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NEW CELL THEORY AND ITS FACTUAL BASIS

[Comment: This report gives information on the "new cell theory" of O. B. Lepeshinskaya, from an article by L. N. Zhinkin and V. P. Mikhaylov (Leningrad) published in Uspekhi Sovremennoy Biologii (Progress of Contemporary Biology), Vol 39, No 2, Moscow, March-April 1955. Another article by Zhinkin and Mikhaylov on the same subject appeared in Archiv Anatomii, Gistologii i Embriologii (Archives of Anatomy, Histology, and Embryology), No 2, 1955, pp 66-71.

A. N. Studitskiy has replied to the attack made on his work by Zhinkin and Mikhaylov. Studitskiy's article, "In Defense of the New Trend in the Development of the Cell Theory," appears in Uspekhi Sovremennoy Biologii, Vol 40, No 1 (4), July-August 1955, pp 94-107.]

O. B. Lepeshinskaya's works on the development of cells from non-cellular substance began to appear in 1934. Originally, the object of her research was chicken embryos. She described how cells which took part in the formation of the embryo (the endoderm and blood islands) were formed from the yolk. Her sphere of interest then expanded. In a book which appeared in 1945, she introduced personal data on (1) the development of cells from the living substance of crushed hydras, (2) the formation of the nucleus before the beginning of cleavage in eggs of the sturgeon family, (3) the formation of cells from the yolk during the development of birds, and (4) the formation of cells during the healing of skin wounds in mammals.

Both the factual material and the theoretical concepts of O. B. Lepeshinskaya elicited various responses from different investigators at the time.

In 1950 there was a special conference of the Biological Department of the Academy of Sciences USSR devoted to the problem of living substances and the development of cells. Lepeshinskaya herself read a paper to this conference entitled, "The Development of Vital Processes in the Precellular Period." A paper entitled "O. B. Lepeshinskaya on the Development of the Precellular Stage in the White of a Bird Egg" was presented by her co-workers V. G. Kryukov and V. I. Sorokin.

A large number of scientists presented papers at the conference, and all of them agreed unanimously with O. B. Lepeshinskaya's conclusions. They acknowledged the importance and convincing nature of her work and accepted the basis of the "new cell theory," which she says is in agreement with dialectical materialism. The conference passed a resolution which recognized the necessity for extensive research in the field of the development of cellular and non-cellular forms of life, and recommended that biologists in various specialities engage directly in the development of this "progressive field of the science of life." The conference considered it necessary to popularize the ideas developed by O. B. Lepeshinskaya extensively and to utilize them in the practice of medicine and agriculture.

The resolution of the conference has now begun to be reflected in official programs and in textbooks for higher educational institutions and schools.

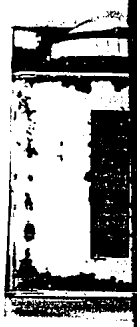
Beginning in 1950, a large number of special works devoted to the development of cells and tissues from noncellular living substances began to appear. The new cell theory has been presented as a singularly correct and absolutely proven theory in the Bolshaya Sovetskaya Entsiklopediya (Large Soviet Encyclopedia) and in a number of brochures and books.

Thus, the convincing nature and provability of the new theory, it seems, are not subject to doubt. It should be noted, in addition, that from 1950 on hardly any criticisms either of the theory itself or of the facts underlying it have appeared in print. This in itself is a circumstance which testifies to the fact that everything is not well, since no science can develop without a conflict of opinion. Moreover, in this field there is no conflict of opinion, since any scientist who says anything against the progressive cell theory is soon relegated to the ranks of the idealists, metaphysicists, or Virchowites. This situation was created by Academician T. D. Lysenko, who wrote in the forward of O. B. Lepeshinskaya's book: "It is natural that the theoretical propositions and conclusions of O. B. Lepeshinskaya may seem unacceptable to those scientific workers who have not divorced their scientific thinking from metaphysical approaches and who may reject the conclusiveness of parts of her work since this work does not agree with their theoretical views. For scientific workers who are in agreement with the genuine theory of development, the theory of dialectical materialism, the works of O. B. Lepeshinskaya are, in my considered opinion, completely acceptable." (1950, p V)

Academician T. D. Lysenko emphasized that anyone who did not agree with O. B. Lepeshinskaya or who doubted her factual data was formerly a metaphysicist and not an adherent of dialectical materialism. This proposition and the article by N. N. Zhukov-Berezhnikov, I. N. Mayskiy, and L. A. Kalinichenko, "On Noncellular Forms of Life," which was published in Bol'shevik in 1950, established to a great degree the incorrect path along which the development of the study of cells has proceeded since that time. A situation was created which caused the journals to be filled with a large number of mediocre and sometimes simply fantastic descriptions. Under the banner of progress, these works were given top priority in the publication schedule; i.e., articles devoted to the development of cells from noncellular living substance were printed in Arkhiv Anatomii, Gistologii i Embriologii (Archives of Anatomy, Histology, and Embryology), No 6, 1953, within a few months after their submission date, whereas the normal period is a year and a half. Forgetting that any investigation must be founded on concretely tested, proven facts, the editorial departments of these journals did not exhibit the fundamental requirement of scientific study -- conclusiveness.

This led to the appearance in our journals of a number of works which are a discredit to Soviet science. For example, an article by G. A. Melkonyan, on the development of bone from Echinococci which had been extracted from bones and had been immersed in formalin for a number of years, was published in Uspekhi Sovremennoy Biologii (Progress of Contemporary Biology) in 1950. The "newly formed" bone was lamellar, although, as is well known, Haversian systems are formed in a living organism around functioning blood vessels, while in the described instance there could not logically be any such vessels, and, indeed, the author did not mention them. This fact did not disturb the editorial staff, however, and the article appeared in the "News of Science" section. Many other similar examples could be cited, but we are not concerned here with individual works. Our interest is in this general trend and in the conditions which, in the recent past, have given rise to the cell theory.

It would be impossible to treat all the problems connected with the theory of living substance. We will therefore only examine those which are related, in the main, to the factual basis of the "new cell theory." We will not consider either the philosophical or factual aspects of the contemporary status of the cell theory. A special article should be devoted to these problems.



Among the arguments introduced as proof of the new cell theory, great attention is devoted to works on the formation of various blood and connective tissue cells from noncellular living substance (O. B. Lepeshinskaya, 1950; Ye. Ye. Malovichko and T. N. Rupasova, 1953; and V V. Averburg, 1954).

O. B. Lepeshinskaya conducted experiments with white mice on the backs of which skin wounds had been inflicted. She studied the regeneration process with the aid of histological sections and laminate preparations, prepared according to G. V. Yasvoin's method. According to her description, all the stages of the transition from very fine granules formed as a result of the decomposition of fat cells, phagocytized "blood granules," to actual lymphocytes could be seen in the region of infiltration on the fixed and stained preparations. "All these transitional stages from the fine granule to the lymphocyte," writes the author, "lead one to the conclusion that the granule, which has been excreted by a wandering cell, is nothing more than part of a cell, 'living substance,' which grows and produces a granule of medium caliber, then becomes larger, and finally is transformed into a lymphocyte." (1950, p 169)

Ye. Ye. Malovichko and T. N. Rupasova also studied the healing of skin wounds on mice. Proceeding from the proposition that "to repeat exactly the experiments of O. B. Lepeshinskaya is superfluous, since the results which she obtained do not need confirmation" (1953, p 23), they modified her experiments. Burns were inflicted on the animals and the processes which occured in the lesions were studied under the microscope using specimens taken from the surface of the burn with an object glass. These specimens were fixed with methyl alcohol and stained according to Romanovskiy's method. On the basis of outlines visible in these prepared specimens, the authors came to the conclusion that fibroblasts, produced by the decomposition of neutrophils (pus), after passing through a "compact sphere" stage, were formed.

V. V. Averburg studied the characteristics of cellular and phagocytic reactions of guinea pigs to tuberculosis bacilli (BCG) on fixed smears prepared from the exudate which formed at the site of injection. On the basis of a study of these smears, the author came to the conclusion that the nuclear segments of the decomposed polynuclear cells "were transformed into a very fine granule which became the source of origin for new polynuclear cells at the site of inflammation. On the other hand, due to the decomposition of the polynuclear cells, the surrounding nuclear segments grow and are transformed into lymphocyte-like cells, which undergo further transformation into lymphocytes and then into mononuclear cells like monocytes and polyblasts." (1954, p 106)

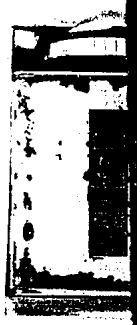
The photomicrographs which illustrate the works of O. B. Lepeshinskaya, Ye. Ye. Malovichko, T. N. Rupasova, and V V. Averburg are all identical in character: various sizes of normal blood cells, cellular elements in a state of decomposition, and granules of various dimensions are depicted on them. All these pictures can and should be treated not as stages in the progressive development of cells, but as stages in their degeneration. O. B. Lepeshinskaya is fully aware of this. She very definitely pointed out in the second edition of her book that conclusions about the development of connective tissue cells during the healing of wounds from noncellular living substance were made on the basis of indirect considerations. In her opinion, the possibility of the formation of cells from simple protoplasmic spheres isolated from the cells of a hydra, and the sharp increase in the quantity of cells at a focus of inflammation, which is not accompanied by a significant quantity of mitoses, are evidence of this. "These considerations compel us," she wrote, "to acknowledge the neoformation of cells by means of the transformation of the living

substance which is eliminated during the destruction of cells into new cells. It is necessary to make such a hypothesis on the basis of certain facts which we now have, and to try to prove this hypothesis with the aid of every modern method of research. In order to do this, we must not limit ourselves only to histological experiments, but must utilize the tissue culture method and investigate the process of healing wounds with the aid of 'ultraopaque' [sic] in a living state." (1950, pp 169-170) Unfortunately, without having carried out these experiments, O. B. Lepeshinskaya substituted a more categorical formulation for this cautious one.

In an article printed in Voprosy Filosofii (Problems of Philosophy), she wrote the following: "We studied the processes which occur in wounds, paying attention to the transformation of living substance excreted by decomposing cells, and were convinced that the blood cells which flow out of wounds decompose into granules. New cells then develop from these granules through a number of stages. The fact, established by us, that the granules, formed during the decomposition of cells, give rise to a new quality, new cells, advanced the scientific thought of Soviet histologists concerning certain important problems." (1953, p 133)

Thus, O. B. Lepeshinskaya herself has given her own hypothesis the status of a fact. Doubtlessly, this evolution was facilitated by the uncritical speeches of a number of comrades who, propagandizing in favor of the new cell theory, presented O. B. Lepeshinskaya's data on the neoformation of connective tissue cells from blood granules as a firmly established fact. We will introduce only two examples. N. N. Zhukov-Verezhnikov, I. N. Mayskiy, and L. A. Kalinichenko, in an article entitled "Noncellular Forms of Life" wrote: O. B. Lepeshinskaya also demonstrated that even in the case of the destruction of cells and the production of cell-less living substance, the cells can reconstitute themselves, reacquiring all their former structures and vital characteristics." (Cited from the collected work Vnekletochnyye Formy Zhizni [Extracellular Forms of Life], 1952, p 196) P. V. Makarov in a public lecture, published by the All-Union Society for the Dissemination of Political and Scientific Knowledge, writes without any circumlocution: "The neoformation of cells was studied by O. B. Lepeshinskaya during the healing of wounds. In this instance, the cells are formed from the blood plasma, at the expense of the living substance excreted by the destroyed tissues in the wounding process." (p 15)

An article by A. A. Safronov was published recently in Vnekletochnyye Formy Zhizni. Safronov developed a method of treating purulent wounds "by drawing off all the nonliving elements of the wounds and simultaneously attracting wholesome living substance from deep within the wound." (1952, p 176) A table showing the results of treatment with the author's proposed method was appended. Out of 112 patients, positive results were obtained with 110. Clinically positive results are indisputable, and it can only be hoped that the author has such success in his future work. The theoretical treatment of his method, which he bases on the theories of Lepeshinskaya is more open to question. He correctly indicates that he removes the pus and decomposition products not only from the surface of the wounds but from deep within it as well. We are in full agreement with this. This action undoubtedly plays a decisive role in the healing. The reasoning of the author concerning the role of the blood, the intratissue liquids, and the protoplasm of the cells in the raised granulating edge of the wound--"which are transformed into living substance, capable under favorable conditions of developing into whole cells and connective tissue fibers" (p 186)--is completely unsubstantiated and unproven.



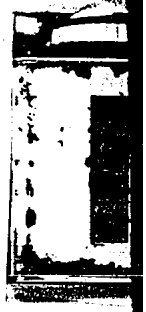
Innovational works which advance any field of science or force us to reconsider what have seemed to be firmly established positions are always welcome. However, the data upon which these works are based should be incontrovertible from a factual point of view. This cannot be said of the works introduced by O. B. Lepeshinskaya, Ye. Ye. Malovichko, T. N. Rupasova, and V. V. Averburg. All of them are incorrect from the methodological point of view. Their treatment of the pictures observed in the preparations is completely uncritical. They ignore two important methodological details: (1) the pictures showing the transformation of small grains and agglomerations into cells could be introduced with equal justification as proof of the opposite process, i.e,, their decomposition, and (2) the distribution of decomposing cells of one type (neutrophils or fat cells) and elements of normal types of cells (lymphocytes or histocytes) in one and the same microscopic field cannot, without justification, be considered as evidence of a genetic relationship between them.

Does all that has been said mean that the dynamics of the transformation of certain cellular structures cannot be studied by using histological preparations? Naturally, no. The problem of the possibility of correlating individual histological preparations each of which represents certain details of a momentary process is very complicated. A correct interpretation can be made in a given case only if the following details are observed: (1) the existence of sufficiently complete, well worked over data which can explain the whole dynamics of the process; (2) an account of all aspects of the process in its entirety, including the migration, proliferation, and degeneration of the cells; (3) an account of the numerous bibliographic references which reflect the enormous experience of previous investigators; and (4) a comparison of the preparations with analogous data obtained through the study of tissue elements during embryogenesis and during pathological conditions in an organism both in the living state and in tissue cultures.

Modern hematology is based on an enormous amount of factual data. In order to explain the interrelationships between various types of blood cells on the one hand and between blood and connective tissue elements on the other, experimental data based on conditions in an intact organism and in tissue cultures, comparative histological observations, and different types of clinical material have been utilized. Naturally there are still many disputable and indeterminate problems in the field of histology. The dispute between the unitarians and the polyphiles is still going on. As before there is still no exact definition of the nature of monocytes. Nevertheless, the basic outlines of the interrelationships between the blood elements have been sufficiently exactly clarified and, in addition, have been tested in live form in clinical laboratories where a study of the laws governing the development of the blood has been used successfully for diagnostic purposes.

At the present time it can be considered an established fact that among mammals: (1) small lymphocytes are capable of transforming into histocytes and then into fibroblasts (A. A. Maksimov) and, under certain conditions, into special myelocytes and leukocytes (Ryum). (2) myeloblasts are capable of transforming into small lymphocytes, histocytes, fibroblasts, and also erythroblasts and granulocytes (Timofeyevskiy and Lepeshinskaya).

There have been no observations or facts in modern hematology which point to the development of blood cells or connective tissue from granules formed as the result of the decomposition of granulocytes or fat cells. The "discoveries" of O. B. Lepeshinskaya, Ye. Ye. Malovichko, T. N. Rupasova, and V. V. Averburg are based on data which contain nothing original either in relation to setting up the experiments or in the preparation of specimens. Their conclusions are based on considerations which are the exact opposite of all the known illustrations of the various stages in the decomposition process which cells undergo after the initial stage of their neoformation.



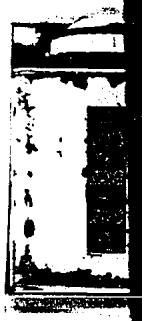
In their search for facts which might confirm the "new cell theory," certain investigators have turned to the study of various polynuclear structures. As is known, there are formations in the make-up of various tissues and organs in an organism which do not have a cellular structure and which consist of protoplasm and a small or large number of nuclei. The transverse striated skeletal and heart muscle fibers, the polynuclear giant cells of the bone marrow, and giant cells which develop in an inflammation focus belong to this category. Certain epithelial cells under normal conditions, i.e., in the testicles, repeatedly lose their cell boundaries. A single syncytium is then formed and consists of a mass of protoplasm with nuclei disseminated in it. All of these formations develop from individual cells either as the result of their coalescence or because of multiple cleavage of the nuclei without accompanying plasotomy. On the other hand the isolation of nucleo-protoplasmic territories from similar symplastic structures and formation of cells from them is a well-known fact found in every textbook. The discovery of symplastic structures and of the intermediate substances which are formed in every complex multicellular organism as a result of the vital activities of the cells, at the time, brought about an important correction in cell theory. The cell theory was initially contrived as a theory of the structure of an organism and was then correctly recognized as a theory of the development of an organism.

It is the normal practice in histology to designate all these formations, i.e., muscle fibers, symplasts, and plasmodia of various origin, as "noncellular" structures in contrast to ordinary cells having a single nucleus. It would be more correct to call them "supracellular."

A number of investigators have utilized this long-established designation in order to place, essentially in a completely formal manner, all these structures in the category of noncellular living substance. On the basis of the well-known definition of living substance given by O. B. Lepeshinskaya -- "living substance is a protoplasmic mass containing nuclear substance in one form or another, i.e., in a diffuse or disseminated state, but not in the form of a nucleus" -- symplastic structures (muscle fibers, polynuclear cells, and various plasmodia) cannot belong to the category of noncellular living substance since they consist of protoplasm and a certain number of typical nuclei. Nevertheless, a number of authors feel that by describing the development of cells from symplasts and by substituting the terms "noncellular living substance" or "noncellular substance" for the established terms "noncellular structures," they are developing O. B. Lepeshinskaya's theory and enriching it with new material.

As an example of such proofs, one can introduce the history of the work of A. N. Studitskiy on the regeneration of lung tissue. The process of regeneration occurs in the lungs in a very complicated manner. Analysis of the true picture is made difficult by the irregularity of alveolar surfaces, the presence of pulmonary macrophages, and continual participation of bacteria in the processes taking place. A. N. Studitskiy has been working on the study of the regeneration of the lungs for a long time. At the conference on the problems of living substance and the development of cells which took place in Moscow 22-24 May 1950 in the Department of Biological Sciences, Academy of Sciences USSR, he, taking part in the discussions, made an attempt to present his data on the regeneration of lung tissue in rabbits in conformance with the basic postulates of O. B. Lepeshinskaya's theory. Relying upon fundamental concepts, he described what he had observed in the following words:

"During regeneration, the surface tissue of the injured bronchi begins to phagocytize. The cellular structure of the phagocytizing system is disrupted. Huge complexes of protoplasm arise which encompass accumulations of cells destroyed by the injury to the lungs. The process of phagocytosis leads to the conversion of the function and structure of the tissue. Tissue is converted



from integumentary tissue into one of the forms of connective tissue which consists of giant polynuclear cells. These, in turn, break down further into individual, typical, connective tissue cells. This process of transforming the structure of a tissue which has changed functionally occurs, as we have observed, as the result of the destruction of the old structure and the emergence of a new structure from the destroyed material." (1951, pp 150-151)

A. N. Studitskiy, as an experienced histologist, knew full well that the phenomena which he described had no relationship whatsoever to the new cell theory. In the complex process of reparative restoration, complicated by infection, giant cells are formed which take part in the phagocytosis. In time, they are partially destroyed and partially broken down into isolated fragments. As to what this has to do with noncellular living substance, he explained that his data serve as "an illustration of the idea of the universal significance of the processes of destruction of an old form during the transition to a new form which corresponds to the changed function of the tissue." (1951, p 151)

Having started out on this course, however, A. N. Studitskiy went further. In 1952, in a report at a conference on the problems of the development of cellular and noncellular forms of living substance, he, utilizing the formal generality of the term "noncellular," spoke concretely of the conversion of the "cellular phase of the development of living substance into the noncellular phase" during the process of lung tissue regeneration. According to his description, a symplast which has no cellular structure and in which nuclei begin to dissolve is formed from the distension of the bronchial epithelium. As a result of this, in the center of the symplast "a substance is formed in which the assimilated material of the absorbed blood corpuscles and dissolved nuclei of the symplast can completely correctly be considered as living substance, at the expense of which new cellular elements should (authors' underlining) be formed." (1954, pp 76-77) A. N. Studitskiy, however, was not able to trace the ensuing process of secondary formation of cells from this noncellular living substance. He says that "an acute basophilia was noticeable along the periphery of the symplast. Accumulations of nuclei of various sizes and shapes were observed which produced the impression (authors' underlining) that they were islands where the neoformation of cells was taking place." (p 77) Nevertheless, in conclusion, he writes that his data "are directly related to the solution of one of the tasks elicited by the new cell theory, namely, the task of determining the regular relationships between the cellular and noncellular phases of the development of living substance." (p 79)

A very interesting thing then occured. The conference, paying no attention to the fact that A. N. Studitskiy had not observed the development of cells from noncellular living substance, or that he, using general terms, spoke only of an "impression" which he had received from his work, remarked in its resolution that his data had the character of established facts. We read the following in the resolution: "The data reported by Prof A. N. Studitskiy concerning the fact that the symplastic formations which play a significant role in the development of lung tissue during the healing of injuries are of a noncellular character and actually represent an accumulation of living substance from which cells develop are new. This is the first time that this method of cell evolution from living substance has been observed. This phenomenon extends, and to a significant degree changes, existing conceptions concerning the mechanism whereby tissues and organs are restored after injuries." (p. 270) Thus, incorrectly reporting facts, and arbitrarily using them as substantiation, the leaders of the conference have advanced one more "proof" in support of the new cell theory.

In recent times, a number of works have appeared on the neoformation of nuclei from the sarcoplasm of regenerating muscle fibers (A. N. Studitskiy, 1953b, 1953c; F. S. Balakin, 1952; E. Z. Yusfina, 1954 et al.).

However, before reviewing all these works, we must examine briefly exactly what a skeletal muscle fiber is. O. B. Lepeshinskaya herself, and V. I. Sorokin particularly, speak and write about "skeletal muscle cells" etc. From their point of view, a muscle fiber is a cell. As is well-known, a muscle fiber consists of sarcoplasm and as many as several hundred nuclei. The fiber is covered by the sarcolemma. There are myofibrils in the sarcoplasm. Such a type of structure is usually, as was indicated above, called subcellular or noncellular. Muscle fibers develop from cell myoblasts which have clear contours, reproduce karyokinetically, and possess a single nucleus. The development of the fiber proceeds by means of the fragmentation of the nuclei (amitosis) and the fusion of myoblasts. As a result of this, muscle tubes are formed which have nuclei in the center and myofibrils along the periphery. These well-known facts have been demonstrated in numerous experiments, in particular, in the works of A. N. Studitskiy and A. R. Striganova (1951). Consequently, a muscle fiber is not a cell but a histological structure of noncellular composition developed from cells. It has been necessary to make this explanation since the idea of considering a muscle fiber as a cell does not agree with reality.

The work of F. S. Balakin was carried out on an unknown animal resembling a mammal. (The author did not name the precise subject of subjects used in his investigation. Judging by the caption under one of the sketches, it was a rabbit.) F. S. Balakin maintains that neither mitotic or amitotic division occurs in the muscle buds which form during regeneration and that the number of nuclei increases as a result of their neoformation from the noncellular living substance formed during the reorganization of the protoplasm. In addition, myoblasts may be formed from small protoplasmic lumps, "which remind one of yellow spheres." The four photomicrographs introduced by the author do not justify his conclusions. The schematic sketches which should show the course of the entire process do not correspond with the pictures which can be discerned in the photomicrographs.

F. S. Balakin's conclusions are completely unproven. Moreover, he himself in 1949, reporting on what was evidently the same investigation at the Fifth All-Union Congress of Anatomists, Histologists, and Embryologists, described the amitotic cleavage of the nuclei of muscle fibers from the 2d to the 4th day after muscle fiber injury. (1951, p 452)

An analogous picture can be seen if we examine the work carried out by E. Z. Yusfina on rats and rabbits. Citing A. M. Vasyutochkin, N. G. Khlorin, and Z. S. Katsnel'son, who worked with various subjects, the author maintains that "there is still no unified opinion on the problem of the method by which the number of nuclei in muscle fibers increases during regeneration." (p 123) She writes that she has not succeeded in observing either mitosis or amitosis, and is of the opinion that the nuclei arise anew from the sarcoplasm. It should be noted that the author shows a nucleus forming on photomicrograph 1, indisputably, as the result of amitotic division. Analogous pictures can be seen in the two subsequent sketches. E. Z. Yusfina points out that the nucleus of a muscle fiber "in the majority of cases does not show signs of degeneration." (p 125) One might ask: "Does degeneration occur in a lesser number of cases? Why doesn't the author describe it?" E. Z. Yusfina is a little more careful in her conclusions, but the manner of discussion, and the veritability of their work is identical.

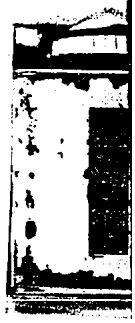
The investigations of A. N. Studitskiy are the most detailed works devoted to the problem of the neoformation of muscle nuclei from sarcoplasm. He conducted his experiments on chicks and rats. Since the observations of the chicks gave clearer results, he made a detailed study of them. In a period of one or 2 months, the biceps or sartorius muscle of a chick was subjected to perforation by a needle through the skin (25-50-100 punctures). As a result of this treatment, the fibers in the injured muscle thickened, the number of nuclei increased progressively from the periphery to the central portions, and myoblasts divided and formed new muscle fibers. The changes increased during the course of the experiment. Muscles were also found to change in an analogous manner after perforation of the skin alone over previously injured muscles. (The author considers these changes due to a conditioned-reflex mechanism.)

According to A. N. Studitskiy's data, the basic part of a nucleus is formed in the sarcoplasm from chromatin spheres containing desoxyribonucleic acid. In his basic work, printed in the journal Arkhiv Anatomii, Gistologii i Embriologii, No 4, 1953, A. N. Studitskiy illustrates various phases in the development of the chromatin spheres with a number of sketches made from preparations dyed according to Feulgen's method. The chromatin spheres, proceeding from the pre-nucleus stage, are converted into a primary nucleus which divides mitotically. Separating themselves together with the sarcoplasm surrounding them from the muscle fibers, these nuclei are transformed into cell-myoblasts.

One must give A. N. Studitskiy his due in that he does not brush aside the controversial questions which arise during the course of his experiments as do F. S. Balakin and E. Z. Yusfina. He examines them. He emphasizes that the number of nuclei is increased not only as the result of their neoformation from chromatin spheres but also by means of mitosis and amitosis. He points out that the chromatin spheres are observed "mainly in the vicinity of cell nuclei" (1953b, p 13) and thus, "that one may assume that they have split away from the nuclei as the result of their fragmentation." However, A. N. Studitskiy is of the opinion that this hypothesis is not entirely justified since "rather frequently" the chromatin spheres are not connected with the nuclei. A. N. Studitskiy has devoted his main attention to the most serious argument which can be made against his data, namely, the treatment of the chromatin spheres as a stage in the degeneration of muscular nuclei. He, however, considers "the hypothesis concerning the degenerative character of the described process" to be supported by two facts: (1) the regular sequence of the observed stages of development of nuclei from chromatin spheres--"The latter are already formed within the 2d to 3d week after the beginning of the experiment as the result of the 2 first traumatizations of the muscles. Intensive processes of spontaneous decomposition still have not developed in the muscles during this period." (p 15)--and, (2) the direction of the process--"A muscle subjected to systematic traumatization does not show the signs of depression which might be caused by the phenomenon of degeneration. On the contrary, the increasing neoformation of muscle fibers testifies to the intensity of vital processes. The structures which arise while the muscles are in this condition cannot have a degenerative character." (p 15)

A. N. Studitskiy, however strange it may seem, has, without a doubt, not sufficiently analyzed the character of the reactive changes occurring in muscle fibers during their regeneration.

Muscle fibers of the skeletal musculature, as has been known for a long time, possess a significant degree of plasticity. During regeneration, there is a certain degree of differentiation of the muscle fiber accompanied by a marked increase in the quantity of nuclei. Myoblasts separate from the reorganizing fiber, and muscle buds protrude out of it. (These processes may coincide with one another.) Next, in the succeeding stage of regeneration,



during differentiation, the number of nuclei decreases almost to normal. Those that are superfluous are absorbed naturally. The degeneration of excess nuclei occurs in completely viable, differentiating, young muscle fibers. (This often occurs during embryonic development. Let us remember that processes of neoformation and degeneration occur constantly in growing bone.)

The "two facts" that A. N. Studitskiy introduces as proof that chromatin spheres are transformed into muscular nuclei indicate the reverse.

A. N. Studitskiy maintains that chromatin spheres represent "living nuclear substance" since they have the capacity to grow. It is hardly necessary to dwell long on his "proof" of this. The fact that "one can observe dozens of chromatin spheres having most varied dimensions in one and the same section" (p 13) is more correctly explained as an illustration of the degeneration of nuclei by a type of pyknosis during various stages.

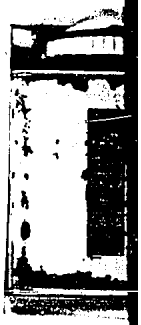
Consequently, A. N. Studitskiy's widely propagandized investigations do not possess the characteristics required of any investigation, namely, conclusiveness and provability.

Ye. V. Dmitriyeva presented a report on the problem of the neoformation of nuclei during regeneration at a recent meeting of the plenum of the All-Union Society of Anatomists, Histologists, and Embryologists in Leningrad. She studied the regeneration of the muscles of the tongue of a rat using a histochemical method. She demonstrated that the sharp increase in the number of nuclei in the regenerating muscle fibers was brought about by the amitotic division and fragmentation. The oxyphilous nuclei observed in the sarcoplasm, "shadows of nuclei," vacuoles with and without nucleoli inclusions, and granules of various dimensions containing desoxyribonucleic acid which F. S. Balakin, E. Z. Yusfina and A. N. Studitskiy described, represent various stages in the destruction of superfluous numbers of nuclei as the result of their lysis and pyknosis. The fact that all these pictures were observed, not during the early stages of regeneration when the number of nuclei is increasing, but, as is correct, in the later stages, i.e., after 7 to 10 days, when the numbers begin to diminish, serves as proof of this.

It may be stated with complete justification that the neoformation of nuclei from the sarcoplasm of muscle fibers was not proven in any of the works introduced.

V.

O. B. Lepeshinskaya, as is well known, in studying the development of a fertilized sturgeon egg in relation to the old observations of V. V. Zalenskiy, did not observe the development of a morphologically formed nucleus in it during the early stages. According to her description, the nucleus developed later from protoplasmic granules. The process of formation of the female pronucleus, according to her representation, reflects the stages in the phylogenetic development of a cell from noncellular living substance. These observations by O. B. Lepeshinskaya were recently carefully checked by T. I. Faleyeva (1953) in the Laboratory of the Fundamentals of Pisciculture of the Main Administration for Pisciculture of the Ministry of the Fishing Industry. T. I. Faleyeva demonstrated that a nucleus in various of its states was present in the eggs of sturgeons during every period of their development. Every egg was divided into a series of more than 200 sections 7 microns thick, and the nucleus was observed in only one or two of them. T. I. Faleyeva's investigations explain the errors made by O. B. Lepeshinskaya. (At a conference of embryologists held in Leningrad 25-31 January 1953, B. N. Kazanskiy reported the results of his work on an analysis of the processes of egg-cell maturation, ovulation, and fertilization in sturgeons. The data obtained by him speaks in support of the succession of nuclei in ovocytes during this period of ovogenesis. [Theses of the Conference, pp. 11-13])



Precisely this erroneous data of O. B. Lepeshinskaya initiated a review of a problem of the development of gametes which has great general biological significance. T. D. Lysenko insisted on the necessity for a review of this problem in his report at the conference on the problem of living substance. Regarding embryonic development and the laws governing the differentiation of embryonic tissues in a simplified manner, he asked: "How can the simple division of an egg cell give rise to the cells of various tissues and organs which it does not resemble in either form or content?" (1951, p 110). The process of differentiation of various elements in the tissues of developing embryos and the processes of organogenesis have been well studied. Not being informed of this, however, he came to the conclusion that "it is not possible to imagine the development of an organ from an embryo or from a germ cell without recognizing the formation and origination of cells from noncellular substance. (p 110)

An analogous picture was presented in the report of A. A. Avakyan, who dogmatically postulates the necessity of the formation of phasicly young embryonic cells and the tissues of the callus from a living substance having no cellular structure. Basing his arguments on general considerations rather than facts, he says that "the formation of new cells from noncells should be considered a necessity in organic nature." (p 104)

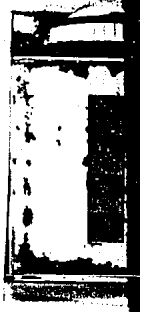
The investigations of N. S. Stroganova (1952), B. A. Yesdanyan (1953), and A. V. Abuladze (1953) were published after this conference. In them, these authors tried to prove the development of gametes from noncellular living substance. We will review their works briefly.

N. S. Stroganova investigated the testicles of white rats. In addition to the preparation of the usual histological sections, she made extensive use of slides containing testicle specimens. A number of the slides were fixed and stained, while others, after dilution with a physiological salt solution, were merely covered with cover glasses. The study of the enclosed drop was carried out at 37°C in a "living state." The work is accompanied by sketches and photomicrographs.

The author describes the formation of early spermatogonia in the testicles of young rats from anuclear protoplasmic drops which, "evidently," are formed from the interstitial substance in which "one should find" the substances liberated during the degeneration of follicular cells and gonocytes within the testicular tissues. The author describes basophilic drops of a dark blue color and having various dimensions in the testicles of half-grown rats. Fine stratifications without any structure can be seen. "Their presence is expressed by a violet tint along the periphery. Starting with this it is possible to trace all the details of a series of subsequent transitions ending with the formation of a small structure morphologically similar to a nucleus from a basophilic drop." (p 49) These structures, according to N. S. Stroganova's observations, do not initially have protoplasm and develop like "bare" nuclei. Their protoplasm appears later.

On the basis of her observations, N. S. Stroganova comes to the conclusion that "the ontogenesis of a gamete begins with a living substance having no cellular structure." (p 47)

What can be said of this work? The sketches which should illustrate the author's data do not acheive their purpose. As an example, one can analyze the six sketches in Plate No. 1 which are supposed to show the development of spermatogonia from anuclear drops in the testicle of a 30-day-old rat. Sketch No 1 on this plate represents the usual view of the convoluted tubules in the testicle at an average enlargement. The remaining five sketches are great enlargements of isolated parts of various slides prepared according to



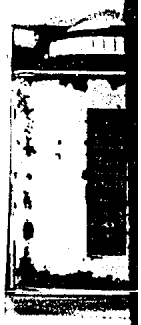
to Feulgen's method and stained with eosinazure. Individual cells, some kind of mounds, and traces like spots where cells have touched the glass are visible on the photomicrographs. In order to speak of any kind of succession from one to another of these essentially diverse formations, in addition to daring, one must possess a significant degree of imagination. Treating the basophilic drops (sketches No 3, 3a, 4, 5, and 6 of Plate No 2) as early stages in the development of spermatogonia in half-grown rats is simply unprovable. Isolated cells of the usual type and of various dimensions and certain degenerating cell elements are visible in the photomicrographs.

These pictures should more correctly and logically be treated as illustrations of various stages in the destruction of individual cells, a process which occurs continuously during normal spermatogenesis.

B. A. Yezdanyan investigated the testicles of white rats and rabbits using histochemical methods in nucleic acid. In his opinion, he has succeeded in tracing the conversion of basophilic spheres, drops as described by N. S. Stroganova, in the walls of the seminiferous tubules. According to his data, some of these spheres pass through the walls of the tubules to the basement membrane and are converted during this process into young spermatogonia. An analysis of the sketches accompanying this work and a critical comparison of them with the text leaves no doubt that the author arbitrarily describes a process which is actually proceeding in the opposite direction and regards the various stages in the degeneration of the individual cells which make up the walls of the tubules as their neoformation. It is understandable that, during the destruction of a cell, the nucleic acids entering into its composition do not disappear immediately and can be observed histochemically in the form of globules and granules of various sizes among the cellular debris. This, however, is the terminal stage in the decomposition of a cell and not the initial phase of its development.

A. V. Abuladze studied the histological changes in transplanted ovaries of 2- to 4-month-old rabbits. She studied the ovaries for 2-40 days using histological preparations stained with hematoxylin-eosin. The changes in the tissues of the successfully transplanted ovaries can be divided into two periods. The first period is characterized by degenerative changes which encompass all the tissues of the transplant to a certain degree. During this time, a "large part" of the egg cells in the primary follicles undergo granular regeneration; and the secondary follicles, Graafian vesicles, and corpus luteum decompose. This period lasts from 4 to 6 days. During the second period, in addition to the continuing degenerative processes, regenerative processes begin. After the 4th to 6th day, new primary and then secondary follicles are formed.

"One can assume," writes A. V. Abuladze, "that the primary follicles originate along the course of the blood vessels and capillaries and that the cells which cover the follicles (the follicular cells) are directly related to the vascular walls." (p 47) The data of the author concerning the connection of the developing follicular cells with the elements of the vascular walls is not conclusive since her method of staining does not afford a basis for determining the histological interrelationships between connective tissue elements and other cells. We will not dwell on this problem however. Within the scope of this article we are interested in A. V. Abuladze's data concerning the formation of egg cells. In her opinion, they develop from noncellular living substance carried in by the blood. Initially, the egg cells are represented by an anuclear protoplasmic formation. The nucleus appears later. The author did not observe the neoformation of egg cells from noncellular living substance directly.



She based her conclusions only on indirect considerations: the formation of primary follicles along the course of blood vessels, the correspondence in time of the appearance of capillaries and a specific stage in the decomposition of old egg cells, and the fact that she was unable to observe either mitosis or amitosis in forming egg cells. "These observations," writes A. V. Abuladze, "form a basis for assuming (authors' underlining) that the egg cells in primary follicles do not originate by the division of previously existing cells, but arise anew from structureless living substance carried in by the blood, since their formation is directly connected with the appearance of functioning blood vessels in the transplant." (p 50) The author writes in just as unprovable but even more dogmatic a manner in relation to the secondary follicles. "The egg cells contained in them arise spontaneously at the expense of the substances introduced into the conditions of the medium by blood containing decomposition products." (p 50)

From what has been said, it is clear that there is no special necessity for spending much time on a review of the proofs advanced by A. V. Abuladze in support of the development of egg cells from noncellular living substance. Her conclusions are not based on concrete facts, but on indirect considerations treated from a biased point of view and essentially of a hypothetical nature.

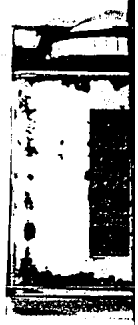
Nevertheless, adherents of the new cell theory immediately accorded the data of A. V. Abuladze the status of firmly established fact. L. M. Plyushch used her data as an example of the provable correctness of the new cellular theory in an article published in Voprosy Filosofii (Problems of Philosophy), No 4, 1953.

A. N. Studitskiy in an article entitled "Towards the Creative Development of the Problem of Species Formation" (1953a) wrote that A. V. Abuladze's experiments "left no doubt about the fact that the source of the neoformation of gametes is the living substance carried into the transplanted ovaries by the blood." (pp 22-23)

In reading the works in which authors attempt to prove the development of spermatogonia and ovogonia from lumps of noncellular living substance, basophilic drops, etc., the following question involuntarily arises. If gametes can be formed and are formed from particles of structureless living substance, repeating, from the point of view of O. B. Lepeshinskaya and her followers, certain phylogenetically infinitely remote stages in the development of the organic world, why do spermatogonia, spermatocytes of various types, and spermatids exist in the testis or ovary of a given animal? What biological meaning do all these cellular forms have from the point of view of biogenetic law as it is understood from the position of the new cell theory? This question still has not been answered.

The idealistic nature of A. Weissman's theory of embryonic plasma leads to the concept of the continuity of the embryonic tract. This concept, which is not acceptable from the ideological standpoint, is supported at the present time by a large number of facts in the fields of comparative embryology, regeneration, etc., which we will not analyse here. It should only be remarked that, although we do not recognize the continuity of germ cells, we do not consider it necessary to accept obligatorily, as certain authors do, the development of germ cells from noncellular living substance.

The question of how germ cells originate in animals should be decided on the basis of strictly proven facts.



In the critical analysis of the material underlying the "new cell theory" we have only touched upon a few questions. From our point of view, the data of O. B. Lepeshinskaya, Ye. Ye. Malovichko, T. I. Rypasova, and V. V. Averburg concerning the formation of various blood cells and connective tissue from granules remaining after the decomposition of granulocytes and fat cells is factually unproven. The same is true of the works of N. S. Stroganova, B. A. Yesdanyan, and A. V. Abuladze on the development of gametes from noncellular living substance carried in by the blood or formed as the result of the decomposition of the cellular elements of a gamete. The widely propagandized data of F. S. Balakin, E. Z. Yusfina, and A. N. Studitskiy concerning the development of nuclei from the sarcoplasm of a muscle fiber during its regeneration can likewise not be considered conclusive.

We did not analyze a number of other morphological works, i.e., those of G. K. Khrushchev, L. S. Sutulov, Kh. M. Karolinskaya, M. Ya. Subbotin, V. M. Lumpova, N. N. Kusnetsov, F. S. Ragol'skaya, etc., in which the authors have made attempts to demonstrate the formation of cells from noncellular living substance, since they are equally unproven. It is only necessary to notice that the authors of the majority of these works, knowing full well the insufficient basis for their conclusions, usually describe the process of cell neoformation with such reservations as "evidently," "one can assume," "produces the impression," "it is highly probable," etc.

Turning to a review of the facts produced by O. B. Lepeshinskaya herself, it is necessary to establish in respect to the material presented above, that the formation of cells during the healing of wounds in mammals is completely unproven. Unfortunately, O. B. Lepeshinskaya and especially her commentators have changed their originally cautious formulations into dogmatic assertions having no basis in fact. In the light of new investigations during recent years, the formation of a nucleus before the beginning of cleavage in sturgeon egg cells was also not confirmed. There is a nucleus in the ovocyte which never disappears, and O. B. Lepeshinskaya simply did not observe the first division at the end of the prophase and beginning of the anaphase, the chromosomes of which are dispersed just as they usually are during karyokinetic division.

On 14 April 1954, P. V. Makarov and V. Ye Kozlov gave a report to the Leningrad Society of Anatomists, Histologists, and Embryologists entitled "On the Nature of Morphogenetic Processes in Substances Isolated From Cells." Having repeated the experiments on the grinding of hydra, the authors duplicated the phenomena which O. B. Lepeshinskaya described, but they were not able to confirm her basic hypothesis that cells were formed anew from living substance during this process. The same transformations were also observed during the use of ground material killed with formalin and osmic acid. The fifth thesis of their report reads as follows: "On the basis of data obtained by us the conclusion must be reached that the phenomena described by O. B. Lepeshinskaya in her work on hydras were based on not biological, but physicochemical processes." (The work of V. Ye. Kozlov and P. V. Makarov appeared in Vestnik Leningradskogo Universiteta (Herald of Leningrad University), No 7, 1954, pp 55-59, after our article had already been submitted to the printers.)

Thus, even P. V. Makarov, who propagandized and presented these data in a detailed manner in his 1953 book, did not confirm them. Consequently, the basic material of O. B. Lepeshinskaya, aside from the development of cells from yolk spheres has either been refuted or cannot be considered proven.

[A work by V. N. Orekhovich, M. I. Levit, and T. P. Levchuk-Kurokhtina came out after our article had already been submitted to the printers. The authors,

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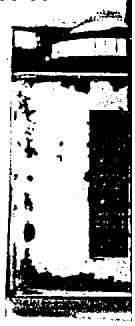


using labled amino acids, demonstrated that the synthesis of protein molecules does not occur in the protein or bile of a developing chick embryo. From this they concluded that "the development of cellular elements from proteins of the yolk or the protein membrane appears highly improbable." Biokhimiya (Biochemistry) 19, 5, 1954, pp 610-615. Thus, the neoformation of cells from the yolk is doubtful in the light of this latest data.)

At a conference of embryologists held in January of this year A. G. Knorre, in a report entitled "Certain Laws of Embryonal Histogenesis", reported that, according to his data, the yolk was not transformed into cells during the development of a chick embryo (Theses of the Conference, pp 32-35)

In this work, we have not touched upon O. B. Lepeshinskaya's concept of "living substance." This question should be the subject of a special article. It is only necessary to point out that it is completely undefined. This fact was noted in print after the conclusion of the work of the Second Conference on the Problem of "Noncellular Forms of Life", 5-7 May 1953. (K. Draganov, 1953)

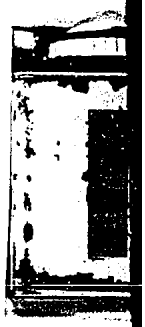
The definition, which O. B. Lepeshinskaya gave for living substance in her monograph is essentially different from that which she gave in conjunction with V. G. Kryukov in volume 15 of the Bol'shaya Sovetskaya Entsiklopediya (Large Soviet Encyclopedia).

The term "living substance" is used at the present time in relation to blood plasma, various "destructured tissues," the white and yellow of birds' eggs, the abdominal fluid of the silkworm, and, finally, the content of ordinary mononuclear cells during the stage of mitotic division. We must review the last-named example of "living substance" in a more detailed manner.

According to O. B. Lepeshinskaya's concept, mitotic division "begins with the transformation of the living substance of the cell into a noncellular form." (1952, p 89) This is manifested by the cell's loss of the characteristic differention between the nucleus and the protoplasm. In other words, in her opinion, a cell, in the mitotic state, repeats a certain primeval phylogenetic stage which existed on earth before its emergence. It is hardly necessary to dwell in any detail upon the erroneousness of such a treatment of the process of mitotic division. Her only basis for this is the temporary disappearance of the nuclear membrane and the nucleolus during a specific stage in the development of the nucleus. The nucleus does not disappear, however, during the metaphase, but is transformed into another state, another form. During mitotic division, the cellular organoids, i.e., the cytocentrum, the Golgi apparatus, and the chondriosomes, are preserved in the cytoplasm. In the divided cell these organoids represent the phylogenesis of unquestionably new formations. This also, once again, indicates the fact that cells do not return to a state of primary living substance during cell division. There are no serious bases for O. B. Lepeshinskaya's dogmatic assertion concerning the transition of a cell into a noncellular form during mitosis.

It is appropriate that we remember certain scholars "who have confirmed and developed" the new cell theory. O. B. Lepeshinskaya herself indicated in her report on 22 March 1950 that the data of G. M. Bosh'yan and M. M. Nevyadomskiy (together with the data of a number of other authors) confirm her theory. In her 1952 book, she only mentions one of these two authors, M. M. Nevyadomskiy, and does not cite G. M. Bosh'yan at all.

N. N. Zhukov-Verezhnikov, I. N. Mayskiy, and I. A. Kalinichenko wrote an article for Bol'shevik (1950) which was afterwards reprinted several times in various editions. Among these, in the book, Filosofskiye Voprosy Sovremennoy Biologii (Philosophical Problems of Contemporary Biology), 1951, without any



justifications, explanations, or references, they omitted all mention of the works of G. M. Bosh'yan whose data had appeared in several textbooks. Evidently, in order not to create the impression that there are weak points in the theories and facts which support her work, the authors and commentators did not wish to mention the fact that the "views" of O. B. Lepeshinskaya determined who were the persons who had "mystified Soviet science." (Meditsinskiy Rabotnik, 1954)

The theory of the formation of cells from living substance has found zealous converts among the scientists who formulated the new theory of species formation. Academician T. D. Lysenko writes the following about it: "We envision the matter so: Within the body of a wheat plant organism during the interplay of accompanying life conditions the grains of a rye body are engendered. This engenderment does not, however, take place by a transformation of wheat cells into rye cells, but by the emergence of grains of the body of another species within the interior of the body of the organism of the given species from a substance having no cellular structure. These grains, initially, likewise cannot have a cellular structure. Later, the cells and embryos of the other species are formed from them. This is what the works of Olga Borisovna Lepeshinskaya contribute to the development of the theory of species formation." (1951, p 111) O. B. Lepeshinskaya herself connects her works with T. D. Lysenko's theory of species formation. Thus, the "facts" concerning species formation, as described by T. D. Lysenko and his followers, are one of the arguments used to support the correctness of her theory. On the other hand, they use her data as a basis for their theory.

The discussion which is going on concerning the problems of species formation have shown the falseness of T. D. Lysenko's theory, and consequently the connection of species formation with the emergence of cells from living substance, which is purely speculative, has not been confirmed by any facts.

Conclusion

In drawing conclusions from all that has been said, one must recognize that the "new cell theory" is based on material which is not sufficiently founded on or confirmed by fact.

All this, from our point of view, forces one to review the entire theory. We are of the opinion that any theory should be based on rigorously proven facts, should proceed from the objectively, actually existing laws of nature, and should correctly and objectively reflect nature.

O. B. Lepeshinskaya's theory does not satisfy these basic requirements.

If there are no facts which prove it, then this must be stated, and, in any event, it should not be presented dogmatically to pupils in school or to the students in Vuzes.

We have not examined all the "facts." It would be impossible to do this in one article. We wish to emphasize once more that, although cells during their developmental history were formed from noncellular living substance (of which we have no doubt), it cannot be construed to mean that this once completed process is presently being repeated in every animal and plant.

The "new cell theory," created by O. B. Lepeshinskaya and widely propagandized by a number of contemporary scholars, is factually unfounded and in no way represents progress.

It is necessary to initiate a free discussion of the problems of the cell theory, the development of cells, and the concepts concerning living substance.

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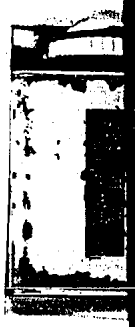

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