o'-the-wisp of philosophy. You may think you have it in your hand but will find that you have merely the shadow of something else. You will pursue that something else; you will touch it, and again it will feel real until you find that your consciousness of its touch is no more than the tingle of your own blood as your hands clasp upon it. Reality is the most alluring of all courtesans, for she makes herself what you would have her at the moment; but she is no rock on which to anchor your soul, for her substance is of the stuff of shadows; she has no existence outside your own dreams and is often no more than the reflection of your own thoughts shining upon the face of nature.

THE CHANGING BACTERIA[1]

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I HAVE been asked to sum up the discussion on bacterial variability to which we have listened this morning chiefly as a compliment to my years, because I have lived through more radical changes in our concept of the bacterial cell than have fallen within the lifetime of many of those present. I am here in the capacity of the innocent bystander, as a witness to the assault which the younger generation of bacteriologists are making on the concepts which in the past were held most sacred.

I happen to have been born in the year 1877, the year in which Nägeli published his famous book emphasizing his concept of pleomorphism, which assumed an almost unlimited variability, involving mutual transmutations between bacteria of the most widely separated groups. His extreme position was quickly overthrown by the work of Koch, Cohn and Migula and their followers, and for a period of thirty years bacteriology was ruled by the concept of relatively fixed and simple bacterial types.

We did know all along that certain variations occurred in the physiological reactions of bacteria, but these variations were for the most part closely and directly related to environmental conditions. We knew, for example, that *Bacillus prodigiosus* produces no red pigment at 37°. We knew that the virulence of many organisms could be enhanced by passage through suitable animal hosts. We knew, too, that virulence could be attenuated by exposure to unfavorable environmental conditions, as in the production of anthrax vaccine by Pasteur. Such variations as this, however, variations which were held to be gradual in their development, quantitative in nature and directly dependent upon the maintenance of the environment which called them forth, did not materially disturb our concepts of bacterial stability.

The first real threat to the older ideas was in the work of Neisser (1906) and Massini (1907) upon *B. coli-mutabile* and in the simultaneous work of Twort on the acquisition of new fermentative powers by organisms of the colon-typhoid group. These observations were confirmed but still regarded as representing exceptional phenomena. Twort's work was, however, continued and broadened by Penfold and elaborated by Ledingham in England, while Eisenberg in Germany was bringing forward convincing evidence of new types of bacterial variability. In 1917, came the work of Weil and Felix on Proteus X 19, in 1921, the recognition of rough and smooth forms by Arkwright; and very shortly the universality of the phenomenon of bacterial dissociation was demonstrated beyond any question. No one can read Hadley's magnificent monograph on this subject without being convinced that we are dealing here with a wide-spread and fundamental characteristic of the bacterial cell.

It is an extraordinary evidence of the fact that we see with our minds and not our eyes that this phenomenon should have remained so long undiscovered. For thirty years, bacteriologists had had rough and smooth colonies staring them in the face and had refused to see them because they did not fit into preconceived concepts of what should be there.

It is now at any rate clear that bacteria of very widely separated groups in pure line cultures, sometimes cultivated from a single cell, break up into two or more different strains with characteristics clearly differentiating them from each other. These characteristics may manifest themselves in cell morphology and capsule formation, in colony type, in biochemical characters and in virulence. The variants may breed true for generations, but in a vast majority of instances they tend in whole or in part to revert to the parent type or to change from one type to another, if suitable environmental stimuli are provided. There is no wild or random variation, for certain fundamental characteristics remain constant and the behavior of a rough or a smooth dissociant of a given species may be just as characteristic as that of the parent strain from which it was derived. The process is not one of mutation in the ordinary biological sense, since it is generally reversible and a true mutation is not. Dissociation is also markedly influenced both in

[1] Address delivered before the Society of American Bacteriologists, Baltimore, December 28, 1931.

amount and in direction by environmental factors. Yet the relation is in no sense direct and specific, as is the case with impressed variations. On a single culture plate, with essentially uniform environmental conditions, we find colonies of various dissociation types growing side by side. Furthermore, dissociation differs from the phenomena of impressed variation in the fact that it is relatively discontinuous, giving us 2, 3 or 4 well-defined strains which are usually much more common than are intermediate forms. (In certain instances, as in Marshall and Jared's recent work on Brucella, the shift from S to R forms fails to show such discontinuity). Finally, in widely separated groups of bacteria, dissociation seems to operate on general parallel lines, as evidenced by the fact that we can apply such terms as "rough" and "smooth" to the resulting strains.

Hadley lists the characteristics of the smooth form as follows, those of the rough form being generally the opposite:

R, Mutant Type

Agglutinative growth in broth.
Sedimentary suspension in 0.8 per cent. salt sol.
Often expansive growth on agar.[2]
Colonies rough, irregular, flat.
Seldom generates secondary colonies.
Agar growth harder, translucent.
Agar growth seldom so fluorescent.
Agar growth nonpyocyanogenic.
In motile species, nonmotile.
Noncapsulated.
Biochemically less active.
Often pure R; may have some O or S.
Lacks the "specific soluble substances."
Flocculent precipitate only in immune serum.
Slightly or nonvirulent (nontoxic[3]).
More common in carriers and convalesc.
More common in chronic infections.
More resistant in aging.
Less sensitive to bacteriophage.
Product of adaptations.
Tendency to short rods and cocci.
Not transformed in S immune serum.
Transformed to S in R immune serum.[4]
Susceptible to phagocytosis.

In general the smooth strain is the more virulent one; although with the cocci this relationship is reversed; and in general there is a tendency for the less virulent form to predominate, after cultivation outside the animal body.

Meanwhile, the concept of the simplicity of the bacterial life cycle has been upset during the past fifteen years by evidence of an entirely different kind. It had been known from the earliest days of the science that many bacteria went through a spore stage as a part of their life cycle; but this was the only exception to the general rule of binary fission. In 1916, however, Hort in England demonstrated the formation of gonidial bodies forming a definite reproductive stage in the life of colon-typhoid organisms. In the same year Löhnis and Smith in the United States and Enderlein in Germany described a whole life cycle involving complexities like those characteristic of certain of the higher fungi; and more recently it has been demonstrated that bacteria of widely separated groups may pass through a filterable stage which is later able to reproduce the original type of cell from which it was derived. The phenomena of gonidia formation and of filterability are now established beyond any question; and such work as that of Morton Kahn, in which the entire process of cell-disintegration and reintegration has been observed under the microscope in single-cell cultures, should convince the most skeptical. Evidence for a form of sexual reproduction in certain bacteria is also impressive, if not completely conclusive. Kuhn and Sternberg have recently attempted to explain all the phenomena of bacterial variation as due to the presence and influence of new hypothetical protozoon-like organisms which they call Pettenkofer bodies; but their assumptions seem wholly gratuitous.

Hadley and others believe that the two sorts of phenomena which have been here discussed are fundamentally related and that dissociation is the result of sexual reproduction. I must confess that I am not yet convinced of any such essential relationship and I believe it is wiser at present to recognize two distinct types of bacterial variation, which we may for convenience call dissociative and cyclogenic, and to leave the question of their interrelationship open for further exploration.

I must confess that it is not easy to distinguish clearly and sharply between these two phenomena on philosophical grounds. Both represent essentially discontinuous and reversible changes in morphological and physiological characteristics. Both are influenced by the environment; yet one senses a certain fundamental difference between the two types of variation. The cyclogenic variation, as its name implies, suggests an analogy with the normal life cycle of the higher forms of life, while dissociation similarly recalls mutation in the higher forms. As stated above, however, this latter analogy can not be a true one because of the reversibility of dissociation phenomena and also because discontinuity in dissociation is only relative. For the present we can perhaps only recog-

[2] Apparent exception in case of *B. proteus*.
[3] Relation to toxicity established only for *B. diphtheriae* and *B. enteritidis;* suggested for *B. dysenteriae* Shiga and for *B. botulinus*.
[4] Established for *B. subtilis*.

nize the two distinct types of variation and hope for further light as to their significance and mutual relationship. I do not, however, believe that more than two new types of variability need not at present be postulated; and I would suggest that efforts be made to correlate any fresh phenomenon of variation with either the cyclogenic or the dissociative type of variability, before introducing new terminology or new philosophical concepts.

Bacteriophagy I conceive as a third and quite distinct phenomenon, arising from the influence upon bacteria of a self-perpetuating substance (probably an organism) of independent origin. I can not believe with Hadley that bacteriophage is a result of dissociation; nor can I agree with my colleague, D'Herelle, that dissociation is necessarily and always a result of bacteriophagy. Rough strains are commonly lysogenic and a symbiosis between bacterium and bacteriophage might explain the appearance of certain "rough" characteristics. It seems quite certain, moreover, that action of bacteriophage is one of the commonest and most powerful stimulants to both cyclogenic and dissociative variation. It may well be, however, that other incitants would prove to be of equal generality if they were tested as extensively.

As one who has been long interested in systematic bacteriology I would point out that all this new knowledge does not involve a return to Nägeli's pleomorphism nor does it invalidate the conception of bacterial specificity. The fact that under certain conditions the colony of typhoid bacilli produces papillae of lactose-fermenting organisms is just as definite a characteristic of the typhoid bacillus as the fact that most of its cells fail to ferment that sugar. What we are getting from these studies is not a negation of bacterial specificity, but a conception that the characteristics of each species are vastly more complex than we had supposed.

Nor is there any danger that these new discoveries will overthrow the fundamental bases of epidemiology. It is just as true as it ever was that typhoid fever is normally caused by the presence of the Eberth bacillus and diphtheria by the Klebs-Loeffler bacillus. The simple concepts of specificity have proved their value. They are relatively, if not absolutely, sound, as proven by the empirical results obtained through their application. On the other hand, the new knowledge opens enormous possibilities of explaining obscure phenomena and of obtaining new methods of defense against communicable disease. The serological relation of Proteus X 19 to typhus fever and of *Salmonella suipestifer* to hog cholera, the association of Pfeiffer bacilli and streptococci with influenza and poliomyelitis may all perhaps be elucidated by future discoveries in this field. It may be that exposure to a non-virulent but immunizing phase of the diphtheria bacillus and the streptococcus may account for the development of immunity which takes place during childhood and which always seemed a difficult phenomenon to explain on accepted principles. The use of nonvirulent dissociants like the bacillus of Calmette and Guerin may widen our resources in the production of artificial immunity.

The brilliant work of those who have presented papers to-day, and of their predecessors, has opened up new fields in bacteriology which are full of hope and promise. They have given us a new concept of the marvelous properties of the organisms with which we work. They have multiplied the fascination and the practical possibilities of our science.

SCIENTIFIC EVENTS

THE ANNUAL EXHIBIT OF THE BRITISH PHYSICAL AND OPTICAL SOCIETIES

The twenty-second annual exhibition held jointly by the Physical Society and the Optical Society was held at the Imperial College of Science and Technology, South Kensington, in January. The exhibit was open to the general public. The London *Times* reports that the bulk of the floor space was occupied by the exhibits, many of them new, of the firms of scientific instrument makers. On the top floor and at a few other stands, however, there may be seen groups of apparatus displayed by some thirty contributors to the Research and Experimental Section.

The exhibitors here include many official bodies, such as the Meteorological Office, the Government Laboratory, and the National Physical Laboratory, the last of which showed a great variety of apparatus, including an interesting optical test of the effects of glare on the eye. The Post Office Engineering Research Station showed, among other apparatus, an "artificial ear," which has acoustic effects upon a telephone receiver equivalent to application to a human ear.

Mr. R. G. Bateson, of the Forest Products Research Laboratory, exhibited a direct-reading humidity meter operating on the wet and dry bulb thermometer principle, and enabling calculations of humidity to be made by inspection without reference to the usual tables or charts. A new humidity control apparatus for use in small testing rooms and laboratories was shown by the Wool Industries Research Association, together with a meter for testing the permeability of fabrics by the air, an extensometer for testing the elasticity of individual fibers, and a combined electrical