There is something stimulating in the creation of things which exist physically, which you can look at or feel, which does not exist in any purely intellectual achievement. This being so, I would not for a moment desire that the training of engineers for the future should so over-emphasize the purely intellectual side of our profession as to blot out the training which will enable men to produce things physically.

We must always have in mind that our engineers, in the last analysis, must be the creators of physical things if they are to be real producers, have a real understanding of their profession, and be able to play the enlarged part which I foresee to be the province of our successors.

As a telephone engineer I get a tremendous kick, whenever I go across the continent, merely in looking out of the car window and seeing such a simple thing as the pole line which carries the transcontinental circuits. Why? Because I realize that some of the best and happiest years of my life were spent in the creation of that very physical thing. At the present time I deal with similar problems almost wholly in an abstract way. I decide what sort of things should be done and I pass judgment on the work of others, but in the main I have no part in the construction of the things themselves. My life is given up almost entirely to paper-shuffling and various forms of intellectual gymnastics, which leave in me relatively little satisfaction.

ON POSTULATES OF PROOF IN PROBLEMS OF THE BACTERIAL LIFE CYCLE

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INTO many of the etiological questions of modern bacteriology there have been introduced problems of far-reaching biological consequences, which must be approached with the grim logic of the bacteriological forefathers unless we are to flounder in a bewildering confusion. These are the matters of the filterable stages of true bacteria and the suggested cyclic relationship between bacteria and the ultramicroscopic viruses. These two questions have often been confused with each other and there is a growing school of investigators from whose work it is often unclear whether they advocate one of these theories only or whether, in claiming the truth of one, they mean to imply that of the other as well. In regard to these developments, bacteriology is in much the same confusion with which it was threatened in the early etiological era, when countless false leads were laboriously followed out by investigators who attached etiological conclusions to the mere isolation of any organism from an animal or man suffering from a specific disease. And the formulation of his postulates by Koch was the warning of an uncompromising disciple of the truth against the dangers of allowing faulty reasoning to leap across experimental chasms. It is time for us to set up, in consultation, similar postulates in regard to the problems alluded to, if we are to avoid the obstructions to permanent progress which loose reasoning always produces. For there is no room for two schools of theory in any of these matters. Either a proposition is demonstrable by experiment, and confirmable, or it is not. And it can only delay the successful pursuit of the truth to claim, as established fact, conditions which have not been so established by observation. No one would be more delighted than the writer of these notes if most of the claims that have recently tended to establish a traceable cyclic relationship between invisible and visible forms of bacterial life could be substantiated. Such an achievement would enormously increase the capacity of bacteriologic methods to clarify important biological and medical problems. But we gain nothing in this direction unless we set down clearly the criteria of proof which alone can justify us in incorporating these new conceptions into the premises of our science. Regarding such criteria opinions may differ. It is with the purpose of clarifying this issue that these notes are written.

Let us consider first the question of the existence of filterable forms of true bacteria. The impulse for the present activity in this field was the great progress made in the knowledge of bacterial dissociation. And, in regard to this, it is gratifying to realize that the horizon of bacteriology and immunology has been infinitely enlarged by the studies of the so-called "mutations" in which cultural and colony studies and their immunological and chemical correlations constitute a series of discoveries achieved by the most rigid observance of that type of self-criticism in experiment which, it seems to us, is often lacking in the fields of inquiry which are the subject of this discussion. That all methods of bacterial filtration are complicated by a host of experimental irregularities is well known. And that there is no satisfactory method of appraising any of the ordinary laboratory filters except by actual test is acknowledged by every one who has worked with these methods to any extent. In our own work, we have found that neither the measurement of the amount of freshly distilled water which will pass through a filter, under a stated negative pressure, in a given time, nor the measurement of the pressure which will push air through the filter under water, possess any reliable relationship to the permeability of the filter for bacteria. Also, Ward and Tang in our laboratory showed, some years ago, that the passage of a virus through a filter depended as much upon the suspension fluid as it did on other factors and that the agents of vaccinia and of herpes would pass through a filter with far greater ease when suspended in certain types of broth than when taken up in any of the various isotonic salt solutions, irrespective of pH. Grinnell, then, testing all our Berkfeld and Mandler filters with *B. prodigiosus,* showed that all the "V" candles and most of the "N" ones would let these organisms through under relatively low pressure (10 cm Hg) provided the bacteria were taken from old cultures and were suspended, for filtration, in a hormone broth at about pH 7.8. Moreover, to be sure of the "tightness" of filters so tested, we found, in connection with our early typhus work, that control cultures of filtrates could not be regarded as sterile until they had been incubated for at least two weeks, since many of our controls showed the first prodigiosus growth as late as twelve and thirteen days after filtrate inoculation. From these facts alone it is apparent that the mere passage of bacteria through a filter—even a Berkfeld "N"—is not proof of a filterable form.

It is, of course, quite likely that bacteria, which multiply by fission, may well degenerate into granular fragments far smaller than the characteristic species-forms. It is not only conceivable but even likely that such fragments, containing chromatic materials, may be viable and grow out eventually to the adult stages.[1] But this does not constitute a filterable phase of a cycle. It is biologically far less significant and modifies in no respect our fundamental conception of bacteria.

In order to truly demonstrate the principle of a cycle between filterable and non-filterable—or, more exactly, large and minute forms of a morphological cycle, we would set up the following postulates:

(1) It must be possible to filter a suspension of a well-defined pure culture of bacteria through a filter which holds back the characteristic forms; and these original forms should not appear in the filtrate or in cultures made with adequate amounts of the filtrate on suitable media after incubation of at least two or three weeks.

(2) There must be evidence of growth of some kind in cultures made of this filtrate, but without evidence of the presence of the original normal forms.

(3) The culture of the filterable or minute form must be carried in a series of several generations.

(4) It must be possible to recover the normal forms from such successive ''filterable attributes.

Such requirements have not, as far as we know, been fulfilled by Mellon, by Rosenow or by Kendall, who are among the chief protagonists of the existence of filterable stages. They have been reported, we believe, only by Hadley, who gives details in regard to his Shiga bacillus filtration, but this work has not yet been sufficiently confirmed. Hadley, incidentally, is also quite definite in rejecting any implication that he suggests identification of his "filterable bacterial forms" with the so-called "ultramicroscopic virus" groups.

When we come to the suggestion that infectious agents, such as those of herpes, poliomyelitis, etc., are merely filterable or ultramicroscopic forms of well-known bacteria, we are confronted with a problem that threatens still greater dangers of possible confusion. It is of course, an obvious thought that has come to every one who has been frustrated by the difficulties which confront those who are laboring for a break-through in this field of investigation. It is not originality, but rather boldness—we might say intellectual recklessness—which seems to us to characterize the claims for such a cycle on anything less than convincing evidence. It is a fascinating way out of our difficulties, and the voice of caution is too apt, just now, to be suspected of unimaginatively academic hostility to new ideas, which is justly regarded as the opposite pole of obstruction to progress.

The claim of such cycles has been made, either in statement or implication, by a number of workers who need not be named, both in connection with herpes encephalitis, poliomyelitis and fox encephalitis. And the point of view has become widely disseminated among clinicians. To those who work with the ultramicroscopic viruses, however, a number of attributes of these agents are obvious which caution them to demand complete proof before they permit themselves to regard them merely as stages in a cyclic metamorphosis of bacteria. These properties, apart from

[1] Every one who has worked with the cholera spirillum and many other similar organisms knows that old cultures show almost no characteristic individual forms. Smears from such cultures are swollen, granular and unrecognizable as true spirilla. Yet, on transfer, the typical morphology reappears. We were, at one time, tempted to interpret, as possible evidence of a new type of bacterial life, the fact that our filtrates of typhus material, controlled with prodigiosus, showed no growth in cultures for as long as twelve days, after which period the original forms appeared in the tubes. This is, however, much less sensationally explicable on the basis of latency of a few organisms under conditions of the unusual environment furnished by filtrates containing many fresh tissue constituents.

the usually ultramicroscopic magnitudes which determine filterability, are the following:

(1) Except for the as yet insufficiently confirmed experiments of Eagles with tissue extracts, no filterable virus has been cultivated except in the presence of living cells in tissue culture.[2]

(2) Many of the viruses have been serially cultivated in tissue culture without reversion to the bacterial form.

(3) They produce diseases which are specific and unlike those produced by any known bacteria, even those produced by the bacteria supposed to have been developed out of the viruses themselves.

(4) The pathological histology characteristic of the virus diseases is entirely unlike that of any of the true bacterial lesions but, on the other hand, there is much similarity between the histological strategies aroused in animal tissues against the various filterable agents.

(5) In the lesions of most (almost all) filterable virus diseases characteristic "inclusion bodies" are present.

(6) There are many indications which render it likely that the theater of conflict in the virus diseases is an intracellular one.

(7) Active immunization in the virus disease is (with two exceptions which are not yet clearly understood) impossible unless living virus is used.

(8) The protective bodies differ from bacterial antibodies both in their limited concentration, even with hyperimmunization, and in the difficulty and uncertainty of demonstrating any *in vitro* reactions.

(9) There is a striking concentration of virus in specific tissues like nervous system and skin.

(10) There is a likelihood of persistence of the viruses in the animal body as long as immunity persists.

In addition to these points there are many minor facts, such as resistance to glycerine, to chemical agents and to heat; relationship to oxidation and reduction and to salt concentrations such as those recently demonstrated by Clark, all of which demand more study—but which, taken together, should caution us against any rash assumptions of relationship to bacteria, however attractive and startling such speculation may appear to be.

We do not want to be understood as throwing out of court the theory of cyclic relationship between bacteria and the virus group. Indeed, the possibility of such a relationship is perhaps the most important problem confronting the bacteriologist to-day. However, there is little sense and no utility in piling up our literature with repeated assertions of the existence of such a condition, unless definite postulates of proof can be fulfilled; and such postulates we would set down as follows:

Starting with a virus capable of producing a characteristic disease with all the clinical, pathological and immunological criteria necessary for its recognition, the investigator must:

(1) Repeatedly cultivate a bacterium of a single well-defined species.

(2) He must carry this bacterium through a number of culture generations. (If he can produce the disease, in the animal susceptible to the original virus and in a characteristic way, with these cultures, all the better. But this need not be required since virulence may change with form. However, we would attach no importance to such experiments as those of Rosenow with poliomyelitis, in which the bacterium produced a disease in rabbits and ginea-pigs—species entirely resistant to the original virus.)

(3) After a number of bacterial culture generations, it must be possible to get back the virus itself—apart from the bacteria—either by culture or by animal inoculation; the culture generations must be sufficient in number to insure complete removal of the original virus by adequate dilution; and such recaptured virus must possess all the original characteristics as to filterability, specific pathogenicity, etc., of the original material.

Such demands have not, to our knowledge, been fulfilled by any of the investigators who have been protagonists of the cyclic idea. Until such postulates or similar ones—adjusted to new knowledge—are required, however, we will get no farther, and this phase of bacteriology will remain sterile. We might add to all this the modest requirement that the experiments reported in such cases should be repeatable by other qualified investigators.

We sincerely hope that our point of view will be vigorously criticized by those who hold these cyclic metamorphoses to be demonstrable facts. The questions involved are of such fundamental importance that they call for the cooperative efforts of serious bacteriologists to remove them from the realm of speculative reasoning and place them upon a basis of experimental proof comparable to that which has been demanded for every other great bacteriological discovery.

[2] We believe that we are correct in assuming that neither the cultivation of the so-called "globoid bodies" in poliomyelitis—nor the cultivation of the agent of mosaic disease are regarded as accomplished facts any longer—even by their original proponents.

SCIENTIFIC EVENTS

PLAN FOR A CHEMICAL CENTER IN CHICAGO

ON January 30, 1932, representatives of the Chicago Section of the American Chemical Society and of the Chicago Chemists Club signed agreements by which both groups will in the future hold their meetings in the Midland Club. In addition, the Chicago Chemists Club signed a lease for quarters considerably larger than they have previously occupied in the Midland Building, 176 West Adams Street, in which the Midland Club is located. The signing of these