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Monkeypox virus: ecology and public health significance

L. KHODAKEVICH,[1] Z. JEŽEK,[2] & D. MESSINGER[3]

Recent investigations have revealed that monkeypox virus infections occur with a high prevalence in several species of squirrels belonging to the genus Funisciurus, *less frequently in squirrels of the genus* Heliosciurus, *and rarely in forest-dwelling primates. These squirrels commonly inhabit the secondary forests around human settlements in the rural areas of Zaire, especially where oil palms are grown, and are rare in the primary rain forest.*

Human infection with monkeypox virus occurs most frequently in the 5–9-year-old age group, particularly in small villages where the children hunt and eat squirrels and other small mammals. As the populations are now increasing in number and can no longer feed on wild life alone for their animal protein requirements, the development of animal husbandry as a source of meat will certainly decrease the risk and the incidence of human monkeypox, even in areas where monkeypox virus is present in the local population of squirrels.

Although population growth and economic development in western and central Africa will probably reduce the risk of human infection with monkeypox virus, visitors to these areas who are likely to come into contact with wild animals should be offered smallpox vaccination as a protection.

INTRODUCTION

In 1959 a new disease agent in the genus Orthopoxvirus, which was called monkeypox virus, was discovered in captive Asian monkeys in Copenhagen, and several similar findings were reported subsequently (*1–3*). Interest in this virus increased greatly when it was found to be the cause of a smallpox-like disease in western and central Africa in 1970, and special investigations were carried out to determine whether human monkeypox constituted a risk to the smallpox eradication programme. In December 1979 the Global Commission for the Certification of Smallpox Eradication concluded, based on the evidence then available, that it did not constitute such a risk, but recommended that "WHO should organize and assist a special surveillance programme on human monkeypox, its epidemiology and its ecology" (*4*).

Following this recommendation, intensive studies on the epidemiology of human infections were carried out in Zaire from 1980 till 1987 (*5*, *6*). Research on the ecology of monkeypox virus was strengthened from 1984 onwards, and has resulted in a better understanding of how the virus circulates in wild animals and how it is transmitted to human beings. This article presents a summary of the research carried out in the 1980s and analyses the results.

Early studies on the ecology of monkeypox virus

The fact that the virus was isolated from monkeys and that several outbreaks had occurred in primates in captivity initially directed the search for reservoir hosts towards this group of animals. Monkeypox-virus-specific antibodies were detected in several species of forest-dwelling monkeys: *Cercopithecus ascanius*, *C. petaurista*, *Colobus badius* and *Allenopithecus nigroviridis* (*3*, *7*, *8*).

Epidemiological investigations of 67 primary human monkeypox cases revealed that 64.5% of the patients had been in contact with monkeys at the presumed time of contracting the infection and that 11.8% had contact with both squirrels and antelopes (*6*). Most of the animal contacts were described as healthy, though in two reports a sick squirrel and a chimpanzee were associated with the occurrence of the disease in children (*9*, *10*).

[1] WHO Team Leader, AIDS prevention and control programme, Ethiopia. Requests for reprints should be sent to Dr. L. Khodakevich, c/o WHO Representative, P.O. Box 3069, Addis Ababa, Ethiopia.

[2] Medical Officer, Global Programme on AIDS, World Health Organization, Geneva, Switzerland.

[3] Research Worker, National Institute of Biomedical Research, Kinshasa, Zaire.

MATERIALS AND METHODS

Identification of the reservoir of monkeypox virus was considered by the WHO Committee on Orthopoxvirus Infections in 1984 to be a high priority in the research on monkeypox (*5*). In 1985 a specialized team was established in Zaire for this purpose. Led by a biologist, the team carried out a series of surveys in various parts of the country (Fig. 1), which included studies on the flora and fauna in monkeypox enzootic areas and the collection and sampling of animals (with preliminary taxonomic identification) for virological and serological studies. The preserved sera and organ samples were shipped to the two WHO Collaborating Centres in CDC (Centers for Disease Control), Atlanta, GA, USA (Chief, Dr J. Nakano) and at the Moscow Research Institute for Viral Preparations, Moscow, USSR (Chief, Dr S. S. Marennikova), where they were tested. The final identification of the animals was carried out by Dr Marc Colyn in the Musée Royal de l'Afrique Central in Tervuren, Belgium.

In October 1986 an experimental laboratory was set up in the virology department (Chief, Dr B. Goussard) of the Institut National de Recherche Bio-Médicale in Kinshasa (Director, Dr J.-J. Salaün), where a team of researchers (Dr. E. Shelukhina, Dr S. Polie, Mrs D. Messinger, and supporting staff) studied the transmission of monkeypox virus among squirrels and some terrestrial rodents.

A new approach to research on virus ecology, in which terrestrial and arboreal rodents and bats were given priority over primates and other large mammals of the tropical rain forest, followed from the results of the earlier surveys and of human surveillance in Zaire (*11*, *12*). The sites for the surveys were determined more precisely by an analysis of the locations where humans had contracted the disease, and the behaviour and movements of persons of different age groups.

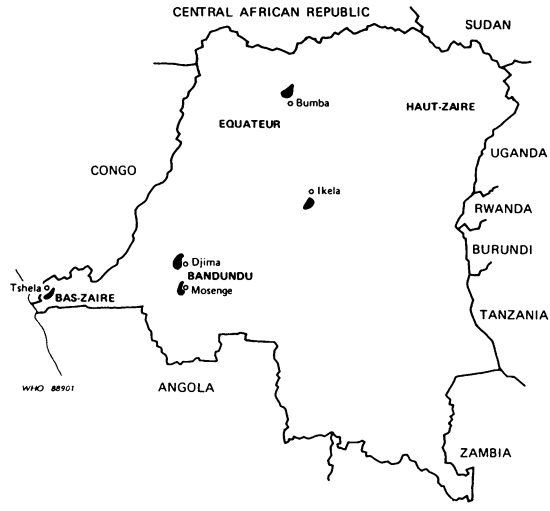

Fig. 1. Map of Zaire showing survey zones for investigating the ecology of monkeypox virus in the north, central and western regions of the country.

RESULTS

Ecological features

The studies initially covered 12 villages in several parts of Bumba zone and revealed three clearly demarcated areas around the dwellings: the settlement area, comprising the village and immediate surroundings; the adjacent agricultural area, with both cultivated and abandoned agricultural fields; and the primary (closed) rain forest, which was usually 3 to 4 km away from the village (*11*). A similar pattern was observed in other places like Mosenge and Djima (Fig. 1) (Dr Lubini Ayingweu, unpublished report).

It was also found that most members of the population remained in the settlement or agricultural areas throughout the year. Only adult and adolescent males moved out occasionally to visit the primary forest for hunting.

The larger wild mammals occupying the original forest had abandoned the agricultural areas where only terrestrial rodents, arboreal rodents and bats now remain. The settlement area is inhabited by commensal rats and mice; domestic cats, goats and sheep usually dwell around the houses and in the nearby agricultural areas. No systemic study was made on the fauna of the primary forest, but these were apparently less affected by human activities. The fact that human monkeypox was most common among children who stayed in the settlement and agricultural areas, rather than among the hunters, focused attention on the animals found in these areas.

Serological studies

During the first survey carried out in the north of Zaire (Bumba zone) blood samples were collected from 120 sheep and goats, 67 domestic cats, 172 terrestrial rodents and 21 squirrels from the areas where human monkeypox cases had previously been reported. Monkeypox-virus-specific antibodies were not detected in the samples collected from the domestic animals and terrestrial rodents, but two out of 18 squirrels (*Funisciurus anerythrus*) were seropositive. One of the two seropositive animals had pock-like lesions on its skin, and culture of its skin and organs yielded monkeypox virus (*13*).

Following these findings the study areas were

Table 1. Results of the surveys, using radioimmunoassay, on the ecology of monkeypox virus in four areas

Animals	Bumba		Ikela		Bandundu		Bas-Zaire		Total	
	No. tested	No. positive[a]	No. tested	No. positive	No. tested	No. positive	No. tested	No. positive	No. tested	No. positive
Terrestrial rodents and insectivores	1024	0 (0)[b]	—	—	98	0 (0)	—	—	1122	0 (0)
Primates	41	3 (7.3)	112	9 (8)	—	—	—	—	153	12 (7.8)
Squirrels:										
Funisciurus spp.	320	79 (24.7)	96	16 (16.7)	124	3 (2.4)	119	58 (48.7)	659	156 (23.7)
Heliosciurus spp.	37	6 (16.2)	23	3 (13)	10	0 (0)	31	6 (19.4)	101	15 (14.9)
Total	1422		231		232		150		2035	

[a] Monkeypox positive by radioimmunoassay.
[b] Figures in parentheses are percentages.

extended to the central and western parts of Zaire (Fig. 1), and screening was concentrated on arboreal animals such as squirrels and primates in the forests; terrestrial rodents and insectivores were also studied in parallel. None of the 1122 terrestrial rodents and insectivores tested was found to have antibodies to monkeypox virus (Table 1). Among the primates (mainly *Cercopithecus ascanius*) the antibody prevalence rates ranged from 7.3% to 8.0%. In all areas, the highest prevalence rates were observed among squirrels of genus *Funisciurus* followed by another squirrel (*Heliosciurus rufobrachium*), in which the antibody prevalence rates ranged from 13.0% to 19.4% (Table 1).

Studies on transmission

The experimental studies carried out at the Kinshasa laboratory showed that monkeypox virus was very efficiently transmitted through air and excreta (vomit and faeces) among captive squirrels, and by skin scarification. Ants (*Crematogaster* species) were also tested because in nature they represent a significant part of the diet of squirrels and they consume the tissues of dead mammals. No virus was found in ants fed on the infected tissues of squirrels (E. Shelukhina, J. Nakano, unpublished observations).

Incidence of infection in different animals

The foregoing data and the monkeypox antibody prevalence rates among human beings (*14*) indicate the order of preference for various animals and man in the circulation of the virus in nature (Table 2). Among the animals studied, squirrels of the genus *Funisciurus* stand out as the potential reservoir host, i.e., a host which ensures maintenance of the virus population in nature (Fig. 2). These animals are very common in the agricultural areas, their numbers in favourable conditions reaching several hundreds per km^2 (*15*). During their daily activities they form groups of several individuals and frequently share the nests of their neighbours, even those of different species.

Heliosciurus species of squirrels are also involved in virus transmission, but appear to be less frequently infected and probably may not be able to sustain circulation of the virus in areas where *Funisciurus* does not occur. The incidence rate among non-human primates is less than that among squirrels, hence they may be considered as occasional or incidental hosts. The incidence in man is the lowest, probably because of the relatively rare contact with wild life and the practice of food hygiene and cooking. Among wild animals it is possible that the virus is transmitted through direct physical contact, or via the air or excreta. Man is infected mainly by eating the unprocessed organs from any mammal which is infectious with monkeypox virus at the time. As the infectious period in animals only lasts a few days (as indicated

Table 2. Estimated incidence of monkeypox virus infection among various animals and human beings[a]

	Antibody prevalence rates (P)	Lifespan (t) (years)	Incidence (I) (cases/year/1000 individuals)
Funisciurus spp.	0.24	2	240
Heliosciurus spp.	0.15	4	75
Non-human primates	0.08	7	23
Human beings	0.01	50	0.04

[a] The calculation of the incidence rates is based on the following formula adapted from Freeman & Hutchison (*24*): $I = P/(t/2) \times 1000$.

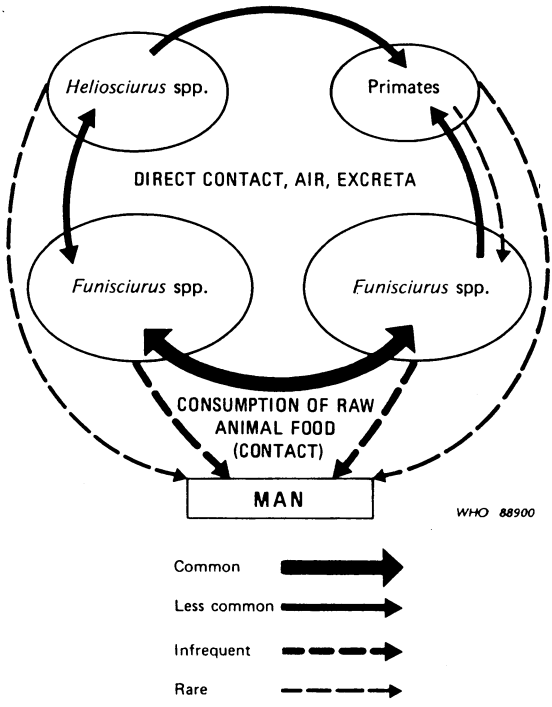

Fig. 2. Diagram to illustrate the transmission of monkeypox virus in nature and from animals to man.

by the Kinshasa studies) and rarely coincides with their consumption by man, human monkeypox is a rare sporadic disease.

DISCUSSION

Extent of the monkeypox enzootic area

Although the present studies were conducted only in Zaire, it should be possible to determine the areas in other African countries where the virus could circulate, the critical requirement being the presence of the reservoir host. The surveys in Zaire showed that the circulation of monkeypox virus was maintained through squirrels inhabiting various types of degraded or secondary humid tropical rain forests. Even in the most remote areas of Bumba and Ikela zones of Zaire, at least 50% of the primary (closed) forests have been converted into secondary forest, and in places far from human settlements, forests of this type supporting *Funisciurus* (*16*) are found alongside streams and on hills which are not capable of sustaining the primary rain forest (*17*).

The squirrels of the genus *Funisciurus* make their nests 2–10 metres above the ground. In the primary (closed) forests no small mammals are found at this level, whereas, on the contrary, various types of secondary forests are densely populated by squirrels. The nuts of oil-palm trees (*Elaeis guineensis*) provide plentiful food for squirrels and facilitate maintenance of their population. These trees grow widely in secondary forests and in plantations throughout West Africa, occupying an almost uninterrupted belt of 50–250 km width along the coastline from Sierra Leone in the west to southern Cameroon (*18*, *19*). This belt widens in Gabon and Congo and occupies nearly the whole basin of the Zaire river up to 25° East.

In general the known areas where monkeypox virus occurs extend from longitude about 12° West to 25° East, and is limited by the tenth parallel on the North and by the eighth on the South. Within this wide area the virus circulation is determined by the prevalence of populations of *Funsiciurus*, which in their turn are determined by the type of forest. The areas covered by either degraded, secondary humid tropical forests or semi-deciduous forests with a significant number of oil-palm trees may be considered as monkeypox enzootic areas. Whether or not monkeypox virus is actually present in any particular area may be determined by testing the squirrels for antibodies to this virus.

Public health significance of monkeypox virus

Three factors determine the chances of transmission of monkeypox virus to human beings in enzootic areas.

(1) *Methods of food preparation*. The importance of food preparation methods in the infection of human beings from a wild animal source was established by our observations in several monkeypox enzootic areas where the cultural and economic conditions of the population were different. The two areas that were compared, Bumba zone in the north and Tshela zone in the west, have populations of *Funisciurus* with 25% and 49% monkeypox antibody prevalence rates, respectively. In Bumba zone 107 human monkeypox cases were recorded from 1972 to 1985, while none was reported in the whole of the western (Bas-Zaire) region, where there are relatively advanced health services as compared with the northern region of the country.

The nutritional habits in Bumba and Ikela zones differ from those in Tshela. In the former, rodents which are trapped by children from the age of 5–6 years onwards, represent 60–85% of all wild animals captured by the rural population and are sometimes consumed without cooking. After the age of 9–10 years the children copy their parents and cook

the meat. In Bas-Zaire, on the other hand, children start hunting wild animals at the age of 12–13 years and small mammals are relatively rare targets. Moreover, consumption of uncooked meat is unusual, probably because of better general education; in Bas-Zaire region nearly twice as many children complete primary and secondary schooling compared with Equateur region in the north, where Bumba zone is situated (*20*). Further, the population density in Bas-Zaire is four times higher than in Equateur region (36.6 and 8.4 persons per km^2, respectively), and animal husbandry is more advanced than in the north.

Human monkey is a disease of mainly the rural population, 90% of the patients living in small villages inhabited by less than a thousand persons; only three cases were reported from towns of more than five thousand residents (*6*). This difference is probably related to the fact that in the rural areas with low population densities the people rely almost entirely on wild animals as the source of animal protein. With the increase in population density, animal farming was established as a source of protein. Thus in the course of general economic development, traditional nutritional practices are disappearing and it is expected that infection with monkeypox virus will decrease.

(2) *Past vaccination against smallpox.* The second factor relates to the susceptibility of the population to monkeypox virus, which is determined mainly by smallpox vaccination carried out in the past (*6*). Between 1980, when smallpox vaccination was stopped in Zaire (and in most countries of west and central Africa), and 1983 the proportion of vaccinated children below 5 years of age in Zaire declined from 43.7% to 12.4% and there is a gradual decrease in the older population as well. In several years therefore the whole population will become susceptible, and every close contact with a monkeypox-affected animal may be expected to result in infection in a human. Thus the probability of the virus entering a human population depends on the balance between the rate of decline of immunity due to smallpox vaccination and the rate of advance of social and economic development of the population in the enzootic areas.

(3) *Person-to-person transmission.* The third factor affecting the incidence of human monkeypox is the transmissibility of the virus between humans. Several episodes of person-to-person transmission have been reported in Zaire (*5*, *6*), in one of which there were probably four generations of transmission (*21*). Secondary attack rates of human monkeypox in unvaccinated contacts are 12.3% within affected households and 3.3% for others (*6*), figures that are several times lower than the rates recorded for smallpox in Asia and Africa (*22*).

Using the data on human transmission in Zaire, a stochastic model was developed for person-to-person infections with monkeypox virus among the population according to three levels of vaccination coverage—50%, 25%, and zero (*23*). The model clearly indicated a diminishing number of cases in successive generations and eventual cessation of transmission.

Risk of infection for visitors to enzootic areas

So far we have discussed the monkeypox threat to the local population in enzootic areas. Visitors to these areas, including persons from other countries, may also come in contact with monkeypox infected animals in the course of their occupational activities or hobbies. Though humans are mainly infected through food, it is possible that the virus could enter the human body through skin abrasions (like vaccinia virus) or the respiratory tract (like smallpox virus); both routes of virus transmission were proved to be very efficient among animals in the Kinshasa study.

Some persons in the enzootic areas are frequently required to handle wild animals during their work (e.g., to capture them alive, nurse the recently captured ones, or dissect them). These persons should be considered at risk, i.e., they belong to the category of "investigators at risk" which was mentioned by the Global Commission for the Certification of Smallpox Eradication (*4*), so that in addition to enforcing personal precautions it may be wise to offer them smallpox vaccination.

For the populations living in the endemic areas, health education on food hygiene, especially for children attending primary schools, may significantly reduce the chances of contracting the infection from wild life.

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RÉSUMÉ

ORTHOPOXVIRUS SIMIEN: ÉCOLOGIE ET IMPORTANCE EN SANTÉ PUBLIQUE

Des travaux récents ont montré que les infections à orthopoxvirus simien surviennent avec une forte prévalence chez plusieurs espèces d'écureuils appartenant au genre *Funisciurus*, sont moins fréquentes chez les écureuils appartenant au genre *Heliosciurus*, et sont rares chez les primates arboricoles. Ces espèces d'écureuils vivent en général dans les forêts secondaires qui se développent autour des établissements humains dans les zones rurales du Zaïre, notamment dans les régions de plantations de palmiers à huile, et sont rares dans la forêt ombrophile primitive.

L'infection humaine par l'orthopoxvirus simien survient très fréquemment entre 5 et 9 ans, notamment dans les petits villages où les enfants chassent pour les manger des écureuils et d'autres petits mammifères. Toutefois, les populations de ces régions deviennent plus nombreuses et ne peuvent plus se satisfaire des seuls animaux sauvages comme source de protéines animales; le développement de l'élevage réduira certainement le risque comme l'incidence de l'orthopoxvirose simienne de l'homme, même dans les régions où l'orthopoxvirus simien est présent dans la population locale d'écureuils.

Bien que l'expansion démographique et le développement économique de l'Afrique occidentale et centrale puissent probablement réduire le risque d'infection humaine par l'orthopoxvirus simien, les visiteurs de ces régions qui sont susceptibles d'entrer en contact avec des animaux sauvages se verront proposer la vaccination antivariolique à titre de protection.

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