Reports

Are There Any "Acellular Animals"?

The cell theory, one of the greatest generalizations of biology, has been unwisely attacked. In no uncertain terms, Dobell (*1*) claimed that Protozoa must not be considered as cellular organisms. In fact, he viewed all Protista as noncellular, in spite of "their obvious structural resemblances in certain features" to the cells of Metazoa. More recently, Hyman (*2*) in volume I of her most scholarly and useful series, *The Invertebrates,* has also adopted the view that Protozoa are acellular and has, along with Dobell, defied all the laws of morphological homology and logic in doing so.

Both authors agree that individual Protozoa have the same fundamental organization as is to be found in the cells of Metazoa. Upon what considerations then have these claims of noncellularity been based? Refreshing as views alternative to the customary blind following of current usage have always been to me, I cannot admit the validity of the arguments that Dobell, first, and later, Hyman, have used in their own support, and I wish to show that their interpretation is neither justified nor desirable.

To begin with, Dobell states definitely that the protist individual is not the homolog of a single cell in the body of a multicellular animal or plant, but is instead homologous with a whole multicellular organism. This claim is a contradiction of every valid demonstrable criterion of homology, "morphology's central concept." We say, on the contrary, that because of their essential structural correspondence part for part with the cells of Metazoa, Protozoa are undoubtedly cellular. Thus nuclei are the homologs of nuclei; cytosomes with their constituent parts are each homologs of the corresponding parts of the cells of Metazoa. Indeed, all the major and many of the minor cell parts are recognizable in the cells of many organisms, although the limiting membranes may be temporary or slightly developed in some. There is no useful purpose to be gained by denying these real homologies, and if they exist, a protozoan is the homolog of a single cell in a metazoan.

Dobell and Hyman appear to be in agreement, at least as far as the Protozoa are concerned, that a cell can be a part of an organism, but never a whole organism. This interpretation leads to the strangest conclusions about zygotes and gametes! According to both authors, a fertilized egg is not a cell, but after the first cleavage the two-celled stage is cellular as are all subsequent stages. This is of course a denial of Virchow's aphorism *omnis cellula e cellula,* and the denial is openly made by Dobell. But Hyman's statements are contradictory, for she first affirms Virchow's aphorism and later by implication denies it. Thus on p. 12, Hyman states, "Cells come into being only by the division of preexisting cells," but later (p. 248) it is said that, "No direct proof exists of the origin of the Metazoa from the Protozoa, but such origin, besides being necessitated by the principle of evolution, is strongly indicated by the facts of embryonic development, in which each metazoan passes from an acellular to a cellular condition." Dobell is also in trouble in the case of gametes and parthenogenesis. A gamete of a metazoan is a cell because he interprets it as a part of an organism, not a whole organism. And the unfertilized egg that develops into an organism parthenogenetically is a cell, but the fertilized egg before cleavage is not a cell! This intellectual sleight-of-hand, which is used in order to appear to be consistent, is obviously forced and arbitrary and not at all helpful to their interpretation.

What was hoped for from these illogical conclusions? Dobell wished to emphasize that an individual protist could act as an individual metazoan, which within limits is true. He also wished to make it clear that the Protista are not necessarily simpler, lower, or more primitive than Metazoa. These are challenging statements to which I am entirely sympathetic, and they are worthy of careful consideration. And the view that Metazoa probably became cellular by changes in internal organization, rather than by colonial aggregation as Hadži (*3*) has maintained for some time, I am also willing to accept. But none of these ideas can possibly excuse or justify considering Protozoa to be acellular, nor do they require it.

Hyman explains her interpretation of the Protozoa as "acellular" in the following statements (p. 44). "The study of the invertebrates begins with the Protozoa, animals that are usually defined as consisting of a single cell. This point of view, inherited from the heyday of the dominance of the cell theory in the conception of organisms, which were regarded as aggregations of cells, is not only without advantage, but conveys an erroneous impression. The protozoa are not loose cells moving about, but complete organisms that may be of more complicated construction than the simplest Metazoa. We therefore prefer to refer to the Protozoa as *acellular,* rather than as unicellular animals, that is, as animals whose body substance is not partitioned into cells." This statement has a curious *non sequitur* in it—naturally the body substance of a single cell is not further partitioned into cells, but there is no necessity for denying that it is a cell for that reason. The main reason for denying the cellularity of Protozoa thus appears to be the great complexity of some, and this reason appears to be of more importance to her than the admitted fundamental agreement in structure between protozoan and metazoan cells. "Acellular organisms and the various types of cells found in cellular organisms all exhibit much of the same fundamental construction, and this fact permits the somewhat idealized description of a typical cell found in books" (p. 5).

I suggest that not one of the reasons advanced separately by these authors in support of the interpretation of Protozoa as acellular, nor all of them together, is sufficiently cogent to warrant the denial of the essential homologies that exist in all cells. Nor have any additional reasons been given by Lwoff (*4*) or by Hutner and Provasoli (*5*), who have accepted Dobell's interpretation. There may have been a time when the complexity of some protozoans and the integration of the metazoan individual were underestimated. Even so, every one of the valid objectives of Dobell and of Hyman can be reached without the adoption of their interpretation of Protozoa as acellular. Recent students of the origin of protoplasmic systems—for example, Haldane (*6*)—believe that cellular organization was a necessary step in the evolution of such systems and was early achieved and has been consistently maintained since. Neither the individuality of each protozoan nor the extremes of complexity reached by some requires a denial of

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their cellularity. In the face of the admitted fundamental agreements in the structures of protozoan individuals and metazoan cells, the arguments advanced by Dobell and by Hyman become irrelevant and of no vital consequence. The cell theory stands as one of the valid generalizations about the protoplasmic systems of animals.

ALAN BOYDEN
Department of Zoology, Rutgers University, New Brunswick, New Jersey

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31 October 1956

Reticular Activating System of Brain Stem and "Animal Hypnosis"

During the evolution of animals and man, certain basic types of reactions to stimuli from the external environment are to be found, the manifestations of which may differ at various evolutionary stages, but whose mechanism is principally identical. These basic types of reactions are called "biological radicals" by Kretschmer (*1*), and their mechanism is considered by this author to be "phylogenetically preformed." Such a biological radical is the so-called "panic reaction" (*Bewegungssturm*); another is the *Totstellreflex,* which is also called "animal hypnosis." The latter phenomenon has a number of analogs in clinical pathology in the form of various manifestations of the stupor-hypnoid syndrome of Kretschmer (*2*).

The onset and the dynamics of "animal hypnosis" as an experimental model of some psychiatric and neurological syndromes have been reported in a number of papers (*3*). In this report, a part of the electroencephalographic analysis of animal hypnosis is brought forward.

Animal hypnosis in a rabbit was experimentally elicited by standard rotation of the animal about its vertebral axis in a special apparatus. After this phenomenon had been evoked, changes characteristic of the onset of sleep and later electric activity of deep sleep appeared in the electroencephalographic record.

When the animal, in a state of animal hypnosis, is exposed to arousing stimuli, then there are changes present in the EEG record that are identical with those produced by arousing stimuli during normal, natural sleep. It is demonstrated in Fig. 1, where the first part of each record represents the wakeful EEG rhythm and the second part represents the rhythm during animal hypnosis, that the applied stimuli (indicated by arrows) lead to a change in the EEG record from the electric activity of sleep to a rhythm of greater frequency and of lower amplitude (record *A,* nociceptive stimulus; *B,* clapping of the hands three times in quick succession; *C,* labyrinth mechanical stimulus; *D,* labyrinth galvanic stimulus). This change can be seen simultaneously in all the electrodes, even though the depression of sleeping activity is not as marked in every electrode. The significance of the arousing stimuli in animal hypnosis is different. Labyrinth stimulation was found to be most effective, with nociceptive, olfactory, acoustic, and optic stimuli following in succession.

The simultaneous appearance of the EEG arousing reaction in animal hypnosis in all the cortical regions at the same time indicates that Magoun's brainstem reticular activating system is capable of function during this inhibitory state. This system represents—in contrast to the classical sensory and sensitive tracts, leading to the primary cortical receptor regions—a secondary afferent tract with a diffuse cortical projection via the thalamic and extrathalamic tract (*4*). The presence of the EEG arousing reaction from animal hypnosis shows that in the course of this form of generalized central inhibition, this system, which is important to the animal's existence and which insures the waking up from sleep, remains functionally active. It is known that, during central inhibition that is evoked, for example, by narcosis, this system is functionally eliminated (*5*).

It is perhaps possible to assume that this observation of the function of one of the most important brain systems during animal hypnosis can contribute toward the elucidation of the mechanism of those human pathological syndromes that appear during regressive forms of human behavior and of which the animal hypnosis represents an experimental model.

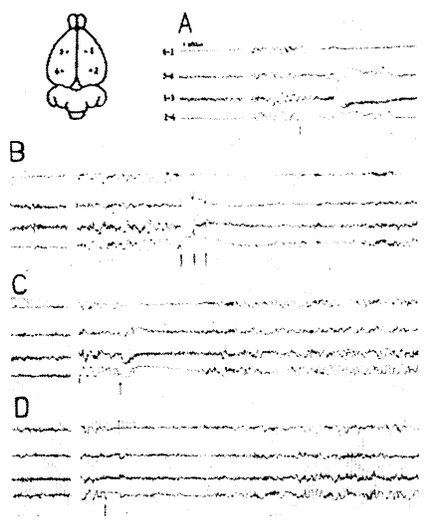

Fig. 1. Electroencephalographic rhythms of animals awake and during "animal hypnosis."

DOMIN SVORAD
Institute of Physiology, Czechoslovak Academy of Sciences, Prague, Czechoslovakia

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11 September 1956

Antileukemic Action of Reserpine

During the course of studies in our laboratory on the effect of lysergic acid diethylamide and *d*-amphetamine on the toxicity and marked depression of animals that were administered large (25 mg/kg) doses of reserpine (*1*), we have directed our attention to the metabolic alterations produced by reserpine and reserpine derivatives. Since large doses of reserpine produce marked changes in the normal metabolic patterns (*2*), it was thought possible that reserpine might alter the metabolism of tumor cells more extensively than it did that of normal cells and thereby prove detrimental to the tumor. The data presented here show that reserpine can exert an antileukemic action (*3*).

Hybrid male mice [(BALB/cAn × DBA/2J)F_1] (8 to 10 weeks old and of weight 20 to 25 g) were inoculated in the right hind leg with 0.1 ml of a suspension of leukemic (L1210) cells (*4, 5*). The animals were allowed to develop leukemia until the local tumor had reached a diameter of approximately 9 to 12 mm (estimated by palpation) at which time the disease is generally systemic as well as local. When the disease had reached this preterminal stage, the mice were randomized and the designated groups were treated with a single injection of reserpine. The animals were weighed daily and observed for mortality. The size of the local tumor at the site of leukemic inoculation was obtained by palpation.

The results of a typical experiment are summarized in Fig. 1. A single treatment with reserpine produced an almost threefold increase in the remaining lifetime of mice with advanced leukemia. The mean survival time was an increasing function