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Keynote Address:

The Ecological Approach to the Study of Zoonotic Diseases

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“When we survey the history of thought, and likewise the history of practice, we find that one idea after another is tried out, its limitations defined, and its core of truth elicited The proper test is not that of finality but of progress.”

A. N. Whitehead, 1929, *Process and Reality*, p. 19. Cambridge University Press.

The ecological approach to the study of zoonotic diseases is to study the natural parasitic infections of wildlife in relation to those found in man and domestic animals. In searching for natural foci of disease agents in wildlife, it is logical to study habitat types which have a large and relatively stable wildlife population. In this type of biome one does not expect to observe disease in the animal population, but if viruses, rickettsia, bacteria, fungi, protozoa or helminths set up chains of infection in aberrant hosts, this may result in epidemics of disease, sometimes associated with a high mortality. We should always be alert to the occurrence of disease in wildlife because this is the best source of specimens for study. A single sick bird, bat, mouse, rat, squirrel, rabbit, skunk, fox, etc., is a valuable specimen for study. Likewise, sporadic cases of disease in man and domestic animals gives us an indication of where to look for a disease agent in wildlife. We can then do a population study of the wildlife in the immediate area and try to determine which animal was the source of the infection. It is also important to study the site where an epidemic began. This may indicate the geographic source of the disease. In order to determine whether a given domestic species is the natural host of a parasite, we should study the same species as it occurs in the wild, i.e., wild cattle, pigs, goats, sheep and fowl. In regard to the common human parasites, we can compare the incidence of infection in urban populations and aboriginal tribes which live a nomadic and isolated existence. I will come back to this subject in discussing specific infections.

The literature contains an enormous amount of information about parasites found in animals. There are two common methods of investigation of parasitic infections, one the examination of the sick or dead animal to see what caused the disease, the other, a survey of an animal population looking for a specific parasite. We know a great deal about helminthology because the parasite can be seen without

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magnification. When we deal with micro-organisms we need special media or living host systems in order to isolate the parasite. The use of the infant mouse as an experimental animal resulted in the isolation of a great number of previously unknown viruses and much information was obtained about the epidemiology of some of the well known viruses. The development of cell culture test systems for isolation and identification of viruses resulted in the isolation of a Pandora's box of pathogens from specimens taken from the respiratory tract and the gastrointestinal excretions of man and domestic animals. The study of virus infections in the urinary tract is just beginning but it is already evident that many different viruses can be found in the urine of man and animals. As we look at this miasma of parasitic agents we wonder where they all came from. It seems impossible that they could have been maintained by man before he developed an urban civilization with frequent contact between individuals and an ample supply of susceptible hosts.

The scientific approach to a problem is to ask questions such as why, what, where and how. Why do we have epidemics of disease? What is the nature of the parasite that makes us sick? Where does the parasite come from? How is it transmitted from one individual to another? What diseases are the result of man's culture? Let us begin with man's place in nature. Our cultural history goes back about 10,000 years. We have had written information for about 5,000 years but there is little written information from the period prior to the 15th century. How was man living 10,000 years ago? What was the total population, several hundred thousand or several million? I would choose the former figure. On the basis of what we know of the early culture of man and from the study of the food gathering and hunting families now living, it seems that prior to the domestication of plants and animals, man must have lived in small family units of less than 50 individuals, with little contact between these small population groups. It is unlikely that man caused much disturbance in the natural vegetation and animal populations during this period of history. Much has been written about man the hunter. The common assumption is that large game such as deer, goats, antelope, bison, etc., were the main source of food. The books are full of paintings of the cave man gnawing on large bones. Having observed the collection of animals by aboriginal tribes and nomadic hunters, I believe that the best source of game was small mammals and birds. Only after the development of powerful weapons, for example, the bow and arrow and spear, did man begin to take large game animals for food. Since the development of firearms the destruction of large game has been rapid.

What is the situation today? There is little arable land which does not show the effect of agriculture. The great deciduous forests of the riverine plain of Asia Minor, Asia, Europe, and North America have been cut and the land plowed and seeded with domesticated varieties of plants and trees. The cutting of the tropical evergreen forest is more recent, yet increasing steadily. The northern coniferous forest has been exploited both in Europe and North America, partly for agriculture and partly for pulp wood and timber. Man has increased from a relatively rare species to the most abundant species of large mammal on earth. Likewise, the domesticated animals have almost completely replaced their wild ancestors; large herbivorous animals other than domesticated ones seem to be on the way to extermination. The American bison, which less than 200 years ago numbered in the millions, is now extinct except in National Parks. If you want to study the viral population of bison, you at least know where to set up your field laboratory. The deer and antelope would have been exterminated by this time if they had not been protected by sanctuaries and hunting regulations. In view of the current war in Cambodia I am fearful that the last of the wild cattle which are found there will be killed and eaten before they have been studied in their natural environment.

It is estimated that there are about 3 billion people now living. There are about an equal number of domesticated animals. The annual turnover of domesticated species such as cattle, pigs, goats, sheep and chickens is high, thus insuring a constant

supply of susceptible hosts for the parasitic infections which are maintained in them. The same is true for pet animals such as dogs, cats and birds. When we consider diseases involving bird hosts, we think of chickens. It is difficult to obtain information about the total population of chickens in the world, but an idea can be obtained when we look at the production of chickens in the State of Georgia which alone produces over a million a month.

The present human population and the frequent contact of individuals and rapid transportation makes it certain that man will sooner or later become infected with every parasite in nature to which he is susceptible. Man's curiosity takes him into caves, jungles, deserts, forests and every nook and cranny of nature, often sleeping in close contact with wildlife and drinking surface water. He also likes to make pets of exotic forms of wildlife and this predisposes to infection with parasites with which he would never be exposed in his usual habitation.

As man developed an urban civilization he became associated with para-domestic wildlife such as house mice, rats, sparrows, pigeons and a great variety of birds, rodents, squirrels and bats which find man-made structures suitable for occupancy during part or all of the year. The storage of water in clay jars resulted in the domestication of certain species of mosquitoes. Certain flies adapted to the piles of garbage and dung heaps associated with village life. Cockroaches, bed bugs, reduvid bugs, fleas, ticks, lice and mites became associated with man. Each brought the capability of transmitting certain diseases to man from wildlife. Whereas once the water supply was from springs and wells, it became necessary to impound water from streams and rivers to supply cities. In many villages and cities of Asia surface water is drunk without any treatment other than allowing it to settle in clay jars. In the United States the water is purified to some extent but we know that the coliform counts are often high and we do not test the water for pathogenic viruses. One can expect that bacteria and viruses infecting the intestinal tract of wild animals and birds will sooner or later reach man via contaminated water or food and infect him if he is susceptible. This is perhaps the best reason for trying to isolate all the micro-organisms which parasitize wildlife. Having the organism we can do serological tests to determine whether man has been infected with them.

Where do we find the vegetation types which favor a large and relatively stable population of plants and animals. The semiarid plateaus and the mountain valleys of the Temperate Zone with forest, park woodland, grassland and desert brushland have a large population of both small and large animals. When man lived as a food gatherer and hunter he evidently liked this environment because of the abundance of animal life and the great variety of plant food. In dense deciduous or evergreen forest, there is little ground vegetation and there are no cereal grasses or other plant foods which attract herbivorous animals. The wildlife that exists in dense forest is most abundant in the canopy where there are nuts, fruits and insects. The moist dark floor of the tropical evergreen forest is very quiet and it is difficult to find any animal life. It is on the edges of such forests, along water courses and in clearings, that we find high populations of small mammals.

There are certain species which live their whole life in a limited area of a few hundred square feet, others move about over a few miles and some migrate hundreds or thousands of miles from south to north and back again each year. Some move in great arcs along the shores of the land masses, others cross great oceans. In the Far North, migratory birds and bats find solar radiation continuing nearly 24 hours a day during the summer and enormous numbers of these animals go there during the breeding season because of the abundance of insect life which they can use to feed their young. The migration of birds and bats is not as obvious as one might expect. The migration continues for about three months, both spring and fall. Some species migrate by day, others by night. Some aggregate in large numbers, others move in small groups of individuals. There are certain places where there is a concentration of migrant species where they roost, cross water barriers or where they move along

a mountain ridge. Colonial bats use caves as resting places during migration and some bat caves will harbor millions of bats at one time during the peak of migration. The rivers are like highways for certain of the migratory birds and bats. There is local migration related to fruiting of grasses and trees. As we study the various species of birds and bats we come to the question of total populations. One cannot get a satisfactory answer but it seems that 100 million is about the top figure for any of the common species. The information just reviewed makes one cognizant of the possible role of birds and bats in moving parasitic infections from one place to another and the sites of concentration of the population along routes of travel which predispose to infection of aberrant hosts along the way. This is especially important when we are studying the arthropod-borne diseases.

In looking for parasitic infections in wildlife which may infect man, we turn first to the mammals because we are mammals. Among small mammals, mice, rats and bats constitute the great majority of the wildlife population. There are also great populations of ground squirrels and gophers. In the Temperate Zone we think of the large populations of small mammals in the coniferous forest north of 50° latitude. This is the source of much of the fur bearing animals such as mink, ermine and fox. The lucrative trade in furs is related to the high population of small mammals in this region which serve as food for the carnivores. The small rodents remain through the winter but the bird and bat population fluctuates with the seasons. We must consider the potential role of bats and birds in bringing parasitic infections from the northern forest to the more temperate or tropical regions as they migrate south in the late summer or fall. The fact that mosquitoes can transmit certain arboviruses during the epidemic season does not negate the possibility that other arthropods such as simuliids and culicoides flies may be more important hosts in the transmission of the infection in the northern forest. In the tropical zone we have large populations of bats and rats. In regions with large tracts of tropical forest there may be more than 100 species of bats and some of these may have populations of many millions of animals. I believe that bats are the most numerous of the animals in the tropical forest, yet they have not received much attention as sources of parasitic infections until recently.

I now wish to discuss some specific disease problems of man. How much do we know about the parasites which are responsible for the major epidemic diseases of man such as bubonic plague, smallpox, cholera, typhus, malaria, yellow fever and influenza. What about the source of these parasitic infections in nature?

Plague

Bubonic plague has been called the great teacher because so much has been learned about the control of infectious diseases from the study of plague. There have been three great epidemics of plague in modern times: the Justinian Plague, the Black Death, and the widespread epidemic of the 19th century. The Justinian plague of the 6th century killed half or more of the inhabitants of the Empire. The second great epidemic, the Black Death, began in Asia during the first half of the 14th century. This was the most frightful epidemic of recorded history. From 50-75% of the population of Europe and Asia died during a period of three years. There have been many other local epidemics of plague such as the one in London during the 17th century and the one in Marseilles in 1720-21, the latter resulting in the death of 39,000 persons in a population of 90,000. During 1903-04, more than one million people died of plague in India.⁷ What do we know about plague today? Where does it come from? We know that there are foci of endemic plague in certain areas of the semiarid plateau regions of North and South America, U.S.S.R., Africa, and Asia. From time to time there are dieoffs of marmots, ground squirrels and other small mammals and at such times it is usually easy to isolate

the plague organism from fleas and from tissues of sick and dead animals. Between such outbreaks there is no sign of the disease, and we can only assume that some species of animal in these regions harbor the plague bacillus as an inapparent infection. Despite all the work that has been done on plague, we do not know the natural reservoir host. Outbreaks of plague in wildlife require the presence of large populations of susceptible rodents, and there seems to be a critical population number below which the disease cannot be maintained. Once introduced into villages and cities where there is a large population of rats, plague can be maintained as a migrating epidemic in rats for many years. The infected rats ordinarily die of the disease. The usual series of events in an outbreak of urban plague is first a rat-fall or dieoff of rats. Subsequently, the disease appears in man as a flea-borne or bubonic plague. There may be direct transmission from man to man. This is called pneumonic plague and this appears to have been the major cause of death during the great epidemics. When it was found that plague was spread by rats and rat fleas, sanitary measures of rat and flea control were adopted. The development of insecticides active against fleas has been a major factor in the control of plague. Now having several therapeutic agents effective against plague, we do not worry much about this disease. It is now clear that the rat is an aberrant host of plague and we do not know the natural host of the plague bacillus. Studies of an outbreak of plague which began in northwestern Iran in 1947 indicates that desert gerbils of the *Meriones* genus may be the natural hosts of the plague bacillus in that region.² I believe that the natural host of plague in the United States is some small mammal of the semiarid plateau and that the plague organism exists as a symbiont in the respiratory or intestinal tracts of the natural host. In searching for the plague bacillus in desert animals, I suggest testing nose and throat swabs and feces rather than blood specimens. The most probable means of setting up aberrant cycles of infection is when population numbers reach a level where there is fighting and cannibalism and the more susceptible hosts develop bacteremia, thus making possible transmission by fleas. The kangaroo rats do not seem to be affected in the dieoffs of plague and therefore they should be studied as possible reservoir hosts.

Smallpox

What about smallpox? This disease has been feared because of the high mortality and disfigurement of those who recover. The mortality in recent epidemics has been about 20% but it was probably higher during the 17th and 18th century epidemics. Smallpox cannot be maintained in man unless the infection can spread from person to person as a migrating endemic or epidemic infection. Therefore, it must have originated from a nonhuman source. It will be interesting to observe what happens after the vaccination program breaks the man to man cycle in India. We know that cowpox is a natural infection of cattle and this strain of the virus produces a mild form of the disease in man. This is the source of the smallpox vaccine virus. There is also a mild form of human smallpox called alastrim. There is a disease of house mice called ectromelia. This virus can be used to immunize man against smallpox. It is interesting to speculate as to whether the house mouse of Asia was the source of the smallpox virus which has caused such terrible epidemics in man in that country. One can hypothesize that the virus once introduced into the human population may have increased in pathogenicity. This seems to be a characteristic of many parasitic organisms when they are propagated in aberrant hosts, either naturally or artificially. There is good evidence that smallpox was not known in the New World prior to colonization by Europeans. The mortality from smallpox among American Indians showed that they had had no prior experience with this virus. From 1617-19 about 90% of the Indians living along the Massachusetts Coast died of smallpox.¹³ Smallpox epidemics later decimated the Indian population in Central and Western United States. Having this information I do not believe that we will find the natural host of this virus in North America.

Cholera

Cholera is another disease associated with large urban populations where cultural practice results in heavy fecal contamination of drinking water. The interepidemic host is unknown. There are vibriotic infections in domestic animals such as cattle and swine. There are vibrios in birds, fish, reptiles, amphibians and insects. Cholera is endemic in the delta of the Ganges in India and this would be a good place to look for the natural host of this organism. Knowing the water-borne character of the disease, one is inclined to think of a natural host that lives in the water but here again it may be some rodent that contaminates the water supply at its source.

Typhus

Typhus is one of the most complex of the zoonotic diseases. This disease has been associated with war, famine and migrations of people. This disease is caused by a rickettsial organism, and various host systems are known, for example, classical human louse-borne typhus, murine flea-borne typhus, mite-borne tsutsugamushi disease or scrub typhus and rickettsial pox, tick-borne spotted fever, and Q fever. In our studies of arboviruses in California and Oregon, we have encountered several strains of rickettsia in testing blood specimens of meadow mice, *Microtus montanus*. These strains are of low pathogenicity for infant mice but can be maintained by intracerebral passage in this host. We have not isolated this type of organism from other small mammals in the same area. The serum from mice infected with these rickettsia show some serological relationship to strains of Rocky Mountain spotted fever rickettsia. The *Microtus* mice studied were heavily parasitized by mites such as *Laelaps kochi*, *L. alaskensis*, *Haemolaelaps glasgowi* and *Hoplopleura acanthopus* lice. All of these arthropods have a worldwide distribution. Ticks were not found on the *Microtus* mice trapped in the meadow environment. Rocky Mountain spotted fever was known to occur in nearby forested areas. I was living in New York during the outbreak of rickettsial pox which occurred in 1946.⁸ Rickettsia were isolated from *Alloperomys sanguineus* Hirst, collected in housing developments which had been constructed in a meadow environment. I do not know of any studies of the *Microtus* mice at the time of the outbreak. Spotted fever rickettsia were isolated from a naturally infected meadow mouse *Microtus pennsylvanicus*, in Virginia.⁹ In the studies of scrub typhus carried out in Japan after World War II, it was found that *Microtus montebelli* was the principal wildlife host for the rickettsia in some regions. In other regions *Apodemus speciosus speciosus* was the principal host.¹⁴ Recent studies of scrub typhus in Australia demonstrated that the *Melomys banana* rat was an important source of rickettsia. There is a small mammal in Australia called *Mastacomys* which looks like a meadow mouse and has the same ecology as this animal and it would be of interest to study this animal as a possible host of rickettsia. It lives in a mountain environment much like that where we isolated rickettsia from *Microtus* mice in Western United States.⁵ The rickettsial diseases are ordinarily arthropod-borne but Q fever in man is usually the result of airborne infection. On the basis of the ease with which rickettsial infections have spread to man in laboratories and what is known concerning the epidemiology of Q fever, we should consider the possibility that the usual route of infection in a microtine host may be by the respiratory tract. I suspect that the various rickettsial diseases noted above have a common origin in nature and that the antigenic difference between strains may be explained by selection of different rickettsial characters by the different arthropod and mammalian hosts and incorporation of host characters by the organism. I have been interested in the epidemiology of louse-borne typhus which seems to be related to cold environments, suggesting origin in mountain valleys where there are many microtine rodents.

Malaria

I shall not say much about malaria, although I have worked with this disease, especially avian and simian malaria. I suspect that man is an aberrant host for the malarial parasites we find in him. What do we know about natural hosts of human malaria? We do know that monkeys are naturally infected with malaria parasites and some of these can produce a malaria infection in man. Are any of the malarial parasites found in rodents, bats and other wildlife infectious for man? The establishment and maintenance of malaria parasites in man evidently occurred as the result of domestication of some anopheles mosquitoes. We did not know that man was susceptible to *P. cynomolgi* until there was accidental exposure to mosquito bite in the laboratory. If human malaria is eradicated in tropical regions where the disease has been present for long periods of time, we may discover the natural foci when there are sporadic cases of infection from nature. Subsequent investigation of such foci may give us information about the natural host.

Yellow Fever

Yellow fever is now a rare disease but it used to be one of our most serious epidemic diseases. The epidemic cycle depended on transmission of the virus from man to man by the *Aedes aegypti* mosquito, a domesticated species. For a time it was thought that man was the sole host of this virus. After the elimination of urban yellow fever, cases were observed in man engaged in clearing tropical forest for agriculture. This led to the discovery of what is called jungle yellow fever. In this instance human infection was related to transmission of yellow fever virus by a forest canopy feeding mosquito. The discovery that monkeys were involved in the forest cycle led to the conclusion that monkeys were the natural host of the virus. The high mortality associated with outbreaks of yellow fever in monkeys in South America makes one believe that this animal is an aberrant host. The monkey is a good sentinel animal for yellow fever because dieoffs of monkeys may be the first evidence of the presence of the disease and the migratory course of the monkey epidemic can be followed by looking for diseased monkeys. The occurrence of sporadic cases of yellow fever in man where there are few or no monkeys indicate that there are other natural hosts of this virus. I have visited several endemic foci of yellow fever in Columbia, Brazil and Bolivia and also one where there was an outbreak of the disease. I also visited sites where there had been small outbreaks in the past. The presence of an abundant population of a fruit bat, *Carollia perspicillata*, in each of these regions and the lack of other likely mammalian hosts, makes me suspect that this bat may be either a natural or amplifying host for yellow fever virus in South America. These bats migrate, following the fruiting of different plants and trees. This may be a means for the spread of the infection. Migrating epidemics involving monkeys do occur but this seems to be a dead end in the transmission of the virus in nature. The isolation of many different group B arboviruses from bats, at least one of which has been identified as yellow fever virus, warrants comparative studies of the various group B bat viruses to determine whether some of these will produce immunity in animals to yellow fever virus.¹ My experience with Modoc virus isolated from deer mice and Rio Bravo virus isolated from Tadarida bats can be used to illustrate the possible role of different group B viruses in setting up new cycles of infection in wildlife. The Modoc and Rio Bravo viruses are easily distinguished by serological tests including the neutralization test, but mice immunized with Modoc virus are immune to intracerebral challenge with Rio Bravo virus. However, when mice are immunized with Rio Bravo virus most of them sicken and die when challenged intracerebrally with Modoc virus. This indicates that Modoc virus has the greater antigenic coverage and that Rio Bravo virus is probably a variant of

Modoc virus which has lost some of the natural heterogeneity of the virus by passage in bats. Before leaving this subject of group B viruses in bats, I want to mention that the dengue viruses should be studied in relation to these viruses.

Other Arboviruses

This brings me to the subject of arboviruses which produce less spectacular outbreaks of disease. We now have more than 200 strains of arboviruses but only a few of these cause major disease problems. Tick-borne encephalitis has been a serious disease problem in the USSR and the group B virus responsible for this disease has been isolated in several other European countries. There are several different strains of this virus, each with a different epidemiological pattern. The occurrence of an epidemic of Kyasanur forest disease in India, which proved to be caused by a variant of the group B tick-borne complex, seems to be an example of an aberrant cycle of transmission of this virus. The virus caused massive mortality in monkeys similar to that observed in outbreaks of yellow fever in South America. In Malaya there is a variant of the same virus called Langat virus and in this area there is no disease problem related to the virus. In the British Isles there is Louping Ill virus which belongs to the same complex of viruses. In North America the Powassan virus is the representative of this group of viruses. I recently isolated a strain of Powassan virus in California by primary cell culture of the kidney of a spotted skunk. There was no evidence of active virus by the direct test of the kidney tissue but the cell culture produced Powassan virus. We have no evidence of tick transmission of this virus in California. We are now trying cell culture as a means of isolating this virus from small mammals in the area where we found the virus. What is the natural host of the tick-borne encephalitis virus as it occurs in various parts of the world? The viruses of this complex have been isolated from a great variety of small mammals and birds but there is no satisfactory evidence to incriminate a particular genus.

The major tick-borne virus disease in the United States is Colorado tick fever. In California the major arthropod host is *Dermacentor andersoni* but *Dermacentor occidentalis* is also found infected. We have isolated this virus from five species of small mammals, that is, golden-mantled ground squirrels, *Citellus lateralis*, chipmunks, *Eutamias amoenus*, a wood rat, *Neotoma fuscipes*, a pocket mouse, *Perognathus parvus* and a deer mouse, *Peromyscus maniculatus*. Although we have obtained only one isolation of the virus from pocket mice, I suspect that this animal is the most likely natural host of the virus. It has the geographic distribution of the disease and the tick studies suggest that the source of the virus is one of the small mammals that serve as hosts for the larval form of the tick. The golden-mantled ground squirrel and the yellow pine chipmunk are evidently amplifying hosts.⁹

Among the group B mosquito-borne viruses the Japanese B virus has been responsible for the most severe epidemics. West Nile, Murray valley and St. Louis viruses have also caused serious epidemics of disease in man. The epidemic cycle of these viruses is well known but the interepidemic host or hosts are unknown. The same is true for the group A encephalitis viruses. There is good evidence that birds are important hosts during the epidemic cycle but we do not know where the virus is maintained in nature. Migratory birds evidently move these viruses over great distances and wherever there are high populations of resident birds and a good mosquito vector, the virus may be amplified and spill over to a variety of aberrant hosts, including man and horses. The Brewer's and red-winged blackbirds appear to be especially important in the spread of encephalitis viruses in central and western United States. There is also evidence that a great variety of birds may be involved in the movement of the virus from one region to another. The studies in Central and South America show that fresh water swamps with dense vegetation and trees are good sites for the isolation of these viruses. The northward migration of birds occurs at a time when the mosquito population is low in the Temperate Zone and this is the most likely reason why transmission does not occur at that time. It is a

different situation when the birds migrate south in June, July and August. The question is what is the source of the infection in the Northern Temperate Zone? Where is the virus maintained in the winter? I believe we should study the small mammal insectivores such as shrews, meadow mice, red backed voles, moles and bats in the search for natural hosts of these viruses. There is evidence that the bird-mosquito-bird cycle can be maintained through the winter in the warmer parts of the United States but this does not appear to be a regular occurrence.

Although some arboviruses are arthropod-borne during the epidemic cycle, it is not known whether arthropod transmission is necessary for the maintenance of the virus in the natural host system. The known tropism of many of the arboviruses for excretory organs allow a variety of means of transmission by aerosol exposure or ingestion. Cannibalism is another means for the transmission of the viruses. Our studies of Modoc virus in California have shown that this group B virus has a marked tropism for the kidney and the virus may be excreted in the urine of experimental animals for up to five months. We have also shown that the virus may be recovered from the kidney by cell culture up to 14 months after experimental infection.¹¹ The *Peromyscus maniculatus* deer mouse appears to be the natural host of Modoc virus. It has not been isolated from any of the other small mammals in California. The *Tadarida brasiliensis* bat appears to be the natural host of Rio Bravo virus. In this host the virus has a tropism for the salivary glands and may be excreted in the saliva for many months.⁴ We have recovered two rod shaped viruses in California, one the Kern Canyon virus from *Myotis yumanensis* bats and the Klamath virus from *Microtus montanus*. They are similar in appearance to the VSV viruses. These viruses should be studied as possible pathogens for domesticated animals. The Hart Park virus was isolated from mosquitoes and wild birds. This virus does not appear to produce infection in mammalian experimental animals but may be a pathogen for domesticated fowl. The Turlock virus has been isolated from mosquitoes and birds but we do not know of any disease problem related to this virus.

Among the wildlife viruses which are pathogenic for man and not transmitted by arthropods, or rarely so, I wish to mention Lymphocytic Choriomeningitis (LCM) and Argentinian and Bolivian hemorrhagic fever. The discovery that the *Calomys callosus* mouse was the source of Bolivian hemorrhagic fever and that this virus was excreted in the urine of this mouse was an important and new development in our knowledge of wildlife viruses.¹² We have known that LCM was excreted in the urine of *Mus musculus* but little has been done on the epidemiology of this virus infection in recent years because there are so few cases of infection with this virus.

Rabies

I have a special interest in myxoviruses. I consider rabies virus as a member of this group of viruses. In the study of the epidemiology of rabies, I have become convinced that canines such as dogs, foxes, coyotes and jackals are aberrant hosts of this virus and the natural host or hosts are to be found among the carnivores which do not suffer epidemic disease from this virus, such as the spotted skunk, weasel, ermine and mongoose.¹⁰ The occurrence of sporadic cases of rabies in such animals in the absence of obvious involvement of other species of domestic or wild animals, points to the source of the virus in nature. The only other likely source is in some animal which serves as food for these carnivores. A study of the associated small mammals has failed to reveal any strains of rabies virus. The possible exception is the bat but in this instance the distribution of bat rabies does not fit the geographic distribution of the disease.

Influenza

I mentioned influenza as one of the great epidemic diseases. The epidemics of this disease recorded in recent times show us that this disease has all the characteristics of an aberrant infection as it occurs in man. It appears suddenly, runs a rapid course with a high morbidity and at times a considerable mortality, and then disappears. We know of three types of this virus, that is, A, B, and C. It is the A strain which produces the most severe disease. What are some of the possible sources of influenza A virus in domestic animals and wildlife? We know of strains of this virus from swine, horses, chickens, turkeys and ducks. The virus has also been isolated from terns collected on a bird island off South Africa.⁸ In all of these hosts the infection is associated with disease and one can suspect that the virus is derived from some other source. What has been the geographic origin of the recent outbreaks of influenza A? The Asian flu of 1957 and the Hong Kong flu of 1968 had their origin in southern China. What are the possible sources of a myxovirus such as influenza A in this region? What ecological situation is present there which might predispose to transfer of a myxovirus from wildlife to man? I have been interested in bats for many years. This began with my study of vampire bats. I have since studied bats in different parts of the world. In Asia we find enormous numbers of bats in caves and some of these caves are visited occasionally for religious services. Other caves are historical sites, and some are used for human habitation. In China caves have been used extensively for human habitation and there are large Buddhist caves carved out of the sides of the mountains. Situations such as this offer an excellent opportunity for man to come in contact with large numbers of bats. In studies of the susceptibility of bat lung cultures to influenza B virus, we found that the virus grew readily in these cells without cytopathic effects.

I do not know of any large scale studies of bats for myxoviruses. A good method to use for this type of study would be to prepare lung and kidney cell cultures from different species of insectivorous and fruit eating bats, pooling several individuals of the same species for each culture. The cultures could then be observed for cytopathic effects, hemagglutination and hemadsorption. We have begun such studies with insectivorous bats. In searching for myxoviruses in bats in Asia, I would recommend the study of fruit eating bats which are not found in the Temperate Zone. Influenza B and C viruses have no known geographic distribution and in this instance we might look for the virus in insectivorous bats.

There are a great number of other parasitic infections we could talk about, for example, the 160 respiratory and enteroviruses which parasitize man, for example, the parainfluenza viruses, reo viruses, adenoviruses, rhinoviruses, measles, rubella, mumps, chickenpox, respiratory syncytial virus, hepatitis virus, polio virus, echo viruses and Coxsackie viruses. We know of the relationship of measles, dog distemper and rinderpest. Do they have a common origin in some natural host? The outbreaks of pleurodynia caused by some Coxsackie viruses surely fit the epidemiological pattern of an aberrant infection from some animal source. We can also find wildlife sources for the salmonella infections. Amebiasis, schistosomiasis, guinea worm, hook worm, ascaris and tape worms should all be studied in relation to wildlife. The same is true for diseases caused by borellia, leptospira, spirocheta and brucella. Tularemia is one of the major diseases derived from wildlife. Glanders and infections with a variety of *Pasteurella* organisms are also related to wildlife sources.

From what I have said, you will note that little is known about the origin of most of our serious parasitic diseases. This should be a stimulus to the study of parasitic infections of wildlife. I believe that the primary cell culture method for the isolation of viruses from wildlife will prove to be the best means for the detection of the natural host of our common arboviruses. The fluorescent antibody test has been an excellent tool for the study of the pathogenesis of a variety of parasites and it is particularly useful for the demonstration of parasites of low pathogenicity.

I have given you some general ideas about the ecology of the zoonoses. It seems that almost all of our serious disease problems are related to our cultural inheritance. You will note that regions in Europe with a stable agricultural environment have little trouble with wildlife disease. It is the abrupt change in the environment such as deforestation, reforestation, plowing up of land for agriculture, especially when associated with irrigation and the building of urban communities in otherwise natural environments, that predispose to outbreaks of disease.

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