



View Point

# KFD-Present State of Knowledge

PK Rajagopalan

Former Director, Vector Control Research Centre, Indian Council of Medical Research and formerly: WHO STAC Member, WHO Consultant and WHO Expert Committee Member on Malaria, Filariasis and Vector Control.

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## I N F O

**E-mail Id:**

leelaraj2004@gmail.com

**Orcid Id:**

<https://orcid.org/0000-0002-8324-3096>

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Leland B. Yeager believes that armchair theorizing is more than just the “simple sterile juggling of arbitrary assumptions” that occurs in the absence of fieldwork or the conventional scientific process. The scientific approach, which requires active examination of nature through data collection, contrasts with armchair scholarship. Even if an empirical scientist and an armchair philosopher use distinct methodologies, they might work together to uncover new facts or insights. The anthropologist Bronislaw Malinowski was a vocal opponent of armchair theory, and his ideas are frequently summed up by the phrase “get off the verandah.” Encouraging fieldwork and observation. There are hundreds of publications on Kyasanur Forest Disease during the last several decades, mostly from data already published, a computer analyzed and dished out with fancy titles. It never mattered to science.” I have been trying to tell the same thing to our Indian colleagues, particularly during the last two or more decades, who are wedded to theorizing from stale data collected by others and stored in computers.

They, instead, should go to the field, stay there and face the wilderness, work over a period of time and collect data themselves- and observe what is actually happening in nature, instead of writing irrelevant papers and publish them. But then the Arm Chair Epidemiologists and apron-wearing biologists think that research should be done wearing a white apron, in air-conditioned comforts with a computer as aid. The anthropologist Bronislaw Malinowski, whose arguments are frequently summed up by the phrase “[come] off the verandah,” encouraged fieldwork and participant observation and was a vocal opponent of armchair theorizing.

As recently as Dec 2021, Gen.D.Raghunath, the former Director General of the Armed Forces Medical Research, stated, “I would like to emphasize the role of fieldwork in identifying fall-outs of environmental degradation. Numerous infections have arisen in a similar manner. When one sees the evolution of disease investigation in recent times the lack of quality fieldwork is evident. In short, wearing out shoe leather should form the basis of epidemiology, of course, supported by the newer molecular methods, not vice versa. It is an unfortunate fact that this important lesson has not been sustained. It needs to be fostered and expertise re-established”. Dr Jorge Boshell Manrique, a Colombian scientist, from the Rockefeller Foundation, who, though a medical man, was an ecologist and field worker out and out he discovered



the sylvan cycle of Yellow Fever in South America and discovered a new mosquito species transmitting the virus to monkeys at the tree tops. He elaborately studied the Epidemiology of Kyasanur Forest Disease (KFD) in India and wrote a brilliant paper on “Ecological Considerations” in the American Journal of Tropical Medicine and Hygiene (1968). No medical man had achieved such a feat in our country because he stayed in the KFD forest for more than 6 years.. He was my mentor. It was a common sight in those days to see a Khaki-clad foreigner and a khaki-clad Indian walking in the deep forest, the former carrying a machete, and the latter 12 bore a Winchester shotgun! He was a walking encyclopedia on many subjects. I really learnt a lot from him while walking behind him. Every word uttered by him was knowledge to me. The man-monkey-tick-small mammal- birds involvement in the KFD cycle was well established by him and his assistant (me). The leader left India in 1966, and I continued for a few more years, and then the field station was closed down.

There are many gaps in our knowledge still left. Later I isolated the KFD virus from insectivorous bats, *Rhinolophus rouxii*, and from *Ornithodoros* ticks collected on these bats and from their roosting places adding some new information on possible reservoirs.

Till today no new information has been added. In recent years many states in the Western Ghat part of India from Kerala, to Gujarat, (e.g., Karnataka, Goa and Maharashtra, Tamil Nadu, etc.) had reported sporadic human cases of KFD as well as monkey deaths in isolated pockets. The virus appears to cause monkey deaths, human disease, and infection in ticks. Then it disappears. This is all what the present-day research workers, wedded to molecular science, are doing. They publish papers, and there ends their Safari research!

But no one has ventured to find out anything beyond. Probably because there are not many human deaths, whenever such episodes are reported, the authorities had also lost all interest in studying this disease. Now KFD is clubbed with other neglected tropical diseases. Boshell’s study was so thorough, that a lot of information was generated on the role of common cattle in taking the role of distributing adults of *Haemaphysalis* ticks, which were once parasitizing wild animals. Development works like Sharavathy Valley Hydro Electric project came; the wild animals moved away, the forest became denuded, and man along with his cattle moved in. This also created miles and miles of interfaces between the forests and the developed land, which was highly conducive for the proliferation of small mammals and passerine birds. The invasion of the area by the shrub Lantana, through birds, made the area very hospitable for passerine birds and small mammals.

In 1967, this author came across a colony of insectivorous

bats, *Rhinolophus rouxii*, in an abandoned well in a distant village (Kasarguppe) in Shimoga District, while researching the natural cycle of the Kyasanur Forest Disease (KFD) virus. They are nocturnal, eat only insects, and can be observed flying around after nightfall searching for them. The ticks that parasitize them in their habitat must also be fed by them. These bats were discovered to be infected with *Ornithodorids*, a soft tick of a novel species known as *O. Chiropterphila*. Ticks removed from the field carrying the KFD virus were a wall of the wells, and as ectoparasites of bats (Ind.J.Med.Res. 1969, 905-8). It was significant that no other genera of ticks like *Haemaphysalis* and *Ixodes* were found on these bats. Thus, there seems to be a bat-*Ornithodoros* - bat zoonotic cycle silently existing in nature. But the mystery is how the virus get out of the bat-soft tick cycle and enters the *Haemaphysalis* monkey man cycle to cause monkey mortality and human disease.

We have so far evidence to show that there are many cycles occurring in nature:

- A Zoonotic cycle (bat-*Ornithodorids*-bat cycle)
- An enzootic cycle between ticks both *Haemaphysalis* and *Ixodes* and small mammals
- A Transmission cycle (Similar to over-wintering) involving adults of *Ixodes* and nymphs of *H.turturis*
- A natural zoonotic cycle involving bats, small mammals, monkeys, cattle, and of course both *Ixodid* (*Ixodes* sp), *Haemaphysalis* sp., and Argasid (*Ornithodorids*) tick

The role of *Ornithodorids* had been totally ignored by all the investigators (including me) all these years. This species seems to have a crucial role in the maintenance of the virus for two simple reasons, the multiple nymphal stages which enable a wider range of feeding hosts, and the large life span (more than 7 years) as adults, while still retaining the virus (as shown in Karshi virus).

A long-term study, therefore, must be undertaken in many pockets along the Western Ghats on every one of the above mentioned factors, particularly on the zoonotic reservoir status of bats for KFD. Firstly exploration of the roosting places of micro chiropterans should be undertaken followed by a search for *Ornithodoros* ticks, which has never been done. There are many questions yet unanswered. Earlier investigations by the Rockefeller Foundation-led the group (Boshell and Rajagopalan) had shown several possibilities. There is the interplay of so many factors, with many missing links.

Another important aspect is that KFD human cases were occurring during the dry season (November-March), but during the monsoon, there were no human cases and monkey deaths. The virus was detected in *Ixodes* adult ticks collected on small mammals, esp. the shrew, *Suncus murinus* and in free living nymphs of only *Haemaphysalis*

*turturis* (trans monsooning ticks) collected in drags, and free living adult *Ixodes* spp found in flag drags, and as parasites on the common shrew, *Suncus murinus*. They had the virus during the monsoon. The hosts of *Ixodes* adults during the monsoon, the shrew, itself circulated high titres of the virus, and they had also the highest population turn overs among the small mammals in the area. The shrew, *Suncus murinus* thus plays a very important role to maintain the virus during the monsoon. The five striped palm squirrel, *Funambulus pennanti*, trapped during the monsoon in the forest, also had high titres of virus, and were hosts for *Ixodes* adults. But the squirrels were not as abundant as the shrews. Two species of wild rats, *Rattus rattus wroughtoni* and *R.r.blanfordi* also had virus and ticks, but they are much fewer in numbers than the shrews.

And then there is the question of the soft tick, *Ornithodoros rhinolophi*, parasitic on the bat, *Rhinolophus rouxii*. KFD virus has been isolated both from the bat and the tick. Significant to note that no *Haemaphysalis* tick has been collected off these bats. Is there therefore, no bat-*Haemaphysalis* connection? The *Ornithodoros* tick itself could be the reservoir (It is important to note that *O.savignyi*, the vector of African sleeping sickness, is known, as a fed adult, to live for several years, with virus intact in them. It is also relevant to note that Bhatt and Goverdhan (1973, Acta Virologica, 17, no. 4), working on another species, *Ornithodoros crossi*, in the laboratory showed that this tick, once infected as larvae, carried the virus through all stages and the virus was present in the adult for up to 395 days! ).

There appears to be many cycles of virus, with no evidence yet of their being interconnected happening in nature. The small mammal-hard tick-monkey-man cycle must be a very fascinating story by itself. The crucial finding in 1967, about virus isolations from the insectivorous bats, and their tick ectoparasites, *Ornithodoros* should have stimulated interest among the researchers. But alas, even subsequent findings in recent years by others about the bat connection to viruses such as Ebola, Marburg, and Corona etc the officialdom and research bodies just ignored it.

Compared to previous epidemics of KFD in 1957-60, the finding of virus in bats in 1967 (Ind.J.Med.Res. 1969, 905-8) should have resulted in a serious search for virus in bats, and their tick parasites, but ignored due to reasons unexplained. Nor were the present day researchers interested when sporadic cases and monkey deaths occurred in different pockets throughout the Western Ghats, and a few of them became epidemics. There was of course a flicker of enthusiasm among some, only for some time, when there were quite a few human cases and monkey deaths, in Thirthahalli area, an old theatre, in January 2019.

Quite a lot of noise is always made by the media, authorities as well as researchers whenever a new site is found with

monkey deaths/human cases, but their enthusiasm wanes the moment the area became silent. Many institutions send teams to these spots, more out of compulsion than out of real interest, and undertake field trips for a very short duration (call it a picnic, safari, or obeying orders of their bosses, or by people in Institutions who are just ignorant), and they collect specimens from sick humans, dead monkeys, and ticks and send them to laboratories, where virus is isolated (if present). Bang comes a paper, giving the details of work done, with hypothetical explanations, etc. Their job is over. The government is satisfied, their CV is enhanced, their interest ceases, and the matter is forgotten until the next episode in some other site! There is no persistence of interest or efforts to find out why such sporadic outbreaks occurred!

When KFD was first discovered in 1957, with massive monkey mortality and human cases and everybody was talking about it, because of the suspected yellow fever connection, as both monkeys and men were dying, but the curiosity over the years now seems to be over. Now no one wants to know about what is the source of this virus and from where it has originated.

KFD requires the investigator to go deep into the forest and stay there, and study ecological and environmental changes which had occurred. Though hard field work in remote areas in inhospitable territory is required, our present day Sarkari scientists are just not interested. To be fair to them, the authorities expect too much from them, and without giving them even elementary facilities. When I started my career, over seventy years ago, the Rockefeller Foundation (RF) it was a pleasure to work for them, because they looked after our working conditions and encouraged us.

KFD is a Zoonotic Disease, and its Eco-epidemiology is elucidated in a magnificent exposition by Jorge Boshell in the American Journal of Tropical Medicine (1969). You name a mammal or a bird, it is involved in some way, including our common cattle, apart from man and monkeys which are the victims. And of course the arthropod vectors, ticks. Dr Boshell worked for nearly six years in the jungles of Shimoga District, the homeland of KFD, and set an example of how a scientist should work in the field! Our modern Johnnies would not have even heard about him. His paper "Ecological considerations in KFD" explained how 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. The bat angle was established in 1967 after Dr Boshell left India.

### The Facts Known so Far

- Virus has been isolated from several species of ticks free living and those parasitizing small mammals.

Many of these mammalian hosts were also found to have a quick population turnover, circulate high titers of KFD virus for varying lengths, infect their Ixodid ectoparasites, and play a crucial role in dispersing infected ticks across the region of their mobility inside the forests

- The immune hosts are quickly replaced by new susceptible ones. *Haemaphysalis*, the main human disease vector, and the two *Ixodes* species *I. petauristae* and *I. ceylonensis* are among the tick species
- The most significant small mammal is the common shrew, *Suncus murinus*, an insectivore (sometimes mislabeled as a rodent) that is simultaneously parasitized by *Ixodes* sp. and *Haemaphysalis* species, both of which are severely out of proportion to its size
- *Ixodes* and *Haemaphysalis* gathered from the forest floor have a virus that has been frequently isolated. and as ectoparasites from rodents and shrews throughout the year. After several years of continuous studies within the forests, it had been found reasonable to conclude that the little mammals, particularly the shrews, play big in the transfer of infection to *Ixodes* spp. from *Haemaphysalis* ticks. This can be vital within the epidemiology of the 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 is evidence that tick burdens were littered with extrinsic factors, likely linked also to the local climate. Intrinsic factors were also found to affect tick burdens. Larval and nymphal tick burdens were positively correlated with host body size. After body size, the residual variation in tick burdens for *Ixodes petauristae* larvae and nymphs were attributed to unmeasured qualities of rodent and shrew species. None cares nowadays to check population variables. The role of rodents and shrews as important hosts for immature stages of ticks, especially larvae need to be highlighted. My studies also showed that tick burdens on rodents and shrews are stricken by a fancy combination of local climate and host factors, making some individuals more likely to contribute to the life cycle of ticks and therefore the enzootic transmission cycle. For a better understanding of tick-borne transmission, one must put more emphasis on intrinsic factors since these have an impact on small mammals' contribution to enzootic transmission.<sup>6</sup> What about the bats, hosting these soft ticks? Bats are related to many viruses reported. The very fact that KFD springs up from unexpected foci far from one another but within the Western Ghat forest range makes the bats a possible reservoir of the KFD virus. The most important question that continues to be answered is, "From the closed bat-*Ornithodoros*

tick cycle how does the virus enter the complex forest ecosystem of birds and tiny mammals, the *Ixodes*/*Haemaphysalis* and also the - tick-monkey-man cycle? This is often the sole question that continues to be answered to know the natural cycle of KFD". I tried to talk to many younger Sarkari scientists holding high positions, but they have no time to even listen to an experienced old (92 years old) vintage scientist! I had written critical articles (J.Com.Dis, 51(4)2019; 52 (1), 2020; 52(2) 2020; Frontline, August 4, 2017, April 10, 2020) and several others. I contacted the chief of the only Virus Research Centre, (now National Institute of Virology), and he says (December 2020) that "they stopped field ecological studies on Bats (and on small mammals) from 1980 to 2005", i.e. for 25 Years. Since this institute was the only one to study Arboviruses, can there be a bigger tragedy? Also, I felt Entomologists (Biologists) who did pioneering studies in the past, are now donning white aprons rather than Field uniforms and sitting with a computer. Can we blame it all on the Molecularization of Virus research, ignoring Ecological, entomological and epidemiological aspects

It is never too late. From a purely academic interest, if not epidemiological, the mechanism of survival of the virus within the ecosystem must be investigated particularly when there's no episode of KFD in man or an epizootic in monkeys. Who could explain the sporadic and sudden appearance of human cases or monkey deaths sporadically in several parts of India in recent years? It needed special ingenuity and willingness to plan and pursue future investigations within the field which the Rockefeller Foundation did (1950-70). Such in-depth studies should be started from where they were left off in 1970, expanded in scope and may be pursued with greater vigour if you wish to grasp what triggers an episode. Every new focus must have an original source to start out with. Since KFD has been proved to be an animal disease, the initial source seems to be bats. The Ugandans and thereafter the Australians have done excellent work in trying to find bats as the source of the many viruses. We've also got the recent example of the "Chinese bat woman", Shi Zhengli, who did marvellous work, as recently as January 2020, implicating bats as the reservoirs of the Covid-19 virus. The Ebola virus, though not affecting India, is a major problem in Africa, has also been traced to bats. Scientists all over the world, except in India, have many publications on the role of bats.

Among the Macro chiropterans, there is only one group, the fruit-eating Flying Foxes (*Pteropus giganteus*, *Rousettus leschnaulti*, and *Cyanopterus sphinx*) which have been studied by our researchers, but without any evidence of being reservoirs. Since it is very easy to collect these bats, numerous publications about experiments with these

bats have come out recently. But no one seems to have ventured into inhospitable jungle terrain and searched for insectivorous bats, living in abandoned caves, structures and forests in the present day. Among the smaller insect-eating Microchiroptera, two families, Rhinolophidae and Vespertilionidae, are important as reservoirs of dangerous KFD virus (*Rhinolophus rouxii*), Ebola Virus, (*Miniopterus inflatus*) and Corona Virus (*Rhinolophus sinicus*). Though Ebola virus has yet to strike India in dangerous proportions, the other two are already there. While we are still fighting how to contain the pandemic Coronavirus, and have no time to look for reservoirs, what about KFD? Sporadic episodes, some epidemics too, have been regularly reported from many areas throughout the Western Ghat region, but only spotty and sketchy short-term (Safari?) visits were done by teams sent by several institutions, resulting in quickie publications. You must study insectivorous bats living in abandoned cave structures in remote areas in the forests, where closed cycles of KFD virus must be going on.

What is happening among the present-day researchers on KFD? At least one epidemiologist has called the phenomenon a crisis in its own right an “epidemic of armchair epidemiology, a term coined by Silicon Valley technologist, Aaron Ginn, in an article called “Evidence over hysteria-Covid 19.” I think there is a lot of hysteria over the KFD amongst workers now.