Rabies-related viruses

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The history of the rabies-related viruses had its origins in the discovery of bat-associated rabies in the Americas, where the viruses which occur in insectivorous and vampire bats have all proved to be biotypes of rabies virus proper. Findings in the Americas aroused worldwide interest, and Lagos bat virus was discovered in 1956 in Lagos in Nigeria, when it was isolated from fruit bats in a deliberate attempt to determine whether bat-associated rabies also occurs in Africa. The virus was subsequently isolated in surveys from bats in 1974 in the Central African Republic (one isolation) and in 1985 in Senegal (two isolations). There was no indication that the bats tested in deliberate surveys behaved abnormally.

During an epidemic of dog-rabies in Natal in 1980 and 1981, however, positive (cross-reactive) rabies immunofluorescence was recorded in several fruit bats which behaved abnormally, i.e. were caught by pet dogs and cats during daylight, or were found dead in gardens or swimming pools. Three isolations were made from such bats and all proved to be Lagos bat virus. A further isolation of Lagos bat virus was made from a fruit bat which was apparently found dead by dogs in a garden in Durban in 1990. Furthermore, Lagos bat virus was isolated in 1982 from a cat in Stanger, Natal, and in 1986 from a cat in Dorowa, Zimbabwe.

Suspicion that the cats were infected with a rabies-related virus was aroused by the facts that both cats had been vaccinated, that the cases occurred remote from any other known cases of rabies at the time, that fluorescence was weak with anti-rabies conjugate and that the signs of illness in the cat in Zimbabwe (lethargy and paresis), were not typical of rabies. Presumably the cats became infected from contact with bats.

Mokola virus was first isolated from shrew in Nigeria in 1968 (4 isolations) in the course of a survey for arthropod-borne viruses in small mammals in Mokola Forest, near Ibadan. Isolation of the virus from the cerebrospinal fluid from a young girl with nervous disease in Ibadan, Nigeria, was tentatively reported in 1969, but for a variety of reasons this isolation is no longer regarded as valid. An isolation made in 1971 from the brain of a girl who died in Ibadan of nervous disease, is regarded as valid.

Mokola virus was subsequently isolated in surveys from a shrew in 1974 in Cameroon and a rodent in 1983 in the Central African Republic. In 1981 and 1982, the virus was isolated from six cats and a vaccinated dog in Bulawayo, Zimbabwe, which were tested for suspected rabies. Suspicion that a rabies-related virus was involved was aroused by atypical signs of illness and weak fluorescence with rabies conjugate.
The incident in Zimbabwe prompted re-examination of a stored virus obtained in 1970 from a cat in Umhlanga, Natal, which had fluoresced atypically, and this also proved to be Mokola virus. It is notable that Mokola virus has never been obtained from bats, and it is surmised that the cats and dog gained infection from shrews or rodents -possibly there was an epizootic in small mammals in Bulawayo in 1981-82.

Duvenhage virus was first isolated in 1970 from an adult male living in Warmbaths district, Transvaal, South Africa, who died from rabies-like disease five weeks after being bitten by an insectivorous bat. The only other isolations of the virus came from an insectivorous bat caught in daylight by a cat in Louis Trichardt, Transvaal, in 1981 and another caught in a survey in southern Zimbabwe in 1986.

Prior to 1985, there were 12 isolations of "rabies" from bats in Yugoslavia, Turkey, Germany and Poland (only insectivoros bats occur in Europe) and one from a human who died in Russia in 1977 after being bitten by a bat. Most of the isolations were made in surveys, but some of the bats had behaved abnormally, e.g. were active during daylight. The viruses were initially identified as "rabies" virus in tests which cannot distinguish rabies from the related viruses, and most were discarded, but three of the early isolates from Germany were preserved and subsequently found to be closely related to Duvenhage virus.

At this stage there was speculation that Duvenhage virus may have been imported into Europe in bats, as for instance in ships carrying fruit from South Africa. In 1985, however, there was a further isolation of virus from a bat, which attacked a woman in Denmark, another from a bat zoologist who died in Finland, as well as an isolation from a person who died after being bitten by a bat in Russia.

These isolations prompted the conducting of surveys in Europe, with the result that during the remainder of 1985 and over the ensuing few years there were over 450 isolations from bats in Denmark, Poland, Germany, Netherlands, Spain, France and Czechoslovakia. Many of the bats from which isolations were made behaved abnormally, particularly in Denmark, and it seems probable that an epizootic situation existed in Europe in 1985 and the following years. The number of isolations made in surveys currently amounts to about 40 per annum in Europe.

As mentioned in the talk by Dr King, the results of monoclonal antibody studies indicated that there are two subtypes of European bat virus, associated with serotine and myotine bats, and that these are distinct from Duvenhage virus which occurs in southern Africa. Unpublished studies with monoclonal antibodies at several reference laboratories in Europe, failed to identify rabies-related viruses among thousands of isolates from terrestrial vertebrates, apart from the human isolates mentioned above.
Studies conducted in South Africa (National Institute for Virology) with panels of monoclonal antibodies received from Dr King at Weybridge, and from the Wistar Institute in Philadelphia, and the Centres for Disease Control in Atlanta, failed to reveal rabies-related viruses among 120 isolates from humans and domestic and wild animals in South Africa, apart from the bat and cat isolates mentioned above, thus confirming observations made by Dr King on southern African isolates. The position in Africa appears to be similar to that in Europe: although rabies-related viruses could theoretically adapt to terrestrial vectors and spread to cause problems similar to rabies, this does not appear to have happened yet.

It has been suggested that diagnostic laboratories should include tests with a selected small panel of monoclonal antibodies in their screening of field specimens in order to detect rabies-related viruses. However, misleading results may be obtained with abbreviated panels of monoclonal antibodies, and some laboratories in Africa have not yet mastered or instituted adequate routine diagnostic procedures.

Moreover, the low incidence of infection with rabies-related viruses likely to be encountered in diagnostic laboratories, does not seem to justify the extra work and expense involved in screening all specimens with a large panel of monoclonal antibodies. In those rare instances where rabies-related viruses are encountered in diagnostic laboratories, there are usually clues which assist in arriving at the correct diagnosis, such as the involvement of an unusual host (e.g. bat, shrew), or a history of the affected animal having been bitten by such a host, atypical signs of illness, the occurrence of the case in isolation from other known cases of rabies and the appearance of atypical or weak fluorescence in tests with anti-rabies conjugate. It makes more sense to apply the monoclonal antibody tests only in instances where there are features which suggest that rabies-related viruses may be involved, and the tests on such viruses are probably best conducted at regional or international reference laboratories.

The monoclonal antibody tests on rabies isolates in South Africa referred to above, also confirmed the finding of Dr King that separate biotypes of rabies virus circulate in dogs and mongooses in southern Africa.