains to be discovered, although he interpreted the segmentation of the germ of cephalopods in the same manner as Bergmann. Mr.

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* Karsten, De Cella vitâle Dissertatio. Berlin, 1843.

† Karsten, Ann. and Mag. of Nat. History, vol. xiii, p. 268. London, 1864.

‡ Karsten, Ann. and Mag. Nat. History, vol. xiii, p. 281.

§ Henle, Traité d'Anatomie Générale. Trad. d'Allemand, par A. J., Jourdan, 2 vol., Paris, 1843, tom. 1, p. 374.

‖ Kölliker, Entwickelungsgeschichte der Cephalapoden. Zurich, 1844.

Paget,* so well known from his Lectures on Surgical Pathology, suggested in 1846, that a cell might arise in some other way than from a nucleus, since he had met morbid growths composed entirely of fibres, in which not a nucleated cell was present. Most of these statements are, however, reconciled by the information which has since been added to our knowledge of the subject.

MARTIN BARRY, 1840.

It was in his first series of embryological researches, published in Part II of the "Philosophical Transactions" of the Royal Society of London, for 1838, p. 310, that Dr. Martin Barry declared "that the germinal vesicle (which he regarded as the nucleus), and its contents constitute throughout the animal kingdom the most primitive portion of the ovum." In his second series, Part II, 1839, in stating that the germinal vesicle returns to the centre of the cell, *post coitum*, he first pointed out that the nucleus does not always accompany the cell through the whole vital process at the periphery (the original position according to Schleiden and Schwann), but that it also passes to the centre, as we now well know. Here, also, he declares, but in his third series, Part II, 1840, he *demonstrates*, that there arise in the parent vesicle, two or more infant vesicles, the parent vesicle disappearing by liquefaction. And in his third series, p. 529, he says, "The germinal vesicle does not burst, or dissolve away, or become flattened, on or before the fecun-

* Paget, Report on the Progress of Anatomy and Physiology, Br. and For. Med. Rev., July, 1846.

dation of the ovum as hitherto supposed. It ceases to be pellucid." And on page 531, "The germinal vesicle fills with cells, and these become filled with the foundations of other cells; so that the germinal vesicle is gradually rendered opaque."

He also describes in this series, in great detail, the mode in which these cells are produced from the germinal *spot*, which he considers in the light of a nucleus to the germinal vesicle. Part II, 1839, p. 360. And though the minute details may not precisely accord with those of the most recent observations, the correct idea is clearly grasped. In fact, it may be said that in minuteness of detail alone does he differ from later observers, and had he simply stated that the young cells arise from the nucleus or nucleolus of the parent cell, he would accord precisely with the most recent observers. But he is, if possible, even more explicit when he says, "The process inherited from the germinal vesicle by its offspring, reappears in the descendants of these. Every cell, whatever its minuteness, if its interior be discerned, is filled with the foundations of new cells, into which its nucleus has been resolved." Again he says,* "Schleiden has seen the nucleus undergoing such changes (division), but failed to recognize them." And finally, in "Philosophical Transactions" for 1841, pp. 207–8, we have the following striking paragraphs, which would seem also to correct some previous errors:

"§ 77. I am very much inclined to believe, that

* Barry, Philosophical Transac., 1840, p. 348, § 385.

in the many instances in which authors on 'cells' have described and figured more than one nucleolus in a nucleus, there has been either an incipient division of the nucleus into discs, or the nucleus has consisted of two or more discs; the nucleoli of those authors having been the minute and highly refracting cavities or depressions in the discs. If this has really been the case, it affords additional evidence, I think, *that the reproduction of cells by the process I have described—namely, division of the nucleus of the parent cell—is universal*—so numerous have been the instances in question. I may refer to the figures given by Schwann, who examined nearly every tissue, and to those of Schleiden, whose observations have been so extensive on plants. I think, indeed, that many of the figures of Schwann afford evidence of the division in question having taken place. It is to be recognized in his delineation of the cells of cartilage, cellular tissue, middle coat of the aorta, muscle, tendon, feather, etc. The same remark is applicable to a figure given by Reichert of ciliated epithelium cells. Dr. Henle found that in the layers of his 'pflaster-epithelium' cells, the nucleus, very distinct in the lower cells, had almost disappeared in those situated in the upper part. From this observation, and from the presence of two nucleoli in some of the nuclei figured by this observer, as well as from the nucleus becoming more granular, I think it extremely probable that these cells (including those of the epidermis), are reproduced by the process just referred to,—*division of the nucleus;* additions being no doubt continuously made at the lower part of the layer, by 'which cells previously there are pushed farther out.'

"§ 83. The nuclei which various observers have found lying among the fibres of various tissues, have been considered by them as the 'remains of cells.' This may have been the case, but so far from thinking with those observers, that the nuclei in question were 'destined to be absorbed,' I am disposed to consider that they were sources from which there would have arisen new cells."

Without doubt, we can say, as did Goodsir,* in the above by Martin Barry, we have the "first consistent account of the development of cells from a parent centre, and more especially of the appearance of centres within the original sphere." Nothing more definite, or directly to the point, could be desired, and we think it may be justly said of Barry, that he completed the expression of the cell theory inaugurated by Schleiden and Schwann, in modifying the mode of origin to conform to most recent observation.

PROF. JOHN GOODSIR, 1845.

In 1845, Prof. John Goodsir published his paper on "Centres of Nutrition,"† in "Anatomical and Pathological Observations," in which he clearly grasped the two important principles of the modern Cellular Pathology; *first*, the *activity* of these centres (nuclei), their power "to draw from the capillary vessels, or from other sources, the materials of nutrition, and to distribute them by development to each organ or texture after its kind;" *second*, the *origin* of such centres or nuclei

* Goodsir, Turner's Edition of Anatomical Memoirs. Edinburgh, 1868. Note on p. 390.

† Goodsir, op. citat., p. 389.

from previously existing nuclei. In this short paper of three pages, are contained, as stated, the essentials of the cell doctrine of Virchow, and as it has recently assumed additional interest on controversial* grounds, it may be well to introduce as much as bears directly upon the subject. "The centre of nutrition with which we are most familiar, is that from which the whole organism derives its origin,—the germinal *spot* of the ovum. From this, all the other centres are derived, either mediately or immediately; and in directions, numbers, and arrangements, which induce the configuration and structure of the being. As the entire organism is formed at first, not by simultaneous formation of its parts, but by the successive development of these from one centre, so the various parts arise each from its own centre, this being the original source of all the centres with which the part is ultimately supplied.

"From this it follows, not only that the entire organism, as has been stated by the authors of the cellular theory, consists of simple or developed cells, each having a peculiar independant vitality, but that there is in addition, *a division of the whole into departments*, each containing a certain number of developed cells, *all of which hold certain relations to one central or capital cell, around which they are grouped.* It would appear that from this central cell, all the other cells of its department derive their origin. It is the mother of all those within its own territory.

* Edinburgh Monthly Medical Journal, February and April, 1869, pp. 766 and 959.

It has absorbed materials of nourishment for them while in a state of development, and has passed them off after they have been fully formed, or have arrived at a stage of growth when they can be developed by their own powers.

"Centres of nutrition are of two kinds,—those which are peculiar to the textures, and those which belong to the organs. The nutritive centres of the textures are in general permanent. Those of the organs are in most instances peculiar to their embryonic stage, and either disappear ultimately or break up into the various centres of the textures of which the organs are composed.

"*A nutritive centre, anatomically considered, is merely a cell, the nucleus of which is the permanent source of successive broods of young cells*, which from time to time fill the cavity of their parent, pass off in certain directions and under various forms, according to the texture or organ of which their parent forms a part."

Prof. Goodsir does not fail to state in the first paragraph of his paper, that with many of these centres anatomists have been for some time familiar, but further remarks, that with few exceptions they have looked upon them as embryonic structures. He alludes in a note to the observations of Bowman and Barry, the former on "Muscle," and the latter "On the Corpuscles of the Blood," in Philosophical Transactions, respectively, of 1840 and 1841, and states in a second note that "for the first consistent account of the development of cells from a parent centre, and more especially the appearance of new centres within the original sphere, we are indebted to Martin

Barry."* We have carefully read the references in each instance. In Bowman's paper† we can recognize a brief reference to a possible influence of the cell upon nutrition, but none as to its origin, in the following sentence: "It is, however, not impossible, that in all these cases, there may be during development, and subsequently, a further and successive deposit of corpuscles (nuclei) from which both growth and nutrition may take their source." That Dr. Barry's paper is more explicit has been shown.

REMAK, 1853–55.

Remak‡ defended most effectually the view that cells originate from previously existing cells *by division*, and that at least in the early stages of the development of the embryo, no other mode of cell development occurs than by division. Remak also contended for, and according to Stricker,§ established the same law in respect to the pathological development of cells, although Stricker admits also that Virchow played an important part in the extension of our knowledge in this direction.

HUXLEY, 1853.‖

Allusion has already been made to Prof. Huxley

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* Goodsir, Anatomical Memoirs, vol. ii, p. 389, and note on pp. 390–91.

† Bowman, "Muscle," Philos. Transac., 1840, pt. i, p. 485.

‡ Remak, Untersuchung über die Entwickelung der Wirtelthiere. Berlin, 1852–55.

§ Stricker, Manual of Human and Corporative Histology. New Syd. Soc. Transl., 1870, p. 34.

‖ We presume it will scarcely be inferred by any reader, that in connection with Wolff, of whose theory he has been the able exponent. In the same paper* he has given us his own views—"conceived in the spirit, and not unfrequently borrowing the phraseology, of Wolff and Von Baer." We present them, as far as may be consistent with brevity, in his own words:

"Vitality, the faculty, that is, of exhibiting definite cycles of change in form and composition, is a property inherent in certain kinds of matter. There is a condition of all kinds of living matter in which it is an *amorphous germ*—that is, in which its external form depends merely on ordinary physical laws, and in which it possesses no internal structure. Now, according to the nature of certain previous conditions, the character of the changes undergone, or the different states exhibited—or, in other words, the successive differentiations of the amorphous mass will be different.

"The *morphological* differentiation may be of two

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the views of Prof. Huxley here presented are brought forward as those now entertained by him, and with which the public have been made so generally familiar through his lecture on "Protoplasm," or the "Physical Basis of Life," delivered at Edinburgh, November 18th, 1868, and originally published in the "Fortnightly Review" for February, 1869; but also largely republished in numerous English and American periodicals, as well as in a separate pamphlet, to be had of the publishers of the Yale College Courant, New Haven, Conn. To one closely observing, however, we think that these latter views will appear to be foreshadowed in the theory here given, and which we think of sufficient historical importance to justify its presentation here.

* Huxley, Review of the Cell Theory. Br. and For. Med. Chir. Rev., October, 1853, p. 305.

kinds. In the lowest animals and plants,—the so-called unicellular organisms—it may be said to be *external*, the changes of form being essentially confined to the outward shape of the germ, and being unaccompanied by the development of any internal structure.

"But in all other animals and plants, an internal morphological differentiation precedes or accompanies the external, and the homogeneous germ becomes separated into a certain central portion, which we have called the *endoplast*, and a peripheral portion, the *periplast*. Inasmuch as the separate existence of the former necessarily implies a cavity in which it lies, the germ in this state constitutes *a vesicle with a central particle*, or a 'nucleated cell.' *There is no evidence whatever* that the molecular forces of the living matter (the 'vis essentialis' of Wolff, or the vital forces of the moderns), are by this act of differentiation localized in the endoplast to the exclusion of the periplast, or *vice versa*. *Neither is there any evidence that any attraction or other influence is exercised by the one over the other*; the changes which each subsequently undergoes, though they are in harmony, *having no causal connection with one another*, but each proceeding, as it would seem in accordance with the general determining laws of the organism. On the other hand, the 'vis essentialis' appears to have essentially different and independent ends in view, in thus separating the endoplast from the periplast.

"The *endoplast* (nucleus) grows and divides; but, except in a few more or less doubtful cases, it would seem to undergo no other morphological change. It frequently disappears altogether; but as a rule it undergoes neither chemical nor morphological metamorphosis. So far from being the centre of activity of the vital actions, it would appear much rather to be the *less important histological element.*

"The *periplast*, on the other hand, which has hitherto passed under the name of cell-wall, contents and intercellular substance, is the subject of all the most important metamorphic processes, whether morphological or chemical, in the animal and plant. By its differentiation, every variety of tissue is produced; and this differentiation is the result, *not of any metabolic action of the endoplast*, which has frequently disappeared before the metamorphosis begins, but the intimate molecular changes in its substance, which take place under the guidance of the 'vis essentialis,' or, to use a strictly positive phrase, occur in a definite order, we know not why.

"The metamorphoses of the periplastic substance are twofold,—*chemical* and *structural*. The former (*chemical*), may be of the nature either of *conversion*,—change of cellulose into xylogen, intercellular substance, etc., of the indifferent tissues of embryos, into collagen, chondrin, etc.,—or of *deposit*,—as of silica in plants, of calcareous salts in animals. The *structural* metamorphoses, again, are of two kinds, *vacuolation* or the formation of cavities, as in the intercellular passages of plants, the first vascular canals of animals; and *fibrillation*, or the development of a tendency to break up in certain definite lines rather than in others."

These views he illustrates by examples from vegetable life in the *sphagnum* leaf, and from animal life in *connective tissue* and striped *muscle.*

As characteristic and distinguishing features of this theory, we desire to point out, first, the substitution of the term "*endoplast*" for "nucleus;" that of "*periplast*" for "cell-wall," and "intercellular," "substance." Second, the absolutely passive nature of the "endoplast," which is neither itself the author of changes nor the subject of changes. Third, the passive nature as well of the "periplast," so far as it is the author of changes, though it is pre-eminently the *subject* of changes, the *seat in which changes take place.* And herein, we believe Huxley to have been misinterpreted by some who have presented his views elsewhere, as Dr. Beale,* who represents him as believing the periplast active, that it is the efficient agent, that it sends in partitions, etc. But that Prof. Huxley considered it passive we believe may be legitimately inferred from his text. As the *seat* of change, however, accomplished not as "the result of any metabolic action of the endoplast, but of intimate molecular changes in its substance, which take place under the guidance of the *vis essentialis,*" the *periplast* is differentiated into every variety of tissue. Finally, we have the distinct admission, as seen in the sentence last quoted, and also throughout the entire expression of the theory, of a controlling, guiding principle, through which the differ-

* Beale, Microscope in Medicine. Third Edition. London, 1867, page 147. Beale, Structure and Growth of the Tissues, London, 1865, pp. 9, 10.

entiation is accomplished. This principle, which is here referred to as the "vis essentialis," is elsewhere included under the expressions "vitality," and "general determining laws of the organism." Though this admission is seemingly so at variance with the views of the same observer in 1870, when, in common with other physicists, he emphatically denied the existence of "vital force," or even such a thing as life itself, yet, as already intimated, we deem it possible to detect a foreshadowing of his more modern views, in the following paragraph of the paper whence we have derived our information:

"We have therefore maintained the broad doctrine established by Wolff, that the vital phenomena are not necessarily preceded by organization, nor are in any way the result or effect of formed parts, but that the faculty of manifesting them resides in the matter of which living bodies are composed, as such; or, to use the language of the day, that *the vital forces are molecular forces.*"*

Huxley moreover says that the three botanical data upon which Schwann's theory was based, viz.:

1. The anatomical independence of the vegetable cell as a separate entity.

2. His conception of the structure of the vegetable cell, and

3. Its mode of development, were all erroneous.

Since first, he (Huxley) considers that the fact that by certain chemical or mechanical means, a plant may be broken up into vesicles, corresponding

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* Huxley, loc. citat., p. 314.

with the cavities which previously existed in it, is of no more value in proving the independence of these vesicles, than the fact that a rhombohedron of spar, broken up with the hammer, into minute rhombohedrons, is evidence that those minuter ones were once independent, and formed the larger by their coalescence.

Second, Schwann's view of the anatomy of the cell was incorrect, since he regarded the nucleus as invariably present, whereas in certain vegetable cells (as in Hydrodictyon, Vaucheria, Caulerpa, Sphagnum), it is indubitably absent; and since he did not include the nitrogenous primordial utricle, discovered by Mohl, in 1844,* as one of the elements of the cell.

Finally, Schwann's mode of cell-development is erronous, having "been long since set aside by the common consent of all observers;" cell-development always occurring by *division*, except in the embryo sac of the Phanerogamia, the sporangia of Lichens, and of some Algæ and Fungi; and even the free cell-development of the latter is quite different from that of Schleiden and Schwann, being by the development of a cellulose membrane (periplast) around a mass of nitrogenous substance (endoplast), which may or may not contain a nucleus.

The difference between the views of Schwann and Huxley are best expressed by the latter in the contrast he draws between those of Schwann and Wolff:

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* The existence of the primordial utricle is denied by many botanists of the present day.

"For Schwann, the organism is a beehive, its action and forces resulting from the sêparate but harmonious action of all its parts. For Wolff (and Huxley), it is a mosaic, every portion of which expresses only the conditions under which the formative power acted, and the tendencies by which it was guided."

The statements of Prof. Huxley with regard to *cell-development* entirely accord with the most recent observations on the subject, and are quite important to us in tracing out the present state of the cell doctrine.

J. HUGHES BENNETT, 1855.*

Dr. Bennett, of Edinburgh, considered that "the ultimate parts of organization are not cells nor nuclei, but the minute molecules from which these are formed They possess independent physical and vital properties, which enable them to unite and arrange themselves so as to produce higher forms. Among these are nuclei, cells, fibres, and membranes, all of which may be produced directly from molecules. The development and growth of organic tissues is owing to the successive formation of histogenetic and hystolytic molecules. The breaking down of one substance is often the necessary step to the formation of another; so that the histolytic or disin-

* Bennett's Practice of Medicine. Am. Ed. of William Wood & Co., N. Y., 1866, p. 118.

Prof. Bennett has further elaborated his views in the Edinburgh Medical Journal, March, 1868, and The Popular Science Review, January, 1869, but his conclusions are substantially the same as quoted.

tegrative molecules of one period become the histogenetic or formative molecules of another."

Again: "As to development, the molecular is the basis of all the tissues. The first step in the process of organic formation is the production of an organic fluid; the second, the precipitation in it of organic molecules, from which, according to the molecular law of growth, all other textures are derived either directly or indirectly."*

Figs. 4, 5, 6, 7, illustrate these views amply.

FIG. 4. FIG. 5. FIG. 6. FIG. 7.

Fig. 4, Molecular structure of the scum on its first appearance, in a clear animal infusion. Fig. 5, Molecular structure of the same six hours afterwards. The molecules are separated, and the long ones (so-called vibriones) in active movement. Fig. 6, The same on the second day. Fig. 7, Filaments (so-called spirilla) formed by aggregation of the molecules, in the same scum on the third and fourth days, all in rapid motion. 800 diam. linear. (From Bennett's Practice.)

Prof. Bennett contends, also, that morbid growths may easily be shown to originate in a molecular blastema, though not to the exclusion of pre-existing cells. The accompanying figures are sufficiently explanatory.

It should be stated also that this author, in common with others not accepting the cell doctrine in its entirety, admits the production of cells by buds, division or proliferation, without a new act of generation, and that "this fact comprehends most of the admitted observations having reference to the cell doctrine."†

* Op. citat., p. 119. † Op. citat., p. 123.

We have in the expression of this theory, a practical admission of the spontaneous origin of animal life, of which Dr. Bennett, in the paper referred to in the *Popular Science Review*, for January, 1869,

FIG. 8.

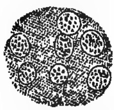

FIG. 9.

FIG. 10.

FIG. 11.

Fig. 8, Nuclei imbedded in a molecular blastema. Fig. 9, Young fibre-cells formed by the aggregation of molecules around the nuclei of Fig. 8. Fig. 10, Cancer cells, one with a double nucleus. Fig. 11, Histolytic or so-called granule-cells, breaking down from fatty degeneration. 250 diam. linear. (From Bennett's Practice.)

openly declares himself the advocate, while the views are in no way essentially different from those of Schwann.

Closely allied to this theory is the so-called investment or cluster theory (Umhüllungs-theorie), described by Virchow on page 53 of *Cellular Pathology* (Am. Ed. of Chance's Translation): according to which "originally a number of elementary globules

FIG. 12.

Diagram of the Investment (cluster) theory. *a*, Separate elementary granules. *b*, Heap of granules (cluster). *c*, Granule-cell, with membrane and nucleus.

existed scattered throughout a fluid, but that under certain circumstances they gathered together, not in the form of vesicular membranes, but so as to constitute a compact heap, a globe (mass, cluster—Klümpchen), and that this globe was the starting-point of all further development, a membrane being formed outside and a nucleus inside, by the differentiation of the mass, by apposition, or intussusception."

TODD AND BOWMAN, 1856.

Notwithstanding earlier approximations to the truth, we find free cell formation still admitted by the eminent authorities, Todd and Bowman, as one mode of origin of cells, so late as December, 1856, though the spontaneous origin of organs is spoken of as exceedingly doubtful. After describing the elements of the ovum, considered in its entirety as a nucleated cell, and referring to the period after fecundation, it is stated, "At this period the embryo consists of an aggregate of cells, and its further growth takes place by the development of new ones. This may be accomplished in two ways: first, by the development of new cells within the old, through the subdivision of the nucleus into two or more segments, and the formation of a cell around each, which then becomes the nucleus of a new cell, and may in its turn be the parent of other nuclei; and, secondly, by the formation of a granular deposit between the cells, in which the development of the new cells takes place. *The granules cohere to each other in separate groups, here and there, to form nuclei, and around each of these a delicate membrane is formed, which is the cell membrane.* The nuclei have been named *cytoblasts*, because they appear to form the cells; and the granular deposit in which these changes take place is called the *cytoblastema.*

"In every part of the embryo the formation of nuclei and of cells goes on in one or both of the ways above mentioned, and, by and by, ulterior changes take place, for the production of the elementary parts of the tissues."*

Thus did physiologists adhere to the original free cell formation of Schleiden and Schwann. Singularly, Dr. Carpenter,† who expressly states, in his Manual of Physiology, edition of 1865, that he has been led to the view of Professor Beale by comparison of the results of the recent inquiries of several British and Continental histologists with those of his own studies, says, a few pages further on (p. 150), "New cells may originate in one of two principal modes; either directly from a previously existing cell, or by an entirely new process in the midst of an organizable blastema." He then proceeds to give the two methods in detail, without in any way denying the latter.

VIRCHOW, 1858.

Less than two years later, August 20th, 1858, Prof. Virchow published his "Cellular Pathology, as based upon Physiological and Pathological Histology." According to him, the cell is the only possible starting-point for all biological doctrines. This cell can only originate from a previously existing cell, taking its primary origin from the ovum, and the Harveian maxim *omne vivum ex ovo*, becomes in its special application, *omnis cellula e cellulâ*. This

* Todd and Bowman, The Physiological Anatomy and Physiology of Man. Am. Edit., Philadelphia, 1857, p. 63.

† Carpenter, Manual of Physiology. London, 1865. Note on p. 14.

is true of all physiological and pathological processes in the vegetable and animal. In all editions of "Cellular Pathology" which we have met, the typical cell is described as consisting essentially of "cell-wall," "cell contents," and "nucleus;" the "nucleolus," though usually met in fully developed older forms, is not considered an essential constituent of the cell. The object of the "nucleus," according to Virchow, is entirely connected with the *life* of the cell, that which maintains it as an element and which insures its reproduction. While to the "cell contents" over and above the nucleus, that is the "residual cell contents," is due the *function* of the cell, that to which is due the contractility of muscle, the neurility and sensation of nerve, and the secretory office of the gland cell.*

To secure the universal application of the cell doctrine, it becomes necessary to eliminate from the vegetable cell, the external non-nitrogenous membrane known as cellulose, and restrict it to the nitrogenized portion comprised in the *primordial utricle* as the *proper cell-wall*, and in the *protoplasmic* contents of the cavity as the proper cell contents, which contain also the nucleus. "It is only when we adhere to this view of the matter, when we separate from the cell all that has been added to it as an after-development, that we obtain a simple, homogeneous,

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* Virchow, Cellular Pathology, as based upon Physiological and Pathological Histology. Second Edition. Translated by Frank Chance, M.B., etc. Am. Edition, Philadelphia, 1863, p. 37.

extremely monotonous structure, recurring with extraordinary frequency in living organisms."*

More recently, however, Virchow is reported as not regarding the "cell-wall" as an essential part of the cell, as stated in Cellular Pathology; but *that a nucleus surrounded by a molecular blastema was sufficient to constitute a cell*; then he says that the outer part of this cell blastema consolidates and forms a cell-wall as Beale has shown, and that this takes place in the amœba when placed in water.†

As thus defined, the cell is the seat of pathological and physiological processes rather than the blood, or the nerves. The cell is active—the ultimate morphological element in which there is any manifestation of life, and beyond which the seat of real action cannot be removed. Hence the term *Cellular Pathology* rather than humoral, or neural, or solidistic. The so-called *exudations* are not such in the strict sense of the term, and the cells which they contain, whether of pus or organizable lymph, are the result of proliferation of previously existing cells. Even "fibrin, wherever it occurs in the body external to the blood, is not to be regarded as an excretion from the blood, but as a local production," resulting from the activity of the cells of the tissue in which it is found, and conveyed to the surface by the transudation of the *serous* fluids alone.‡ In the

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* Op. cit., pp. 31, 34.

† Letter from Berlin, in Edinburgh Medical Journal, February, 1865.

‡ Virchow, op. cit., pp. 435–6.

above statements we have the *first* distinctive feature of Virchow's theory.

Again, since every organized body is usually made up of a number of these cells, each independent in itself, yet combined and arranged for the attainment of a special end, and therefore mutually dependent, there result certain communities or cell territories into which the body is portioned out by Virchow. But not only is the relation of these cells to each and to the central cell whence they took their origin mutually dependent, but in many animal tissues, at least, we have the so-called *intercellular substance*, in a certain definite manner dependent upon the cell or cells which it surrounds, "so that certain districts belong to one cell and certain others to another." Especially is this the case in pathological processes, where sharp boundaries may often be drawn between cell territories. Herein have we the *second* distinguishing character of Virchow's theory.

There are also a *third* and *fourth* distinctive features. It has already been explained that the principle of the theory of Schleiden and Schwann lay in this, that every tissue, healthy or morbid, results from the apposition of cells, and that this principle is still observed as correct, the mode of origin of the primary cell being alone the object of dispute. According to Virchow, however, it is a special cell which becomes the starting-point of physiological and pathological processes, and by its various metamorphoses constitutes the healthy or morbid tissue, excepting epithelial formations. This cell is the so-called *connective tissue corpuscle*, or cell of the connective tissue, which, according to Virchow, is a cell with all its essential constituents (cell-wall, cell contents, and nucleus), and not a nucleus alone, as originally described by Schwann, and later by Henle* and Landois.† From the well-known universal prevalence of connective tissue, this view receives support. Thus, it is from the connective tissue corpuscles of the soft, silk-like connective tissue, so universally present in muscle, that the muscular fasciculi are primarily developed. It is from these that nerve-

FIG. 13.

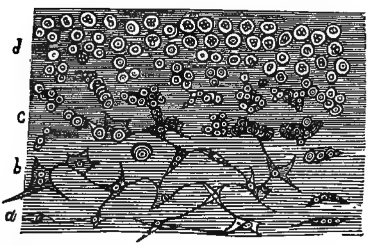


FIG. 14.

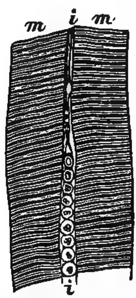


Fig. 13. Purulent granulation from the subcutaneous tissue of a rabbit, round about a ligature. *a*, Connective tissue corpuscles. *b*, Enlargement of the corpuscles with division of the nuclei. *c*, Division of the cells (granulations). *d*, Development of the pus-corpuscles. ×300. (From Virchow.)

FIG. 14. Interstitial purulent inflammation of muscle in a puerperal woman. *m m*, Primitive muscular fibres. *i i*, Development of pus-corpuscles by means of the proliferation of the corpuscles of the interstitial connective tissue. ×280. (From Virchow.)

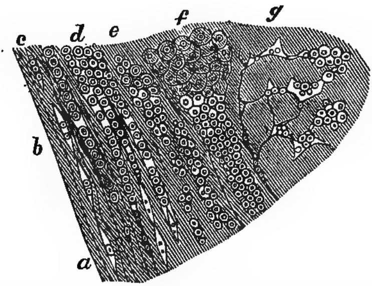
fibres take their origin. It is by the rapid proliferation of these corpuscles that pus is formed (Figs. 13 and 14); it is from the perverted growth and de-

* Henle, Bericht über die Fortschritte d. Physiol., 1859; 1866, p. 41.

† Landois, Zeits. f. wiss. Zool., Bd. xvi, p. 1.

velopment of these that tubercle and cancer arise (Fig. 15), and similarly all pathological new formations. None of these products are exudations from

FIG. 15.



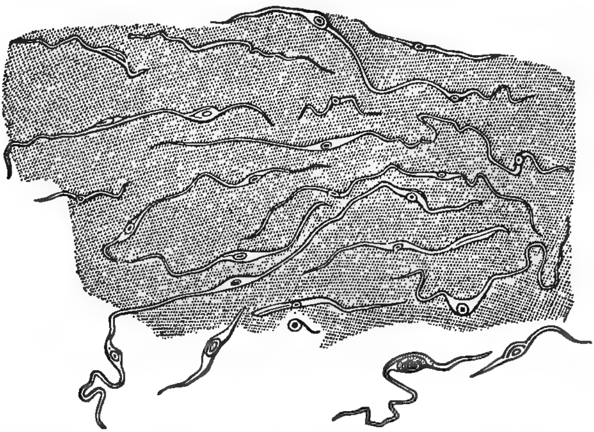
Development of cancer from connective tissue in carcinoma of the breast. *a*, Connective tissue corpuscles. *b*, Division of the nuclei. *c*, Division of the cells. *d*, Accumulation of the cells in rows. *e*, Enlargement of the young cells and formation of the groups of cells (foci, Zellenheerde), which fill the alveoli of cancer. *f*, Further enlargement of cells and groups. *g*, The same development seen in transverse section. (From Virchow.)

the blood, according to Virchow. They are entirely local in their origin. In these views he is supported by the majority of German observers.

Another mode of formation of pus is however admitted by Virchow, in the growth and development of new cells in *epithelium*, whether in cuticle or mucous membranes. Whether forms of suppuration exist which may be referred to muscular, nervous, and capillary elements, he considers doubtful.

A *fourth* and final distinctive feature of Virchow's views, concerning which there is less unanimity, even among German histologists, is his peculiar system of canals or tubes, produced by the anastomosis of one cell with another, and which he considers must be classed with the great canalicular system of the body, as forming a supplement to the blood and lymphatic vessels, and as filling up the vacancy left by the old vasa serosa, which do not exist.* (See Fig. 16.) Of

FIG. 16.



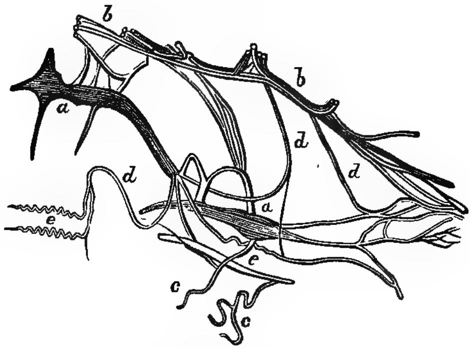
Connective tissue from the embryo of a pig after long-continued boiling. Large spindle-shaped cells, connective tissue corpuscles (Bindegewebeskörperchen), some isolated and some still imbedded in their basis substance, and anastomosing one with the other. Large nuclei with their membrane detached; cell contents in some cases shrunken. ×350. (From Virchow.)

this system he also considers the cordlike fibres of yellow elastic tissue as forming a part.† These he considers, with Donders,‡ as originating by a trans-

* Virchow, op. citat., p. 76.
† Virchow, op. citat., p. 133, a. f.
‡ Donders, Siebold und Kölliker's Zeitschrift, Bd. iii.

formation of the connective tissue corpuscles themselves. He says, "The transformation of these latter into the former, can gradually be traced with such distinctness, that there remains no doubt, that even the coarser elastic fibres directly result from a chemical change and condensation of the walls themselves.* Where originally there lay a cell, provided with a delicate membrane and elongated processes, there we see the membrane gradually increasing in

Fig. 17.



Elastic networks and fibres from the subcutaneous tissue of the abdomen of a woman. *a a*, Large elastic bodies (cell bodies), with numerous anastomosing processes. *b b*, Dense elastic bands of fibres on the border of larger meshes. *c c*, Moderately thick fibres spirally coiled up at the end. *d d*, Finer elastic fibres, at *e* with more minute spiral coils. ×300. (From Virchow.)

thickness and refracting the light more strongly, whilst the proper cell contents continually decrease and finally disappear.

"The whole structure becomes in this way more

* Virchow, op. citat., p. 133.

homogeneous, and to a certain extent sclerotic, and acquires an incredible power of resisting the influence of reagents, so that it is only after long-continued action that even the strongest caustic substances are able to destroy it, whilst it completely resists the caustic alkalies and acids in the degree of concentration usually employed in microscopical investigation. The farther this change advances, the more does the elasticity of the parts increase, and in sections we usually find these fibres, not straight or elongated, but tortuous, curled up, spirally coiled, or forming little zigzags (Fig. 17, *c*, *e*). These are the elements which by virtue of their great elasticity, cause retraction in those parts in which they are found in considerable quantity, as, for example, in the arteries. The fine elastic fibres, which are those which possess the greatest extensibility, are usually distinguished from the broader ones, which certainly do not present themselves in tortuous forms. As regards their origin, however, there seems to be no difference between the two kinds: both are derived from the connective tissue cells, and their subsequent arrangement is only a reproduction of the original plan. In the place of a tissue consisting of a basis substance and anastomosing reticulated cells, there afterward arises a tissue with its basis substance mapped out by long elastic networks with extremely compact and tough fibres." This may be looked upon as the least well determined of the important points of Virchow's doctrine, though most German histologists also favor it. Among these may be classed Kölliker,* C. O. Weber,† Leydig,‡ Friedreich,§ His,‖ Donders,¶ Wittich,** Böttcher,†† Billroth,‡‡ and Stricker. They are opposed by Schwann, Reichert, and Henle, and find little favor among English and American histologists.

A part of this system, also, according to Virchow, are the so-called dentinal tubules, the lacunæ and canaliculi of bone, even the continuity traced by Gerlach,§§ between the ciliated cells of the aqueduct of Fallopius; that by Heidenhain‖‖ and Brücke¶¶ between the lacteals and cylinder epithelium of the intestinal villi of the rabbit, by means of corpuscles of connective tissue; in the epithelium of the endocardium by Luschka;*** and the results of similar

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* Kölliker, Manual of Human Microscopic Anatomy, p. 41, 1860. Also recent paper, in which he completely assents to Virchow's views, according to N. Y. Quart. J. Pschy. Med., July, 1869.

† Weber, C. O., Virchow's Archiv, Bnd. xiii–xv.

‡ Leydig, Handbuch der Histologie, 1856.

§ Friedreich, Virchow's Archiv, Bd. xv.

‖ His, Beiträge zur Normalen und Pathol. Histol. d. Cornea. Basel, 1856.

¶ Donders, loc. citat.

** Wittich, Virchow's Archiv, Bd. ix.

†† Böttcher, Virchow's Archiv, Bd. xiii.

‡‡ Billroth, in Beiträge zur Pathol. Histol., 1858, admits all but the tubular nature of the processes.

§§ Gerlach, Mikrosk. Studien, 1858.

‖‖ Heidenhain, Moleschott's Untersuchungen, Bd. iv, 1858, p. 251.

¶¶ Brücke, Moleschott's Untersuchungen, Bd. viii, 1862, p. 495.

*** Luschka, Virchow's Archiv, Bd. ix, p. 569.

observations by Eckhart,* Billroth,† and Friedreich.‡

The other fibrous element of areolar or connective tissue, which forms the mass of its bulk, the *pure white fibrous* or waving, does not, according to Virchow, have its origin in cells, but is a modification of a previously homogeneous intercellular substance, deposited between the cells; a view which in its glaring departure from the primary proposition that the cell is the starting-point, and that every tissue is composed of cells or some modification of cell forms, presents one of the few inconsistencies traceable in the theory of Virchow.

We think it proper, in a historical memoir of this kind, to refer to some severe critical remarks which appeared in the *Edinburgh Medical Journal*, of February and April, 1869, in which Prof. Virchow is accused of appropriating the observations of Prof. Goodsir as his own. That there are points in common, it will be recollected, and, also, that these are 1st, the invariable origin of cells from previously existing cells, and 2d, the division of the tissues into cell territories. Now on the one hand we deem that the dedication of Virchow's volume to Prof. Goodsir is as handsome an accredit as could possibly be given for whatever of common there may be in the writings of the two authors, and on the other hand we have seen that Martin Barry is acknowledged even by

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* Eckhart, Beiträge Anat. und Physiol., 1855.

† Billroth, Müller's Archiv, 1858.

‡ Friedreich, loc. citat., p. 538.

Goodsir, to be the author of the "first consistent account of the development of cells from a parent centre." The idea of *cell territories* seems, however, to have originated with Goodsir, nor do we believe, for the reason stated, that Virchow intended to usurp his prerogative. The merit of Virchow consists in his application by actual demonstration of the first of these points to so large a variety of physiological and pathological processes, to which is added original conception in the prominence given to the connective tissue corpuscle and the canalicular system, whatever may be the truth with regard to either.

SARCODE OF DUJARDIN—PROTOPLASM OF MAX SCHULTZE. 1835–61.

Dujardin* had, in 1835, discovered in the lower animals a living, moving, contractile substance, which he called *sarcode.* The peculiar appearances of this substance attracted the attention of many observers, among whom were Kühne, Reichert, Ecker, Henle, Meyen, Huxley, Max Schultze, John Müller, and others. It was thought peculiar to the lower animals, and there was assigned to it a property of "irritability without nerves."†

The observation of Siebold,‡ that the yolk globules (vitelline spheres of the egg) of Planaria exhibit contractions and expansions, which with suitable care continue for hours, and the discoveries which fol-

* Dujardin, Ann. d. Sciences Nat., tom. iii et v.
† Schultze, Max, Organis. d. Polythalamien, 1854.
‡ Siebold, Froriep's Notizen, Nr. 380, p. 85.

lowed of similar movements and changes in form, in colorless blood-corpuscles, pigment cells, and elsewhere, led Kölliker* to express the conjecture that the contents of all cells are contractile. Virchow† attributed the ciliary movement to a contractile substance. Leydig‡ and Ecker considered the movements of the yolk spherules as phenomena of life, and Kühne§ had studied physiologically and chemically, sarcode and muscular tissue, and pointed out the similarity of the phenomena presented in the act of dying, by both. But all considered sarcode as something different from the animal cell, as a body *sui generis*.

According to Hæckel‖ the protoplasm or sarcode theory, that is, the theory that the albuminous contents of animal and vegetable cells as well as the freely moving sarcode of Rhizopoda, Myxomycetæ, etc., are identical, and that in both cases this albuminous material is the original active substratum of all vital phenomena, was brought forward in its elementary form by F. Cohn¶ in 1850, and by Unger in 1855.** Hæckel says also that it may be considered one of the greatest achievements in modern biology and one of the richest in results. It was further de-

* Kölliker, Wurzb. Verh., Bd. viii.

† Virchow, Archiv, Band v., 1853.

‡ Leydig, Handbuch der Histologie, 1856.

§ Kühne, Müll. Archiv, 1859, p. 817.

‖ Quart. J. Mic. Sc. July, 1869, p. 223.

¶ F. Cohn, Nachträge zur Naturgeschichte des protococcus pluvialis, Nova Acta Ac. Leop. Carol., vol. xxii, pars. 2, 1850, p. 605.

** Unger, Anatomie und Physiologie d. Pflanzen, 1855.

veloped by Max Schultze in 1858, and finally established by him in 1861.* He first showed the analogy between sarcode and the contents of the animal cell, and that the entire infusorial world, simple or compound, is made up of cells, thus extending the typical formative element of Schwann to the entire organized creation.

The comparison between sarcode and the protoplasm of plants on the one hand, and that of animal cells on the other, was also made by Pringsheim,† E. Brücke,‡ E. Hæckel,§ and W. Kühne,‖ and by their efforts, together with those of Max Schultze, Unger, and Cohn, our knowledge of the independent life of the cell was extended, in a very short space of time, further than in the twenty years previous.¶

The name *protoplasm* for a portion of the contents of the animal cell had already been brought into use by Remak, who extended it from the layer which bore that name in the vegetable cell to the analogous element in the animal cell.**

* Schultze, Max, Müll. Archiv, 1861, p. 17.

† Pringsheim, Untersuchungen über d. Bau. u. d. Bildung d. Pflanzenzellen, 1854.

‡ Brücke, E., Elementar-organismen, Wien. Sitzungsb., 1861.

§ Hæckel, E., Die Radiolaren, 1862.

‖ Kühne, W., Protoplasm und die Contractilitat. Lpzg., 1864.

¶ Stricker, S., Handbuch der Lehre von den Geweben des Menschen und der Thiere. Leipzig, 1868, p. 3, German Ed.

** Sterling, J. H., As regards Protoplasm in relation to Prof. Huxley's Essay on the Physical Basis of Life. Edinburgh, 1869, p. 14. Conf. also McNab, Monthly Microsc. J., No. xvii, vol. iii, 1870, p. 33.

Pringsheim had also shown, in 1854, that no such membrane as a primordial utricle existed, but that *all within* the *cellulose* wall of the living vegetable cell was *protoplasm* and cell fluid, however complex its composition.

"He admitted that in the cortical layer of the protoplasma a distinct arrangement into layers often occurred, and these he distinguished as the cutaneous and granular layers of the protoplasma, but he denied that the primordial utricle could be differentiated as a membrane from the subjacent protoplasm. If, in animal cells, partly from their relatively small size, and partly from their greater average wealth in protoplasma, it is more rarely possible to make a sharp demarcation between a cortical layer of protoplasm and a cell fluid, there nevertheless exists a difference in the constitution of the former, such that a cutaneous layer, destitute of or scantily supplied with granules, incloses the remaining more granular material. The white blood cell may serve as an example. This is, however, very different from a proper membrane."*

Unger† (1855), had been struck with the close similarity of the mobile phenomena of the Polythalamiæ with those of the processes of protoplasm stretched across the cavity of many vegetable cells. Although he had not personally investigated the former, he became convinced from Schultze's description that a resemblance amounting to identity existed

* Duffin, A. B., On Protoplasm. Quart. Jour. Mic. Sci., N. S., vol. iii, 1863, p. 252.

† Unger, op. citat., p. 280.

between their movements and the protoplasm streams of vegetable cells.*

Leydig,† in 1856, claimed for the contents of the cell a higher dignity than for the membrane or cell-wall. He claimed that a *cell was but protoplasm* (klumpchen-substanz) *inclosing a nucleus.* The cell membrane, according to him, was simply the hardened periphery of the substance of the cell.

To Max Schultze, however, as already stated, belongs the credit of having fully overturned the vesicular idea of cells. In 1861,‡ he insisted upon some modification of prevailing views, respecting the relation of cell-wall to cell contents, and contended for a higher position for that part of the cell corresponding to the protoplasm of Von Mohl (that within the so-called primordial utricle), and showed how a careful study of the phenomena presented by the pseudopodia, extended by the various Rhizopods, might aid in clearing up the life of the elements of the cell.

He also defined the cell as "*protoplasm surrounding a nucleus.*" The importance of this definition, as stated by Stricker,§ lay not so much in the fact that many cells were denied a cell-wall, as that the so-called cell contents could now be made to harmonize with the animal primordial substance or sarcode. Schultze illustrates his definition by the em-

* Duffin, A. B., loc. citat., p. 252.

† Leydig, op. citat.

‡ Schultze, Max, Ueber Muskelkörperchen, in Reichert and Dubois Reymond's Archiv, 1861.

§ Stricker, op. citat., 5. (German Ed.)

bryo cells resulting from the segmentation of the ovum, as typical cells, which are thus composed of protoplasm surrounding a nucleus, which nucleus, as well as protoplasm, are products of like constituent parts of another similar cell. "The cell leads in itself an independent life, of which the protoplasm is especially the seat, although to the nucleus also undoubtedly falls a most important, though not yet precisely determined role. Protoplasm is for the most part no further distinct than that it will not commingle with the surrounding medium, and in the peculiarity that with the nucleus it forms a unit. Upon the surface of the protoplasm, there may form a membrane, which, *although derived from it*, *may be chemically different*, and the assertion that it *is the beginning of a retrogression* may be defended. A cell with a membrane cannot divide itself, unless the protoplasm within the membrane divides itself. A cell within a membrane chemically different from protoplasm, is like an encysted infusorium."*

Brücke† went even further in his definition, and said that it was not shown that the nucleus even is an essential element of the cell. In proof of which he adduces the cells of cryptogams and says: "We have no positive knowledge either of the origin or function of the nucleus, and, indeed, the constancy of its occurrence seems subject to certain limitations if we take into consideration the cells of cryptogams,

* Schultze, Max, Protopl. d. Rhizopoden. Leipzig, 1863.
† Brücke, E., Die Elementar-organismen, p. 18–22. 1861.

and do not start out with the belief that the nucleus is there even though we do not see it." Facts in justification of Brücke's doubt are adduced by Stricker* in the discovery by Max Schultze,† in the Adriatic Sea, of a non-nucleated amœba (Amœba porrecta), by Hæckel,‡ in the Mediterranean, of a non-nucleated protozoon (Protogenes primordialis), and by Cienkowsky§ of two non-nucleated monads, namely, Monas amyli and Protomonas amyli. Hæckel says of his Protogenes primordialis that it multiplies by division. Stricker's‖ own observations on the fecundated egg of the frog, which confirm those of Von Baer, incline him to adopt the view of Brücke, and to omit the nucleus in a theory of elementary organization.¶

Such is the history of and such the properties of the substance known as "protoplasm." But of late

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* Stricker, op. citat., p. 6. (German Ed.)

† Schultze, Max, Organis. d. Polythalam. 1854.

‡ Hæckel, Zeitschr. f. w. Zoolog., 1865, Bd. xv.

§ Cienkowsky, Max Schultze's Archiv, 1865.

‖ Stricker, op. citat., New Sydenham Society's Translation, vol. i, p. 8, London, 1870. See also Stricker's paper On the Development of the Simple Tissues, in vol. iii, London, 1873.

¶ Hæckel[1] also considers that by no phenomena is the correctness of the "protoplasm theory" so thoroughly proved, and at the same time in so simple and unassailable a manner, as by the vital phenomena of the Monera, by the processes of their nourishment and reproduction, sensitiveness and motion, which entirely proceed from one and the same very simple substance, a true "primitive slime."

[1] Hæckel, Ernst, Monograph on the Monera, and Remarks on the Protoplasm Theory. Q. Jour. Mic. Sci., N. S. vol. ix, 1869.

years another meaning has been given to the term, an anatomical one, in which the original general application has been altogether ignored, and that is *that part of the cell outside of the nucleus* without regard to the properties of the matter, corresponding to the "cell contents" in cells which have a cell-wall. Thus we speak of the protoplasm of the colorless corpuscle or the liver-cell, or of the squamous epithelial cell, whereas the properties of the substance thus named are vastly different. In the former two instances living growing matter is meant, in the latter dead formless material, incapable of growth and reproduction through its own inherent properties. These differences should be always remembered.

With these general considerations in the history of "protoplasm," we are the better prepared to take up the theory of

DR. BEALE, 1861.

In April and May, 1861, Prof. Lionel S. Beale delivered the lectures before the Royal College of Physicians of London, in which he promulgated the views which have since been further elaborated and become permanently associated with his name. These views were published in part, in Beale's "Archives of Medicine," and in September, 1861, in a volume "On the Structure of the Simple Tissues of the Human Body," in the preface to which he says, "he thinks it right to state that the conclusions which have now assumed a definite form have gradually grown upon him during the course of observations extending over a period of several years. In fact some of the drawings in this volume, and others which have been published elsewhere, equally favorable to this view, were made long before any specific theory had been arrived at."

The "*cell*," or "*elementary part*," as Dr. Beale prefers to call it, is composed of matter in two states, matter which is *forming*, and matter which *is formed*; matter which has the power of *growing* by producing matter like itself *out of pabulum* or food, and matter which possesses no such power, but results from the death of the forming matter. The former is known as *germinal* or *living* matter, the latter as *formed* matter. The former, in varying quantity in different cells, is *central* in its situation (see frontispiece, Fig. 17), and includes what has been called by others nucleus, cell contents, protoplasm, endoplast. The latter, also present in different quantity in different cells, is *peripheral* (frontispiece, Fig. 17), and includes what is known as cell-wall, periplast, intercellular substance, and products of secretion.

In its structural characters, germinal matter is *soft*, *transparent*, *colorless*, and as far as can be determined by the highest powers, *structureless*, being visible only through its difference in refracting power as compared with the menstruum in which it floats, or by the granular matter it may entangle; and these characters are the same at every period of its existence. In the simplest vegetables they may be studied, in the thallus of the sugar fungus, among the lowest animals, in the amœba (frontispiece, Fig. 16), and in higher animals in the mucus-, pus-, or white blood-corpuscles (frontispiece, Fig. 10), all of which are composed almost purely of germinal matter; the very thin periphery of formed material being scarcely appreciable or distinguishable from the diffraction band.

In its *endowments* and *properties*, germinal matter is *acting*, *living*, *growing*, and *moving*, through some inherent power of its own. It alone, as stated, is capable of producing material like itself out of pabulum, and of multiplying by division, or dropping off of a portion of itself, which portion immediately assumes an independent existence, and grows, maintains, and reproduces itself like the parent germinal matter. It is also capable of being stained by an ammoniacal solution of carmine, and the younger it is, or more recently formed, the deeper is the stain it assumes. And since the latest formed always appears in the centre of the mass, successive tints, or zones of color, will often be produced in the staining process, growing deeper from without inward, as seen in Fig. 17 of the frontispiece.

It has been stated that what is called nucleus by Virchow and others, is included in germinal matter. This is true, though the nucleus is not always the whole of the germinal matter. There may be other older germinal matter beyond the nucleus, on its way to conversion into formed material, but still germinal matter, which assumes a tint with carmine, but not so deep as the nucleus. Thus, the entire mass of the pus-corpuscle (frontispiece, Fig. 10), except, perhaps, its extreme periphery, is germinal matter, yet there is within this another younger portion of germinal matter, taking a deeper tint with carmine, but which alone of the elements of this cell we are in the habit of calling "nucleus." The "*nucleus*," then, is nothing but a *new centre* of germinal matter, and the "*nucleolus*" is a younger centre. And there may even be within this a still younger portion of living matter, taking even a deeper stain, which might be called a "*nucleoleolus*." By this staining process may we distinguish the nucleolus from a minute oil-drop often mistaken for it, and which will not admit of being stained.

On the other hand, germinal matter in a comparatively quiescent state is often quite destitute of nuclei. But let the mass be freely supplied with nutrient matter, and nuclei and nucleoli rapidly make their appearance.

So with regard to the "cell contents" over and above the nucleus, although they may all be germinal matter, yet this is not necessarily the case. Thus in the white blood-corpuscle and mucus-corpuscles, what Virchow would consider cell contents is all germinal matter; but the superficial epithelial cell lining the interior of the mouth has its nucleus alone composed of germinal matter, and much that has been described as cell contents is really formed matter. (Figs. 5 and 6 of frontispiece.) More nearly does the germinal matter of Beale* correspond with the "protoplasm" of Max Schultze, with which, indeed, it seems identical, except that the latter observer seems somewhat at a loss how to dispose of the nucleus, of

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* Beale, Protoplasm; or, Life, Force, and Matter. London, 1870, p. 38.

which he does not speak as a new or young centre of protoplasm.

Formed material, instead of being *active*, so far as the vital acts described as characteristic of germinal matter are concerned, is *passive*, *non-acting*, *dead*, and can only increase at the expense and death of the germinal matter, on the periphery of which it is formed. It differs widely in its appearance, and is often "structured" as in muscle and nerve, but not necessarily so, as is seen in the intercellular substance of hyaline cartilage. It possesses also certain properties, different in different situations, and widely different also from those of germinal matter. Thus it is contractile in the sarcous tissue of muscle, exhibits neurility in the nerve, is protective in epithelium, is diffluent as the formed material of the milk-cell (milk), and in the formed material of the liver-cell (bile). Again, it is hard and elastic in the intercellular substance of cartilage and epidermis, horn and nails. It does not become stained on being soaked in weak solution of carmine in ammonia, and if by reason of the strength of the solution it should happen to be stained, the color will wash out on soaking in glycerin, which is not the case with the coloring of the germinal matter.

The cause of this permanent staining of the germinal matter by an ammoniacal solution of carmine, is thought by Dr. Beale to be due to an acid reaction of this matter, in consequence of which the carmine is precipitated from its alkaline solution. This view would seem to be confirmed by the researches of Ranke on the *Reaction of the Tissues*.

The *size* of the elementary part, as thus composed, is extremely various. The smallest particles of germinal matter, measured by Dr. Beale, are less than $\frac{1}{100000}$ of an inch in diameter, and would not be called cells in the ordinary sense of the word, yet they are functionally such; that is, they grow, multiply by division, and under appropriate circumstances assume the characters of fully formed cells. On the other hand, the largest epithelial cells, including their germinal matter and formed material, are often as large as the $\frac{1}{250}$ of an inch in diameter, or larger; cells of morbid growths are sometimes $\frac{1}{200}$, while the human ovum, which is a typical cell, varies from the $\frac{1}{240}$ to $\frac{1}{120}$ of an inch. Pure germinal matter is rarely seen in masses as large as the $\frac{1}{500}$ of an inch in diameter, without breaking up into smaller particles of germinal matter, and as constituting the nuclei of fully formed cells, is usually from $\frac{1}{6000}$ to $\frac{1}{3000}$ of an inch in diameter.

The *method of production of formed material* is best studied in the epithelial structures, particularly in the epithelium lining mucous cavities, of which sections may be easily made down to the vessels whence their nourishment is obtained. In the deep layers, next the nutrient surface, the cells will be found to consist of almost pure germinal matter (frontispiece, Fig. 1), imbedded in a soft, mucus-like, yet continuous formed matter. These masses of germinal matter divide and subdivide, pushing the older masses towards the surface, to make up for those which are constantly exfoliated. While this is going on, however, the germinal matter keeps increasing in size until the cells arrive half way towards the surface, by absorption of nutrient pabulum, which has to diffuse itself through any formed material already existing. At the same time, a portion of the germinal matter is being converted into formed material, which accumulates on its surface, within that already formed, stretching it, and becoming more or less incorporated with it. *Thus, both constituents of the cell increase up to a certain point, the cells constantly growing in consequence.* As new cells are, however, produced from below, the older ones are removed farther and farther away, the formed matter becoming more and more impervious to nutrient pabulum. At length a point is attained when the entire cell ceases to increase in size, since no pabulum reaches the masses of germinal matter, though the latter is still being converted into formed material. Hence, the masses of germinal matter actually grow smaller as the cell increases in age; and when the periphery is reached, there remains but a small nucleus of germinal matter, with a large quantity of formed material. Thus, we are enabled to judge of the age of the cell by the relative quantity of germinal matter and formed material; if the former be large, and the latter small, the cell is young, whereas, if the opposite relation exists, the cell is old and almost ready to exfoliate. But exfoliation in health probably does not take place until the last particle of germinal matter dies, and the entire cell becomes a mass of passive, lifeless, formed material.

The production of formed material from germinal matter may also be studied in the conversion of the white blood-corpuscle into the red. In the spring of the year many white corpuscles can be found in the blood of the frog and newt, undergoing conversion into formed material at their edges, where the usual granular appearance is being substituted by the smooth and slightly colored. This goes on until all except the nucleus is thus converted. In mammalia this change goes on until the whole white corpuscle is thus converted into the red.

Secondary Formed Material.—There are certain kinds of formed material to which this term is applied by Dr. Beale. These are the oil of the fat-cell or vesicle and the starch-granule of the vegetable cell. It results, as does all formed material, by a conversion of the germinal matter into this special form. The young fat-cell, as all young cells, is almost pure germinal matter; as it grows older, however, and is exposed to oxidizing influences, the conversion of germinal matter takes place, partly into the cell-wall proper of the fat-vesicle, and partly into the secondary formed material or oil, until finally it becomes a mere dot on the inner surface of the cell-wall, or disappears altogether.

The increase of cells, according to Beale, takes place in several ways; *every cell coming from a pre-existing cell*, but the germinal matter is always the portion in which it originates.

There is not generally a symmetrical division of the nucleus into two, and these into four, as is so often described, and as is often seen in the vegetable cell, but there is rather a budding, and subsequent dropping off of the portions of germinal matter which is to produce the new cell, and which almost always assumes the spherical form when allowed to float freely. (See Figure 10 of frontispiece.) The formed material is never active, according to Beale, but entirely passive in the process of cell multiplication.

Nutrition of Cells.—So, too, in the nutrition of the cell, the germinal matter is the sole active agent. The formed material may act as a filter to the nutrient matter, but is quite passive. The pabulum, which is coursing through the bloodvessels, becomes converted into germinal matter, which in turn becomes formed material, and so long as this is kept up, the cell continues to grow. The course taken by the pabulum, and the order of conversion, is shown by the arrows, in Figure 17, of frontispiece, and will be readily understood by reference to the explanation. Occasionally, and especially in disease, the formed material may become the pabulum for rapidly multiplying cells, and thus be consumed.

Intercellular substance has already been spoken of as formed material. We have it most strikingly present in the white fibrous tissue, or tissue of tendons, and in hyaline cartilage. If the former be stained by carmine, and examined in thin section under the microscope, it will be found composed of beautiful bands of gently waving fibrous tissue, or tissue exhibiting a fibrous appearance, at varying intervals in which are noted nuclear masses of germinal matter, which have assumed the tint of carmine. Or, if dilute acetic acid be added to the specimen, the fibrous appearance will at once become homogeneous, while the nuclei will be rendered distinct, and clearly visible. In young tendon (frontispiece, Fig. 11), the masses of germinal matter will be found very abundant, and the intercellular fibrous substance in smaller quantity than in old tendon where the masses of germinal matter occur only at long intervals. These masses of germinal matter, or connective tissue corpuscles, it will be recollected, are considered by Virchow as perfect cells, presenting cell-wall, cell contents, and nucleus, and the fibrous intercellular substance as a subsequent modification of a homogeneous matrix, deposited between the cells by the bloodvessels. These connective tissue corpuscles are regarded by Beale as simple masses of germinal matter, the conversion of which into formed material produces the fibrous intercellular substance, as seen in Fig. 11, frontispiece, and between which and the intercellular substance immediately adjoining, there is no line of separation, constituting a cell-wall.

As the tendon grows older, the masses of germinal matter become less abundant, because a larger number have been totally converted into formed material; and the bands of indestructible material which sometimes join them, and which are considered by Virchow as a part of his canalicular system, are, according to Beale, *nothing but imperfectly converted formed material*, or rather germinal matter, which has not been converted. While the twisted and curling cord-like fibres of the so-called *yellow elastic tissue*, also considered by Virchow as a part of his canalicular system, are thought by Beale to be composed in part of true yellow elastic tissue, such as is found in the ligamentum nuchæ, and likewise formed from nuclei (frontispiece, Fig. 14), but in part also of the remains of nerves and vessels, which were active at an earlier period of life.*

So, also, with *hyaline cartilage*. According to Beale, the intercellular substance of cartilage results from the conversion of the so-called cartilage-corpuscles or cells into formed material, and here also the germinal matter is directly continuous with the matrix, no proper cell-wall intervening.

Cartilage is not to be considered as a distinct class of tissue from epithelium, nor can the latter, in all cases, be distinguished from cartilage by the existence of separate cells, since in many forms of epithelium, at an early period of existence, the formed material corresponding to the masses of germinal matter is continuous throughout, and presents no indication of division into cells.† A "cell," or "elementary part," then, of fully formed tendon or cartilage, would consist of a portion of germinal matter, with a proportion of formed material about it, extending to a line midway between that mass of germinal matter and the masses immediately adjacent, of which the cartilage or tendon is composed; and such a line would correspond to the outer part of the surface of an epithelial cell.‡ In very young cartilages, as in very young epithelium, the cells consist

* Beale, On the Structure and Growth of the Tissues, and on Life. London, 1865, pp. 95, 96, and 101.

† Beale, Protoplasm; or, Life, Force, and Matter. London, 1870, p. 51.

‡ Beale, Protoplasm, pp. 51–2.

of germinal matter only, with a small quantity of soft formed material intervening; and to understand the true relation of the cells to the intercellular substance, the tissue should be studied at different periods of its growth.

So, too, a "cell" or elementary part of muscle or nerve, would consist of a mass of germinal matter (the so-called nucleus), with a portion of muscular or nervous tissue corresponding with it, and with which it is uninterruptedly continuous.

In the formation of the *contractile tissue or muscle*, the germinal matter seems to move onward, undergoing conversion at its posterior part, into the muscular tissue, while it maintains itself by absorbing and converting pabulum. This will be understood by reference to Fig. 13, of frontispiece. The fibres of *yellow elastic tissue* are formed in precisely the same manner. (See frontispiece, Fig. 14.) *Nerve fibres*, which in their completed state consist almost wholly of formed material, are similarly produced. In the young state, the fibre is composed of masses of germinal matter, linearly arranged, and in close proximity. As the conversion takes place and the fibre is produced, these become more widely separated, and the *tissue* resulting from such conversion is nerve (frontispiece, Fig. 15).

The "Cell" or "Elementary Part" in Disease.

Here, as in normal nutrition, the germinal matter is alone active. It is impossible to state precisely every instance, but it is probable that in the majority of cases of disease, the morbid state consists essentially in a modification of the healthy nutrition of the cell, that is, the cell is made to grow more or less rapidly, or is perverted in its mode of growth, though it is likely that within certain limits, the conditions under which cells ordinarily live may be modified without deviation from health. But in *inflammatory* processes attended by local products, as *pus* or *lymph*, and in the production of *tubercle* and *cancer* we see the results of excessive multiplication and perversion of germinal matter consequent upon the appropriation of an *excess of nutrient pabulum*. In other instances, as *cirrhosis*, where there is shrinking, and hardening, and wasting, we see the effects of a diminished supply of pabulum, either through a diminution in the quantity supplied, or an impermeability in the septum through which it is compelled to pass.

An increased supply of pabulum may be admitted to germinal matter, either in consequence of the removal of barriers through which it is ordinarily compelled to pass, or in consequence of the nature of the fluids by which it is bathed. A simple illustration is seen in suppuration in epithelium, or the germinal matter of any tissue; for, according to Beale, suppuration and morbid processes generally, are not restricted to any one kind of germinal matter, as the connective tissue corpuscle, but may occur in all germinal matter to which the conditions are supplied. Using epithelium by way of illustration, as the result of the increased supply of pabulum, the germinal matter first grows, as seen in the frontispiece, Figs. 7 and 8, then in the luxuriance of its growth, even at the expense of the formed matter, sends out buds or processes, which soon drop off and become separate pus-corpuscles. (Figs. 9 and 10.) These are produced so rapidly that there is not time for formed material to form upon their surface in any quantity, and they have not time, therefore, to pass on into epithelium. Hence pus-corpuscles are almost pure germinal matter. So soon as the process ceases, in consequence of the supply of pabulum being diminished, the germinal matter multiplies less rapidly; opportunity is permitted for the production of formed material on its periphery, and the cell now passes through the different grades of epithelium, as described on pages 88, 89, and 90. The pus-corpuscles are analogous to the deepest layers of epithelial cells there referred to, which deep cells are in fact the "mucus-corpuscles," so-called, well known to be morphologically identical with pus-corpuscles; the former being simply the young epithelial cell on its way to become perfect epithelium, while the latter is the same also, though never allowed to pass into the perfectly formed state.

Again, in *pneumonia*, and here we note where the paths of Virchow and Beale separate more widely, the so-called "exudation," or product which fills up the vesicular portion of the lung, is regarded by Beale as the result of a proliferation of *minute particles of germinal matter* (very much smaller than white blood-corpuscles), which have passed out through the capillary walls with the liquor sanguinis.

In all inflammatory processes and fevers, this is believed by Dr. Beale to take place to a greater or less extent, the little masses of germinal matter or nuclei in the capillary walls also taking part, often increasing in size to such degree that they materially obstruct the passage of the blood, and by dropping off portions give rise to bodies floating in the blood precisely similar to white blood-corpuscles, or pus-corpuscles; indeed, Dr. Beale considers that this may be one of the sources of origin of the white blood-corpuscle.*

So, also, *tubercle* is believed by Dr. Beale to result either from the multiplication of masses of germinal matter which have passed through the capillary walls from the blood, or from the masses of germinal matter usually termed nuclei, in connection with the capillary walls. He says, in illustration: "In a case of tubercle, which was very rapidly developed upon the surface of the pia mater, in a man of tubercular constitution, I proved most distinctly that the tubercles were connected with the vascular walls, and that if the nuclei had not given origin to them, they were certainly implicated. My own opinion is, that these nuclei gave origin to the tubercle-corpuscles, in consequence of receiving from the blood peculiar nutrient matter. In the lung I have seen appearances which point to a similar conclusion."† Would not these views arise from appearances pre-

* Beale, Microscope in Clinical Medicine, third ed. London, 1867, p. 166.

† Microscope in Clinical Medicine, third ed., 1867, p. 205.

cisely analogous to those represented as giving support to the view, that tubercle originates in the perivascular sheaths of bloodvessels? The views of Beale, H. Charlton Bastian,* and Cornil,† would then constitute simply different modes of expression of the same truths.

ROBIN,‡ 1867.

Robin, who may be considered the mouthpiece of the French school of histologists, reduces the human body to elementary parts, usually microscopic, which he calls *anatomical elements.* The forms he makes threefold,—*fibres*, *tubes*, and *cells*.

The *fibres* are generally of considerable length, sometimes extending from the lower part of the spinal cord to the extremity of the foot. Their diameter is, however, small, often not exceeding .001 millimeter, or .00003987 of an inch.

The *tubes* offer as objects of study the walls and the cavity.

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* Bastian, H. C., Tuberc. Meningitis, Edinb. Med Jour., 1867, p. 875.

† Cornil, Tubercle in Connection with the Vessels, Archiv. de Phys. Norm. et Path., Jan. et Fev., 1868.

‡ Our information with regard to M. Robin's views, is derived from an admirable exposition of them published in vol. iv, 1867, of the New York Medical Journal, by Dr. William T. Lusk, who there states that he has them mainly from a course of familiar and private instruction, furnished to him by M. C. H. Georges Pouchet, assistant to M. Robin, Lecturer upon Anatomy and Histology to the Ecole Pratique, author of "Un Précis d'Histologie," etc., and son of the eminent physiologist, Prof. F. A. Pouchet; so that they may be said to be the views also of the elder Pouchet.

The *cells* of *vegetables* have a wall, a cavity, and contents (air, oil, etc.). The *cells* of *animals*, on the contrary, are, as a rule, homogeneous. Animal cells containing a cavity are only found exceptionally. The substance of cells is ordinarily granular. Most cells contain an ovoid nucleus more granular than the substance itself.

In all cells the nuclei afford different chemical reactions from those of the substance of the element. Each cell is an independent organism, passing through various stages of development, from birth to death.

The birth (origin) of the elements takes place by 1st, segmentation; 2d, genesis; 3d, epigenesis; 4th, germination.

1st. *Segmentation.*—The human ovum is a small hollow sphere, containing in its interior the vitellus or yolk, which consists of granular matter in a hyaline substance. At the end of a certain time *particles of the granular matter approximate, unite, and form a nucleus in the vitellus.* Next, the nucleus elongates, takes an hour-glass form (biscuit), then divides. The division of the yolk occurs simultaneously. In the same way, the division takes place into 4, 8, 16, and more parts. These divisions of the vitellus have received the name vitelline globules. Their mode of formation is called segmentation.

2d. *Genesis.*—When the vitelline globes have become very small by successive segmentation (diameter .008 millimeter, .00031396 of an inch), these little bodies take the name of *embryonic cells.*

According to M. Robin, these cells dissolve. From the fusion results a blastema, in the midst of which nuclei make their appearance. This is known as *genesis.* It is the second and most frequent mode of the formation of anatomical elements. It is characterized by the appearance of an anatomical element in a fluid termed blastema, in which the element did not previously exist.

3d. *Epigenesis.*—When the embryonic cells dissolve, the embryo-plastic nuclei are produced by *genesis* in the blastema which results from their fusion. Then little cone-like prolongations of transparent matter are observed at the extremities of the nuclei, giving rise to the *fusiform* bodies, which are the *connective tissue corpuscles.* This mode of formation by growth upon another element is known as *epigenesis*, and is the mode in which connective tissue is developed. The prolongations of these fusiform bodies constitute the non-elastic fibres or white fibrous tissue element of connective tissue. Sometimes the substance deposited by epigenesis upon the nucleus has several prolongations, forming a *stellate cell* or connective tissue corpuscle. These fusiform and stellate cells are likewise known as *embryo-plastic* or *fibro-plastic bodies*, and this latter term is a most common one in French histology.

The *elastic fibres* of connective tissue are likewise formed by epigenesis, but upon special nuclei, and the prolongations are insoluble in acetic acid.

There is an early period of fœtal life, previous to the formation of connective tissue, in which we find only embryo-plastic nuclei and fusiform bodies in amorphous matter. This is called embryo-plastic tissue. Growth at this epoch is most rapid, the fœtus reaching in a short space of time the dimension of .030 millimeter (.0118 of an inch).

4th. *Germination.*—This is very frequent in vegetables, but in animals only one example is known, viz., at a period previous to the fecundation of the ovum. Before segmentation takes place the vitellus is observed to retract. The hyaline substance pushes out a prolongation, which becomes round, separates, and constitutes an independent anatomical element exterior to the vitellus, and bearing no part in the future development of the ovum.

The following account of certain special elements illustrates and further explains the views of M. Robin. *Red blood-globules* (hematies), diameter, .007 millimeter ($\frac{1}{3500}$ of an inch); thickness .002 millimeter ($\frac{1}{12752}$ of an inch). Blood-globules are elastic,—a property enabling them to elongate, and pass through capillaries which have a calibre less than the diameter of the blood-globule. They are homogeneous throughout—i. e., *have no cell-wall. Blood-globules are formed by genesis in the blood plasma.* In the fœtus they make their appearance before the white blood-globules (leucocytes). In man there are two kinds of red blood-globules, viz.: first, embryonic; second, normal. The *embryonic* blood-globules are double the size of the normal ones. They have a slightly granular nucleus, situated nearly in the centre, which is insoluble in acetic acid. The *normal* blood-globules are not a transformation of the embryonic. They appear by genesis in the midst of the blastema of the blood. After the fourth month, the embryonic globules cease to form, and as the mass of the blood increases, the proportionate number diminishes with great rapidity.

Leucocytes, or white blood-globules, are found in many tissues, in the blood, on the surface of mucous membranes; *in a word.they are the pus-corpuscles.* In form, they are round, with pale, well-defined borders, and contain extremely fine gray granules. They possess a very thin envelope, and a granular cell contents. The normal diameter is .008 millimeter ($\frac{1}{3000}$ of an inch). On the addition of water, the leucocytes swell, the granular particles are agitated by a peculiar movement (first observed by Brown), and finally, *a considerable number of these particles unite, so as to form two or three little masses, that have been mistaken for nuclei.* Upon the addition of acetic acid the same reaction follows, but with greater rapidity.

The mode of production may be followed, step by step, upon the surface of wounds, especially little ones. At first a hyaline liquid appears. At the end of a couple of hours, this liquid becomes finely granular, and then all at once, in the midst of the granulations, we perceive small granular bodies analogous to leucocytes, offering the same chemical reactions, but measuring only .003 millimeter (.000118 of an inch) in diameter. They are, in fact, leucocytes of young growth. When leucocytes are retained in the economy, as in shut sacs, they increase in size, and reach a diameter of .012 millimeter ($\frac{1}{2500}$ of an inch). Then they fill with fat-granules, and are known as *corpuscles of inflammation* (exudation corpuscles, compound granule-cells). Finally the substance and investing membrane of the leucocytes disappear, the granules dissolve and are reabsorbed.

Capillaries.—The finest capillaries are anatomical elements of tubular form, with transparent resistant walls which measure .001 mm. (.00003937 of an inch) in diameter. These walls contain granular ovoid nuclei, which project, sometimes exteriorly, sometimes upon the inner surface of the tubes. These nuclei measure .006 mm. (.00023622 of an inch) in the transverse, and .008 mm. (.00031596 of an inch) in the long diameter. Their long axis is parallel to that of the vessel. The finest capillaries have a diameter of .007 mm. (.0003756 of an inch), leaving a calibre (after deducting the walls) of .005 mm. (.00019685 of an inch), or .002 mm. (.00007874 of an inch) less than the average diameter of the blood-globules which traverse them.

They are formed as follows: 1st. In new tissues, hollow projections push out from contiguous capillaries, which meet and unite together. 2d. A solid filament forms, in which nuclei make their appearance. Subsequently, the filament becomes hollow, and its nuclei remain the nuclei of the capillary.

A single perusal of these views as thus illustrated, will convince the reader that *spontaneous formation* is the prevailing mode of origin of the elements of tissues, according to the French school. Such perusal cannot fail to convince the reader also of the accuracy of description of the fully formed elements described by Robin.

PROF. HUXLEY,* 1869.

There is one kind of matter which is common to all living beings, and that matter is "*protoplasm*," the scientific name for "the physical basis of life." In illustration from vegetable life, each stinging needle or hair of the common nettle consists of a very delicate outer case of wood, closely applied to the inner surface of which is a layer of semifluid matter, full of innumerable granules of extreme minuteness. *This semifluid lining is protoplasm*, which thus constitutes a kind of bag, full of a limpid fluid, and roughly corresponding in form with the interior of the hair which it fills. When viewed with a sufficiently high magnifying power, the protoplasmic layer of the nettle hair is seen to be in a condition of unceasing activity. Local contractions of the whole thickness of its substance pass slowly and gradually from point to point, and give rise to the appearance of progressive waves, just as the bending of successive stalks of wheat by a breeze produces the apparent billows in a wheat-field.

But in addition to these movements, and independently of them, the granules are driven, in relatively rapid streams, through channels in the protoplasm which seem to have a considerable amount of persistence. The currents in adjacent parts commonly take similar directions, coursing in a general stream up one side of the hair and down the other,

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* Protoplasm; or, The Physical Basis of Life. A Lecture by Prof. Huxley, delivered in Edinburgh, November 18th, 1868.

though partial currents also exist which take different routes; so that sometimes trains of granules may be seen coursing swiftly in opposite directions, within a twenty-thousandth of an inch of each other; and occasionally opposite streams come in direct collision, and after a longer or shorter struggle one predominates. The cause of these currents seems to lie in contractions of the protoplasm which bounds the channels in which they flow, but which are so minute that the best microscopes show only their effects and not themselves.

Among the lower plants it is the rule rather than the exception, that contractility should be still more openly manifested at some periods of their existence. The protoplasm of Algæ and Fungi becomes, under many circumstances, partially or completely freed from its woody case, and exhibits movements of its whole mass, or is propelled by the contractility of one or more vibratile cilia.

In illustration of animal protoplasm, Prof. Huxley adduces the colorless corpuscles of the blood, which, under the microscope, at the temperature of the body, exhibit a marvellous activity, changing their forms with great rapidity, drawing in and thrusting out prolongations of their substance, and creeping about as if they were independent organisms. "The substance which is thus active is a mass of protoplasm, and its activity differs in detail rather than in principle from that of the protoplasm of the nettle. Under sundry circumstances the corpuscle dies, and becomes distended into a round mass, in the midst of which is seen a smaller spherical body, which existed, but was more or less hidden, in the living corpuscle, and is called its *nucleus.* Corpuscles of essentially similar structure are to be found in the skin, in the lining of the mouth, and scattered through the whole framework of the body. Nay, more, in the earliest condition of the human organism, in that state in which it has just become distinguishable from the egg in which it arises, it is nothing but an aggregation of such corpuscles, and every organ of the body was, once, no more than such an aggregation. *Thus a nucleated mass of protoplasm turns out to be what may be termed the structural unit of the human body.* As a matter of fact, the body, in its earliest state, is a mere multiple of such units; and, in its perfect condition, it is a multiple of such units, variously modified." The formula which expresses the essential structural character of the highest animal, very nearly covers all the rest, as the statement of its powers and faculties covered that of all others. "Beast and fowl, reptile and fish, mollusk, worm, and polype, are all composed of structural units of the same character, namely, masses of protoplasm with a nucleus. There are sundry very low animals, each of which, structurally, is a mere colorless blood-corpuscle, leading an independent life. But, at the very bottom of the animal scale, even this simplicity becomes simplified, and all the phenomena of life are manifested by a *particle of protoplasm without a nucleus.*

"What has been said of the animal world is no less true of plants. Imbedded in the protoplasm at the broad, or attached end of the nettle hair, there lies a spheroidal nucleus. Careful examination further proves that the whole substance of the nettle is made up of a repetition of such masses of nucleated protoplasm, each contained in a wooden case, which is modified in form, sometimes into a woody fibre, sometimes into a duct or spiral vessel, sometimes into a pollen grain, or an ovule. Traced back to its earliest state, the nettle arises as the man does, in a particle of nucleated protoplasm. And in the lowest plants, as in the lowest animals, a single mass of such protoplasm may constitute the whole plant, or the protoplasm may exist without a nucleus. Under these circumstances it may well be asked, how is one mass of non-nucleated protoplasm to be distinguished from another? why call one 'plant,' and the other 'animal?' The only reply is that, so far as form is concerned, plants and animals are not separable, and that, in many cases, it is a mere matter of convention whether we call a given organism an animal or a plant."

The researches of the chemist have also shown a like uniformity of chemical composition in "protoplasm" or living matter, proving that whatever its source, it contains carbon, hydrogen, oxygen, and nitrogen, producing in their combination a complex substance, which in our ignorance of its more exact nature, we call *proteinaceous* or *albuminoid matter*.

Further, the matter of life is composed of ordinary matter, and again resolved into ordinary matter when its work is done. Waste is constantly going on, which must be supplied by food, which is converted into protoplasm. A solution of smelling salts in water, with an infinitesimal proportion of some other saline matters, contains all the elementary bodies which enter into protoplasm, yet an animal cannot make protoplasm out of these. And this is characteristic. It must take it ready made from some other animal or some plant, the animal's highest feat of constructive chemistry being to convert dead protoplasm into the living matter of life, which is appropriate to itself. Therefore, in seeking for the origin of protoplasm, we must eventually turn to the vegetable world. The plant, however, takes carbonic acid, water, and ammonia, and converts it to the same stage of living protoplasm with itself, though some of the fungi need higher compounds to start with; and no plant can live on the uncompounded elements of protoplasm, and the absence of any one of the elements renders the plant unable to manufacture protoplasm. These elements, carbon, hydrogen, oxygen, and nitrogen, are related to the protoplasm of the plant as the protoplasm of the plant to the animal.

Thus far it is plain that the views of Prof. Huxley accord with those of many eminent histologists and physiologists, the result of whose observations have been embodied in these pages, and his descriptions will be accepted as undoubtedly accurate. More widely, in common with the school of so-called "physicists," of which he is one, does he differ in his views as *to the phenomena exhibited by protoplasm.*

According to Huxley, *protoplasm once produced*, *all the phenomena exhibited by it are simply its properties, just as the phenomena exhibited by water in its various states are properties.* They do not take place through the guidance of any principle called "vitality," any more than the phenomena of water take place by virtue of "aquosity." Prof. Huxley can discover no halting-place between the admission that protoplasm of one animal or vegetable is essentially identical with and readily converted into another, and the further concession that *all vital action* may, with equal propriety, be said to be the *result of the molecular forces of the protoplasm which displays it. The thoughts to which we give utterance are the expression of molecular changes in protoplasm.* These are admittedly so-called materialistic *terms*. Yet Prof. Huxley says: "Nevertheless, two things are certain: the one, that I hold the statement (above) to be substantially correct; the other, that I, individually, am no materialist, but on the contrary believe materialism to involve grave philosophical errors." Such union of materialistic terminology with the repudiation of materialistic philosophy, he believes to be "not only consistent with, but necessitated by sound logic." This he proceeds to show in this manner: If it be supposed that knowledge is absolute, that we know more of cause and effect than a certain definite order of succession of facts, and that we have a knowledge of the necessity of that succession, then there is no escape from utter materialism and necessarianism. But it is impossible to prove that anything whatever may not be the effect of a material and necessary cause, and no act is really spontaneous, since a really spontaneous act is one which has no cause. Yet any one familiar with the history of science will admit that its object has always meant, and means the extension of the province of matter and causation, and the concomitant gradual banishment from all regions of human thought, of what we call spirit and spontanéity,—that is, the object of all science has been and is to find out the causes of all phenomena; and there is no difference between the conception of life as the product of a certain disposition of material molecules, and the old notion of an Archæus governing and directing blind matter within each living body, except that here, as elsewhere, matter and law have devoured spirit and spontaneity. And moreover, the physiology of the future will gradually so extend the realm of matter and law, until it is coextensive with knowledge, with feeling, and with action. It is this *progress of knowledge*, according to Prof. Huxley, which so many of the best minds conceive to be the *progress of materialism*, which they watch with such fear and powerless anger as a savage feels, when, during an eclipse, the great shadow creeps over the face of the sun. We know nothing of this terrible "matter," except as the name for the unknown and hypothetical cause of states of our own consciousness, and as little of that "spirit," except that it is also a name for an unknown and hypothetical cause of states of consciousness, that is, matter and spirit are both names for the imaginary substrata of groups of natural phenomena. Dire necessity and "iron" law are gratuitously invented bugbears. If there be an "iron" law, it is that of gravitation, and if there be a physical necessity, it is that a stone unsupported will fall to the ground. We know nothing more of this latter phenomenon, except that stones always have fallen to the ground under these conditions, and that they will continue to fall to the ground thus unsupported.

It is simply convenient to indicate that all the conditions of belief in this case have been fulfilled, by calling the statement that unsupported stones will fall to the earth a "law of nature." But when for *will* we exchange *must*, we introduce an idea of necessity which does not lie in the observed facts, and is not warranted by anything that is discovered elsewhere. And with regard to which Prof. Huxley says: "For my part, I utterly repudiate and anathematize the intruder. Fact I know, and Law I know; but what is this necessity, save an empty shadow of my own mind's throwing? But, if it is certain that we can have no knowledge of the nature of either matter or spirit, and that the notion of necessity is something illegitimately thrust into the perfectly legitimate conception of law, *the materialistic position that there is nothing in the world but matter, force, and necessity, is as utterly devoid of justification as the most baseless of theological dogmas.*

"The fundamental doctrine of materialism, like those of spiritualism, and most other 'isms,' lie outside 'the limits of philosophical inquiry,' and David Hume's great service to humanity is his irrefragable demonstration of what these limits are. Hume called himself a skeptic, and therefore others cannot be blamed if they apply the same title to him; but that does not alter the fact that the name, with its existing implications, does him gross injustice. If a man asks me what the politics of the inhabitants of the moon are, and I reply that I do not know;

that neither I nor any one else have any means of knowing; and that, under these circumstances, I decline to trouble myself about the subject at all, I do not think he has any right to call me a skeptic. On the contrary, in replying thus, I conceive that I am simply honest and truthful, and show a proper regard for the economy of time. So Hume's strong and subtle intellect takes up a great many problems about which we are naturally curious, and shows us that they are essentially questions of lunar politics, in their essence incapable of being answered, and therefore not worth the attention of men who have work to do in the world." . . . .

"If we find that the ascertainment of the order of nature is facilitated by using one terminology, or one set of symbols, rather than another, it is our clear duty to use the former, and no harm can accrue so long as we bear in mind that we are dealing merely with terms and symbols. In itself it is of little moment whether we express the phenomena of matter in terms of spirit, or the phenomena of spirit in terms of matter; matter may be regarded as a form of thought, thought may be regarded as a property of matter—each statement has a certain relative truth. But with a view to the progress of science, the materialistic terminology is in every way to be preferred. For it connects thought with the other phenomena of the universe, and suggests inquiry into the nature of those physical conditions, or concomitants of thought, which are more or less accessible to us, and a knowledge of which may, in future, help us to exercise the same kind of control over the world of thought as we already possess in respect to the material world; whereas, the alternative, or spiritualistic terminology is utterly barren, and leads to nothing but obscurity and confusion of ideas. Thus, there can be little doubt that the further science advances, the more extensively and consistently will all the phenomena of nature be represented by materialistic formulæ and symbols. But the man of science, who, forgetting the limits of philosophical inquiry, slides from these formulæ and symbols into what is commonly understood by materialism, seems to me to place himself on a level with the mathematician, who should mistake the *x's* and *y's*, with which he works his problems, for real entities, and with this further disadvantage, as compared with the mathematician: that the blunders of the latter are of no practical consequence, while the errors of systematic materialism may paralyze the energies and destroy the beauty of a life."

These are the views of the "physicists," so-called, a school represented by Prof. Huxley, Prof. Owen, Herbert Spencer, Mr. Grove, Prof. Tyndall, and others. Prof. Owen, in the last pages of vol. iii of *The Anatomy of the Vertebrates*, declares himself the champion of spontaneous generation, and he maintains, also, that the formation of living beings out of *inanimate matter* by the conversion of physical and chemical into vital modes of force, is a matter of daily and hourly occurrence. Mr. Grove says that "in a voltaic battery and its effects we have the nearest approach man has made to an experimental organism," and that in the human body we have chemical action, electricity, magnetism, heat, light, motion, and possibly other forces "contributing, in the most complex manner, to sustain that result of combined action we call life."

ADDISON, WALLER, COHNHEIM (1842, 1846, 1867).

At the annual meeting of the Provincial Medical and Surgical Association of England, held at Exeter, August 3d and 4th, 1842, William Addison read a paper entitled "Experimental and Practical Researches on the Structure and Function of Blood-corpuscles, on Inflammation, and on the Origin and Nature of Tubercles in the Lungs." In the section "On Pus-corpuscles," he says: "The colorless blood-corpuscles appear to form pus-corpuscles." In the section on "Inflammation," we find the following: "The circulation in the web of a frog's foot was watched at intervals for half an hour, and only a few lymph-globules were seen. A crystal of salt was applied, and the examination continued: its first effect was to quicken the rate of the circulation; this soon ceased, and the blood became stationary, the vessels being red and congested. In the capillaries contiguous to the congested vessels, the blood was oscillating to and fro; a little further off, the circulation was very quick. In half an hour the number of lymph-globules had increased considerably, and the circulation in the congested vessels was resumed; but the corpuscles passing through them sometimes oscillated to and fro, sometimes retrograded, and at others hurried or darted through the vessels with the utmost velocity.

The current of the red corpuscles in some of the veins appeared to be confined to the centre of the vessel, and not to touch the circumference, which was occupied by a great many lymph-globules. On the following morning the whole interior of the inflamed vessels appeared to be lined with lymph-globules. By gently altering the focus of the microscope they were seen below the red current, and *many of them appeared to lie externally to the boundary of the vessels.*"

Again, page 258:* "During some of these experiments the islets of tissue between the capillaries became distinctly cellular, and appeared as if overspread with irregular-shaped lymph-globules."

These various statements, while they permit the inference that Addison first conceived that the colorless blood-corpuscle becomes the pus-corpuscle in inflammation, do not allow us to infer that he actually observed its migration through the walls of vessels. Indeed, he says, page 259: "The phenomena observed in the foregoing experiments corroborate the views of those distinguished physiologists who entertain the opinion that the capillary distribution of the blood is situated in the channels of the tissue, and not in vessels with a distinct membranous coat."†

In 1846 Waller‡ more correctly appreciated this migration, but it was not until Cohnheim published his famous paper on "Inflammation and Suppura-

* The Transactions of the Provincial Medical and Surgical Association, vol. xi. London, 1843.

† Müller's Physiology, vol. i, p. 229.

‡ London, Dublin, and Edinburgh Philosophical Magazine, vol. xxix, pp. 271 and 398.

tion,"* in 1867, that the observation attracted the attention it deserved. Since then it has been confirmed again and again, and most conclusively lately by Arnold, of Heidelberg.†

The theory which grew out of Cohnheim's observation was, that it is *the colorless corpuscle of the blood*, rather than the connective tissue corpuscle, which is the starting-point of all new formations, healthy and morbid. It is the accumulation of these corpuscles outside of the bloodvessels, in the interspaces of the fibrillar connective tissue, which forms the beadlike rows of cells figured by Virchow and others. It is these which, accumulated in larger numbers, forms the pus of an abscess. It is these which, perverted in the direction of their development, produce the tissue of tubercle, cancer, sarcoma, and other forms of morbid growth. It is these, also, which become the medium of repair of all injured or destroyed tissues which are capable of regeneration, whatever their complexity or simplicity.

That the colorless corpuscle plays a most important rôle in the production of new formations, healthy and morbid, few now deny; but that it is the sole morphological element, exclusive of the connective tissue corpuscle, thus active, many will not admit. Conspicuous among those who have combated this exclusive view are Stricker and Norris,‡ whose ob-

* Ueber Entzündung und Eiterung, Virchow's Archiv, Bd. xl, 1867, p. 1.

† Ueber Diapedesis, Virchow's Archiv, vol. 58, 1873.

‡ Versuche über Hornhaut Entzündung, Studien aus dem Institute für Experimentelle Pathologie in Wien, aus dem Jahre 1869.

servations and experiments in the production of inflammation in the corneæ of frogs and rabbits have attracted much attention. Their object was to show that the connective tissue corpuscles (the corneal corpuscles here) shared in the formation of the products of inflammation by their proliferation, and that the colorless corpuscles themselves, after their migration beyond the walls of the bloodvessels, also underwent cell division, and thus contributed in a second manner to the formation of pus. They argued, also, that the enormous accumulations of pus in large abscesses could not be reasonably accounted for on the ground that the only source of the pus-corpuscle is the wandered-out colorless corpuscle.

These observations of Stricker and Norris are generally acknowledged as having settled the question in favor of the view, that there are two elements of organization,—the colorless corpuscle *and* the connective tissue corpuscle, either of which may also become the starting-point of pathological new formations.

NEW VIEWS ON THE STRUCTURE OF CELLS AND NUCLEI.—1877–78.

As early as 1867, C. Frommann* published a pamphlet on the "Normal and Pathological Anatomy of the Spinal Cord," in which he states that the presence of fibrils in the nuclei and nucleoli of cells, first observed in ganglion-cells, was demonstrated by him also in the cells of connective tissue, cartilage, and

* Untersuchungen über die normale und pathologische Anatomie des Rückenmarks, 2 Theil. Jena, 4. Mit 6 Taf. p. 17. For abstract of, see Henle and Meissner's Bericht über die Forschritte der Anatomie und Physiologie, in Jahre 1867, Leipzig, 1868.

bone-cells, and in the epithelium of the mouth and capillary vessels. He observed clear shining fibrils proceeding from the nucleolus joining themselves to others proceeding from the nucleus and protoplasm. From the nucleoli of connective tissue arise one, two, and, more seldom, three fibrils. These sometimes dwindle away in the nucleus itself; at others, after a straight or curved course, leave the cell and lose themselves in the neighborhood. Repeatedly was observed the entrance of a nucleolus-fibre into a cell process, and if two cells were united by a process from each, the nucleolus-fibre was seen to pass from one cell to another. So also fibres originating in the nucleus, sometimes as many as six in number, could be followed into the protoplasm, and more seldom beyond the cell. Certain fibres appear to cease in the nucleus by a free extremity, as though cut off. Others have attached to them glistening granules, which in fresh, as well as hardened preparations, are contained in variable number in the nucleus. Frommann believes that the granules of the nucleus and protoplasm are the nodal points of a very fine fibrous network, from which fibrils go off and leave the cell. These are found in the cells of all the tissues named above. In consequence of this complicated structure of the nucleus, Frommann thinks it improbable that it multiplies by division; he believes in a free new formation of the nucleus in the protoplasm, where, alongside of nuclei of ordinary appearance, smaller homogeneous ones make their appearance.

In 1873,* Heitzmann asserted that the substance

* Untersuchungen über das Protoplasma, Sitzungsber., d. k. Akad. d. Wiss. zu Wien, Bd. lxvii und lxviii, Abth. iii, 1873.

of various cells, amœbæ, blood-corpuscles, cartilage-cells, bone-cells, epithelial cells, etc., contain networks of minute fibrils, into which pass fibrils radiating from the interior of the nuclei of these cells.

In 1875, Frommann* again described, in accordance with Heitzmann, a minute network of fibrils in the nuclei of blood-corpuscles of *Astacus fluviatilis*, which passed through the *nuclear membrane* into a similar network in the substance of the blood-corpuscles.

Schwalbe,† in 1875, found the nucleoli in the nuclei of ganglion-cells in the retina often possessed of minute filamentous prolongations, and the nuclear membrane showing prominences on its inner surface. Schwalbe designates as "nucleolarsubstanz," the nucleolus and filaments, nuclear membrane and its prominences, to distinguish it from the rest of nuclear matter, which he calls "kernsaft" or "nuclear juice."

Kupffer,‡ in 1875, maintained that the substance of the lower cells of the frog, the odontoblasts, the epithelial cells of the salivary gland of *Periplaneta orientalis*, is composed of a hyaline (non-fluid) ground

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See also a paper by Heitzmann on the same subject, in the New York Medical Journal for 1877. For the historical facts from this date in the development of these new views, I am indebted to the very valuable paper of Dr. Klein in the Quarterly Journal of Microscopical Science for July, 1878.

* Frommann, Zur Lehre von der Structur der Zellen, Jenaische Zeitschrift f. Naturw., Bd. ix, 1875, p. 280.

† Bemerkungen über d. Kerne d. Ganglionzellen, Jenaische Zeitschrift f. Naturw., Bd. x, 1875, p. 25.

‡ Ueber Differenzirung d. Protoplasma an den Zellen thierescher Gew., Schriften des Naturw. Vereins f. Schleswig-Holstein, Heft iii; and Beitr. z. Anat. u. Physiol., Festgabe f. Carl Ludwig, 1875.

substance, "Paraplasma," and of a granular fibrillar contractile "Protoplasma," imbedded in the former. The relation and distribution of the protoplasmic fibrillar substance varies in cells of different kinds.

Strassburger,* in 1876, observed that in developing cells of *Phaseolus multiflorus*, a network of fibrils is present radiating from the nucleolus, and permeating the interior of the nucleus in connection with a similar network of the cell substance.

In 1876, Bütschli† observed in the nuclei of colored blood-corpuscles of the frog and newt, minute fibres with granular thickenings, but no nucleolus as asserted by Ranvier.

Moyzel,‡ in 1875, found in the epithelium of the cornea of the frog, rabbit, and cat, during regeneration, large round nuclei, in which he observed filamentous masses, either convoluted or radiating from a central point. He regarded these forms as due to a particular stage of division, as described by Bütschli and Strassburger.

O. Hertwig,§ in 1876, also distinguished a "nuclear substance," from a "nuclear juice," and Bütschli,‖ in the same year, a "nuclear matter" from a "nuclear fluid." The "nuclear matter" of the latter com-

* Ueber Zellbildung und Zelltheilung, Jena, 1875. Abstract in Quart. Jour. Mic. Sci., vol. xvi, 1876, p. 138.

† Studien über die ersten Entwickelungserscheinungen der Eizelle, Abhandl. d. Senkenbergischen Naturf. Gesellsch., Bd. x, 1876.

‡ Ueber eigenthumliche Vorgänge bei der Theilung der Kerne in Epithelialzellen, Centralbl. f. Medic. Wissensch., No. 50, 1875.

§ Beiträge zu einer einheitlichen Auffassung der verschiedenen Kernformen, Morphol. Jahrbuch, 1876, Bd. 2, H. 1, 1876, p. 73.

‖ Loc. citat., vol. x.

prises the nuclear membrane, the nucleolus, and a fibrillar stroma, which latter, in some instances, extends in a radial manner from the nucleolus.

E. Van Beneden* saw a fine protoplasmic reticulum in the large axial entoderm cell of Dicyema, which (reticulum) exhibited slow spontaneous movements. In the nucleus of the ripe ovum of *Asterocanthion rubens* he also observed within the nuclear membrane and beside the nucleolus a delicate network of finely granular substance, which he calls "nucleoplasma," including several "pseudo-nucleoli." According to him the germinal vesicle of the ripe ovum of the rabbit also contains a minute network.

Arndt,† in 1876, distinguished in the nucleus a homogeneous ground substance and elementary globules; the former possesses a vesicular structure, and incloses in its meshes the latter.

W. Flemming,‡ in observations on the structure of nuclei found in the membrane of the urinary bladder of *Salamandra maculata*, in 1876, saw a very delicate and dense network of fibres uniformly pervading the interior of the nucleus, and attached to the nuclear membrane. This network, "Gerüstformige

* La maturation de l'œuf, la fécondation et les premières phases du développement embryonaire des Mammifères. Bul. de l'Acad. Royale de Belgique, 2 Ser., t. 40, 1875; also Contributions à l'histoire de la vésicule germinative et du premier noyau embryonaire, in the same journal, January, 1876.

† Über den Zellkern, Sitzungsb., d. Medicin. Vereins zu Greifswald, Nov., 1876.

‡ Beobachtungen über die Beschaffenheit des Zellkerns, Archiv für Mikrosk. Anat., Bd. xiii, 1876, p. 693, and following.

Structur," was seen by Flemming in the nucleus of all cellular elements of the bladder of *Salamandra*, epithelial cells, connective tissue cells, migratory cells, unstriped muscle-cells, nerve-cells, endothelial cells, and blood-corpuscles. With regard to Flemming's observations, Klein* says their clearness and extent leave no doubt that the network in the nucleus represents a definite and pre-existing structure. This has been to a certain extent questioned by Langhans† as regards the fresh cells of the human decidua serotina, but, Klein again observes, "Flemming's assertions cannot be in the least shaken, considering that he observed the above structure, not only after the use of reagents, *e. g.*, acetic acid, chromate of potash, alcohol, chromic acid, with or without subsequent staining in carmine or hæmatoxylin, but also in the absolutely uninjured bladder, *i. e.*, while this organ was being observed in the living curarized animal." And, in a later note, Flemming‡ states that he observed the same network in the nuclei of various cells, also in the living and perfectly uninjured larva of *Salamandra*.

Eberth§ noticed nuclei containing anastomosing filaments in their interior in the epithelium of the cornea and the endothelium of the *membrana Descemeti* under normal conditions. He regards them

* Loc. citat.

† Zur Lehre von Zusammensetz. des Kerns, Centralblatt f. Medic. Wissenschaft, 1876, N. 50.

‡ Zur Kenntniss des Zellkerns, in Centralbl. f. Medic. Wiss., 1877, No. 20.

§ Ueber Kern und Zelltheilung, Virchow's Archiv, Bd. 67, 1876.

as peculiar forms in the development and division of nuclei.

Eimer* found in numerous nuclei that the granules of the "granular zone" surrounding his "hyaloid" are due to protoplasmic filaments, which permeate the interior of the nucleus, and anastomose with each other so as to form a network, which extends to the membrane of the nucleus, and also sends radiating fibrils through the hyaloid into the nucleus. The network of fibrils of the nucleus is, in some instances, also in connection with fibrils and networks of the same belonging to the cell substance itself.

The most recent contribution on this subject is the valuable paper by Dr. E. Klein, already alluded to, and published in the *Quarterly Journal of Microscopical Science*, for July, 1878. In this paper Klein shows by observations† on the ordinary freshly killed newt

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* Weitere Nachrichten über den Bau des Zellkerns, etc., Archiv f. Mikrosk. Anat., Bd. xiv, 1877, p. 94. Also, "Notes and Memoranda" of the April number of the Quart. Jour. Microsc. Sci., 1878.

† The following is the method pursued by Klein: The stomach of a freshly killed newt is cut open and placed into a 5 per cent. solution of chromate of ammonia in a closed vessel, where it is kept for about twenty-four hours. It is then washed in water for about half an hour, and placed after this in a dilute solution of picrocarmine, where it is left till it assumes a deep pinkish-yellow tint. It is now washed in water, and microscopic specimens are prepared in this manner. The mucous surface of the organ is scraped with a small scalpel, whereby smaller or larger flakes may be easily removed; they are placed in a very tiny droplet of glycerin on a glass slide; by slight knocking with the rounded or flat top of any thin rod or needle-holder these flakes are broken up into micro-

(*Triton cristatus*), that the statements of Flemming are correct, and presents in addition several observations he has made with reference to the cell-substance itself, and the relation of it to the intranuclear network.

Dr. Klein examined gland-cells, surface epithelial cells, endothelium, unstriped muscle-fibres, connective tissue corpuscles, and nerve-fibres. And every where the nuclei showed an extremely beautiful network of fibrils. This he designates as the *intranuclear* network, which is imbedded in a homogeneous ground-substance. The network does not in all instances extend up to the nuclear membrane, but leaves a narrower or broader zone next to the membrane unoccupied. But in all instances the network is in connection with the limiting membrane by numerous fibrils. The spaces formed by their anastomoses are not uniform, being sometimes larger in the peripheral parts than in the central, and sometimes the reverse. All forms are found between a network with fibrils as in a net, and a honeycomb of membranous structure as in a sponge. In almost all instances are observed a smaller or greater number of

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scopic fragments, a drop of glycerin is placed on a covering-glass, and this is inverted over the above specimen.

Examined under a moderately high power, say Hartnack's 7 or 8, or Zeiss's D or E, we recognize easily innumerable isolated cells or groups of epithelial cells, and a great many isolated nuclei or fragments of nuclei. If the scalpel has been drawn over the surface of the mucous membrane with a little energy, the preparation contains great numbers of gland-cells, isolated and in continuous masses, and also other elements belonging to the tissue of the mucosa.

minute bright spots, which are shown by careful focussing to be fibrils of the network seen in optical transverse section or at the points of anastomosis. In some nuclei, according to Klein, the more irregularly shaped dots are due to a thickening of fibrils from place to place, although Flemming attributes them altogether to the former cause (transverse sections of fibrils). Whence it is clear, the more shrunk the intranuclear network, or the more twisted and convoluted the fibrils, the more does the nucleus present the appearance of being granular.

The *nucleolus* receives an entirely peculiar explanation at the hands of Klein, in which he seems to be sustained by the observations of Van Beneden, O. Hertwig, Flemming himself, Auerbach, Eimer, and especially of Strassburger, Schwalbe, and Langhans. With regard to it Klein first says with undoubted truth: "Now, to every experienced student of histology, it must have become apparent that if there is one thing unsatisfactory, unreliable, puzzling, and inconstant about the nucleus of vast numbers of cells, it is this very nucleolus." Second, that after a very prolonged examination he has arrived at the conclusion that these large particles (nucleoli) are due to one of two things: in some instances they are distinctly thickenings of the network, in others they appear to be merely due to the shrivelling up and intimate fusion of a part of the network. The inconstancy as regards size, shape, and number of the so-called nucleoli seem to him to point very strongly in the above direction.

The assertions which have been made as regards spontaneous movements of nucleoli by Auerbach, Brandt, Eimer, Kidd, and others, he regards as quite compatible with the above view, for Van Beneden has observed movements in the intranuclear network, and it is quite possible that the above assertions might refer to such movements.

With regard to the *nuclear membrane* already mentioned, Klein says that it is composed of an *outer* thicker portion, which is the *limiting membrane proper* and closely connected with it, an *inner*, more or less incomplete layer, which is a *peripheral condensation of the intranuclear network*, with which it is connected by longer or shorter threads. The clear space sometimes observed between the membrane of the nucleus and the intranuclear network is due to a retraction of the latter from the former.

Klein has also demonstrated a network of fibrils in the substance of cells outside of the nucleus, which he designates as the *intracellular* network, in contradistinction to *intranuclear*, in the meshes of which again is the *interfibrillar* or ground-substance, which in the case of the columnar epithelial cells on mucus-surfaces, known as goblet-cells, is mucus,* but finds them also in the endothelium of the surface, in unstriped muscle-fibres, connective tissue corpuscles, and nerve-fibres.

Klein further traces a *direct connection of the fibrils*

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* They are best seen on the slender goblet-cells of the stomach of the newt, kept for twenty-four hours in Müller's fluid, placed then for half an hour in a mixture of two parts chromic acid ($\frac{1}{6}$ per cent.), and one part methylated alcohol, washed after this in water, and stained with picro-carmine.

of the intracellular with those of the intranuclear network, and along with Eberth, Marchi, and Eimer, traces in the epithelial cells of the foregut of the newt, *the cilia in direct continuation through the cell-cover with the fibrils of the intracellular network.*

The intracellular network is less conspicuous than the intranuclear, but possesses the same general characters.

The importance of this subject has seemed so great that I have added at the end of the volume the essential portions of the plate from the *Quart. Jour. of Micros. Sci.*, for July, 1878, which, with its description, will give a very accurate notion of these new views as confirmed by Dr. Klein, than whom, of modern observers, I consider none more reliable.

SUMMARY—PRESENT STATE OF THE CELL DOCTRINE—AUTHOR'S VIEWS.

Minute analysis of the solids of the organism has long been an object of the histologist and physiologist, which, resulting first in the *partes similares* of Aristotle and Galen, has finally reached the so-called "cell" or "elementary part" as the ultimate physical element of organization, out of which all tissues, healthy or diseased, are formed. Our ideas as to the exact physical constitution of this elementary part have undergone considerable change since the first announcement by Schleiden and Schwann, in 1838, of its exact physiological position. The most important modifications of the original conception of a cell is that which removes altogether its vesicular character. So that the term "cell" is really no longer a correct one, since the object to which it is applied is, in its youngest, most active state, at least, a solid mass or "clump" of living matter without the vestige of a wall or envelope about it. The word has, however, become so intimately associated with histology that it is doubtful whether it will ever fall into disuse, nor does it much matter, so long as correct notions of the elementary part are obtained. This latter term, "elementary part," is, however, to be preferred.

Consistently with the latest determined facts, *the cell* or *elementary part* is best defined as the smallest *mass of living matter possessing the essential life properties of reproduction*, *nutrition*, *growth*, and *development.* To such substance the terms "sarcode," "protoplasm," "germinal matter," and "bioplasm" have been applied, the first by Dujardin, the second by Max Schultze and Remak, and the third and fourth by Beale.

The term "sarcode" has nearly gone out of use, and "protoplasm" has come to be largely used for that part of the cell outside of the nucleus, without regard to its living properties. The term "bioplasm," on the other hand, has not yet received such extension of meaning, while it also etymologically defines the substance it represents, and is therefore much to be preferred.

The Nucleus of the Cell.—In the interior of most cells are found one or more differentiated masses of bioplasm, usually round or nearly so, and more granular or darker in hue by transmitted light than the remainder of the cell, which are called *nuclei.* These nuclei, although strikingly constant, are not invariably present, as pointed out by Brücke,* in 1861, in the cells of cryptogams, and confirmed by the earlier discovery in 1854, of a non-nucleated amœba (Amœba porrecta) by Max Schultze,† in the Adriatic Sea; also later by Hæckel‡ and Cienkowski§ in their discoveries in 1865, by the former of a non-nucleated protozoon (Protogenes primordialis) in the Mediterranean, and by the latter of two non-nucleated monads (Monas amyli and Protomonas amyli). Stricker's‖ observations on the fecundated egg of the frog incline him to adopt the view of Brücke, and omit the nucleus in a theory of elementary organization. Such facts as these prove erroneous the definition of a cell proposed by Leydig and Max Schultze, "protoplasm surrounding a nucleus," and the definition more recently accepted by Virchow,¶ that a cell is "a nucleus surrounded by a molecular blastema;" though if we restrict ourselves to the cells concerned in the organization of the higher animals, the latter may be anatomically correct, but the former involves the confusion already referred to in the use of the word "protoplasm," which is here applied to some-

* Brücke, E., Die Elementar-organismen, p. 18–22, 1861.

† Schultze Max, Organis. d. Polythalam., 1854.

‡ Hæckel, Zeitschr. f. w. Zoolog., 1865, Bd. xv.

§ Cienkowsky, Max Schultze's Archiv, 1865.

‖ Stricker, S., in vol. i, p. 8, Stricker's Histology, New Sydenham Society's Translation, London, 1870; also p. 504, vol. iii, London, 1873.

¶ Letter from Berlin, in Edinburgh Medical Journal, February, 1865.

thing outside of the nucleus to the *exclusion* of the latter, to which, if to anything, should be assigned the term.

For the nucleus possesses pre-eminently three of the properties of bioplasm named, nutrition, reproduction, and growth, and in it usually take place the first steps towards the production of new cells, in, first, its increase of size through nutrition, and second, by fission, which subsequently extends to the remainder of the cell. Indeed the chief function of the nucleus has been heretofore considered as that of the reproduction of the cell. But this is by no means invariably the case, as indeed it is clear should not be, when we recall the properties of bioplasm or germinal matter. For although the nucleus is a separate differentiated portion of bioplasm, it does not in every cell comprise the whole of the bioplasm of that cell. This is perhaps best illustrated by the pus-cell and colorless blood-corpuscle, which are pure bioplasm, but which still contain within them separate centres of germinal matter or nuclei. Consistently with this fact, the pus-cells or white blood-cells multiply not necessarily through a primary fission of the nucleus, but often by separating a portion of the external bioplasm, which becomes an independent cell with the endowments of its predecessor. See Fig. 7, 8, 9, 10, of frontispiece. This fact has further a very important illustration in the fecundated germ or ovum of sexual generation. It is now universally admitted that the non-fecundated germ is a distinctly nucleated cell, and it is almost as generally acknowledged that immediately after fecundation the nucleus disappears, to be replaced, however, by a new one, under favorable conditions, which appears to take no part in the subsequent cleavage processes.*

Recent descriptions of the nucleus include in its anatomy a *nuclear membrane*, which is described by Auerbach as a somewhat thick, highly refractile, doubly contoured membrane, which appears to be less distinctly separated from the cell protoplasm than from the exterior of the nucleus. This membrane is regarded by Auerbach as having been formed about the original droplike nucleus by the differentiation of the inmost layer of the protoplasm into a species of interior cell membrane. According to Klein, it is composed of an *outer* thicker portion, which is the limiting membrane proper, and closely connected with it an inner more or less incomplete layer, which is a *peripheral condensation of the intranuclear network*, with which it is connected by longer or shorter threads. According to Auerbach, the nuclei first appear as clear spaces, vacuoles

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* According to Prof. Stricker ("Development of the Simple Tissues," in vol. iii, of "Human and Comparative Histology," New Syd. Soc. Ed.), precise statement to the effect that the germinal vesicle is persistent and becomes transformed into the nucleus of the cleavage cells, has only been made by Johann Müller in the case of Entoconcha mirabilis (Monatsberichte der Berliner Akademie, September, 1851). But in recording this fact Stricker seems, as many more recent writers have done, to have entirely overlooked the much earlier observation of Martin Barry, who distinctly asserts (Philosophical Transactions, London, 1840, p. 529), that "the germinal vesicle does not burst, or dissolve away, or become flattened, on or before the fecundation of the ovum, as hitherto supposed."

filled with a tenacious fluid mass possessing no distinct wall. Each droplet then acquires a membrane by differentiation of the inmost layer of cell protoplasm and nuclei, and intermediary granules afterwards make their appearance. Once differentiated, the nuclear membrane is an integral part of the nucleus, constituting the latter a true vesicle, isolable as a whole by mechanical means.*

The Nucleolus.—Very commonly also, though not invariably attending it, a second differentiated mass of matter is found within the nucleus, to which the term *nucleolus* is applied. According to Beale, it is possessed of like endowments, and is supposed to be the most recently formed bioplasm, the non-vitalized circulating albumen of the blood being converted through the agency of pre-existing bioplasm into the latter substance. If the cell normally develop, the nucleolus growing becomes the nucleus, the latter being gradually oxidized upon its exterior and converted into the cell-contents and cell-wall, while a younger centre of germinal matter takes the place of the original nucleolus. This living matter exhibits the important property of being stained by weak solutions of various coloring matters, as carmine, anilin, etc., the younger matter taking on the deeper stain, and by these means its demonstration is rendered strikingly easy. In rapidly growing cells, a still younger centre of bioplasm may sometimes be demonstrated within the nucleolus, while the nucleus remains a distinctly differentiated mass capable of also

* Auerbach, Organologische Studien, Breslau, 1873–4.

being stained. To this *youngest* centre of bioplasm, the term "nucleoleolus" might not be inappropriately applied.

Klein has announced in his recent paper "On the Structure of Cells and Nuclei" (Quart. Journn. Microscop. Sci., July, 1878), that after very prolonged examination he has arrived at the conclusion that these large particles (nucleoli) are due to one of two things: in some instances they are distinctly thickenings of the nuclear network of fibrillæ demonstrated by Frommann and Heitzmann, and confirmed by Flemming, Hertwig, E. Van Beneden, Klein himself, and others; or they are merely due to the shrivelling up and intimate fusion of a part of this network.

Auerbach supposes that the nucleolus is formed by the aggregation about a centre, of nucleolar substance, which is derived either from the periphery of the nucleus itself or from the inmost layer of cell protoplasm. According to him, nucleoli may also multiply by fission. This division is associated with a movement of the new nucleoli through the nuclear ground-substance, the cause of which is not understood. The reverse, or the fusion of several nucleoli into one, also occurs. Auerbach says also that many facts speak for the identity of nucleolar substance and cell protoplasm. In optical appearance, nucleoli and the substance of young cells agree, and vacuolation may occur in either, large nucleoli being seldom free from clear spaces. Both are amœboid, the movements in nucleoli having been described by many observers. Lastly, nucleoli have, as Auerbach himself shows, that characteristic of vital protoplasm, the power of multiplication by division. That is, nucleoli have all the capabilities of elementary organisms, and are in truth *cytodes*. Regarded in this light, they are real daughter cells, which have arisen by an endogenous process, and the nucleus is the chamber in which they develop. It is now merely necessary for them to find a way out through the body of the mother cell, in order to begin life as independent beings. That this method of increase has become obsolete in the cases of a majority of cells of higher adult animals, or perhaps only occurs in pathological processes, may be quite true, according to Auerbach, without offering any obstacle in the way of such a hypothesis. In the specialization of function which appears as we ascend the animal series new means of gaining the same end present themselves, while the old vanish or are made use of for other purposes. The phases in the act of propagation of a unicellular organism may be less significant, and have a far different outcome in a unit cell of a more complex creature.*

The fact of the total or partial disappearance of the nucleus or germinal vesicle shortly before or immediately after fecundation, has been amply confirmed by recent observers, although there are some slight differences in the exact mode of its acceptance. The most important recent contributions on the sub-

* Auerbach, Organologische Studien, Breslau, 1873–4, or see abstract of Auerbach's paper, by Priestley, in vol. xvi, Quart. Jour. Microsc. Sci., 1876, whence I have obtained the above views of Auerbach with regard to nuclei and nucleoli.

ject have been by Auerbach,* Strassburger,† Hertwig,‡ and Van Beneden,§ to whom may be added Bütschli,‖ Oellacher,¶ Kleinenberg,** and Balfour.†† Under the influence of the fertilizing act the ovum again becomes nucleated, the nucleus arising in a fusion of pronuclear bodies, one of which may possibly be derived from the fertilizing element (spermatozoid). The nucleus then begins series of changes, about which most observers are agreed, but for the details of which the reader is referred to the sources named in the footnote.

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* Organologische Studien. Breslau, 1873–4.

† Ueber Zellbildung und Zelltheilung, Jena, 1875.

‡ Beiträge zur Kenntniss der Bildung, Befruchtung, und Theilung des thiereschen Eies, Morpholog. Jahrbuch, 1, 1875.

§ La Maturation de l'œuf, la Fecondation et les Premières Phases du Développement Embryonaire des Mammifères, d'après des Recherches faites chez le Lapin. Bruxelles, 1875.

Excellent abstracts of these four papers, by John Priestly, are found in the Quart. Jour. of Microsc. Sci., for July, 1878, vol. xvi, new series. In the same number will be found an original paper by Van Beneden, entitled "Contributions to the History of the Germinal Vesicle, and of the first Embryonic Nucleus," in which he compares the views of Hertwig with his own.

‖ Vorläufige Mittheilung über Untersuchungen betreffend die Ersten Entwickelungsvorgänge in Befruchteten Ei von Nematoden und Schnecken, Zeitsch. für Wiss. Zoologie, Bd. xxv; and "Vorläufige Mittheilung Einiger Resultate von Studien über die Conjugation der Infusorien und die Zelltheilung, Zeitsch. für Wiss. Zoologie, Bd. xxv, 1875.

¶ Beiträge zur Geschichte des Keimblaschens im Wirbelthierei, Archiv für Mikrosk. Anat., Bd. viii, 1872.

** On the Anatomy and Development of the Fresh-water Hydra. Leipzig, 1872.

†† Balfour, Developmental History of Elasmobranch Fishes, in the Journal of Anatomy and Physiology, January, 1876.

As already stated, previous to the researches of Müller alluded to, no one doubted the disappearance of the germinal vesicle after fecundation. This was thought to have been established by Purkinje* and Von Baer.† But immediately after Müller made his announcement, others followed in its confirmation. Among these were Leydig,‡ Gegenbauer,§ Fol,‖ Leuckart,¶ Pagenstecher,** Mecznikow,†† Hæckel,‡‡ Kölliker,§§ and Van Beneden,‖‖ as the result of his earlier researches. Still later, however, of the above-named

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* Purkinje, Symbolæ ad ovi avium historiam ante incubationem, 1825.

† Baer, C. E. v., Untersuch. u. die Entwicklungsgesch. der Fische, 1835; and Untersuch. u. die Entwicklungsgesch. der Thiere, Bd. ii, Konigsberg, 1828.

‡ Leydig, Ueber den Bau und die Systematische Stellung der Roderthiere, Zeit. für Wiss. Zool., Bd. vi, p. 102, 1856.

§ Gegenbauer, Beiträge zur Näheren Kenntniss der Siphonophoren, Zeit. für Wiss. Zool., Bd. v; Zur Lehre vom Generationswechsel bei Medusen und Polypen, p. 24; Untersuch. über Pteropoden und Heteropoden, Leipzig, 1855. Ueber die Entwickelung der Sagitta, Halle, 1856.

‖ Fol, Die erste Entwickelung des Geryonideneies, Jenaischi Zeitsch., Bd. vii, 1873, p. 474.

¶ Leuckart, Die Menschlichen Parasiten, Bd. ii, 2te Lief. p. 322, 1863.

** Pagenstecher, Die Wochenen, Leipzig, 1865.

†† Mecznikow, Embryologische Studien an Insecten Zeitsch. für Wiss. Zoologie, Bd. xvi, p. 484, 1866.

‡‡ Hæckel, Zur Entwickelungsgeschichte der Siphonophoren, Utrecht, 1869.

§§ Kolliker, Die Schwinimpolypen von Messina, Leipzig, 1853.

‖‖ Van Beneden, Recherches sur la Composition et la Signification de l'œuf basées sur l'Etude de son mode de Formation et des Premières Phénomènes Embryonaires, Mem. Couronné de l'Acad. Roy. de Belgique, 1. xxxiv.

more recent observers, Auerbach, Strassburger, Oellacher, Kleinenberg, Bütschli, Balfour, and Van Beneden, in accordance with fresh researches made on account of the doubts which those of Oellacher and Kleinenberg had created in his mind, all agreed that the germinal vesicle disappeared entirely either before or during fertilization. Hertwig and Van Beneden both furnish a carefully detailed account of the steps in the destruction of the germinal vesicle, the former in the unripe ova of *Toxopneustes lividus*, and the latter in the ovum of the rabbit. While agreeing in many particulars, they differ in their account of the final dissolution. According to Hertwig, the whole structure, after having become peripheral, disappears, leaving behind, of its contents, the germinal spot, or nucleolus, which becomes the nucleus of the ovum ready for the changes of fertilization. Van Beneden, on the other hand, believes that all the constituents of the germinal spot disappear *in toto*.

It seems also that the view of Hertwig, that a part of the germinal vesicle remains to form the nucleus of the ovum, was previously suggested by Derbès and Von Baer. The former, in 1847,* described the ovarian ova as consisting of three zones, the germinal spot, the germinal vesicle, and the yolk, of which the *middle one only disappears*. Von Baer† also states that in the case of echinoderms, the germinal

* Derbès, Observ. sur le Mecanisme et le Phén. qui accomp. la Formation de l'Embryon chez l'Oursin Comestible, Ann. des Sc. Nat., Zoologie, 1847, vol. viii.

† C. E. v. Baer, Neue Untersuch., über die Entwickel. der Thiere, Froriep's Neue Notizen, vol. xxxix, 1846.

spot remains as a nucleus of the ovum when the germinal vesicle is no longer seen.

Similar statements were made by Leydig,* and Bischoff,† the former with regard to Piscicola, and the latter in the case of mammals.

The Cell-contents and Cell-wall.—As cells grow older and are farther removed from the bloodvessels which nourish them, there is found to be, exterior to the nucleus, a portion which no longer admits of staining by carmine solutions of the strength which will tinge the nucleus. Further, the extreme periphery of this is often found condensed so as to present under the microscope a double contour, and to form an actual limitary membrane to the cell. To the former the name "cell-contents" has come to be applied, and to the latter, "cell-wall."

With regard to the "cell-contents," it is plain that a strict adherence to the term would require to be included the nucleus and nucleolus when present, and such was the original scope of the term when a cell was defined as a "closed vesicle or bag with certain 'contents,' among which is essentially a nucleus," a definition now very properly rejected. It is to this portion of the cell also, that the German histologists of the present day apply the term "*protoplasm*," instead of to the nucleus and nucleolus, which in many cells, at least, alone possess the endowments suggested by the word protoplasm (πρωτος, first, πλασμα,

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* Leydig, Zur Anatomie von Piscicola Geometrica, Zeitsch. f. Wiss. Zoologie, vol. i, 1849.

† Bischoff, Entwickelungsgeschichte des Kaninchen eies, 1842.

a thing formed). It is for this reason that I would prefer to reject the term altogether, but it has come to be so closely associated with this portion of the cell, that such omission would now seem impossible.

It is at least probable that this "protoplasm" or cell-contents, the portion of the cell exterior to the nucleus, is derived from the latter by a change in its structure and composition, a change which in the absence of more accurate knowledge we may characterize as of the nature of oxidation. But whatever this change is, its effect is to alter entirely the properties of the matter in which it has taken place. So that it no longer possesses the power of growth through active efforts of nutrition, that is, by converting the pabulum of the blood into material like itself, but continues to grow at the expense of the nucleus or bioplasm, which is gradually converted into it. It is this to which Beale has applied the name of "dead" or "formed" material, but for which I prefer the term *non-germinal*, since this accurately marks the property which it has lost, and it is not always lifeless in any other sense, because in it still reside properties which are inconsistent with the state known as death. Thus the function of the tissue of which the cell forms a part commonly resides in the cell-contents or non-germinal matter, as that of "contractility" in muscle and "neuridity" in nervous tissues. In some situations it is truly dead, as where it becomes the secretion of glands, as milk and bile.

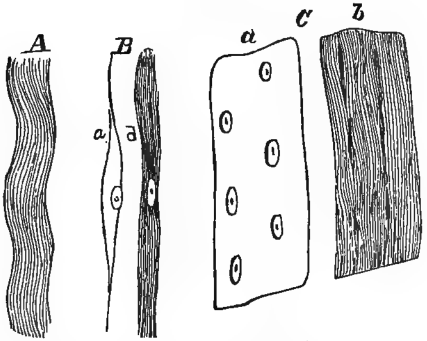
It has already been stated that the "*cell-wall*" when present is simply condensed periphery of cell-contents, and is therefore a part of the formed or non germinal matter, and is in no way essential to the constitution of the cell.

In *structure* the cell-wall when present is usually homogeneous, transparent, in a word *structureless.* Recent observations have, however, shown this to be not invariable. Thus, it is not difficult to demonstrate with the higher powers certain lines or striæ in the outer thickened edge of the columnar cells capping the villi of the small intestine, which are perhaps correctly interpreted by Funke, Kölliker, and others, as porous canals in the cell-wall, through which the fine particles of the emulsified fats are absorbed. These may at least be discovered occupying corresponding situations with great distinctness. Schroen has also described similar markings in the thickened cell-wall of the *rete Malpighii* of the human skin.

Intercellular Substance.—Closely allied to the cell-wall is the so-called intercellular substance of tissues. Although it is true that all tissues originate from cells, yet there are comparatively few which in their perfect state are composed purely of cells, but the latter are more or less separated by a substance between them. Thus cartilage or "gristle" is composed of cells and an intercellular substance, which is either hyaline or fibrous, and all the connective tissues, under which are included bone, cartilage, already alluded to, white fibrous tissue, yellow elastic tissue, and even teeth, are similarly composed of cellular elements, and a something between them, which is either homogeneous or structured.

The mode of origin of this intercellular substance has given rise to considerable discussion. Schwann assumed that there originally existed spindle-cells, the caudate corpuscles, and that out of these cells, fasciculi of connective tissue were developed by splitting up of the body of the cell.

FIG. 18.



A, Bundle of common, wavy, connective tissue (intercellular substance) splitting at its end into fine fibrils. B, Diagram of the development of connective tissue, according to Schwann. *a*, Spindle-shaped cell (caudate corpuscle, fibroplastic corpuscle of Lebert), with nucleus and nucleolus. *d*, Cleavage of the body of the cell into fibrils. C, Diagram of the development of connective tissue, according to Henle. *a*, Hyaline matrix (blastema) with nucleolated nuclei regularly distributed through it. *b*, Fibrillation of blastema (direct formation of fibrils), and transformation of the nuclei into nucleus-fibres.

Henle thought that originally there were no cells, but *nuclei* only were developed in the blastema at certain intervals, while the fibres which afterwards appeared were produced by a direct fibrillation of the blastema, and that while the intermediate substance was thus being differentiated into fibres, the nuclei gradually became elongated, so as at length to run into one another, and thus give rise to peculiar longitudinal fibres (*nucleus-fibres* or kernfasern).

Reichert contended that there were cells in great abundance between which was deposited intercellular substance, with which the membrane of the cells became subsequently blended, reaching thus a stage in which there was no longer any boundary between the cells and the intermediate substance. The nuclei he thought also disappeared in some instances. The intercellular fibres he said were a false interpretation of an optical image.

Virchow, with Schwann and against Henle, be-

FIG. 19.

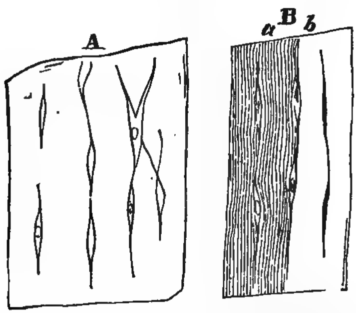


Diagram of the development of connective tissue, according to Virchow's investigations. A, Earliest stage, hyaline basis (intercellular) substance, with largish cells (connective tissue corpuscles); the latter drawn up in rows at regular intervals; at first, separated, spindle-shaped and simple; at a later period, anastomosing and branched. B, More advanced stage; at *a*, the basis-substance which has become striated (fibrillated) presents a fasciculated appearance on account of the cells imbedded in it in rows, the cells becoming narrower and smaller; at *b*, the striation of the basis-substance has disappeared under the influence of acetic acid, and the fine and long-anastomosing fibre-cells (connective tissue corpuscles), still retaining their nuclei, are seen.

lieves that spindle-shaped cells indisputably exist, and with Henle and Reichert and against Schwann, a splitting up of the cells into fibres does not occur, but that a previously homogeneous intercellular substance becomes fibrillated, and that the cells themselves preserve their integrity. In young connective tissue, cells undoubtedly exist, with at least their more important parts as nuclei and protoplasm, but in fully formed fibrous tissue the only portion of the cell which I have been able to satisfy myself, in an almost daily study of healthy and diseased structures, is constantly present, is the *nucleus.*

Max Schultze, in Germany, Beale, in England, and Leidy, in this country, believe the intercellular substance to originate as the cell-contents and cell-wall by a conversion of the nucleus or bioplasm at its periphery, and a pushing off of this converted matter by the deposition of new bioplasm within the nucleus. In fact, according to them, the intercellular substance is simply the oldest cell-wall or formed material, under which term Beale consistently includes all intercellular substance. See Figs. 11, 12, frontispiece.

This view seems to me also to be most consistent with observation, and until something more reasonable is offered I shall adopt it. One of the most potent arguments in its favor is the fact that the cell-wall and intercellular substance are often so closely continuous that they cannot be separated, either visually or by dissection. On this account Beale has also described a "cell" or "elementary part" of cartilage and similar structures, as including in its formed material the intercellular substance extending to a point midway between it and its neighbor.

The Structure of Cells.—As to structure, cells have been heretofore described as structureless, or variously granular, and with powers not exceeding 250 diameters, they may still be so described. Few cells even with these powers are structureless, while on the other hand, a highly granular condition of a cell is considered indicative of some pathological change, except in the case of nerve-cells, which in many situations are admittedly highly granular in the normal state. The same may be said of the nucleus. Occasionally, however, even previous to 1867, certain nerve-cells were described as *striated* in appearance. Examples of structureless cells are most striking in the unicellular organism, as the *amœba* (Fig. 16, frontispiece), in which we have a structureless nucleated mass, which owes whatever of structure it possesses to foreign particles, which it takes up as food. So far as the structure of the elementary part of the more complex organisms, however, is concerned, the recent discoveries, already described (see p. 117) as discernible by a power as low as 300 diameters, demand a total change in the description of the structure of cells. Henceforward we must describe not only the nucleus but also the cellular substance (protoplasm) as fibrillar in structure, made up of a network of delicate fibres the meshes of which are filled with an "interfibrillar" or "ground substance," which is structureless, and that the fibrillæ of the *intracellular* and *intranuclear* networks are continuous. And if Klein be correct we must define the *nucleoli* as merely local thickenings, natural or artificial, of the *intranuclear* network. The *intranuclear* networks are much more distinct than the *intracellular*. See plate at end of volume.

The Shape of Cells.—The *shape* of cells is extremely varied. In its fully developed state each tissue is composed of cells which may be said to be characteristic of it. *First*, the typical form of a cell may be said to be *spherical*, and this is the shape of all young cells in whatever situation found. See Fig. 10, frontispiece. *Second*, in *glandular* tissue, where perhaps cells are changing more rapidly than in any other situation in health, their deviation from the round shape is only such as results from mutual compression, forming more or less *polygonal* cells, as seen in Fig. 3, p. 39. *Third*, in *epithelial* structures we have upon the extreme periphery either flat scales containing a small proportion of bioplasm (nucleus) in proportion to the non-germinal matter (cell-contents), and of irregular outline, forming the so-called *squamous* epithelium, Figs. 3, 4, 5, 6, frontispiece; or *fourth*, similar scales, of regular outline, many-sided and with their edges so adapted as to form a pavement-like structure, forming *tessellated* epithelium; or *fifth*, elongated nucleated cells, which from their shape are called *columnar* cells. *Sixth*, in certain situations, as the respiratory passages, these columnar cells are further provided with hairlike prolongations, known as cilia, which in health exhibit a constant *waving* motion, whence the cells are called *ciliated* cells. Wherever columnar cells are present in successive layers (as is usually the case), they lose their characteristic shape and approach more and more the spherical outline as we recede from the surface, until the deepest and therefore youngest cells are again spherical. *Seventh*, in nervous tissues again, we meet cells which from their prolongations, which may be one or many, are called *polar* cells, and unipolar, bipolar, or multipolar, according to the number of processes they possess. *Eighth*, in the so-called *connective* tissue again, we have a variety in the shape of the cells. Thus in areolar tissue or connective tissue proper, we have young round cells composed almost wholly of germinal matter, exhibiting amœboid movements and all the characters of the leucocyte or colorless corpuscle (Fig. 10, frontispiece), as well as the elongated spindle shaped nucleated cell, so characteristic as to have long ago received the name *connective tissue corpuscle* (Fig. 16, frontispiece, Fig. 18, B.). These latter cells also possess prolongations, which unite with those extending from adjacent cells, and being hollow thus form a canalicular system, of exceeding fineness, which is believed to be capable of conveying nutrient juices in the absence of bloodvessels of sufficient size to conduct the corpuscles of the blood. The appearance of this system is shown in Figs. 16 and 19, from Virchow's *Cellular Pathology*. *Ninth*, the cells of *striated muscular tissue* exhibit a *prolonged oval shape*, sometimes resembling that of the connective tissue corpuscle, while the cells of *unstriped muscular tissue* are typical *spindle-cells*, with bellied centres and staff-shaped nuclei.

Again, in cartilage we have cells exhibiting various modifications of the spherical shape, while the cells of *bone* give us a *tenth* form. These are contained in correspondingly irregular cavities in its substance, and are almost fantastic in their irregularity, exhibiting also prolongations which unite with those of neighboring bone-cells, and with the Haversian canals which conduct the bloodvessels through bone. The shape of the cells through whose agency the *teeth* are formed is also seen to be peculiar, those whence the dentine is developed being provided with a single long process, giving an *eleventh* form of cell. Those producing the enamel are columnar, while the *crusta petrosa*, or portion of bone-like substance covering the fang, contains cells similar to those of bone.

Finally, the cells of *adipose* or *fatty* tissue require allusion. They are spherical or compressed vesicles or sacs of considerable size, are filled with oil, and exhibit in consequence a brilliant, highly refracting character, under the microscope, indicated by a broad dark border and a transparent centre. In the beginning they are in no way different from other young cells, but, according to Beale, their bioplasm, instead of being converted into the ordinary non-germinal matter of albuminous composition, undergoes a fatty conversion, in the course of which it gradually diminishes in size and is thrust towards the wall of the cell, where it may sometimes be demonstrated by staining as a small flattened nucleus. The oil thus produced is termed by Beale *secondary* formed material, to distinguish it from the albuminous nongerminal matter. The same term is applied by him to the secondary product, *starch*, found in the shape of concentrically laminated granules in many vegetable cells. According to most other histologists, however, the fatty contents of the *fat*-vesicles are an infiltration of fat from the blood, *superadded* to the protoplasm or cell-contents, pushing the latter with the nucleus to one side, without substituting it or being derived directly from it as is alleged by Beale.

In *pathological formations* all the different forms of cells here alluded to are met with, and there is now no special type of cell which is known by its shape to have a pathological impression. It is rather by the rapidity of growth of cells, their arrangement and relation to the intercellular substance, as well as peculiarities in the latter substance itself, that we know a structure to be a pathological formation. The "cancer-cell," which was so long an object of wonder and fear, and eagerly sought for as such, is no longer acknowledged to be anything peculiar as to form. At the same time, when cells from a suspected growth are observed to be very large, to contain numerous nuclei or centres of bioplasm, and to exhibit great variety in shape, we have evidences of that rapidity of growth which is more or less characteristic of malignant formations.

The Size of Cells.—This is likewise extremely various. They may be particles of such extreme minuteness as to be recognized as mere dots by the highest powers of the microscope, the smallest particles of germinal matter measured by Dr. Beale being less than the $\frac{1}{100000}$ of an inch (.000024 mm.) in diameter, while the largest epithelial scales are $\frac{1}{250}$ of an inch (.1 mm.) in diameter, and the cells of morbid growths often reach the $\frac{1}{200}$ of an inch (.127 mm.). The human ovum, which may be regarded as a typical cell, with nucleus, nucleolus, and contents, varies from the $\frac{1}{240}$ to $\frac{1}{120}$ of an inch (.105 mm. to .21 mm.). The smallest particles of germinal matter above alluded to would not be called cells in the ordinary sense of the word, but they are such consistently with our definition, and it must moreover be remembered that the term is only applied to such particles of matter endowed with the life properties of reproduction, nutrition, growth, and development. No particle of oil, inorganic or other matter, which does not possess these properties can be characterized as a living cell, whatever its size.

Pure germinal matter is rarely seen in masses as large as the $\frac{1}{500}$ of an inch (.05 mm.), since it usually breaks up into smaller masses to form independent cells before it reaches this size. As constituting the nuclei of fully formed cells, it is usually from the $\frac{1}{6000}$ to $\frac{1}{3000}$ of an inch (004. mm. to 008. mm.) in diameter. While nuclei exhibit less variation in size than do the cells, they are also more constant in shape, being generally round or oval. Sometimes, however, they also exhibit a stellate shape.

The Origin of Cells.—It is to be regretted that this most important question as to the exact origin of cells is not yet definitely settled. A very short time ago the proposition *omnis cellula e cellulâ* was thought to have been abundantly proven, and that all living things come from previously existing things, was generally admitted. But although this view has been, in the conception of some, shaken by more recent experiment, it still remains the only law of cell formation in the minds of most physiologists, and I believe there are none who deny that it forms in all the higher forms of animal and vegetable life the only method of cell genesis which is constantly before us, while the phenomena of spontaneous generation are confined to the creation of the lowest vegetable and animal organisms, so that the proposition *omnis cellula e cellulâ* may be now considered as generally accepted. Prof. H. Charlton Bastian remains the most eminent English supporter of the doctrine of spontaneous generation, against whom Huxley, Roberts, Tyndall, Beale and others have directed articles and experiments.

In the division of cells to produce young cells, it is usually in the nucleus that the segmentation first begins, extending thence to the protoplasm outside of it, although this is not invariable. For any portion of the bioplasm of a cell may grow, separate and form a young cell. It is the bioplasm or germinal matter alone, however, which can give rise to the cell, and never the non-germinal matter or formed material. It is seldom, also, that we see in the animal cell, except in the segmentation of the fecundated ovum, that symmetrical division of the nucleus into two, these into four, these into eight, and so on, as is constantly seen in the vegetable cell, but it is rather a budding and subsequent dropping off of portions of bioplasm which become young cells, and which almost always assume the spherical form when allowed to float freely (see Fig. 10, of frontispiece).

Strassburger,* in his recent work on *Cell Formation and Cell Division*, admits three methods of increase

* Ueber Zellbildung und Zelltheilung, Jena, 1875.

of cells,—cell division, free cell formation, and renewal (vollzellbildung) of cells. He says that in the animal kingdom cell division seems to be the only authenticated mode of increase of cells. Of methods of free cell formation, only a few instances are recorded in vegetables. The last method, renewal or rejuvenescence, has reference rather to the complete formation or development of cells than to their origin.

Nutrition of Cells.—In the *nutrition* of the cell, the pabulum comes to it from the periphery, being strained through the formed material. The new germinal matter takes its place in or near the centre of the original mass, constituting, according to Beale, a new centre of germinal matter, which may be the nucleus, if no other circumscribed centre be present, or the nucleolus, if it be deposited within such a centre. Other new centres, according to him, may again take position within these, and assume the relation of nucleolus to the original nucleolus, which now becomes the nucleus, an older centre of germinal matter; while the original nucleus has probably been converted into the second constituent of the cell, the formed material. If the nucleolus be what Klein considers it, a mere thickening of the intranuclear network referred to, this order of succession in the formation of differentiated centres of germinal matter is of course impossible, and it can only be said that the new matter takes its position towards the centre of the cell mass.

Amœboid Movement (Diapedesis).—Germinal matter, when free and living, exhibits a power of movement, both in *portions* of its substance, producing changes in shape, and in its *entire mass*, resulting in changes of position. The former, and probably, also, the latter, may have for its object the obtaining of pabulum, as is seen in the amœba, when it embraces by its protrusions a particle of nutritive matter. These movements are less decided in the cells of the higher animals, yet they are of constant occurrence, as in pus and white corpuscles, and when thus occurring they are spoken of as "amœboid movements." Allied or identical with this second class of movements, are those of undoubted occurrence in white blood-corpuscles, first observed by Addison,* Waller,† and Cohnheim,‡ whereby these cells have been seen migrating from the bloodvessels.

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* Addison, Physiological Researches, London, 1841.

† Waller, London, Dublin and Edinburgh Philosophical Magazine, vol. xxix, 1846, pp. 271 and 398.

‡ Cohnheim, Ueber Entzündung, und Eiterung, Virch. Arch. Bd. xl, 1867, p. 1.

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" Eine Bemerkung über weisse Blutkörperchen, Berliner klinische Wochenschr., No. 29, 1876.

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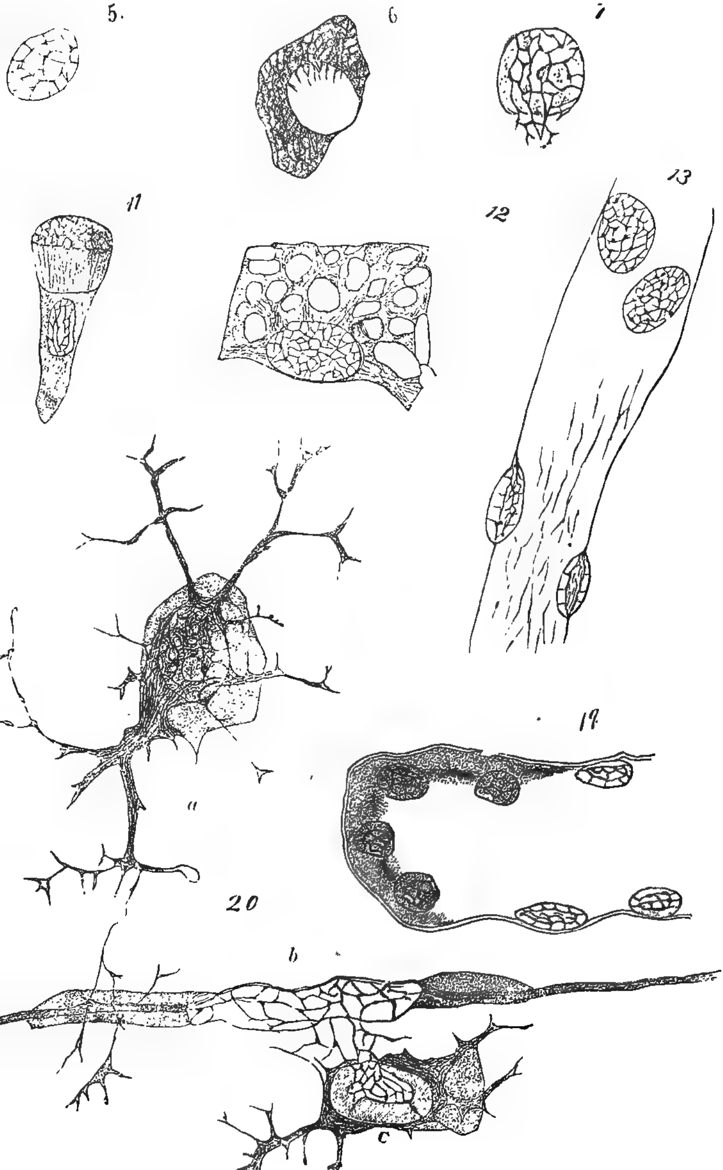
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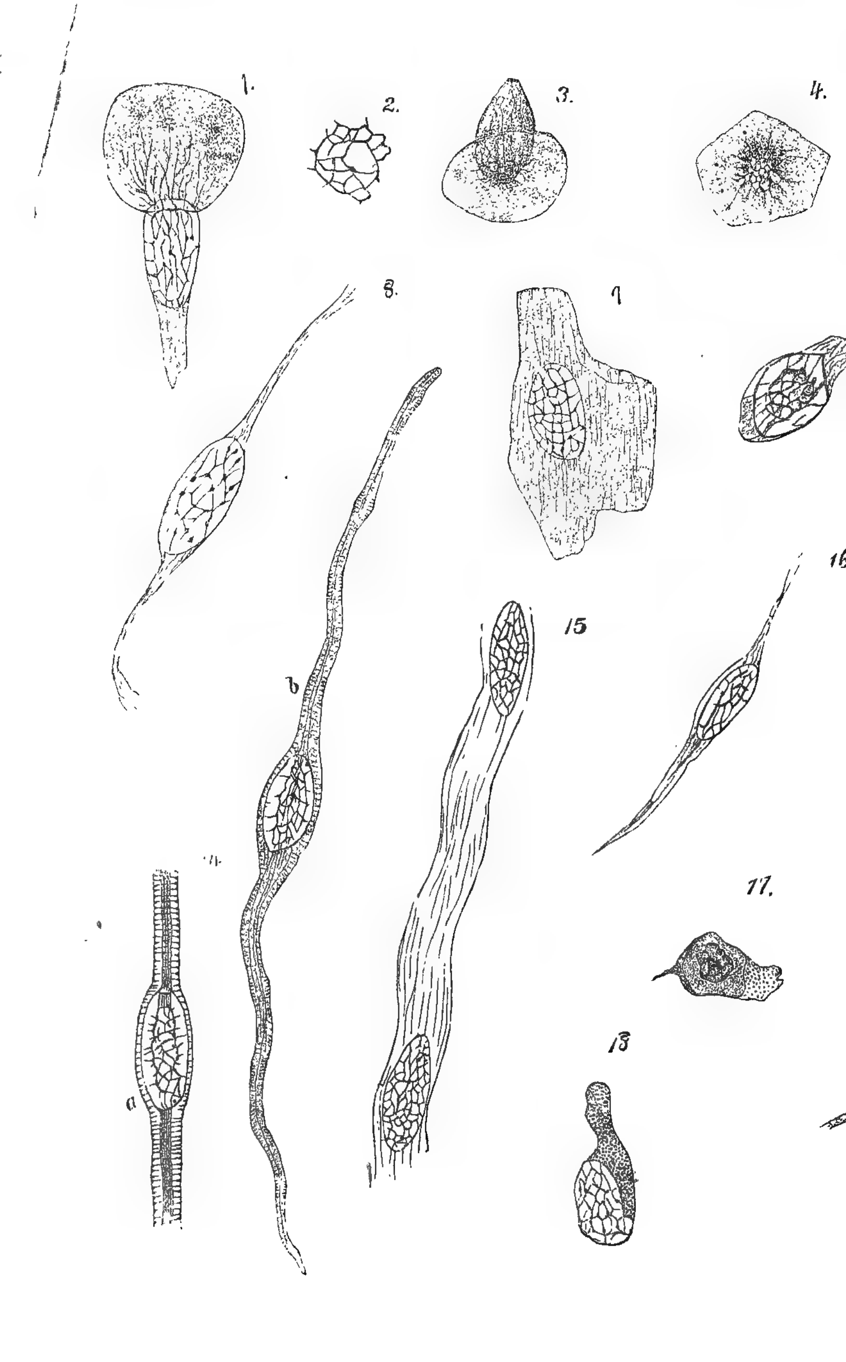
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EXPLANATION OF PLATE,

ILLUSTRATING DR. KLEIN'S PAPER, "OBSERVATIONS ON THE STRUCTURE OF CELLS AND NUCLEI."

(From the Quarterly Journal of Microscopical Science, for July, 1878.)

FIGURES 1–11 (incl.) refer to preparations of stomach, 12–20 to those of mesentery of newt. For method of preparing see text. All figures are represented as seen on Hartnack's small stand with eye-piece III, and Zeiss's objective F.

FIG. 1 represents a goblet cell; the intranuclear network is well shown, and also the fibrils passing from this into the upper and lower part of the cell.

FIG. 2.—The intranuclear network separated from the membrane of the nucleus.

FIG. 3.—A goblet-cell (like that of 1) as seen obliquely from above, showing the intracellular network.

FIG. 4.—The intracellular network looked at vertically from above.

FIG. 5.—Isolated nucleus showing the intranuclear network.

FIG. 6.—A gland-cell, showing the dense network of fine fibrils of the cell-substance; the nucleus has escaped, but there are still left a few fibrils, probably connecting the two networks, viz., the intranuclear and the intracellular.

FIG. 7.—An isolated nucleus of a gland-cell; the wall of the nucleus is broken at one place and the intranuclear fibrils are seen passing outwards.

FIG. 8.—A connective tissue corpuscle—endothelial plate—seen in profile; both the intracellular fibrils and those of the intranuclear network are well shown.

FIG. 9 —A similar cell seen from its broad surface.

FIG. 10 —Portion of a cell; the intranuclear network shrunk.

FIG. 11.—An epithelial cell; the intracellular fibrils are well shown. The top of the cell is seen in an oblique direction, and

the network of fibrils is therefore brought into view. Preparation treated with Müller's fluid, and then with mixture of chromic acid and spirit; see text.

Fig. 12.—Isolated endothelial plate of surface of mesentery. The intracellular and intranuclear networks of fibrils are well shown.

Fig. 13.—A capillary bloodvessel; the two upper nuclei are seen from their broad side, the two lower in profile. They all show the network of fibrils. In the lower portion of the wall of the vessel an imperfect network of fibrils may be perceived.

Fig. 14, *a* and *b*.—Two unstriped muscle-fibres. The intranuclear network of fibrils is well seen; these are in connection with fibrils of the substance of the muscle-fibre; there are seen numerous transverse markings along almost the whole length of the muscle-fibre. That these transverse markings correspond to rings which constitute the cortical part, *i. e.*, the sheath, is well shown in *a*.

Fig. 15.—A non-medullated nerve-fibre of mesentery of newt; the nerve-fibre has a delicate sheath, the nuclei of which contain a distinct network of fibrils.

Fig. 16.—A connective tissue corpuscle seen sideways. The nucleus contains a network of fibrils, in connection with that of the cell-substance.

Figs. 17 and 18.—Two migratory cells; 17, a common pale one, 18, a coarsely granular one. Their nuclei show the network of fibrils very well.

Fig. 19.—A cæcal dilatation of a lymphatic vessel of the same membrane, showing the nuclei of the endothelial cells forming the wall of the lymphatic, and also nuclei of lymph-corpuscles.

Fig. 20, *a* and *c*.—Two connective tissue corpuscles; the distinction between "ground-plate" and "fibrillar substance" is well shown; the "fibrillar substance" is in connection with the intranuclear fibrils.

b, a nucleated plate ensheathing a minute non-medullated nerve-fibre. The intranuclear network is seen in connection with the processes and fibrils of the connective tissue corpuscle *c*.