Bernays (A. C.)

on the relations between cells and micro-organisms –

CHIPS FROM A SURGEON'S WORKSHOP.

CELLS AND MICRO-ORGANISMS.

BERNAYS.

SURGEON GEN'L'S OFFICE
410
LIBRARY

CHIP NO. X.

On the Relations Between Cells and Micro-Organisms.

BY

AUGUSTUS C. BERNAYS,

A.M., M.D. HEIDELBERG; M.R.C.S., ENGLAND; F.R.M.S., LONDON.

Member German Society Surgeons of Berlin; Professor of Anatomy St. Louis College Physicians and Surgeons.

SURGEON GEN'L'S OFFICE
410
LIBRARY

Reprinted from the Journal of the American Medical Association, January 2, 1886.

CHICAGO:
PRINTED AT THE OFFICE OF THE ASSOCIATION.
1886.

ON THE RELATIONS BETWEEN CELLS AND MICRO-ORGANISMS.

The following essay contains the results of years of study with the microscope, begun in Europe, in 1875, at the laboratory of Prof. C. Gegenbaur, and continued in such time as I could devote to the work while engaged in the active practice of surgery in St. Louis, Mo. I feel the many imperfections of this communication but too well, and it is only by the advice of a few friends who are acquainted with its contents that I now venture its publication. I desire to have this paper considered merely a preliminary essay, based upon unfinished investigations; but I believe that an apology for its publication will scarcely be demanded by any person after a careful perusal. The results are so fundamentally at variance with the accepted theories, and are bound to work such a revolution in our current opinions, that I naturally expect very considerable opposition.

I am unable to say when my time will permit publishing the details of the observatious and experiments. My notes are very voluminous, and the execution of the drawings as well as the systematic arrangement of the text and literature would require several years of steady work.

In the meantime I hope this paper will at least draw the thoughts of my fellow-workers in this field of research into new channels, which I am convinced will prove fertile in many ways, more especially in their effects upon the progress of Histology, Pathology and Biology.

The greatest step forward that was ever taken at one time in medical science was by Rudolph Virchow in the years 1855–1858, when he finished his classical work on "Cellular Pathology." It is not saying too much to claim that on the recognition of the cell theory and its application to pathology is built the entire structure of modern medicine, surgery and hygiene. Recognizing the immense benefit which has accrued to mankind from this doctrine, I propose now to inquire into the facts upon which it is based and to ask in which way further progress may be expected.

1. "*A cell is a living body consisting of two bladders, the one within the other of different chemical constitution.*" Virchow.

2. "*Omnis cellula e cellula.*" Virchow.

3. "*All living things correspond in the one point, that they originate from a cell.*" Virchow.

4. "*The cell is the simplest form of life-manifestation.*" Virchow.

5. "*Life is confined to a definite form, the cell.*" Virchow.

6. "*Without a cell there is no life.*" Virchow.

The above six sentences are quoted from Virchow's "Gesammelte Abhandlungen zur Wissenschaftlichen Medicin," pag. 22, Frankfurt-on-Main, 1856.

The commanding influence of Virchow on modern pathological and biological research has so far controlled the opinions and thoughts of European scientists, of whom at least four-fifths are his own disciples, that the above theses have entirely entered into the bone and sinew of the students of natural sciences. Until very recently they have gone unchallenged, except by a very few, and the objections have as yet made little or no impression, as can be seen by a glance at the first pages of any text book of pathological anatomy or biology published during the past ten years.

In a paper purporting to treat of cells, it is proper that we should define this term. If we cannot define the term, it loses its usefulness. The definitions given by Virchow above are insufficient, since we know innumerable instances of living solitary organisms that do not fulfil the postulates. For instance, a micrococcus is certainly a living being, but it is no bladder, nor has anybody ever seen a bladder-shaped substance within it. I chose this instance at this place, because *I expect to prove that the group of micro-organisms, which we call schizomycetes, cannot be classed under the head of what any author up to this day has ever defined to be a cell.* When Virchow says that: "Without a cell there is no life" he *defines* nothing; the statement is of about as much value as if he had said, *Without protoplasm there is no life, or without albumen there is no life.* Such statements are purely hypothetical; they are illogical, because they involve unknown quantities *i. e.* cell, protoplasm, albumen, and finally they are not postulated by anything. I have just shown that Virchow's definition of a cell would exclude the micro-organisms, but no one will doubt that they are living bodies.

C. Gegenbaur, one of the most acute and logical thinkers among morphologists defines cells as follows: "Cells consist of a small lump of soft living substance, which encloses a more compact body, the nucleus." This definition would also exclude the

micro-organisms of the group of the schizomycetes. The text books of Frey, Orth, Toldt, W. Krause and others have accepted the definition of Max Schultze, who defines the cell-substance or protoplasm as a homogeneous, glassy-transparent ground-substance, of a semi-fluid (soft-waxy) consistency, held together by virtue of this property; with a nucleus, a nearly homogeneous, globular, almost solid body, containing a shiny nucleolus. This definition fits the schizomycetes just as little as did the two former. We must therefore conclude that these organisms are not cells at all. But they are living beings. Therefore life is not confined to the definite form called a cell, neither is the cell the simplest form of life-manifestation, and there certainly is life independent of cells.

Before entering more deeply into the question regarding the proper definition of the notion cell we must examine what the term protoplasm means. This question is not easily answered, since the word is used promiscuously by different authors to mean very different things. Confusion reigns in regard to the meaning and use of this word to such a degree that a definition is impossible. Some use the word to designate all living and acting substance; the whole substance of the cell including the nucleus, but excluding the cell-membrane, if one be present. Others mean by protoplasm only the substance of the cell minus nucleus and membrane. Others again use the term only in regard to indifferent or young cells, and do not apply it to the substance of cells which have become specifically differentiated. It appears very difficult where to draw the line in these cases between protoplasm and differentiated or higher cell substances. But few call the cell substance of muscle cells, or of red-blood-corpuscles *protoplasm*, whereas most histologists speak of the protoplasm of ganglion or cartilage or connective tissue-cells. Should any one attempt to answer the problem, whether any given cell substance is protoplasm or when it is no longer protoplasm, he will find himself unable to respond, simply because no one knows exactly what protoplasm is. The recent researches on protoplasm or cell-substance by Fromman, Arnold, and especially by Walter Fleming, on whose works I have largely drawn for the present essay, have shown that there is a definite structure in protoplasm morphologically speaking. This question, as to the nature of protoplasm, has also been studied by Heitzman, and he has arrived at the remarkable conclusion, that the entire body of all animals is one connected mass of protoplasm. Stricker has even denied that cells have

definite boundaries. These last two hypotheses or discoveries, as they are claimed to be, by their authors, directly contradict the experiences of 99–100ths of all observers, and I have seen nothing which would lend even the slightest countenance to such statements. Protoplasm has been analyzed chemically and has been found to consist of albuminoid substances; it is said to be contractile, but that is not proven of everything which is called protoplasm. The protoplasm theory says: "Protoplasm is living material, all life and all organic forms are limited to it and are its products." Does this proposition deserve the name of a theory? Considering that we cannot define the word protoplasm better than the above sentences have shown, is not this theory virtually a *petitio principii*, as much, and even more so, than we were able to show the cell-theory of Virchow to be.

Our conclusions thus far might be called iconoclastic, although strictly logical and scientific. They deserve this appellation unless we can show how the errors just found, may be avoided by future investigators, or if we can advance a better hypothesis in the place of the old ones.

During the past five years two particular subjects in microscopical science have chiefly engrossed the thoughts of all progressive workers in this branch. The first one was the morphology and physiology of micro-organisms, which term I use to include schizomycetes and micrococci only. The second was the morphology and physiology of cell protoplasm and cell-nucleus, especially the phenomena of karyokinesis, or the division of the nucleus and the structure of cell-substance. During my studies on the subjects, I was first of all impressed by the observation that the so-called bacteria or micro-organisms can in no way be compared to what in histology of the higher animals are called cells. Following up this impression by micro-chemical experiments, I soon became convinced that the reactions of the cell-substance or protoplasm in no way corresponded to the reactions of bacteria or schizomycetes under the same treatment. This fact, however, is well established by many investigators. I found, also, that the chemical reaction of the micro-organisms closely corresponds to the reaction of the nuclei contained in the cell-substance; in fact, that it must be very similar to the substance we call nuclein. During the summer of 1884 I spent many days and nights examining and cultivating micro-organisms of different kinds. In many of my open air cultivations with hay infusions

I made the discovery, that there are organisms which can only be called free living nuclei. This observation has been made by a few investigators before me, but has always been denied or disputed by others. I am ready, however, during any summer, to demonstrate and cultivate these organisms to the absolute satisfaction and conviction of even the most skeptical person. In these infusions I not only found free living nuclei, but I saw organisms in almost all stages between a free living naked nucleus to nuclei which were surrounded by a complete shell of protoplasm or cell-substance. I also saw nuclei which had a single protoplasmatic cilium, which they used as an organ of locomotion. Others of these nuclei had three, still others had as many as fifty cilia arranged around their circumference. I could plainly see how a small speck of protoplasm attached to one side of these free nuclei would develop into a hair or cilium, during a few hours that were occupied in the observation of a single organism. I could also plainly discern that within the free living nuclei there were smaller dark bodies, some of spherical, others of bacillar shape, which were in constant lively motion. I am sure also that I often saw them arrange themselves into rather regular figures previous to division. I never succeeded in observing an entire process of division either in a free living nucleus or in an isolated living cell. The cause of this was that I could not keep the organisms alive long enough by any means at my disposal. I can, however, corroborate the observations of Walter Fleming regarding the process of nuclear division on hardened specimens to the very utmost detail. Another observation that I can state with certainty is that the movable bodies contained within the nucleus sometimes leave the body of the nucleus and swim away from it under the cover glass in the water or solution of nutritive salts. I also saw bodies which evidently were micro-organisms, either bacteria or micrococci, enter into these free nuclei, probably through the same pores or holes in the nuclear membrane through which the others had just left the nucleus.

During the summer of 1885 I spent many hours in experiments, conducted with a view to solve the problem as to what would become of a living cell if left to die in a sterilized nutritive fluid. I may be permitted to state that I became almost convinced that the death of cells under these circumstances is attended by the development of micro-organisms.[1]

[1]Experiments are now being made after Koch's method to determine this point, by the makroscopical method on sterilized gelatine in various ways, at my request in New York by experienced bacteriologists.

My observations on this point, however, were not absolutely satisfactory. It is almost impossible to exclude all sources of error, and I do not wish to be understood as having stated this to be a certain fact. Most of these experiments were made with a Zeiss 1–25 inch lens. Before leaving this part of our discourse I must say that all later observers seem to agree on the fact that the nucleus is the essential part of a cell, and that the reproductive function at least emanates from it. The other functions of the nucleus, if there be any, are unknown. The fact, however, that reproduction starts and is principally carried on by the nucleus, sufficiently proves that the nucleus is the most important part of the cell. As long as the idea that a nucleus which is not surrounded by protoplasm or cell-substance does not exist as a living entity controls the mind, it will be very hard to grasp the weight and bearing of the above observations.

Histologists who are accustomed to work almost exclusively with tissues of higher organisms never think of a living nucleus without protoplasm, even as a possibility. After a time, when the fact that there are numerous organisms which are homologous to free nuclei shall have been recognized and corroborated, the supposition that the nucleus is, genetically speaking, the older and most essential part of a cell will seem as evident as it has seemed heretofore that the cell-substance was the important part of the cell. This latter opinion is based upon the hypothesis that the nucleus is only "condensed or differentiated protoplasm." It supposes that protoplasm is the basis of all life. But we know of many organisms, for instance, schizomycetes or micrococci, whose chemical and morphological appearances in no way correspond to those of protoplasm. We know also that the nuclei of cells, as well as the free living nuclei, are not protoplasm. The protoplasm theory must therefore be given up; it is imperfect and is not called for by the facts. I should not wonder if in a few years it will appear strange how such an error as the slighting of the nucleus in favor of the cell-substance, making the latter the more important, and giving the nucleus only a secondary position, could have occurred. The greatest living investigators, men who usually proceed in a most logical and scientific way, have fallen into this prejudice. We know of no example of a cell in the animal kingdom that neither has nor ever had a nucleus. The so-called cell-substance, however, is not really so constant a factor; we find it in the most varying conditions. We do not know that any cell without a nucleus is capa-

ble of division or multiplication, but I have seen the division of the living naked nucleus. These facts all tend to demonstrate the primary and essential importance of the nucleus in contradistinction to the cell-substance. The function or use of the latter is unknown. Possibly it serves the purposes of nutrition in the beginning and is afterwards used for a great variety of purposes, the nucleus always being the essential part so long as it lives.

No one will dare to deny that the great progress made in the natural sciences in modern times is chiefly due to the recognition of the great principle of evolution. This principle itself was established most thoroughly by the two disciplines called comparative anatomy and embryology. It is very evident that the main progress we have made towards a scientific understanding of organic life, has been reached not by study only of the adult or perfect stages of our objects, but by the observations made on the different stages of the growing organism during its development. Gegenbaur says: "Thus ontogeny and comparative anatomy appear as the scientific basis of human anatomy." The latter discipline has been placed upon a more scientific basis, since the introduction of the onto- and phylo-genetic methods of investigation. These methods, I deem, are the ones which should be employed in all instances where a question arises concerning the position of any given organism in the pedigree of life.

Mr. Ernst Haeckel himself has fallen into a grave error here, which undoubtedly will cause the toppling over of his entire structure, grand and wonderful as he has built it. Mr. Haeckel is the author of the biogenetic fundamental law. This law, generally speaking, says: Embryology (ontogenesis) is a condensed and abbreviated repetition of phylogenesis, or the development of the race. We may accept this thesis for the present, reserving the right to modify or amend it in future. Mr. Haeckel started his tree of life upon the foundation of protoplasm, from this he jumped to what he calls monera. These organisms are cytodes without a nucleus, merely small pieces of cell-substance or protoplasm. Next he allows a nucleus to be differentiated out of this protoplasm. These, then, are his *cells*. In order to decide the question where the cells belong in the scale, Mr. Haeckel should have used the methods above mentioned; and under the guidance of his biogenetic law he might have undoubtedly reached the true conclusion.

This now brings me to the main point of this essay. In order to decide what the cell is, let us see whereto

the ontogenetic method will lead us. No sane person will claim that a cell must needs be the lowest living entity. If, therefore, we can observe the ontogenesis of higher organisms, why may we not try to study the development of a cell? I have faithfully tried this method with all the technical appurtenances, aids and ingenuity at my disposal. I have only partially succeeded, but what I have seen is very encouraging. I repeatedly saw a naked living nucleus, while under observation, develop or attract unto its surface (out of the water or nutritive fluid in which the nucleus was examined) small particles of substance which seem to me to correspond exactly in optical appearances to what is usually called cell-substance or protoplasm. The comparative method, when applied to the examination of free nuclei and cells, yielded an almost perfect result. As I stated above, I saw all the stages of living organisms which naturally range between a naked nucleus and one entirely covered by cell-substance. This observation is readily made and can be corroborated by any careful microscopist who is accustomed to work with high powers.

Placing the results thus obtained together with the beautiful work done by Fleming, Rabl, Arnold, Strassburger, Kupfer and others on karyokinesis, the conclusion which seems absolutely unavoidable is that the nucleus existed before the so-called cell and before protoplasm. Protoplasm or cell-substance is a product of differentiation of the nucleus.

I extended my investigations one step farther after I had determined the primary importance of the nucleus. I attempted to analyze the nucleus itself by the methods of development and comparison. As above stated, I plainly saw that within the nucleus there existed active moving bodies of definite forms. Their movements remind the observer of the movements of the smallest micrococci and bacteria. The refraction of light and their chemical reactions also correspond closely to those of these lowest of all known organisms. As above stated, these bodies sometimes leave the nuclei through pores in the nuclear membrane, and others seem to enter into the same places. This, together with the observation, which is not yet well enough established to be convincing, that a cell or its nucleus, when left to die in a sterilized nutrient fluid, will set free micro-organisms, would seem to indicate the hypothesis that the nucleus is a conglomeration of micrococci or a *syncoccium*. This, however, I desire to have understood is by no means a conclusion which deserves any more notice than a

preliminary hypothesis, based as it is on observations which I consider entirely too doubtful for a scientific result.

Before ending my essay I may take the liberty of setting up the following theses as the result of my observations and reflections:

Theses.

I. The hypothesis that protoplasm is the basis of all life is untrue.

II. The hypothesis that cells are the result of the differentiation of protoplasm is untenable.

III. The hypothesis that the so-called cytodes, or cells without nuclei, are phylogenetically the ancestors of cells (with nuclei) is false.

IV. The nucleus is phylogenetically the progenitor of the cell.

V. A cell is an organism which is developed by differentiation and growth from a nucleus.

VI. The process of karyokinesis is a part of the ontogeny of cells.

Hypothesis.

The lowest known stages of the phylogenetic tree of organic beings are:

I. Micro-organisms.
II. Free nuclei = synococcium?
III. Cells.

For the sake of comparison, we give the old hypothesis:

I. Protoplasm.
II. Monera or Cytode.
III. Cells.