Microbiology—Yesterday and Today

A perspective from 50 years ago on the growth and future of microbiology

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“And in today already walks tomorrow”

—Schiller

It is important to attempt the correlation of changes, phases and attitudes in microbiology, since in general there has been a gradual shift in recent years from the endeavors of the individual investigator to those of a team. This shift in emphasis, the difficulties of associating particular eras in a field of science with its eminent representatives and the influence of subsequent developments upon the progress in this field, can best be illustrated by reference to the pioneer investigators in microbiology. These men may be regarded as having set the pace for the science of yesterday.

Early Investigators in General Microbiology

Certain outstanding names in microbiology may be selected to elucidate the changing concepts in the development of this particular field of science. Does the death, 30 years ago, of Wilhelm M. Beijerinck, the great pioneer of yesterday, or, only six years ago, of Sergei N. Vinogradsky, the last of the older giants of microbiology, signify that microbiology of yesterday was brought to an end with the passing of one or the other? Does the sudden death of Albert J. Kluyver, one of the outstanding investigators of recent years, signify that microbiology of today has come to an end and that we must start looking for the microbiology of tomorrow? Or was Kluyver merely a symbol of certain ideas that have been dominating many of the recent concepts in microbiology, and that the modern period as such is far from coming to an end?

Let us attempt to analyze briefly the microbiology of yesterday. Basically, the methods were characterized by observations of the occurrence of microorganisms in nature, by the isolation of these organisms in a pure state, and by the description of many new forms, thus firmly establishing the ecological and botanical aspects of the science of microbiology. The microbiologists of yesterday were largely concerned with a search for organisms responsible for certain known processes, rather than for mechanisms and reactions carried out by such organisms.

A definite forward step in the study of microbes came soon through the pure culture studies of Robert Koch, as well as the contributions to our knowledge of the association of specific organisms with known diseases, largely through the work of Pasteur, Koch and numerous others. The infectious nature of disease thus became gradually elucidated. This development was soon followed by the investigations of Paul Ehrlich in the field of chemotherapy, especially the use of dyes and arsenicals in the treatment of infectious diseases, and of Emil von Behring and Shibasaburo Kitasato, on antitoxins and vaccine therapy.

Simultaneously came the biochemical studies of Winogradsky and Beijerinck on the role of various bacteria in important natural processes, such as nitrification, nitrogen fixation, and sulfur oxidation. These were followed by the work of numerous other microbiologists who, in search for organisms responsible for known processes, concerned themselves with the study of the occurrence, nature, and activities of various groups of microbes. The knowledge thus gained served to broaden further our concepts of general microbiology and of the relation of microbes to natural processes, especially those important in human economy.

It has been said time and again that early microbiology suffered from its emphasis on practical problems. Pasteur was more interested in the isolation and identification of microorganisms in nature, by the isolation of these organisms in a pure state, and by the description of many new forms, thus firmly establishing the ecological and botanical aspects of the science of microbiology. The microbiologists of yesterday were largely concerned with a search for organisms responsible for certain known processes, rather than for mechanisms and reactions carried out by such organisms.
in the processes of fermentation of beer and wine, in the diseases of the silkworm, in the causation and control of rabies and anthrax than in the causative organisms themselves. It should be remembered, however, that during the same period Robert Koch was searching for the organism responsible for the causation of tuberculosis in man and in animals and for the life cycle of the anthrax bacillus; his contributions to methods of control of these diseases were rather secondary in nature. Beijerinck was concerned with the bacteria responsible for the processes that take place in soils and water basins, rather than with the processes themselves. Winogradsky was looking for bacteria capable of bringing about certain autotrophic chemical reactions and thus introduced a new concept into microbiology.

The Older Sciences and the Advance of Microbiology

One must consider first of all the contributions of the general biologists, especially zoologists and botanists, who were the first to offer in many universities courses in bacteriology. The chemist came next with his contributions to our knowledge of the nature and nutrition of microbes. Among those who have made extensive use of the rapidly increasing knowledge of microbes and who contributed greatly to it, the clinician also occupies a prominent place; he was among the first to recognize the great potentialities of this new field of knowledge. If Cohn were to be considered as the representative botanist and Pasteur as the chemist, certainly Koch and Lister would personify, in the very best tradition, the clinicians.

Next must be considered the work of a number of other scientific workers concerned with the nature and activities of microbes. The veterinarian, the plant pathologist, the agronomist, the soil investigator, the sanitary worker, the food expert, the brewer and the distiller, and finally the industrialist interested in fermentation products, ranging from antibiotics to organic acids, have all left their imprint upon microbiology.

Very few of those who are concerned with microbes today, in a period when biochemistry is supreme and when clinical applications appear to have reached their zenith, appreciate the important contributions of the botanist to microbiology. Those who first isolated, identified, and described microbes, whether bacteria or actinomycetes, fungi or viruses, laid a solid foundation for subsequent growth of microbiology. It is often forgotten that the botanists first established the virus-host relationship.

The chemist was also among the first to recognize the great potentialities of microbes as chemical, or rather biochemical, agents. Beginning with Pasteur’s work on the separation of tartrates by molds and the role of lactic and butyric acid bacteria as agents of fermentation, there followed a long sequence of chemical investigators, who studied the production of alcohols, organic acids, vitamins, and finally antibiotics. The chemist, beginning with Paul Ehrlich, followed later by Michael Heidelberger, Gerhard Domagk, and Jacques Trefouel, initiated and developed chemotherapy. The chemist has often utilized the microbe as a model for the investigation of reactions taking place in the metabolism of higher forms of life.

The Microbiologist of Yesterday

Let us now compare the microbiologist of yesterday and today and the approaches and problems with which each has been concerned. First of all, attention was focused upon the methods needed for the isolation and identification of bacteria and other microorganisms, the growth of these organisms in pure culture, and the determination of the role of these organisms in certain processes, such as causation of disease, spoilage of foodstuffs, or the numerous reactions taking place in the soil and in the sea. The life cycles of the organisms thus isolated often played an important part in these investigations. No wonder that the postulates of Koch, so characteristic of microbiology of yesterday, still dominate certain present-day concepts of our knowledge of the relationship of organisms to disease. These concepts, in various modifications, have also influenced our understanding of the role of microorganisms in biochemical reactions taking place in such natural substrates as soil and water.

The foregoing phases of the science were frequently followed and often accompanied by a search for the chemical reactions brought about by the various microorganisms. Almost simultaneously, a search was made for the means necessary to control the microbes responsible for
these reactions. Thus, the studies of Pasteur on microbial fermentations and on the causation of rabies and the work of Ehrlich and Metchnikov on disease mechanisms and immunological reactions were followed immediately by efforts to control the organisms responsible for these processes so important in human economy and in human welfare.

**Fermentation and putrefaction.** None of the contributions made by the chemist to microbiology were more significant than those dealing with fermentation and putrefaction. These concepts, largely enunciated through the classical studies of Pasteur, came to play an important role in the development of our knowledge of microbial nutrition and microbial biochemistry. Gradually the term “putrefaction” was dropped, and “fermentation” eventually acquired great significance.

**Autotrophy.** The original contributions of Winogradsky to our knowledge of sulfur bacteria, iron-oxidizing bacteria, and nitrifying bacteria gave birth to a new concept of bacterial life. It had to do with the ability of certain bacteria to utilize energy liberated in the oxidation of simple chemical elements and compounds. The role of microbes in natural processes thus gained added importance.

**Microbial ecology.** The influence of the environment upon the occurrence and activities of microorganisms came next into consideration. Among the problems involved were those concerned with the effect of the animal or plant host upon the invading parasite and with the significance of symbiotic relationships between plant and animal life, on the one hand, and microbial life on the other. One must also recognize the problems concerned with the effect of the soil and atmospheric environment on the free-living and the saprophilic microorganisms. One may also consider, in this connection, the numerous investigations on the life cycles of bacteria.

**Biochemical concepts.** The growth and nutrition of microorganisms, in pure and in mixed culture, automatically attracted much attention. The development of synthetic and organic media for the growth of various microorganisms involved many problems of physiology and biochemistry. The knowledge thus gained has contributed greatly to a better understanding of the nutrition of animals and man, and tended to bridge the gap between the concepts of microbiology of yesterday and that of today.

**Disease and chemotherapy.** These problems received the greatest consideration by the microbiologists of yesterday. Numerous microorganisms were isolated, cultured, and tested for their effect on experimental animals. Their cells or cell products were used for immunization against infection, in the form of vaccines, and for therapy, in the form of serums and antitoxins. The ability of bacteria and viruses to bring about various immunological reactions in the blood of experimental animals opened new doors into the unknown living world. The sensitivity of microorganisms to various antimicrobial drugs was determined, in order to establish the efficacy of such drugs as potential chemotherapeutic agents. It was soon established that there is a striking parallelism in the activity of such drugs on bacteria in the test tube and in experimental animals.

The initial work of Lister and others on antisepsis and disinfectants, of Metchnikov on immunological reactions, and of Ehrlich on the synthesis of antimicrobial drugs embraced a series of scientific contributions to the field of microbiology that proved of inestimable value to human health. Following the discovery of salvarsan, Ehrlich believed that chemical agents effective against true bacterial diseases were not far away, but a quarter of a century elapsed before the sulfa drugs came into being. There were certain important reasons for this long delay. Chief among these was the dominant idea of Ehrlich of a “maxima-sterilizans” which so impressed itself upon his followers that all their attention was centered upon bactericidal substances rather than upon bacteriostatic agents. The former were too toxic. The latter were either overlooked entirely or were found to have only a weak antimicrobial activity. There was also a lack of appreciation of the selective action of suitable antibacterial agents upon the parasite versus the host.

**Saprophytic microorganisms.** Full recognition of the importance of microbes in the cycle of life in nature was centered on their activities in soils and in composts, in food and in food products, in water and in sewage. Among the problems on the borderline between parasitism
and saprophytism, one may mention the
production of bacterial toxins (botulinum), the
problems of cellulose decomposition in textiles
and paper, and the general damage to industrial
and food materials.

**Taxonomy and descriptive microbiology.** Finally, one should not overlook the thankless
labors of those who worked hard to make microbes recognizable. Although this field is far
from exhausted, as evidenced by the numerous
new species of microorganisms, it must be ad-
mitted that this process of codification of new
genera and species is to be credited to the micro-
biologists of yesterday.

The investigators concerned with these vari-
ous phases of microbiology of yesterday were
primarily biologists, although they frequently
made outstanding contributions to the bio-
chemistry of microorganisms. Their approach
to the problems was primarily biological. They
were ecologists and physiologists, primarily
concerned with cause and effect. Finally, they
were interested in the methods of control of
microbial life. They were concerned with micro-
bial populations rather than with single cells.
They were interested in broad biological activi-
ties rather than in specific biochemical reactions.
It is impossible to conceive of a microbiologist
of yesterday who would be voicing such com-
ment as that made by one of the microbiologists
of today that “Bacteria have no physiology, but
they have a biochemistry.”

**The Microbiologist of Today**

To characterize the microbiologist of today, we
must give first consideration to his use of the
quantitative method and of the biochemical ap-
proach. It is frequently difficult to say with any
degree of certainty where the work of the gen-
eral biochemist leaves off and that of the micro-
biochemist or the microbial biochemist begins.
New concepts have been introduced into micro-
biology, concepts hardly visualized by the mi-
crobiologist of yesterday.

For the sake of illustration, let us consider
the genetic concept. Only yesterday, the genetics
of bacteria was still a dormant or at least a
highly controversial subject. From Mendel to
Morgan and from Darwin to the modern evolu-
tionists, the geneticist dealt entirely with higher
plants or animals. Although some investigators
were occasionally interested in the genetics of
certain groups of microorganisms, as in the case
of Blakeslee’s work on the *Rhizopus* group,
they would scarcely recognize the results of
their efforts in the recent contributions of
G. Beadle and E. L. Tatum, of J. Lederberg and
G. Pontecorvo.

Recent developments in the fields of bacteriop-
phages and of microbial enzymes are other illus-
trations that would characterize the endeavor of
the microbiologist of today. The same is true of
the investigation of metabolic reactions of one
organism under the influence of the products of
another. Microbial populations, when they are
considered at all, are studied from the point of
view of single cultures, with all the complex
reactions involving problems of resistance and
sensitivity, parasitism and saprophytism. No
wonder, therefore, that the field of antibiotics,
involving not only microbiological, but also
chemical and biochemical considerations, could
blossom forth today.

**Metabolism of microorganisms.** The investig-
atior of today is primarily interested in such
questions as the role of specific chemical constitu-
tents of the substrate in the nutrition of micro-
organisms, the transformation of such constitu-
tents into other compounds, either intermediary
or final in nature, and metabolic pathways in
general. These investigations involve problems
of oxidation and reduction, reactions of fer-
mentation, and the various cycles of transformation
involved in biosynthesis in general and the bi-
genesis of specific metabolic products, like anti-
biotics, in particular. The similarity of such bio-
chemical reactions to those involved in parallel
transformations in cells of higher forms of life
has frequently been indicated.

**Enzymatic mechanisms.** The microbiologist
of yesterday was primarily interested in those
enzyme systems which involved questions of
hydrolysis and synthesis, notably those involv-
ing transformation of proteins and amino acids,
starches and sugars. The microbiologist of today
is concerned with problems of enzyme adapta-
tion, with enzymes of respiration and oxidation,
and with numerous other enzyme systems.

**Genetic problems.** These involve problems of
variation, mutation, and selection mechanisms,
of genetic transfers and recombination, of resis-
tance to antimicrobial agents, and the develop-
ment of microbial strains with specific biochem-
ical deficiencies. All of these have tended to
transform completely our understanding of mi-
crobial life and of microbial nutrition, and have placed in the hands of the microbiologist new and effective tools. New vistas of cell growth and cell synthesis have also been opened.

**Viruses and phages.** The chemical purification of viruses and phages, information on the mechanism of interaction of bacterial cells with phages, on the relations of prophage systems to mature phage, and finally the gradually evolving phage-gene concept, have thrown much new light upon the nature and activities at the ultramicroscopic level of life. They have also greatly enlarged our understanding of the relationship between host and parasite, between individual cells in complex populations, problems of reproduction, and a host of other phases of microbial life.

**Formation of growth-stimulating and growth-inhibiting substances.** The formation of vitamins and antibiotics and the knowledge gained from the study of the action of these substances upon the growth of various groups of microorganisms have greatly enlarged our understanding of health and disease, and have provided tools for improving health and extending the life span. Problems of sensitivity and resistance of microorganisms to antibiotics have contributed to a better understanding of microbial populations and the changes they are able to undergo, of problems of virulence vs. avirulence, and a host of others.

**Effect of microbial products upon the growth of other, notably higher, forms of life.** The microbiologist of today has made use of the vast potentialities of certain microbes for producing chemical substances that have the capacity to inhibit or stimulate the growth of other microbes, as well as of higher forms of life. Problems of saprophytism and parasitism are extending the ever-broadening horizons in microbiology and in life in general. The whole subject of chemotherapy has been revolutionized. Add to this the problem of animal nutrition that has gained considerably from our increasing knowledge of microbial products, preservation of food and other biological products, and human health and economy take on a new significance.

Other aspects of microbiology today include a better understanding of cellular morphology, of bacterial serotypes, of the toxin-antitoxin concept, and of quantitative immunology. The para-agglutination phenomena of yesterday have led to recognition of the serological reactions of the bacterial polysaccharides and the transformation of bacteria by deoxyribonucleic acid of today.

Other phases of microbiology have recently made much progress. These include: (a) Problems in medical microbiology, such as the recognition of certain virulence factors and the creation of new types of vaccines. (b) The utilization of microbes in the study of their effects on living cells. (c) The potential use or misuse of microbes as a weapon of warfare.

**Education in microbiology.** We must not, finally, overlook the problem of training of microbiologists. The microbiologist of today is primarily a specialist. He may be completely unaware of the broad biological aspects of the microbes responsible for a given reaction. He may even be accused of considering the microbe as a “bundle of enzymes,” as a “complex method of chemical reactions,” or as primitive forms of life devoid of biological properties and possessing purely biochemical characteristics. In fact, how many microbiologists of today have a microscope handy, to look at the organisms with which they are working? No wonder the academic preparation for a microbiologist stresses a thorough training in chemistry and physics, and places little, if any, emphasis on botany, zoology, medicine, or agriculture.

While microbiology attained the stature as a science, it also became a tool for allied scientific fields. At the same time the contributions of most individual investigators have become diluted in team research. Possible remedies to narrow the gap of difference between the average investigators of today and yesterday may be suggested: Encourage delayed specialization of students, foster broad discussions straddling the remaining demarcation lines of scientific endeavors, place a premium on one or two postdoctoral years in a field different from that pursued during graduate years, and make courses in the history and philosophy of science obligatory, etc. Finally, by all means, encourage long-term fundamental research programs. Give the individual investigator the opportunity to express himself freely, without stifling him by administrative duties and the burden of supervision of numerous technicians.

*This article was abridged from the original, which is available in the online version of this issue.*