A BROADER PERSPECTIVE FOR BACTERIOLOGY

PRESIDENTIAL ADDRESS

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Periodically, there occurs a great event that causes men of science to pause in their work and plans, and attempt to orient their science and their thinking to the influence of the great event. Forces that bring about this self-inspection and analysis have included a change in philosophic thought, the emergence of a new scientific field, the discovery of a new tool for investigation, and the influence of an economic depression. Without entering into the controversy as to whether war is the result or the cause of scientific advancement (and both are apparently true), it cannot be denied that war is a tremendously strong factor in the stimulation of scientific advance. As a forceful event, it is causing scientific men to inspect their position and their science, to relate themselves to the powerful scientific movement of the time, and to plan for alignment with future advancement.

During this time of war, we have much more at stake than merely learning of Nature and applying our learning to the problems of war. We have, it seems, the question of whether we shall have the liberty to continue scientific inquiry without outside pressure or dictation. Under these circumstances, science must consider its association with Mankind, since it depends on human liberties for its freedom and life. For my part, I have little patience for the quibbling over the relative virtues of so-called "pure" and "applied" science. They are not distant cousins between whom we would choose, but siblings whose parents are Science and Mankind. With "pure" and "applied" having the common denominator of a scientific and social parenthood, and with Science and Mankind now in danger, there is in this crisis even less reason for us to choose between the children; how they serve to satisfy man's curiosity on the one hand, and to enrich man's life on the other is what counts.

In surveying a scientific field to determine its status and direction, it is more important to consider its perspective and the points of view of its workers, than to review merely its collection of facts about Nature. The accumulation of details comes, not always easily or as a matter of course, but more certainly if a sound perspective and outlook have preceded. The attitude, however, is more than receptiveness to new ideas; it is a conscious effort to imagine, explore mentally, interpret, synthesize as well as analyze, reach into neighboring fields for techniques and lines of reasoning, develop open-mindedness, and to see one's science in terms of human values. Details then become means to an end and are not ends in themselves. When a science is based on a developing mental attitude, flexibility is one of its characters. Findings that seem to be facts can be regarded as of temporary value to be adjusted or discarded with the acquisition of more knowledge, when the way of thinking is not dogmatic but broad, receptive and mobile.

With these introductory remarks as a background, I should like briefly to consider the science of Bacteriology and to attempt to orient it to modern thought and the influence of the war. In so doing, I shall have occasion also to show the relation of my analysis and resulting suggestions to a cardinal principle of Tropical Medicine.

It is customary to sketch the historical background for a discussion such as this. We can then the better see why a broader perspective can be considered timely. After starting as a curiosity in the hands of Leeuwenhoek, Bacteriology made little progress for 150 years. Then through inquiries into the cause of fermentation and the truth of spontaneous generation, the scientific giants of the times, led by Pasteur, learned about the activity of microscopic forms. When the conception of fermentative action of bacteria was carried over to infectious processes by Lister and Pasteur, the whole field of microbic causation of infectious disease was disclosed. This was a most logical turn of events, which however led to confusion because of the lack of knowledge of those parasitic forms present in and on animal tissues but not primarily concerned with the particular infectious process. In a necessary and scientific solution of

this confused situation, Koch laid down the principles that guided etiologic studies by emphasizing the importance of bacterial form and pure culture.

Thus Bacteriology passed through the phases of initial curiosity, expanding microbic physiology, and restraining morphology. Not until the third decade of this century have bacteriologists recognized that a strict respect for form is not their sacred duty. Aided by the expanding study of viruses, which are recognized chiefly by their action, workers in Bacteriology now think more of what the lower forms do, than of their appearance. This about-face has been a long and painful process that has not simplified our concept of microscopic and sub-microscopic forms, but has no doubt brought us nearer to knowing the complexity of Nature's truths.

As a result of these studies of the last 75 years, man's lot has unquestionably improved. Bacteriology has contributed in no small way to "the alleviation of suffering and the prolongation of life." The yield of the soil has been bountifully increased. The gregarious habit of man has been more pleasantly satisfied by the provision of sanitary conditions and of safer and more varied foods now available from far and near. Microbiology has added to the list of industrial products used and enjoyed by Mankind.

Can we hazard a guess as to the perspective of bacteriologists of this proudly productive era? It is a dangerous generalization, since there are many kinds of persons as well as a great variety of subjects to be considered. Is my opinion correct that we have paid disproportionate attention to techniques and the development of differential media? Perhaps we have worshipped too devoutly the uncompromising goddess of taxonomy, unmindful that she imposes rigid concepts of bacterial properties that really are variable and hence should not be used for natural differentiation of bacteria. We have constantly tried to make procedures easy and determinations final, and have accepted their artificiality without question. We have looked down our test tubes and microscopes so constantly that we have become myopic in regard to the broader outlook.

I do not for a moment minimize the importance of these lines of work, which have step by step led to scientific advances and to the human advantages of which I have spoken. And, if we are critical, we should remember that the perspective has been influenced by the contemporary scientific atmosphere of "getting the facts." Furthermore, the search for the truth about microbic and submicrobic life has assuredly been a source of great satisfaction to the workers, whether they reaped or gleaned in the brotherly fields of pure and applied science.

However, is the present status of bacterial investigation and subjective interest all that we have the right or hope to expect? Are we justified in stopping with the accumulation of observations and the turning of certain findings to practical human use? Is the point of view to be limited to the perspective I have admittedly overdrawn?

Bacteriology has come of age and, in fact, has already given birth to at least two offspring. It has developed its own techniques, its unique principles, and its individual lines of thought. It has roughly staked out its field and forsworn its allegiance to its numerous and dubious parents. As a respected adult, Bacteriology has won the attention and admiration of other sciences. To advance with sister sciences, it must continue to grow in perception, skill and interpretation, and not be content to stay at the level of methods as the aim and end of scientific endeavor.

This, then, is how I analyze Bacteriology, in this critical time that calls for self-analysis and reorientation in the light of the current great event. I venture to do so before this group because I recognize how much Tropical Medicine is concerned with the various phases of Bacteriology. Tropical Medicine looks to Bacteriology and allied fields for the understanding and solution of problems in infectious diseases of warm climates. With the emphasis in medicine being placed on the influence of the region on the incidence and nature of disease, and with the current conflict illustrating daily the importance of that principle of Tropical Medicine, it is pertinent that I suggest, as the basis for further bacteriologic advancement, the recognition of the role of the environment in Bacteriology.

I propose to consider the significance of environment in connection with free-living and parasitic forms.

Let me start the section concerning the free-living bacteria by making some observations, albeit bold, regarding bacterial studies in vitro. Test tube bacteriologists may think that they are delving into the secrets of Nature when they put through its tricks a pure culture of a single-cell

strain, isolated from the soil by a patient worker 50 years before. The unnaturalness of the situation is usually emphasized by the culture being received in the mail from a type culture collection. It arrives in the dry stage in response to a telegram, and the crumbly powder, in an atmosphere of pure nitrogen in a sealed glass tube, is laid on the laboratory table until a synthetic medium is made. Perhaps the only natural constituent intentionally included in the medium is water, to which is added a little chemically purified this and that, and the other elements we consider essential may be included in the water as contaminants or dissolved from the glass. This is the so-called "environment" which provides enough of what the bacterium needs for its structure and physiology, so that in 20 hours (by the automatic timer) a cloud appears in the test tube, to which the worker points with pride. A gram stained preparation is made, and all forms nicely appear with the same size, shape and color.

Now this is all well and good, provided the worker does not deceive himself. The finding is interesting, his curiosity may be satisfied, and perhaps the bacterial growth is of human value. I hasten to defend myself and my colleagues against the charge that this type of work is senseless; it has much sense to it; but too often it has been conducted on the basis of "getting the facts." It has and will have its place, but I plead that the worker recognize the conditions under which he does such work. He must know the artificiality of the conditions and should be willing to say, "This is the environment I set up, not the natural environment. Nature's environment is complex: the pabulum is mixed and variable, the temperature is not set at $\pm 0.5°C$, sunlight is sometimes present, the water supply is irregular, and there is competition with a mixed microbic flora." When this point of view is held, the worker becomes a naturalist and he has progressed from a lower to a higher level of thought and perspective.

The fact is that bacteriologists are beginning to see that the environment is important even under artificial conditions, in respect to the effect of the medium on the regularity of the size, shape, staining, and chemical composition of the bacterium. They are understanding the lability, the variability and the responsiveness of bacteria to some of these environmental factors. Although these conditions of observation are artificial, we are learning by such studies that microbic forms are not static and rigid but follow only broad lines of regularity influenced by factors in their surroundings.

If we turn now to the field of parasitic bacteriology, we find the argument even more pertinent. We bacteriologists do not usually make studies of parasitic forms directly from the sites of the body parasitized. If we did, we should note that the microbic forms are not as regular or as nicely arranged as our textbooks picture them. Instead of building a conception of form based on observations of bacteria in situ, we make cultures right off and then fall back on the artificial culture situation to build our concepts of bacterial morphology and physiology. Useful in diagnosis? Certainly, but not a true picture of Nature, because we have hastened to the use of an artificial environment and neglected the opportunity of acquiring the broader perspective of parasitism.

A basic principle of Bacteriology is pure culture study. Koch, following Henle's lead, emphasized this point in relation to causation of disease and he served the needed function of bringing order out of chaos by insisting on the exclusion of extraneous forms in studies on specific etiologic agents of infectious diseases. This dogma, good in its place and time, is so deeply entrenched in textbooks that the student usually recites the so-called Koch's postulates when questioned for evidence for the specific relation of a causative agent to a specific infectious disease. How much the student misses, particularly the medical student, if he goes no further in his concept of causation than an understanding of Koch's over-simplified enunciation! The breadth of perspective is the measure of our advance from Koch's day. The question now is how far are we willing and able to go in our thinking and teaching.

It is clear by now that one element in the broader outlook I plead for is the inclusion of the environment in the consideration of causation of infectious disease, not as an unnatural concept but as a genuine consideration now supported, although incompletely, by significant controlled observations.

The environment in this connection is a gradient from the immediate surroundings of the parasite in the tissues of the host, to the distant conditions of region and climate so effectively emphasized by Tropical Medicine. I do not propose to enumerate all the stages in this gradient, and for purposes of simplicity I suggest that they be divided into two classes—the intimate and the remote.

Under the term "intimate" may be placed the cell and tissue constituents of the particular surroundings of the parasite, concerning whose various roles we know so little specifically. Why does a certain parasite flourish in a definite part of a tissue or organ of a given host species or strain of a single species? In general, we should consider that when an infection results from an agent that has circulated in the body, its successful localization is due to its finding a favorable intimate environment in a particular part. If I limit myself to considering the unimmunized animal, I should like to ask what is present or lacking in that certain site that favors or discourages microbic growth?

It is becoming increasingly evident that the age of the host is frequently significant, and evidence is accumulating that the nutritional state of the host plays a part in some instances. There are of course those more obvious factors that have to do with this matter of immediate environment, such as trauma and the route of entry of the agent into the animal host; even the numbers of the invading parasite may affect the local situation so that the few survivors of the new population assert themselves effectively.

We must recognize also that what we call a specific infectious disease is not always due to a single microbic species in pure culture. If the infection is of a mucous surface especially, other parasitic and ordinarily non-pathogenic forms may take a significant part in the process. This associative action of different agents sometimes takes a dramatic form, and in numerous instances there is a variation in the properties of the agents as well as a striking alteration of the infectious process itself. Here again, we must accept a modification of the former stereotyped concept of single specific causation of infectious disease and recognize that both etiologically and clinically the effect of the added microbes on the immediate environment of the initial parasite is significant. We err in thinking of the clinical entity of influenza as always being due solely to the influenza virus, of the common cold as being caused by the specific virus alone, of whooping cough as always attributable only to the pertussis bacillus, of smallpox as uncomplicated by bacterial etiology, and hog cholera as occurring naturally without added invasive bacteria.

These types of complex etiology are attributable in part to the physical opportunity of contaminating parasites to enter the lesion begun by specific agents, but more pertinent to the argument is the thought that the intimate environment of a single parasitic species is modified by the associative action of other parasitic species.

The intensive study of viruses in recent years has only emphasized the importance of the role of host factors in the complex host-parasite relation. Virologists have been unhindered by artificial culture work and morphologic studies in their learning of viruses. They have perforce centered their attention on the environment of the virus as supplied by the living experimental host.

After referring to the cellular milieu of the parasite, so strikingly essential in the case of viruses, to the host factors of age and nutritional state among others, and to the associative action of different parasites in relation to etiology of specific disease, need I go further in illustrating the significance in medical Bacteriology of understanding the role of the intimate environment?

My next point needs no elaboration before this group. The remote environment, that is, remote from the parasite, has been amply demonstrated in Tropical Medicine, and during this war is being illustrated and recognized more and more. We think here of such factors as the temperature, altitude, humidity, local customs and living conditions, ectoparasites, and flying vectors of disease. Some of these factors are obvious in their effect, but some, particularly those that seem to exert an influence on the intimate host-parasite relationship, are not so well understood. But they are all factors of environment which we may call "remote" and which bacteriologists, virologists and other microbiologists must recognize above and beyond their laboratory knowledge of the specific agents themselves.

Where does all this bring us? To the proposition that new fields are available and open to Bacteriology and bacteriologists. After having explored its scientific region and established some of its basic principles and methods, Bacteriology is now prepared to turn to a closer study of Nature and to learn what the relation of the natural environment is to the various bacterial forms.

In connection with the free-living, non-parasitic types, the enlarged perspective means the consideration of ecology, in which studies are hardly begun and which in all its ramifications suggests a great variety of challenging, interesting and fruitful problems.

A careful consideration of the environment of

parasitic forms calls for a greater regard being paid to the animal in the host-parasite relation. Too often we have thought of the host as a test tube—inanimate, standard and originally sterile. But so common is the occurrence of a resident virus or bacterium in the experimental animal that virologists are obliged to be constantly on the guard in the study of an experimental virus. This illustrates the many less tangible but clearly natural factors that have to do with parasitism. The whole subject of the selective cellular milieu in the intimate environment of the parasite presents challenges unlimited in scope and promising in application.

Our information on the role of the environment remote from the parasite but affecting the host-parasite relation is as yet somewhat empirical and I fear we are in danger of allowing conceptions to be established that have no substantiation in scientific observation. This is a difficult problem for solution, this host-parasite-climate complex, but progress has been made and surely can be accelerated when the tools, ideas and vision of workers are brought to bear on it. I refer here not only to the environment of warm climates but also to the larger problem of host-parasite-surroundings of all regions.

The war is the current event that is causing us to analyze our respective sciences in an attempt to see if we are progressing in keeping with our times and with the responsibilities we owe to society that nurtures science and currently fights for our liberty of study.

The review of my own science, Bacteriology, leads me to propose that its further development could profitably be in the direction of a higher level of perspective than perhaps now generally held. Without minimizing the importance of the study of bacteria under artificial conditions, the limitations of such methods should be recognized, and the significance of natural conditions and the environment is to be more fully appreciated. Natural conditions are complex and in reference to the parasite include both intimate and remote environmental factors. The importance of the environment is a principle of Tropical Medicine, illustrated and emphasized by world conditions of today. To the degree that Bacteriology, whether applied or pure, accepts this broader perspective, it will the better serve Natural Science and Society.