Mosquito-Borne Arboviruses

Robert H. Kokernot and Botha de Meillon

Texas Tech. University, School of Medicine, Department of Preventive Medicine and Community Health, Lubbock 79409; and Smithsonian Institution, U.S. National Museum, Washington, D.C. 20560.

Today, in order to accomplish goals in education, we hear a great deal about the core program, the symposium, the seminar, elective study, individual study, and special study. The student is said to be increasingly self-motivated by this approach. With this thought in mind, I was motivated to look up Webster's definition of symposium. I wanted to be reassured that the parameters for my presentation would permit more than a scholarly review of factual matter. Apparently the word has two connotations. In one case, the term is applied to "a drinking party, especially following a banquet or a social gathering, at which there is a free interchange of ideas". In this context, the word was indeed reassuring because I was humbled by the invitation to address a meeting sponsored jointly by committees on Epidemiology and Meterology and on Virology of The American Phytopathological Society. Furthermore, I was overwhelmed by our moderator's (Dr. M. R. Nelson) charge to participants in this symposium that you desired a review "of the latest information on measuring, analyzing, storing, and interpreting data on vector population dynamics in relation to disease increase".

If in the minute taken for these few words our rapport had been expedited in a manner expressed by this definition of symposium, I would state that with but few exceptions the art of predicting outbreaks due to mosquito-borne arboviruses has not progressed much further than being able to say; if you have **Many** *Aedes circumuluteolus* in Zululand in southern Africa you can expect Wesselsborn virus; if you have **Many** *Culex tritaeniorhynchus* in Japan, you can expect cases of Japanese B encephalitis; if you are in the central valley of California or the panhandle of Texas, and have **Many** *Culex tarsalis*, you can expect western encephalitis; finally, if you are in McLeansboro, Illinois, or St. Louis, Missouri, and have **Many** *Culex quinquefasciatus* you can anticipate the emergence of St. Louis encephalitis virus. In very short order this strikes at the heart of the matter, which simply stated is that we have a real problem in sampling vector populations in order to determine the status of pathogen transmission. With this unqualified remark, I should have the second cognac and then listen to a "free interchange of ideas".

Perhaps, more appropriate to this occasion is Webster's second implication for the word "symposium"; "a meeting at which several speakers deliver short addresses on a topic or on related topics" or "a collection of opinions on a subject". In keeping with this rather formalized concept, and if our sampling techniques gave accurate and absolute numbers for the population of these primary mosquito vectors, we would be omitting from consideration other important factors that influence the probability of epidemics.

These factors and their complicated relationships in the epidemiology of mosquito-borne arboviruses might be introduced by a brief historical account. This involves classic studies on yellow fever virus. For several hundred years devastating outbreaks due to that virus had taken a heavy toll of human life in North and South America. In temperate climates, these outbreaks were restricted to the warm summer months. Even in the tropics there was a seasonal distribution of cases often related to rainfall and an abundant mosquito population. Occurrence of yellow fever at a time of dense mosquito population was an association noted by several observers. However, to Dr. Carlos J. Finlay of Havana, must be given credit for the theory of the propagation of yellow fever virus by means of the mosquito, which he proposed in a paper read before the Royal Academy in Havana at its session on the 14th day of August 1881.

The question of the causative agent of yellow fever was another matter. The possibility that it might be a virus was suggested by the work of Loeffler and Frosch on foot and mouth disease in cattle. During their investigations they demonstrated that a transmissible agent capable of being passed through a porcelain filter was present in the blebs in the mouth and on the feet of cattle sick with foot-and-mouth disease. This information concerning etiology, and Carlos Finlay's incrimination of mosquitoes was known to members of the special United States Army Yellow Fever Commission that started working in Havana in 1900. Within less than 6 mo they confirmed that yellow fever was in fact caused by a filterable agent which was transmitted to man by the bite of an infected mosquito. Concurrently, the vector was identified and control measures instituted. Within 15 mo from the date the commission arrived in Cuba, the disease was eradicated from Havana. These were dramatic results, because within the proceeding one-hundred and fifty years the annual yellow fever death toll was in excess of 100. Application of similar mosquito control measures was in large part responsible for the successful completion of the Panama Canal Project. The yellow fever infection chain just cited involves man, the vertebrate host, and *Aedes aegypti* mosquitoes, the vector. Transmission occurs in this simple model of urban yellow fever if the virus is present, if there is a susceptible vertebrate population, if a large vector population is present to link the infective and susceptible host population, and if favorable climatic factors are present.

A third factor in this infection chain involving man-mosquito-man was suggested by the occurrence of disease in sparsely populated forested areas in the absence of *Aedes aegypti*. Roberto Franco, a Colombian physician, noted this in 1907. Subsequently it was shown that certain species of monkeys were susceptible to yellow fever virus. This vertebrate represents a type of reservoir host for the virus. That is, yellow fever virus may multiply and depend for its survival on the monkey and under natural conditions it is transmitted to other monkeys by species of mosquitoes other than *Aedes aegypti* which is seldom found far from man's habitation.

This brief account of early work on yellow fever virus has introduced three factors which are basic in the epidemiology of mosquito-borne arboviruses. If we were to imagine this as a type of dramatic theatrical performance, the leading actor would be the virus and the supporting cast would include man the host, monkey the reservoir, and mosquito the vector. The stage itself with curtains and background scenery together with the lighting and sound effects would represent all of the environmental influences. With this analogy in mind, we might list characteristics of each of these components that may be considered in the epidemiology of arthropod-borne virus diseases.

The virus.—At the present time over 250 animal viruses have been reported and shown to be associated with blood-sucking arthropods. Their distribution is worldwide. The majority, however, have not been incriminated in human or animal health. Others, as you know, such as Venezuelan Equine Encephalomyelitis (VEE) virus have been responsible for epidemics involving man and large numbers of equines. Similar involvement has been due to two other viruses referred to as Western Equine Encephalitis (WEE) and Eastern Equine Encephalitis (EEE) viruses. In epidemiologic studies the virus types must be identified through immunologic test. Properties of the virus important in understanding the natural history include animal susceptibility, pathogenicity, virulence, infectiousness, and organ tropism.

The vertebrate host.—The composition of the vertebrate host population may be similarly characterized by counts including age, sex, location, and length of residence as well as immune status resulting from naturally acquired infection, or as a result of inoculations in immunization procedures. Information may be gained regarding potential exposure to vectors by consideration of occupational pursuits, recreational habits, type housing, encroachment on natural foci of infection, and relative attractiveness to vectors.

The reservoir.—It is important to know the relative susceptibility and abundance of the reservoir hosts that serve as sources of vector infections. Species within the population may be characterized by age, immunity status, reproductive rate, attractiveness to vectors, and by the type and location of habitats utilized, especially with respect to proximity to populations of human beings or domestic animals.

The environment.—Important environmental influences in the epidemiology of arboviruses include temperature, rainfall, and humidity, surface water, wind, topography, vegetation, harborage and food supply. The virus, the vertebrate host, the reservoir host and the environment are major components in arbovirus infection chains. The vector is a fifth component which, taken together with the others, results in a complicated natural history. In fact, arthropod-borne virus diseases are the least understood among the entire spectrum of infectious diseases involving man and his domestic animals.

Let us direct our attention to the matter of vector populations in relation to the transmission of pathogens to vertebrates. This is a vast subject, but the problems which face the medical entomologist in his attempts to assess vector populations are by and large similar to those facing the agricultural entomologist. They are basically ones of sampling and even though the techniques may vary considerably the objectives in the main are the same, namely, to aid in the determination, at any stage, of the amount pathogen transmission. If this can be accurately determined, then one can begin to think of measuring the trends of disease incidence, rise and fall of epidemics, the efficacy or otherwise of control measures, and so on. This aspect has been most thoroughly explored in malaria and MacDonald's book Epidemiology of Malaria 1957 (5) is a landmark in this direction.

In any attempt to determine the status of transmission of human and animal pathogens the vector population (among other things) has to be assessed both quantitatively and qualitatively because of the relative unimportance of mechanical transmission. In the classification devised by Kennedy (3) transmission of plant viruses are mostly "stylet-borne", "circulative", and rarely "propagative", whereas, in animal and human infections they are mostly the latter or what we call "biological". This is probably the principal difference between the transmission of plant and animal viruses. Apparently it was as late as 1926 before "propagative" (biological) transmission was demonstrated for plant viruses (9). The extrinsic incubation period of the pathogen in the vector during which there is either plain multiplication, as in the viruses; growth and development, as in the filarial parasites, or growth development and multiplication, as in the malaria parasites, is of basic importance because it means that the life expectancy of the vector is a vital factor in the assessment of its efficiency. If the arthropod does not live longer than the extrinsic incubation period of the pathogen, then no transmission can take place. The mere fact that a pathogen will multiply in an arthropod does not necessarily mean that it will be able to transmit it (6). The known multiplication of virus in a grasshopper, for example, is interesting but it is of no significance as far as human or animal disease is concerned, though it might be important in plant pathology (4, 9).

Before we can speak about vector populations and human or animal disease either epidemic or epizootic it is necessary to point out that vectors do not transmit diseases, but potential pathogens. Whether disease develops, as a result of transmission is entirely a matter of interaction between the transmitted potential pathogen and the human or animal host. Furthermore, a few definitions become necessary to dispel the idea that a vector is simply a loaded syringe with wings. The finding of a known pathogen in an arthropod does not mean *ipso facto* that it is a vector. This is a rather important point the neglect of which has served to confuse epidemiological situations. For the same reason laboratory experiments unless carried further merely show whether the species is receptive to the pathogen or not and even if receptive one still has a long way to go to prove that it is a vector and to demonstrate its efficiency.

It is convenient to segregate vectors into three categories (10):

(i) "Suspected" = free-living arthropods from which a known pathogen has been isolated.

(ii) "Potential" = suspected vectors which can transmit a pathogen experimentally.

(iii) "Confirmed" = suspected vectors which satisfy a further series of requirements.

The main parameters which identify a "confirmed vector" and which also evaluate its "efficiency" (the term "vector capacity" has a special meaning in malariology and is not synonymous with "vector efficiency") are briefly as follows:

1. *Receptivity to the pathogen*. This can be determined in the laboratory without any difficulty by simply feeding clean arthropods on infective hosts and determining if the requisite cycle is completed or the required degree of multiplication is attained.

2. *Transmitting ability*. This again can often be determined in the laboratory by feeding the "primed" arthropod on a susceptible host. "A primed arthropod" is one which has allowed the pathogen (with which it was originally infected) to complete its life cycle to the infective form, or which has allowed the pathogen to multiply to a degree known to be required for successful transmission to the host.

3. *Infection rate in nature*. The rate of infection with a pathogen in the infective stage among wild caught specimens.

4. *Longevity and expectancy of infective life*. These parameters can be determined from the parous rate, the length of the gonotrophic cycle, and by mark-release-recapture techniques.

5. *Blood feeding preferences*. If the pathogen is confined to human beings, as in urban yellow fever for example, then a preference for human blood is important. Any indiscriminate feeding on nonhosts minimizes the efficiency or capacity of the vector. Many human viruses also have a zoonotic cycle which may be maintained by a vector which has little or no contact with man.

6. *Man or animal biting rate*. The frequency with which the arthropod bites is important in determining its efficiency as a transmitter. This is usually determined from the gonotrophic cycle where the arthropod feeds again immediately after ovipositing. Cases where the gravid female (e.g., *Aedes aegypti*) are known to feed again before oviposition truly enchance the importance of the vector but they are probably not frequent.

7. *Density*. Two aspects require consideration (a) the relative density relative to the host and (b) the absolute density. The importance of density is very much influenced by the other parameters mentioned above. It is not so much the absolute density as the density relative to the host, be it man or beast, which makes for efficiency in a vector.

In spite of the fine analysis of the situation and the pinpointing of the parameters by MacDonald (5) and Garrett-Jones and Grab (1), the plain fact remains, that so far, it has not been possible to devise techniques for gathering indisputable data on all counts even in malaria which is one of the best-studied parasitic disease of man (2).

If we turn to the viruses which affect man and animals, the situation is not much better. After many years of thorough and competent research by Reeves (7) and his colleagues on the factors that influence the rise of virus epidemics in California, they failed to forecast the abortion of a threatened WEE Encephalitis Epidemic in 1958 (8). In their own words, "this study fully substantiates that a large mosquito vector population is related to increased virus activity. However, the development of large vector populations and high vector infection rates are not necessarily followed by high transmission rates" (8). In less able and discriminating hands the failure of the epidemic to materialize would have been ascribed to control measures of some sort. This is a most significant document and points to the fact previously mentioned, that crude quantitative vector population estimates, and naturally occurring infection rates in them are not necessarily correlated with successful transmission resulting in disease. Once again, we say that the quantification of transmission is our real goal and sampling our real problem.

SUMMARY.—

1. The problem of assessment of vector populations in plant, animal and human virology is basically one of sampling in order to determine the status of transmission at any given time.

2. In animal and human virology biological transmission is of the greatest importance and this calls for both quantitative and qualitative assessment of the vector population. In plant virology the most important transmission is by contamination, hence quantitative assessment is paramount and here the two disciplines part company.

3. In both disciplines, vectors do not transmit diseases but potential pathogens. Disease is a matter of reaction between potential pathogen and host.

4. In order to clear up some misunderstandings, vectors are classified into "suspected", "potential" and "confirmed". The principal parameters are given which define "confirmed vectors"; they will also serve to determine "vectorial efficiency". "Vectorial capacity" which involves the production of disease is defined.

5. The difficulties involved in gathering the data for quantifying the status of transmission of animal and human viruses at any time is stressed.

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