Book Reviews

A Field of Virology

The Arthropod-Borne Viruses of Vertebrates. An Account of the Rockefeller Foundation Virus Program, 1951–1970. MAX THEILER and W. G. DOWNS. Yale University Press, New Haven, Conn., 1973. xviii, 578 pp., illus. $25.

This large volume is subtitled "An Account of the Rockefeller Foundation Virus Program, 1951–1970." As is acknowledged in the preface, it is certainly not *the* account, which "would run to many volumes." The book is uneven and at times almost prejudicial with respect to recognition of key contributors and laboratories within and outside the Rockefeller group. However, scrutiny of one or another page in the preface and the geographical and institutional index will give an impression, at least by country, of the threads that have been woven into the tapestry of arbovirology. This term refers to an area of advance in basic virology, medical science, and tropical medicine without parallel in global accomplishment in science since World War II.

The preface recounts in some detail certain aspects of the evolution of the arbovirus program, including a résumé of how 35 years of yellow fever research prepared the way. However, all that is said with respect to the inauguration of the program is that in 1950 "the Rockefeller Foundation decided to mount a major program aimed at increasing the store of knowledge about arthropod-borne viruses and the involvement of these agents with human disease." In fairness to those responsible for the idea and to those in the Rockefeller Foundation who made the decision, and in the interest of accuracy, to show that such grand ideas don't happen overnight, there should have been a paragraph recording that from 1948 R. M. Taylor, then director of the Rockefeller Foundation Laboratories in New York, consulted and worked with such creative thinkers as Joseph Smadel, then chief of Walter Reed Army Institute for Research, and yellow fever colleagues Bugher, Johnson, Kerr, and Smithburn to hatch the grand proposal that was accepted by the Board of Trustees late in 1950. In fact, the work of some of these investigators, published in the *Journal of Immunology* in 1952, provided the scientific rationale for the proliferating field activities of that decade through which the Rockefeller laboratories were supplied with the strains and specimens on which the work summarized here was based.

This book is probably the most comprehensive presentation on arboviruses that will appear in the present biomedical era. Nowhere else can such an amassment of data and bibliography be found in one place. Thus it is uniquely valuable even though it will in one way or another disappoint each of those who have devoted their careers to the study of one or more of the some 300 arboviruses now recognized.

With some specifically defined exceptions, the coverage of the book is limited to those agents presumed to be *ar*thropod-*bo*rne *viruses*. The generally accepted criterion for arboviruses is biological; arboviruses are defined as those viruses ingested from circulating blood of an animal host by a hemophagous arthropod in which multiplication ensues and through the mouthparts of which a subsequent animal host becomes infected. Although viral taxonomists initially wished to confine the term arbovirus to those that were physicochemically characterized as cuboid, RNA, lipid-enveloped viruses, thus including some, such as rubella, known not to be arthropod-transmitted and excluding others, such as vesicular stomatitis, that are, agreement has been reached that many so characterized will be classified as togaviruses, leaving arboviruses to a biological definition.

Among the outstanding exceptions are the group B viruses (chapter 7) which have no demonstrable arthropod vector. Especially important are the arenaviruses associated with hemorrhagic fevers. Antigenically related is the Tacaribe group (chapter 11), most of which involve rodents or bats as primary vectors.

For those workers concerned with neutralization, complement-fixation, and hemagglutination-inhibition test results in research or diagnosis, the first four chapters, occupying 91 pages, are essential reading. The essence of the information is why a titer is not a simple measurement and why knowledge of the antigenic nature of the virus and the immunological nature of the antibody vehicle is so important to interpretation of the results. An understanding of this is essential for comprehending the foundations of arbovirology, whether the matter of interest be taxonomic characterization or fundamental epidemiology. These principles are equally applicable to other fields of virology. The discussion of them given here—no matter how laced with seemingly unnecessary and tedious detail—reveals why a well-trained arbovirologist can work effectively in any other field of applied virology.

The second part of the book, the largest portion, is devoted to classification of all the arboviruses that have been examined in the Rockefeller laboratories or those for which there is an adequately characterized immunological relationship derived from other information. The format is a familiar one, following that evolved in the annual reports from which this section of the book is obviously derived. There are three advantages of this over the American Committee on Arthropod-Borne Viruses *Catalogue of Arthropod-Borne Viruses of the World*, edited by R. M. Taylor and kept current by annual addenda published in the *American Journal of Tropical Medicine and Hygiene*.

First, the viruses are characterized and listed according to Casals's concept of antigenic group, the derivation of which is detailed in the introductory chapter of this section. Thus, the reader begins with groups A and B. Along with group C, these are the only ones designated alphabetically. Because of initial confusion with influenza and Coxsackie types the original nomenclature system was changed to focus on geographical names—usually obscure. The name of the first characterized virus in a newly established antigenic group usually became the name of the group. The text moves through the Bunyamwera supergroup to consideration of the so-called minor groups, which, in addition to their established antigenic relationships, exhibit unique features of biological and medical significance.

The second advantage of this format is the annotation of each prototype strain, and characterized group, by a

succinct encapsulation of its geographical origin, host or vector sources or both, and clues to basic epidemiological and disease potential. For example, the chapters on *Phlebotomus*-transmitted viruses and the Tacaribe group viruses synthesize a diversity of virological and epidemiological facts to give the reader a grasp of the importance of these divergent arbovirus diseases in public health.

The third advantage is the tabulation of antigenically related arboviruses, providing a concise display of relevant features that are the basis for concepts of epidemiological importance. Numerous tables identify type of vector, vertebrate host, evidence of pathogenicity for man, and, in some cases, zoogeographical range. With the fairly detailed indices at the end of the book this makes possible quick location of facts known about a particular arbovirus or group as of 1970, a pursuit which would otherwise require a major bibliographic search.

Because this presentation is not a complete distillation of published literature on arboviruses it does not supplant either the *Catalogue of Arthropod-Borne Viruses* or the thousands of references to be found in other bibliographic resources.

The third major segment of the book deals with what the authors term Certain Specific Problems. This is further subdivided into a treatment of biological problems such as distribution, vectors, vertebrate hosts, and human hosts and then a discussion of particular experiences and interests of the authors in yellow fever and dengue in the Caribbean. The last might have better been presented elsewhere because the material is not particularly relevant to the main focus of the book.

Another evidence that this is a virological treatise rather than one for the clinician is the brevity of the discussion of clinical manifestations in man. The pages devoted to this subject are moreover the most confusing in the book and can only frustrate the clinician who seeks helpful information on a suspected arbovirus etiology of illness in a patient. There is an inconsistent mixture of such unfamiliar abbreviations as OHF and AHF with terms such as dengue, yellow fever, encephalitis, and saddle back fever. What relevance epidemics of Rift Valley fever in sheep causing high mortality in lambs and abortion in pregnant ewes have to clinical disease in man is difficult to infer. Perhaps the most useful statement is that "quite similar disease pictures can be caused by completely unrelated viruses . . . two completely different disease pictures can be caused by strains of virus which are immunologically identical." In short, this volume will not be of much ready use in clinical medicine.

In its intention to deal with "the epidemiology of the more important arboviruses" the book fails most seriously, not because what are presented as the important features in the view of its two authors are not significant, but because it fails to highlight the major issues for scientific contemplation and work by the next generation of investigators and researchers, who must gain some inspiration and guidance from what has already been accomplished by the many workers who are not even mentioned here.

On p. 304 begins chapter 13, "Grouped tick-borne viruses not in group B." This succinctly summarizes Casals's years of work characterizing viruses isolated from ticks, showing antigenic relationships of intriguing geographical associations. Since many of these isolates are from ticks associated with migrating birds and far-moving animals, they provide substantive data for new concepts of mechanisms for arbovirus movement and distribution. When integrated with findings concerning bird-tick-associated group B arboviruses (Tuleniy) isolated by Lvov off Sakhalin Island and by Clifford and Yunker off the Oregon Coast, hypotheses begin to emerge that relate not only to the global distribution of disease-related arbovirus complexes but to the evolution of genetically different group stem viruses.

Rather than abruptly ending with yellow fever and dengue in the Caribbean it would have been useful to include an outline and interpretation of the medical and public health importance of arboviruses and a discussion of the major unsolved problems for future research. Among the problems that might have been mentioned are: the implications of antigenic cross-reactivity to immunizing agents, oncolytic activity of arboviruses, questions of overwintering of temperate zone arbovirus pathogens, latent infections of vertebrate hosts, the role of migratory birds and other animals in the dispersal and reintroduction of arboviruses, antigenic modification and mutation, evolution of antigenic types, and multiple vector types.

Recalling that the National Foundation for Infantile Paralysis subsidized publication of the first two editions of Rivers's *Viral and Rickettsial Infections of Man*, which stimulated the interest of, educated, or at least had a significant influence on today's mature working virologists, one regrets that the Rockefeller Foundation, which already has invested $30 million in this arbovirus research program, did not add a bit more to bring this book within easier financial reach of another generation of students and scientists. Being the classic in its field, it should be owned and used by a much larger number of persons and institutions all over the world than its price will allow.

TELFORD H. WORK
Center for the Health Sciences, University of California, Los Angeles

Embryonic Cells

The Cell Cycle in Development and Differentiation. Proceedings of a symposium, Bristol, England, July 1972. M. BALLS and F. S. BILLETT, Eds. Cambridge University Press, New York, 1973. xii, 484 pp., illus. $32.50. British Society for Developmental Biology Symposium.

The task undertaken by this book of trying to relate events at the level of the cell cycle to processes of differentiation and development is a very difficult one. The difficulty lies in our complete lack of understanding of how the cell cycle itself is regulated, let alone of how it may participate in the complex processes of development. In the opening chapter, Mitchison briefly surveys some of the known events and characteristics of the cell cycle and describes two current theories that have been proposed to explain the periodicities associated with the cell cycle. His comments are both provocative and stimulating, but reinforce our awareness of how little we know regarding mechanisms which regulate the cell cycle. Compounding the usual problems that accompany too little understanding are the numerous hazards encountered when one measures the cell cycle and its component parts (G_1, S, G_2, and mitosis). These hazards are enumerated and discussed by Steel in the succeeding chapter, which is particularly valuable for workers measuring cell cycle parameters in cell populations in vivo.

As one might expect from 26 separate contributions, the papers that follow vary greatly in perception and