



Review Article

Do we need Zoonoses Research in India?

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DOI: <https://doi.org/10.24321/0019.5138.202020>

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How to cite this article:

Rajagopalan PK. Do we need Zoonoses Research in India? *J Commun Dis* 2020; 52(2): 74-77.

Date of Submission: 2020-05-10

Date of Acceptance: 2020-06-11

A B S T R A C T

It is not only useful, but necessary, to understand the importance of zoonoses research in India. I do not know how many of the “scientists/ biologists/ administrators” think about zoonoses while planning investigations into diseases of unknown etiology. And, we also need to understand the total epidemiological chain and the natural cycle of the disease agent. Studies on many diseases have been left incomplete, as soon as the disease in humans subsides. There is no more emergency. We have to think of 20-50 years from now and imagine its utility. As long as there is animal-human interface in disease spread, especially when the animals are mammals, the tools of Zoonoses/ field biology will have little or no alternatives.

Zoonoses means diseases which are sourced from animals and transmitted to man. A majority of human infectious diseases are caused by pathogens shared with wild or domestic animals. Zoonotic disease organisms include those that are endemic in human populations or enzootic in animal populations with frequent cross-species transmission to people. Some of these diseases have only emerged recently. Together, these organisms are responsible for a substantial burden of disease, with endemic and enzootic zoonoses causing about a billion cases of illness in people and millions of deaths every year all over the world. Emerging zoonoses are a growing threat to global health and have caused hundreds of billions of US dollars of economic damage in the past 20 years. Zoonotic diseases occur due to various causes, including ecology of pathogens and parasites, environmental modifications due to natural calamities, and other circumstances, such as changes in the dynamics of disease exposure to human beings. In view of present anthropogenic trends, a more effective approach to zoonotic disease prevention and control will require a broader view that emphasizes evidence-based decision making and which integrates ecological and animal, human, and environmental factors.

Given below are examples of three Diseases- Dengue, KFD and Covid-19 here, though there are many more, to explain the importance of Zoonotic Research.

Dengue and Sylvatic Dengue

Dengue strikes annually and about 100 million people suffer with an estimated 50,000 deaths, thriving in the urban environments infested by *Aedes aegypti*, the mosquito species primarily responsible for human



dengue transmission. Meanwhile, the virus' forest-dwelling counterpart - known as "sylvatic dengue" -- continues to flourish in Southeast Asia and West Africa, cycling between non-human primates and the mosquitoes that feed on them. Since the 1970s, sylvatic dengue has received very little scientific attention in India situation that badly needs to be remedied, according to a recent article published in *Nature Reviews Microbiology* with the title: "Fever from the forest: Prospects for the continued emergence of sylvatic dengue virus and its impact on public health". Mosquitoes that carry the dengue and Chikungunya viruses are more widespread than ever, believe scientists mapping the global spread of the insects. There are no treatments or vaccines for these diseases, so knowing where the mosquitoes that transmit them occur and thrive *can help focus research and public health resource.*

Reservoir of Dengue Viruses

Dengue is one of the most rapidly emerging diseases in the tropics. Humans are the principal reservoir of dengue viruses. What we should find out is whether nonhuman primates also serve as a reservoir of human dengue viruses under certain conditions. A serologic survey was carried out to characterize the pattern of transmission of a recently identified dengue virus among macaque monkeys in Sri Lanka. The results indicated that an epizootic dengue virus was active among the macaques. A single epizootic had taken place between October 1986 and February 1987 during which 94% of the macaques within the 3 sq.km study site were exposed to the virus. The epizootic was highly focal in nature because macaques living 5 km from the study population were not exposed to the virus. The transmission of dengue viruses among macaque monkeys in the wild may have important public health implications. "Of all the viruses with the potential to shift from animals into humans, the most likely to do so are those that, like sylvatic dengue, are carried by the non-human primates and/or bats," (Vasilakis. 2016). *Sylvatic Dengue could be capable of similar emergence.* Dengue virus may also be capable of movement from the widespread urban cycles into primates and forest mosquitoes which would establish a new reservoir for human infections. Vasilakis and others identified two factors that make a dengue re-emergence a "clear and present danger": rapid human population growth near and in tropical forests and the fact that little or no genetic change would be needed for *sylvatic dengue to adapt to human hosts and urban mosquitoes.* Active surveillance programs to monitor mosquitoes, non-human primates and humans in areas where sylvatic dengue is endemic, as well as the development of new diagnostic tools that will enable researchers to more easily accomplish those studies is called for. Whether this virus circulates in the forests animals, and economic and ecological pressures are driving people into the forests and get infected, has to

be investigated. There was a successful research program in Malaysia that ended in 1975. There are no records of much work being done on Sylvatic Dengue being done, particularly in areas adjoining forests. *Sylvatic dengue could be capable of re-emergence in such areas, since we know that dengue spillovers had occurred into urban and near-urban settings e.g. in Kottayam, in Kerala, where hundreds of cases were recorded in rubber estates adjoining forests. There are many situations similar in other parts of our country also.* Dengue virus may also be capable of movement from the widespread urban cycles into primates and forest mosquitoes, which would establish a new reservoir for human infections. Two factors that make dengue re-emergence a "clear and present danger are rapid human population growth near and in tropical forests and the fact that little or no genetic change would be needed for sylvatic dengue to adapt to human hosts and urban mosquitoes. *This is an area of research work which has to be undertaken.*

Kyasanur Forest Disease (KFD)

That KFD is a Zoonotic Disease is well known, and its Ecology ably elucidated in an exposition in American Journal of Tropical Medicine, 1969, by Dr Jorge Boshell, who worked for nearly six years in the jungles of Shimoga District, the homeland of KFD. He and his junior colleague P.K.Rajagopalan had set an example of how a scientist should work in the field! Since this is tick transmitted disease, with a complex epidemiology, more detailed explanation is needed. The virus exists in an enzootic cycle with the involvement of several species of small mammals and passerine birds which inhabit the forests adjoining human habitations. Virus has been isolated from several species of ticks parasitizing these small mammals. These mammalian hosts circulate high titers of KFD virus for various durations, infecting their Ixodid ectoparasites, have a quick population turnover and play an important role also in distributing infected ticks within the range of their movement within the forests. *New susceptible hosts replace the immune ones in quicker time.* Among the ticks are several species of *Haemaphysalis*, the chief vector to man and two species of *Ixodes*, *I. petauristae* and *I. ceylonensis*. The most important small mammal is the common shrew, *Suncus murinus* an insectivore (often mistakenly classified as a rodent) which is heavily - proportionate to its size-parasitized simultaneously by both *Haemaphysalis* (the vector to man and monkeys) and *Ixodes* sp.

Intrinsic Factors

KFD Virus has been isolated from *Ixodes* and *Haemaphysalis* collected from the forest floor and as ectoparasites from rodents and shrews. It was reasonable to conclude that the small mammals, particularly the shrews, play a significant role in the transfer of infection to *Ixodes* spp.

from *Haemaphysalis* ticks. *This is very important in the epidemiology of KFD virus, since the population of Ixodes predominates that of Haemaphysalis during the prolonged monsoon season, when both human cases and monkey deaths are rare.* There was evidence that tick burdens were affected by extrinsic factors likely linked also to local climate. Intrinsic factors were also found to affect tick burdens. Larval and nymphal tick loads were positively correlated with host body size. After controlling for body size, the residual variation in tick burdens for *Ixodes petauristae* larvae and nymphs were attributed to unmeasured qualities of rodent and shrew species. The role of rodents and shrews as important hosts for immature stages of ticks, especially larvae has to be highlighted. My studies also showed that tick burdens on rodents and shrews are affected by a complex combination of local climate and host factors, making some individuals more likely to contribute to the life cycle of ticks and the enzootic transmission cycle. To better understand tick-borne transmission one must put more emphasis on intrinsic factors, since these may have major impact on the small mammals' contribution to the enzootic transmission.

Are Bats the Virus Source?

There are several hypotheses which need to be investigated: *whether ticks of Ixodes genus is the medium of survival of the KFD virus during the monsoon season, since they survive for longer duration during the heavy rains. The nymphs of Haemaphysalis turturis have also been found to help in the trans-monsoonal survival of the virus.* And there is also the question of the soft tick, *Ornithodoros rhinolophi* parasitic on the bat, *Rhinolophus rouxi*, from which KFD virus has been isolated. *O.savignyi*, the vector of African sleeping sickness, is known to live, as a fed adult, for more than two years. *So why not the Ornithodoros tick itself act as the reservoir? What about the bats.* They have been associated with many viruses and reported. The fact that KFD sprouts from unexpected foci far removed from each other but within the Western Ghat forest range *makes the bats a natural reservoir of KFD virus.* The main question that remains to be answered is, "From the closed bat-Ornithodoros - tick cycle how does the virus enter complex in the forest ecosystem of birds and small mammals - the *Ixodes/Haemaphysalis* – and the - tick-monkey-man cycle? This is the only question that remains to be answered to understand the natural cycle of KFD". From a purely academic interest, if not epidemiological, the mechanism of survival of the virus in the ecosystem must be investigated particularly when and where there is no episode of KFD in man or an epizootic in monkeys. How could one explain the frequent, sporadic and sudden appearance of KFD human cases or monkey deaths sporadically in different parts of India in recent years? It needs special ingenuity and willingness to plan and pursue long term investigations

in the field similar to what the Rockefeller Foundation carried out (1950-70). Such indepth studies have to be started again expanded in scope and should be pursued with greater vigour, if you want to know what we should do to solve the KFD problem. Every new focus must have an original source to start with. There is strong evidence; the original source to look for is the bats. The Ugandans and the Australians have done excellent work on looking for bats as the virus source. Our young scientists should be enabled to work for long duration in the forests to solve the mystery. There have been no investigations on the original source of the virus, and how (and why) it has entered into the small mammal-monkey-tick-man cycle of disease as no papers have been published.

COVID 19

An acute respiratory illness, Covid 19 is very easily transmitted from person to person, has become pandemic since January 2020, and has gained singular prominence over several other lethal diseases. This is one of the major Zoonotic Disease with real public health impact, caused by zoonotic viruses, viruses that start out in wild animals but can also be transmitted to humans --. We have also the example of the "Chinese bat woman", Shi Zhengli, who did marvelous work, as recently as January 2020, *implicating bats as the reservoirs of Covid-19 virus* (Frontline, April 10, 2020). Bats have attracted increased attention in the last two decades as an important reservoir of many new viruses. This was largely because of the discovery of different highly lethal zoonotic viruses originating from bats, including Hendra, Nipah, SARS, MERS, Ebola and Marburg viruses, among many others Although the notion of bats as the natural reservoir is still being debated for some of these viruses, it is beyond any doubt that bats at least harbour viruses highly related to all of these. The research focus should shift to 'Are bats a true reservoir?'. An epidemic of Ebola killed more than 11,000 people in the recent past in West Africa, and scientists believe "greater long-fingered bat" (*Miniopterus inflatus*), captured near an abandoned mineshaft in Liberia, is the original source (Kupferschmidt, 2019). This bat which lives in many parts of Africa, roosts in caves and feeds on insects. Scientists had previously found two other Ebola strains in a related insect-eating bat, *M. schreibersii*. Ebola is therefore a virus that has multiple hosts, and it might be regionally dependent as to which species carries it.

Since bats were shown to be the carrier of SARS in 2003, not only have many severe acute respiratory syndrome related corona viruses (SARSr-CoV) been isolated from bats, these mammals have been recognized as the natural reservoir for over 100 other viruses including MERS, Ebola virus, Marburg virus, Hendra virus, and Nipah virus, to name a few. Why and how are the bats able to carry and spread

so many viruses? Wudan Yan noted: *1. Bats' high density lifestyle sets up a perfect storm of viral transmission. 2. the tremendous diversity in and among the bat species, which accounts for roughly 20% of all mammals. 3. Bats fly far and wide carrying the viruses to more areas than most mammals. 4. Immunity and body temperature created by high flight.* Shi Zhengli had already implicated bats as a possible reservoir of Covid-19. They have isolated the virus from greater Horseshoe bat, *Rhinolophus sinicus*. (Rajagopalan, 2020). Another species of the same genus, *Rhinolophus rouxi*, and its tick ectoparasite, *Ornithodoros sp.* was found positive for KFD Virus. [Rajagopalan et al, 1969].

Why are Bats (Chiroptera) a Preferred Host for so many Zoonotic Viruses?

Some of their characteristics (food choices, colonial or solitary nature, population structure, ability to fly, seasonal migration and daily movement patterns, torpor and hibernation, life span, roosting behaviours, ability to echolocate, virus susceptibility, and so on) make them exquisitely suitable. Recent observations of outbreaks and epidemics of newly recognised human and livestock diseases caused by viruses transmitted by various megachiropteran and microchiropteran bats have also drawn attention anew to these remarkable mammals. According to literature, 66 viruses have been isolated from bats. Bats are abundant, diverse and geographically widespread. These mammals provide us with resources, but their importance is minimised and many of their populations and species are at risk, even threatened or endangered.

A news report (Woodward, January 30, 2020) said the emerging virus that spread to humans from an animal host are commonplace and represent some of the deadliest diseases known. Given the details of the Wuhan coronavirus (2019-nCoV) outbreak, with a bat origin story, and given that mammals have been the sources of all other such zoonotic corona viruses, as well as a host of other zoonotic diseases, *basic research into the epidemiology of coronavirus needs to be taken up on a war footing. If we know the reservoir species and where they live, we can help the local communities better prepare, and cut down on potential exposure to the virus.*

“Spillover” Events - the Zoonotic Mapping

And this is where zoonotic niche mapping comes in. In India, we SHOULD go to the hideouts of bats and find out what is happening. Our present day researchers must venture out into the field for long duration. These maps are a way to look for patterns where these viruses come out of the forest and into the homes that line the wilderness – scenarios known as ‘spillover’ events. By studying spillover, the scientists better predict where the virus might emerge

in the future and help prepare risk minimizing or mitigation policies and plans. This broad view is essential for the successful development of policies and practices that reduce probability of future zoonotic emergence, for targeted surveillance and strategic prevention and engagement of partners outside the medical community - ecologists, wild life biologists, veterinarians and even management and social scientists to understand the interface.