have been assigned to each man. The assignments are made by many men. Furthermore, it is usually the custom to have the patients assigned to a student in rotation as they enter the ward or clinic, disregarding the relationship of the type of case to the need of the student.

In summarizing the arguments, pro and con, of the several methods of teaching medicine, it is hoped that the reader will appreciate that there is no desire on the part of the writer to quarrel with the protagonists of either form of teaching. Purely didactic, dogmatic methods of teaching have been so completely eliminated from the curriculum of medical schools that such methods will probably never be resurrected. The disadvantages of such a type of teaching are so obvious that no one ever considers nowadays the possibility of relapsing into the scheme of teaching employed thirty and more years ago. There does seem, however, room for the scheduled didactic lecture on the roster of the medical student and it should not be abolished without due thought simply because it is the pedagogic style to do away with it. The ideal arrangement would appear to be a major portion of the student's time devoted to clinical study of his patients combined with a minor portion of the time devoted to didactic lectures in which the head of the medical department could dwell upon the broad and fundamental principles of medicine and at the same time present his subject in a systematic, orderly fashion.

J. H. MUSSER

TULANE UNIVERSITY OF LOUISIANA

ON CYTOMORPHOSIS IN BACTERIA[1]

BACTERIOLOGISTS have been divided in opinion regarding variations in the morphological characters of bacteria. The most generally accepted teaching has been that these characters are invariable except for such pathological changes as may be brought about by an unfavorable environment. But a not inconsiderable minority have maintained that bacteria exhibit a complex "life cycle" similar to that of protozoa or higher fungi, the various stages of which may be found only in varying media. This view has been most elaborately presented in the recent monograph of Löhnis.[2] That the first theory is untenable must be apparent to any one who will patiently apply his eye to the microscope; on the other hand most bacteriologists are not inclined to accept as proven that bacteria show sexual reproduction, alternations of generation, or in general such a complex structure as is implied in the term "life cycle."

I believe that the error in both of these teachings is due to insufficient consideration of the element of time. The first school has been satisfied with its standardized observation of a twenty-four hour culture; the second has tried to patch together a complete picture from isolated observations on widely differing media, both favorable and unfavorable to growth, generally without regard to the phase of growth of the culture. If we are to understand clearly the life cycle of an organism we must observe consecutively all stages in its development. This we may do, with bacteria, either by continuous observation of the growing organisms in the agar hanging block or by removing samples from a growing culture at frequent intervals. The former method yields only a limited amount of information, for after a few cell divisions the cells become so numerous and closely packed together that nothing can be clearly seen. The latter procedure, involving the construction of a picture of the whole from samples, requires the use of statistical methods.

I have been carrying on such quantitative studies of the morphological characters of several species of bacteria and have arrived at a theory different from either of those mentioned. It is, briefly, that the cells of bacteria undergo a regular metamorphosis during the growth of a culture similar to the metamorphosis exhibited by the cells of a multicellular organism during its development, each species presenting three types of cells, a young form, an adult form and a senescent form; and that these variations are dependent on the metabolic rate, as Child[3] has found them to be in multicellular organisms, the change from one type to another occurring at the points of inflection in the growth curve. The young or embryonic type is maintained during the period of accelerating growth, the adult form appears with the phase of negative acceleration, and the senescent cells develop at the beginning of the death phase. Minot[4] has coined the word "cytomorphosis" to designate such progressive changes in the cells of multicellular organisms, and I believe that this term more clearly expresses the real nature of the morphological variations in bacteria than does "life cycle."

This idea is not entirely new. It has been implied in much of the bacteriological literature, but as far as

[1] From the Department of Bacteriology and Immunology, University of Minnesota, Minneapolis, Minnesota. Read before the Society of American Bacteriologists, Washington, D. C., December 30, 1924.

[2] Löhnis, F., "Memoirs of the National Academy of Sciences," Vol. XVI, 1921.

[3] Child, C. M., "Individuality in Organisms." Univ. of Chicago Press, Chicago, 1915.

[4] Minot, C. S., "Modern Problems of Biology." P. Blakiston's Son, Philadelphia, 1913.

I know has not been explicitly stated before. Thus the term "involution form" implies changes associated with senescence and death, and we have long known that motility is usually present only in young cultures and that spores are formed in older ones. But the observation that there is a distinct difference between the cells of young cultures and older ones in practically all species of bacteria has been made only relatively recently by Clark and Ruehl,[5] who have shown that, excepting members of the diphtheria group, the young cells are considerably larger than the older ones. They failed, however, to realize the significance of this phenomenon, for they believed that the increase in size is merely that due to enlargement of the cells preparatory to cell division. If this were the case the maximum size attained would be only twice that of the cells in the original inoculum; or more likely, since in any sample there would probably be just as many recently divided cells as cells just about to divide, the average maximum would be only one and a half times as great as the average size of the resting cells. But I have found in observing developing micro-colonies of Bacillus megatherium that the cells progressively enlarge, reaching a greater size previous to each succeeding cell division, and in measuring samples from a growing culture that the maximum size attained may be as much as six times that of the resting cells. Moreover, the increase in size is accompanied by other changes in morphology; intracellular granules disappear, the protoplasm becomes more hyaline and stains more deeply. And these changes in cell structure are accompanied by physiological variations, for Sherman and Albus[6] have found that such young cultures are more susceptible to harmful agents than are older ones; a condition which also finds its parallel in multicellular organisms, as Child[7] has shown that here also the susceptibility to poisons varies with the metabolic rate.

We may look upon these large cells, then, as a definite morphologic type, the embryonic form, so to speak, characteristic of the stage of active growth. Parallel measurements of cells and cell counts show that the change in size is definitely correlated with the rate of growth.[8] The increase in size commences during the latter part of the lag phase, progresses rapidly during the phase of positive acceleration, reaches its maximum at the moment of most rapid growth, and decrease occurs rapidly during the stage of negative acceleration. This has been repeatedly found true for Bacillus megatherium and in a single observation also for Bacterium coli. The increase involves all dimensions, but the increase in length is proportionately greater than the increase in breadth, so that the larger cells are relatively more slender, the area-length index becoming smaller as the length increases.[9]

If some of the cells be transferred to fresh medium during the period of increasing size they continue to increase in size and will reach a higher maximum than those remaining in the parent culture; if transferred at the period when they have just returned to the original size they immediately begin to increase again; but if transferred a little later, they show an appreciable lag in the new medium.[10] This exactly parallels the results of measurements of the rate of cell divisions when seedings of different age are used; and is also similar to the phenomena observed in tissue cultures, where the cells tend to mature or differentiate if allowed to remain in the same plasma, but revert to the embryonic type if a small portion is transferred to fresh plasma.

If a series of media of the same volume and composition are inoculated with varying numbers of bacteria they will all come to the same level of growth, earlier and more rapidly with the larger seedings. The stage of positive acceleration in growth is therefore more prolonged with smaller inoculums, and it is found that the fewer the cells introduced, the longer is the period of increase in size and the greater the maximum size attained.[11] I have found that, by varying the concentration of the nutrient in the medium, within certain limits (probably determined by the sensitivity of the organism to osmotic pressures) the final level of growth is proportional to the concentration of the nutrient. With the same seedings, then, the phase of negative acceleration must come progressively later with the more concentrated mediums, and it is found that the richer the medium, the longer is the period of increase in size and the greater the maximum size attained.[12]

In multicellular organisms the embryonic stage is followed by cell differentiation. It is obvious that

[5] Clark, P. F., and Ruehl, W. H., *Jour. of Bact.*, IV, 615–629, 1919.

[6] Sherman, J. M., and Albus, W. R., *Jour. of Bact.*, VIII, 127–139, 1923.

[7] Child, C. M., *loc. cit.*

[8] In an earlier paper (Henrici, A. T., Proc. Soc. Exp. Biol. and Med., XX, 179–180, 1922) I have made a statement to the contrary. This error was due to faulty technique in counting the cells.

[9] Henrici, A. T., Proc. Soc. for Exp. Biol. and Med., XXI, 215–217, 1923.

[10] Henrici, A. T., Proc. Soc. for Exp. Biol. and Med., XXI, 343–345, 1924.

[11] Henrici, A. T., Proc. Soc. Exp. Biol. and Med., XIX, 132–133, 1921.

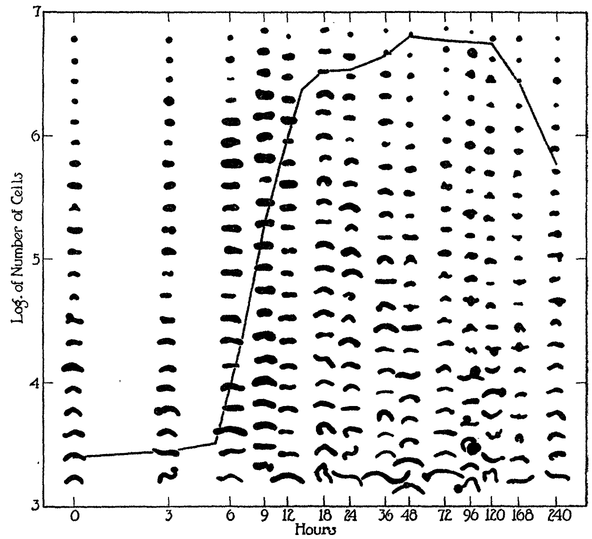
[12] Henrici, A. T., Proc. Soc. Exp. Biol. and Med., XXI, 345–346, 1924.

in bacteria we have no such variation in form as is implied by this term. But with cells uniformly distributed through a nutritive medium these cells should be more uniform in structure than cells nourished by a circulatory system regulated locally by the organism as a whole. We may definitely state, however, that bacteria have a mature form distinct from the embryonic form, characterized by smaller size, granularity of the protoplasm and fainter staining. Minot says that differentiation "consists essentially in this, that something new becomes visible in the protoplasm." In this sense many species of bacteria show differentiation, for they develop spores or metachromatic granules in the mature cells.

Spore formation begins when the culture has nearly reached the maximum growth, at the beginning of the so-called stationary phase. This point of inflection must also come progressively later with small seedings and with concentrated mediums, and so we find that spore formation proceeds less rapidly under these conditions than when the reverse conditions obtain.[13]

Clark and Ruehl found that the diphtheroid group differed from the other organisms studied in that the cells decreased in size during the period of active growth. This I have confirmed.[14] The cells become smaller and deeper staining and form chains; the decrease is greater in length than breadth, so that they appear almost like chains of cocci. The metachromatic granules rapidly disappear. The minimum size, however, is attained not at the mid point of the growth curve, but nearly at the end of growth. The metachromatic granules reappear more rapidly than the cells increase in size. This group will require further study before the different types can be definitely correlated with their proper phases of growth. Unpublished observations show that both the size of the cells and the number of granules are influenced by the size of the seeding and the concentration of the medium, so that these variations are definitely dependent on the metabolic rate.

I have not studied any of the cocci. Clark and Ruehl found that this group varied in size like the bacilli, and will undoubtedly follow the same laws. The spirillum of cholera shows three distinct types of cells, as shown in the accompanying illustration. The rate of growth is shown on this graph by plotting the logarithm of the number of cells against the logarithm of time. The columns of cells represent every tenth cell from a sample of 200 examined at each time interval and arranged in the order of their



area-length index. It will be observed that very little change occurred during the lag phase; that with increasingly rapid growth there appeared a group of new cells, long, plump and relatively straight; with decreasing growth the cells become more slender and curved, the typical "vibrio" form; and when growth is arrested and death begins the cells assume bizarre forms, showing bulgings and "budding" and many become spherical. It is these latter types which Löhnis and others have described as extraordinary reproductive cells; but the trend of the growth curve would indicate that this is not the case. It is noteworthy that only the mature cells are spirilla, the embryonic forms being bacilli and the senescent types cocci!

It is at first glance rather difficult to conceive of these simple variations in the cells of bacteria as being at all comparable to the complex changes which take place in the cells of a developing multicellular organism, but I believe the difference is one of degree rather than kind. There are, as far as I know, no quantitative data available whereby cell changes in a growing embryo may be definitely correlated with phases of growth; but from qualitative observation it would seem that cell differentiation must begin somewhere near the point of inflection in the fetal growth curve. Also, although various recent authors have called attention to the similarity existing between the growth curves for a population and for an individual, it is rather difficult to conceive of these processes as being similar or acted upon by the same causes. But it may well be that fundamentally there is no great difference between a population of one-celled organisms and a multicellular organism which in the last analysis is only a more closely knit together population of cells. At any rate, if the hypothesis here

[13] Henrici, A. T., Proc. Soc. Exp. Biol. and Med., XXII, 197–199, 1924.

[14] Henrici, A. T., Proc. Soc. Exp. Biol. and Med., XX, 179–180, 1922.

presented is correct, it would seem that it will eventually be possible to express cytomorphosis in quantitative terms as a function of the reaction between protoplasm and its substrate.

ARTHUR T. HENRICI
UNIVERSITY OF MINNESOTA

THREE LETTERS BEARING UPON THE CONTROVERSY OVER EVOLUTION

THE three letters appearing below have been used by the writer on a number of occasions, but only the one by President Wilson has been made available by publication.[1]

Since the campaign against evolution is spreading in certain localities and since the statements of Dr. Etheridge and Professor Bateson are widely used by anti-evolutionists in support of their doctrines, it may not be amiss to publish these letters where they will be available for use in the refutation of declarations that pass current. The letter by Wilson is included for convenience of reference and because of its general usefulness.

Washington, D. C.
29th August 1922

My dear Professor Curtis:

May it not suffice for me to say, in reply to your letter of August twenty-fifth, that of course like every other man of intelligence and education I do believe in Organic Evolution. It surprises me that at this late date such questions should be raised.

Sincerely yours,

WOODROW WILSON

Professor W. C. Curtis
Columbia, Missouri

The circumstances connected with this letter are explained in the article just cited. The following comment which was made in that connection is appropriate here:

> If the speaker is correctly informed, Mr. Bryan has recently declared from his Chautauqua platforms that he defies any son-of-an-ape to show that he (Bryan) is neither intelligent nor educated. I make no comment upon what an intelligent and educated ex-President perhaps thinks of the mental caliber of an ex-Secretary of State.

The following letter from Professor Bateson was received in response to a specific request. To the biologist, Bateson's address was, of course, sufficiently explicit, but the writer had found it unsatisfactory, in the case of one teacher who was under fire, to merely state that this distinguished zoologist meant only to question the factors of the evolutionary process.

[1] *Cf.* "Current aspects of the doctrine of organic evolution," *School and Society,* April 14, 1923.

11 December 1922
The Manor House,
Merton
London, S.W. 20

Dear Professor Curtis:

The papers you have sent me relating to the case of Mr. ——— give a curious picture of life under democracy. We may count ourselves happy if we are not all hanged like the Clerk of Chatham, with our pens and ink-horns about our necks!

I have looked through my Toronto address again. I see nothing in it which can be construed as expressing doubt as to the main fact of Evolution. In the last paragraph (copy enclosed) you will find a statement in the most explicit words I could find, giving the opinion which appears to me forced upon us by the facts—an opinion shared, I suppose, by every man of science in the world.

At Toronto I was addressing an audience, mainly professional. I took occasion to call the attention of my colleagues to the loose thinking and unproven assumptions which pass current as to the actual processes of evolution. We do know that the plants and animals, including most certainly man, have been evolved from other and very different forms of life. As to the nature of this process of evolution, we have many conjectures, but little positive knowledge. That is as much of the matter as can be made clear without special study, as you and I very well know.

The campaign against the teaching of evolution is a terrible example of the way in which truth can be perverted by the ignorant. You may use as much of this letter as you like, and I hope it may be of service.

Very truly,

W. BATESON

The paragraph to which Professor Bateson refers above is the concluding one of his address and runs as follows:

> I have put before you very frankly the considerations which have made us agnostic as to the actual mode and processes of evolution. When such confessions are made the enemies of science see their chance. If we can not declare here and now how species arose, they will obligingly offer us the solutions with which obscurantism is satisfied. Let us then proclaim in precise and unmistakable language that our faith in evolution is unshaken. Every available line of argument converges on this inevitable conclusion. The obscurantist has nothing to suggest which is worth a moment's attention. The difficulties which weigh upon the professional biologist need not trouble the layman. Our doubts are not as to the reality or truth of evolution, but as to the origin of *species,* a technical, almost domestic, problem. Any day that mystery may be solved. The discoveries of the last twenty-five years enable us for the first time to discuss these questions intelligently and on a basis of fact. That synthesis will follow on an analysis, we do not and can not doubt.