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View Point

Reservoir Aspects of Viruses

Is There Any Effort by Our National Scientists?

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A B S T R A C T

A Scientist from ***the National Institute of Virology (NIV)***, has been very frank saying in a letter dated 13 December 2020, *that* NIV *had* ***stopped all field ecological studies on bats (and on small mammals) from 1980 to 2005*****, for 25 Years**. This was one of the biggest tragedies in the working of a famous research institute which was established in 1952 by the Rockefeller Foundation and the Indian Council of Medical Research, especially to investigate arthropod-borne viruses in India.

The NIV (formerly VRC) was a **pioneer** in many fields in field ecological studies. See our studies on JE (the wonderful studies in Colair Lake at Akivedu on whether migrant birds brought JE to India, the wonderful studies at Devi Mane Ghats – the results on the Ecosystem studies were yet to be published! Remember these operations involving extensive fieldwork by personnel staying in tents in the midst of tiger-infested jungle (I was one of them)- and then, of course, the KFD studies from 1957 to 1970 (I was again part of it), and so many surveys in many parts of India, of which I was again part of it). Those golden years of progress were entirely due to the Rockefeller Foundation (RF) and their top scientists. In my opinion, the departure of RF coincided with the departure of several scientists en masse from the NIV in 1970. The Molecularisation of NIV also took place at that time, and field ecological studies were given a goodbye. I think this was one of the greatest tragedies for India. Arbovirus research also suffered, because there were at one time only two Entomologists at the NIV, and they were also donning aprons and sitting with computers, rather than in field uniforms. All laboratory computer-based studies in air-conditioned laboratories by apron-clad SCIENTISTS carrying briefcases. Am I not correct, the activities shifted to "**the Microbial Containment complex**" at Pashan? The entomology section had been downgraded with no other field activities. "Total Molecularisation" had taken place. One can't hold any individual particularly responsible, but the real victim was the **Science of Ecology and Zoonoses.**

Though the same scientist wrote that interest has now (2020) been revived in the study of bats and small mammals, **the real reservoir source of many viruses**, we have already missed the bus. For example, Zika virus- though we have known its presence since 1952 (Smithburn, Kerr and Gatne), it is only the Uganda lab that made the first isolation

many years later. We in India are now at a big disadvantage, with a big mania for paper publication with "impact factors" but no problem-solving research. Now that we have the pandemic of Covid, interest has been revived in looking for zoonotic reservoirs.

Let me expand my thoughts as a vintage scientist (age 94 years). Many high-profile epidemics due to viruses have been traced to several species of small mammals, including bats, and scientists are discovering new bat-borne viruses all the time. The animals seem especially adept at harbouring and spreading disease. Evidence has been found about their role in the natural cycle of KFD, Dengue, and Ebola and is suspected in Zika also, and therefore bats can be called Zoonotic reservoirs (Andrew Liston, 2020). According to KF Meyer, the father of Zoonoses research, (I was his student), ***"parasitic diseases of man and animals are a part of a broad evolutionary development".***

The question of whether bats are special is so important that we just can't ignore it anymore. Bats and other species such as small mammals that chronically harbour viruses are known as disease reservoirs (zoonotic reservoirs). Most of the time, these reservoirs stay intact, with infected animals rarely showing symptoms of disease. But sometimes they leak, letting a virus infect new and much more vulnerable species. This is almost certainly what happened with the Ebola outbreak in West Africa, which began with a trickle in December 2014, and has since infected at least 8,900 people and killed more than 4,400. Scientists suspect bats are to blame for this epidemic, which has overwhelmed Guinea, Sierra Leone, and Liberia. The ICMR a few years ago issued a statement that Ebola will come to India anytime and we should therefore intensify our studies, particularly on bats! What have we done? Nothing. Tracing the routes from the reservoir to humans is tricky. Even now, scientists don't know all the pathways. This is where research really starts.

I have been shouting from the tree top for several decades, ever since I isolated the virus from bats in 1967. But who am I to influence studies? Even after retirement in 1990, I have been writing articles and publishing them, but nobody cares probably because they are not **"Sarkari"** views. A recent provocation for me was a brilliant article **"THE VIRUS, BATS AND US''** in the New York Times, (original article by David Quammen- ***"Spillover: Animal Infections and the next human epidemic"***). Now we have a coronavirus pandemic, and bats have been cited as the source. How did this happen? Scientists haven't yet discovered (and **they may never**) just which such encounter brought this coronavirus to humanity. But you can be confident that it didn't happen because some Chinese **rufous horseshoe bat** (*Rhinolophus s*p) flew into Wuhan and bit a poor man on the toe. But then there is a surprise, as their involvement in the natural cycle of Ebola, Corona etc has already been commented upon by me (J.Com.Dis, 51(4)2019; 52 (1),2020; 52(2) 2020; Frontline, April 10, 2020). Bats enjoy a mixed reputation among humans." "They have been calumniated and abused for centuries. And this pattern of antipathy will only be made worse by the **Covid-19 pandemic** — given molecular evidence showing bats as the likely origin of the new **coronavirus** — unless we recognize the merits s of these creatures. Some blame bats for the dangerous pathogens they carry — including, potentially, the precursor of the new coronavirus, SARS-CoV-2. During the current pandemic, the virus **may have gotten into us from one of the several kinds of horseshoe bats from southern China**".

Rabies was the topic that dominated research on bats in this field for much of the 20th century. A few other bat-borne viruses turned up, mostly as incidental discoveries by scientists studying something else. *Rio Bravo* virus, for instance, found among some California bats in 1954 and related to the yellow fever virus, was one. *Tacaribe* virus, carried by both bats and mosquitoes in Trinidad, was another. These viruses yielded scientific papers but not newspaper headlines **because they weren't causing human deaths**. But one did cause human deaths- **Kyasanur Forest Disease** (KFD) which was isolated a few times from *Rhinolophus rouxii* and *Ornithodoros* ticks collected as ectoparasites and from the bats" roosting sites (Rajagopalan et al, Ind.J.Med.Res.1967), in India, There also appeared some new killer viruses, though without (at first) any clear linkage to bats. **Marburg virus** as well as the most lethal and infamous of the **Ebolas,** now known as **Zaire ebolavirus,** caused gruesome illness and death with their first recognized outbreaks among humans, during the late 1960s and 1970s. A few other bat-borne viruses also turned up, mostly as incidental discoveries by scientists studying something else. **Rio Bravo virus**, for instance, found among some California bats in 1954 and related to the yellow fever virus, was one. Tacaribe virus, carried by both bats and mosquitoes in Trinidad, was another. These viruses yielded scientific papers **but not newspaper headlines because they weren't causing human deaths".**

Marburg virus as well as the most lethal and infamous of the Ebolas, now known as **Zaire ebolavirus,** caused gruesome illness and death with their first recognized outbreaks among humans, during the late 1960s and 1970s. But their confirmed (Marburg) or probable (Zaire ebolavirus) connections to bats as reservoirs were not established by science until later. Then, in 1994, a strange new bug spilled out of certain flying foxes in eastern Australia, burned its way horrifically through a stable of racehorses and killed one of the three men who had laboured, shoulder-deep in bloody froth, to save those horses. A second man, a stable hand, got very sick but survived. The third man was a tall veterinarian named Peter Reid. He noted that bats came for the figs. The first infected horse shaded herself beneath

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this fig tree, feeding on grass splotched with virus-laced bat faeces. From her, it passed to the other horses and to the men. That virus got the name Hendra, after the Brisbane suburb where the horse deaths occurred. Nipah virus, in 1998, in Malaysia, also emerged from bats, also passed through an amplifier host (pigs), also killed people and also was named for a place: the village of Sungai Nipah, home to a 51-year-old pig farmer from whose cerebrospinal fluid the virus was first isolated. There have been a few studies on Nipah from the state of Kerala, India, also. But the actual mode of transmission from bats to man, has not been definitely established.

The original SARS virus appeared shortly thereafter, in 2002. It, too, arose from a bat, passed possibly through palm civets, and began sickening people in Shenzhen, China. It spread alarmingly fast to other countries in 2003, with several super spreading events and a high fatality rate, but it was controlled thanks to strong public health measures, and it killed "only" 774 people. The SARS outbreak of 2002-03 was a galvanizing event for disease scientists, who recognized that it could have brought about a disastrous pandemic if just a few factors had differed: (1) a slower response by public health officers, (2) disorganized efforts of containment, or maybe a similar coronavirus but capable of spreading from asymptomatic cases. (Does all that sound familiar? It should. **Discovery of the bat-SARS link two years later strengthened bat-virus research, according to the eminent virologist Charles H. Calisher, "from serendipitous, fragmented, and local, to well-planned, methodical, and global," with attention focused ever more strongly on bats as the reservoirs from which many nefarious viruses have emerged.** Dr Epstein — one of the experts **with a veterinary degree, a PhD in ecology and a master's in public health** — is now a vice president at EcoHealth Alliance, a research and conservation organization devoted to animal and human health. He said, "I'm sure you see the analogy here, the gruesome symmetry that brings consolation to no one**: COVID-19 is a disease catastrophe for humans, with its likely origin in bats, triggered by human action; the white-nose syndrome is a disease catastrophe for bats, with its origin who knows where, triggered again by human action. We humans are one species, abundant, wondrous and powerful. Bats are many species, diverse, wondrous and vulnerable.** That puts some responsibility upon us. Our lives and our health are entangled with theirs. If we could speak to bats, offering armistice, seeking concord, I'd suggest six words for a start: **"Thank you. No hard feelings. Sorry."**

Sorry I have written enough, and quoted from authors. As the Distinguished ICMR chair in Virology and Zoonoses, it is a big responsibility for him. Now that NIV have started the Institute of Zoonoses they are going to be handicapped by the location; Nagpur (very good for oranges!). This should have been located near a Forest Ecosystem – a place near the Western Ghats (which has been a known home for KFD for decades, and nothing seems to have been done systemically except paying safari visits, and publishing a quickie, but with impact factor!) or even Brahmaputra valley. They will find plenty of fruit-eating bats *Pteropus* and *Rousettus* in urban areas, and the *Pipistrellus* in old Temples and Caves like Ellora and Karla. They will do routine studies, isolate some viruses and even publish some papers. **This will not give any clue if you are looking for wild reservoirs.**

One must have dedicated field workers, like the bat woman in China (See my article "Bat Connection" in *Frontline).* You should have people like KF Meyer (MD, DVM, D.Sc), Trained Ecologists, with Public Health training (an MPH ?). You are starting and have the advantage of not being saddled with deadwood. The Rockefeller Foundation gave me a free hand with full powers and even placed two AROs under me (an RA at that time) and I could deliver the goods. Even in VCRC the three DGs of ICMR under whom I served, trusted me fully and supported me, the reason for my success as Director. I think Dr Balram Bharghava and the ICMR make the New Founder Director of the Zoonoses Research Unit (Not at Nagpur though, where you can eat only oranges) but will not have a free hand. You will be bound by the advice of retired conference-loving scientific advisors. A lot of wining (literally, I can certify), dining, tourism, and getting fat allowances- a pleasant money-making holiday.

Please look at the face (Figure 1), a Horse Shoe bat, *Rhinolophus* sp. - a forest dweller, which is connected with KFD, Ebola, SARS, COVID, and many more unknown viruses affecting man.

Figure 1.Horse Shoe Bat

Besides showing great collective diversity, bats also have a high life expectancy. If an infant bat gets past its first birthday, it has a good prospect of surviving to 7 or 8 years. Much longer than a mouse. On average, according to one study, **a bat lives more than three times as long as**

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a non-flying mammal about the same size, and some can reach 30 years, even in the wild. This longevity is not just because of torpor and hibernation, giving long periods of rest. Even non-hibernating bats live to be old, possibly in part because flight allows them to escape from predators, possibly also because escape from predators, lengthening life, has given Darwinian natural selection the time and reasons to eliminate negative mutations. But these are guesses that invite more investigation which is totally lacking in India.

Another conundrum now at the forefront of bat research, with potential medical value for humans, is how their immune systems tolerate viral infection with such aplomb. Bats carry many viruses, and yet they generally don't suffer symptoms themselves. In at least some cases, the concentration of virus in their blood tends to be low. They don't mount the same inflammatory responses as other mammals, which is good for their longevity, because excessive inflammatory responses can be dangerous, sometimes overwhelming the body with a reaction worse than the cause. The sequencing of the genomes of several bat species has revealed that they *carry about half as many immunity-related genes as a human* does. Why would evolution dampen down immune reactions in bats? One hypothesis is that it's a trade-off for flight: Flying entails such physiological stress that an alert immune system might react against unstable molecules produced by the animal's own exertion. In this view, it's better for the bat to ignore the presence of viruses than to suffer autoimmune symptoms from flying. So, could bats help medical researchers understand autoimmune diseases in humans? That's an open question.

Dr Epstein — one of the experts **with a veterinary degree, a PhD in ecology and a master's in public health** — is now a vice president at EcoHealth Alliance, a research and conservation organization devoted to animal and human health. He said "I'm sure you see the analogy here, the gruesome symmetry that brings consolation to no one**: COVID-19 is a disease catastrophe for humans, with its likely origin in bats, triggered by human action; the white-nose syndrome is a disease catastrophe for bats, with its origin who knows where, triggered again by human action. We humans are one species, abundant, wondrous and powerful. Bats are many species, diverse, wondrous and vulnerable.**

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Regards, Rajagopalan

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From bharat sant to Devendra, Dr, Ashwani, sabesan1, ICMR, Jambulingam, Dr, ICMR, me Raj:

My observations on "A letter on Reservoir Aspects of COVID PANDEMIC"

Personally, I feel that when a letter is marked to others, he/she should respond appropriately and contribute to the theme of the letter. To me, Dr Rajagopalan and Dr Mourya are celebrities in the area of virus research, but with an advantage to Dr Rajagopalan for obvious reasons. He is 90+ with virtually unlimited wisdom and fantastic foresight. His letter so sincerely narrates the story of zoonosis research in India since about 1960s (remember KFD work vis-a-vis PKR) till date. He is passionate about taking field-work-inclined zoonoses research in India to great heights for the benefit of mankind, which perhaps may prevent another coronavirus pandemic. His was a breakthrough idea!

It is pertinent at this stage to study some significant publications of Dr PKR. One of his latest, DO YOU NEED ZOONOSES RESEARCH IN INDIA? published in 2020, Issue 2, - Special Issue on COVID is a jewel and can be the benchmark for setting up a School of Zoonoses Research at a suitable place in India. In this review paper, Professor PKR has warned, " ---- basic research into the epidemiology of coronavirus needs to be taken up on a war footing". He strongly advocates, "Our present-day researchers must venture out into the field for a long duration." He further emphasises, " Study of SPILLOVER events through zoonotic mapping to understand 'emergence' of virus and laying down management policies for surveillance and strategic planning.

I understand from the correspondence that an Institute for Zoonoses has been initiated at Nagpur, but probably without any inputs from Dr PKR. Well, that's a decision by decision-makers - often locations are political decisions with or without merits. I have no idea of the scope of the above institute. I tend to agree with Dr PKR about the more-suitable-than-Nagpur location entirely on scientific as well as historical reasons; after all, I was and 'am still imagining a truly interdisciplinary world-class, modern Zoonoses Research Institute, even bigger than NIV. If Dr Mourya and other authorities of the day can re-think the entire Zoonoses Institute project and bring in (nothing personal) the professional Dr. PKR's experiences and foresight, in reality, it will not only be doing justice to zoonoses research, but it may be the best tribute to Dr PKR to his 90 years of service to the nation.

Regards

Bharat Sant

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