Meetings

History of Microbiology

The first conference in the United States devoted exclusively to the history of microbiology convened at Indiana University 29 June–3 July. The sessions were attended by teachers of microbiology and allied sciences from all parts of the country. Most of the speakers were professional microbiologists, rather than historians of microbiology; indeed, it is doubtful whether anyone would admit being confined to such a narrow and esoteric specialty.

L. S. McClung (Indiana University), who serves as archivist for the American Society for Microbiology, described the contents of the archives that are maintained in the Lilly Library. The archives are open to all scholars interested in the developments of American microbiology, particularly those occurring since 1900, and it is hoped that this collection will ultimately serve as a center for historical research in this area.

One of the useful features of the conference was a panel discussion on teaching the history of microbiology at the college or university level. The panel consisted of E. Weinberg (Indiana University), R. N. Doetsch (University of Maryland), F. Engley (University of Missouri), and S. Morrison (Colorado State University). The subject is usually offered as a one-semester course, given generally to senior majors or first-year graduate students. It was agreed that the best method to present these materials of microbiology is either as a series of formal lectures or as a combination of these with seminars and discussions. Emphasis was placed on using original papers ("classics") as primary source materials for these discussions. An interesting suggestion was to use replicas of original experimental apparatus, such as Leeuwenhoek microscopes or Pasteur's swan-neck flasks, as teaching aids.

A course on the history of microbiology would (i) assist in the development of humanistic rather than purely technological scientists; (ii) inspire students with the spirit, adventure, and achievements of microbiologists; (iii) emphasize the importance of microbiology in human affairs (for example, lengthening of life span, control of epidemics, and so forth); and (iv) serve to trace the emergence and development of great ideas and to depict the interaction between the political, social, economic, and scientific features of a given era or society.

R. N. Doetsch (University of Maryland) traced the development of American thought on the cause of infectious diseases. He tried to show that the work of Cotton Mather, John Crawford, John Kearsley Mitchell, and Daniel Drake was in many ways of equal merit to their European contemporaries, but that lack of laboratory development, poor communication, and the challenge of the wilderness prevented its fruition. C. E. Dolman (University of British Columbia) presented a comprehensive survey of the contributions of British microbiologists from 1880 to 1930. One of the interesting features of Dolman's presentation was his superb collection of photographic slides of nearly all the eminent British microbiologists of the half-century about which he spoke. Most of these photographs have never been published, and they certainly constitute a valuable adjunct to the history of that area of microbiology.

Tracing the development of important ideas, R. J. Porter (University of Iowa) spoke on spontaneous generation, and G. Miller (Western Reserve) discussed theories of smallpox in the 18th century. In both of these instances, the speakers emphasized that the development of ideas must be interpreted and criticized in terms of the times in which they were introduced, rather than from the vantage of the 20th century. Porter showed how our ideas on spontaneous generation in 1964 differ from those held in 1864, and he related how Pasteur himself had tried in vain to obtain positive results with a rigorous laboratory technique.

No further publication of these proceedings is contemplated, although the entire program was recorded on tape. This conference, sponsored by the National Science Foundation, together with several symposia held at recent national meetings of the American Society for Microbiology, revealed the growing interest in and the importance of the historical aspects of microbiology in the United States.

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Interferon

Recent research with interferons was reviewed during a special symposium held at the 64th annual meeting of the American Society for Microbiology, Washington, D.C., 4 May 1964.

Last year the program committee of the society decided to test a new kind of scientific session. It proposed to hold one or more "sessions in depth" covering one major topic and consisting of both invited and "offered" papers as an effort toward combining the more desirable features of the traditional symposium and regular scientific session. From the former, the "session in depth" would borrow the element of concentration in depth, with more time allotted to each paper. From the latter, it would take the aura of freshness and novelty of current work and the opportunity for free discussions from the floor.

In discussions of the chemical and physical nature of interferon, T. C. Merigan (Stanford Medical Center) reported that interferons produced in chick, mouse, and human fibroblasts were similar in their molecular weight (about 25 to 35,000); they were, however, distinguishable in their behavior on column chromatography. L. E. Kreuz and A. H. Levy (Johns Hopkins University) obtained similar molecular weights for interferon and determined that the sedimentation constant of this substance was 2.2 to 2.3*S* and the diffusion coefficient, based on chromatography on a Sephadex G-100 column, was 9.5×10^{-7}.

According to Monto Ho (University of Pittsburgh), interferon, unlike some

RNA viruses, is inhibited by actinomycin D. This inhibition is operative only within 1 to 2 hours after adsorption of the interferon inducer. This presumably represents the period during which RNA messengers are formed. The inhibitory effect of actinomycin D on interferon-mediated protection was also noted by S. E. Grossberg. Because interferon formation is also inhibited by puromycin, protein neosynthesis is involved. This suggests that such formation is caused by the release of preformed material. While small doses of mitomycin C do not inhibit interferon formation, large doses do, but, interestingly enough, cause only slight inhibition of virus replication.

In most previous experiments interferon had been produced in vitro. Clearcut evidence that interferon can be formed in vivo, and at a rather rapid rate and in high concentration, has been provided by Samuel Baron and his associates (National Institutes of Health). When a variety of viruses was intravenously inoculated into mice, interferon was found in their serum. Circulating interferon appeared at the onset of viremia, and maximal titers varied from 30 to 400 units/ml. Interferon gave the animals significant protection against subsequent challenge with virus. Similarly, Ho attained high titers of interferon in the serum of rabbits after IV inoculation with Sindbis virus. Activity was noted as early as 1 to 7 hours after inoculation. Preliminary tests showed that blockage of the reticuloendothelial system decreased interferon formation. The presence of interferon in the blood raises the question of where the interferon action occurs. Some contentions are that interferon plays a role in controlling the infectious process at sites distant from the place of interferon production. This is contrary to previously held views that interferon would be expected to act only in the region of its production. In this connection, S. E. Grossberg (Cornell University Medical College) added further evidence in favor of the newer concept. He extended his previous observations on the protection by interferon at a distant organ site in chick embryos. Nonlethal allantoic infection with Japanese encephalitis virus induced the greatest protection against subsequent infection with the neurotropic NWS influenza virus. The protective effect was demonstrable in the brain, suggesting that interferon produced in the allantoic cavity gains access to embryonic blood and organs, including the brain. The latter is thereby protected against subsequent infection. The observations that interferon produced under experimental conditions can find its way into the circulation of the host was complemented by the clinical study of I. Gresser and K. Naficy (Children's Cancer Research Foundation, Boston, Massachusetts). They found that the cerebrospinal fluid from 28 patients in a group of 152 suffering from disease of the central nervous system contained a factor similar to interferon. The highest frequency of positive fluids, 23 out of 58, was among patients with aseptic meningitis (most likely viral). In contrast, only two positive fluids were found among 69 patients with noninfectious diseases of the nervous system; 3 of 25 patients with bacterial meningitis were positive. There was a correlation between the number of leukocytes in the cerebrospinal fluid in patients with aseptic meningitis and the presence of interferon-like substances.

An interesting concept on the mode of action of interferon was presented by R. Z. Lockart, Jr. (University of Texas). His data suggest that interferon acts as an inducer and causes sensitive cells to produce a new protein(s) which, in some yet unexplained manner, is necessary for the inhibition of virus reproduction. The production of the new protein must be of cellular origin and mediated through a DNA-dependent RNA.

The new facts and concepts discussed during the meeting make it obvious that our understanding of the mechanism of production and mode of action of interferon is far from adequate. This in itself is not too disturbing because we have always had at least one comforting feeling —we knew that interferon was made in response to virus infection. But even this bit of equanimity was shattered as the meeting progressed. Judging from the results presented by H. E. Hopps and associates (National Institutes of Health), at least one strain of rickettsiae, *Rickettsia tsutsugamushi*, caused the production of interferon in the tissue culture of chick embryo. Extending this further, J. S. Youngner, in discussing this paper, stated that he and W. R. Stinebring succeeded in producing interferon in chickens by intravenous injection of large numbers of *Brucella*. G. E. Gifford (University of Florida) presented evidence that RNA could stimulate interferon production, and, in fact, products of RNA hydrolysis were even more stimulatory. One of the most potent stimulators was adenosinemonophosphate. Gifford confirmed and extended findings of Rotem and Isaacs and of Jensen. Since many substances other than viruses seem to provoke the production of interferon, the chairman of the session asked whether anyone knew of anything that did not stimulate production of interferon-like inhibitors.

Gifford reported that he could demonstrate an interferon-like substance in noninfected chick embryos. This activity increased with the age of the embryo and seemed to develop in the absence of an obvious stimulus. This raises the question of whether interferon can be produced spontaneously and reemphasizes the uneasy thought that much of what is referred to as interferon (because it has many properties of Isaacs's and Lindenmann's original interferon) may represent different types of inhibitors.

In order to look more closely at these questions and to discuss the nature of interferon and methods of interferon assay, the speakers and several of their guests met informally. As a result an *ad hoc* group (Interferon Reference Club) was formed to serve as a clearing house for ideas and products.

This meeting was sponsored by the Division of Virology of the American Society for Microbiology.

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Mitochondrial Structure and Function—A "Compostium"

On 1 and 2 August, immediately following the Sixth International Congress of Biochemistry, a group of approximately 150 scientists interested in mitochondrial structure and function gathered informally for a discussion meeting at Troutbeck Farm, Malvern, Pennsylvania. The purpose of the weekend was to provide an opportunity for discussion in greater depth and detail of various topics presented at the congress.

A session on the origin of mitochondrial membranes, chaired by A.