RABIES: THE INTERNATIONAL SITUATION

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1 LYSSAVIRUSES AND THEIR GEOGRAPHICAL DISTRIBUTION.

The genus Lyssavirus contains numerous distinct viruses isolated from mammals, fish and arthropods. Some Lyssaviruses have been grouped into 4 serotypes: rabies (serotype 1), Lagos bat (serotype 2), Mokola (serotype 3) and Duvenhage (serotype 4). Serotypes 2, 3, and 4 have so far been found in Africa only.

The serological classification is slowly becoming obsolete with the accumulation and phylogenetic analysis of virus genome sequence data. Based on such information it has been suggested to group the rabies-related viruses into 6 genotypes (Bouhry et al., 1993). Genotype 1 accommodates the old serotype 1, the classical rabies virus strains. It occurs on all continents, except Australia and Antarctica. Genotype 2 replaces serotype 2: Lagos bat virus. Mokola viruses are genotype 3 (serotype 3). Duvenhage viruses are genotype 4 (serotype 4). European bat lyssavirus type 1 (EBL1) is genotype 5. European bat lyssavirus type 2 (EBL2) is genotype 6. EBL viruses are restricted to Europe (Europe?).

With more and more sequence information on different isolates accumulating, it is to be expected that Lyssavirus taxonomy and classification will undergo more changes in the near future.

2 RABIES IN TERRESTRIAL WILDLIFE SPECIES.

The areas for which the association of rabies viruses with populations of wild Carnivora is well documented are limited to North America, Europe, and parts of Southern Africa. The principal rabies hosts of the order Carnivora are all small to medium size (0.4 - 20kg) omnivores, scavenging, and foraging on small vertebrates, invertebrates, fruit, and refuse produced by humans. They reach high population densities (often several individuals/km2) in and near human settlements. High intrinsic population growth rates allow rapid recovery of populations decimated by persecution or disease. They all are able to support initial epidemics of high case density and thereafter an oscillating prevalence over many years.

A particular species may serve as a principal host only in a limited part of its geographical distribution, while in other parts of its range other species are responsible for maintenance and spread of rabies. The disease occurs regularly in a number of other mammalian species in addition to the species recognized as principal host. The occurrence of rabies in these other species may have little or no influence on the course of an epizootic; however, their role is often not so easy to define.

Each principal host species has its specific life history pattern and specific means of social interactions. These host qualities determine what virus variants are capable of survival. It is essential that the virus be transmitted by an infected animal during a period of virus excretion to enough other susceptible individuals. For this to occur, lyssavirus strains must be adapted to the physiological traits and population biology of their hosts (Bacon, 1985; Wandeler, 1991a). They must have a host specific pathogenicity and pathogenesis (length of incubation period, duration and magnitude of virus excretion, duration and extent of clinical illness). We assume that each principal host has its own virus variants adapted for persistence in its populations. With the development of monoclonal antibody technology it became possible to demonstrate that indeed antigenically distinct variants circulate in different host populations (Rupprecht et al., 1991: more recently these epizootic variants can also be characterized on the basis of genome structure, see e.g. Sacramento et al., 1991; Bouhry et al., 1992; Nadin-
Davis et al., 1993). That distinct rabies virus strains circulate in different principal hosts and in separate geographic areas may be considered as support for the hypothesis.

3 BAT RABIES.

Lyssaviruses have been isolated from bats (Chiroptera) from Africa, the Americas, Europe, and Asia. The African bat Lyssavirus isolates are of genotypes (serotypes) 2 and 4, while those from bats in Europe where identified as genotypes 5 and 6. American bat rabies viruses have been categorized as serotype 1, but a more detailed analysis of the large diversity of distinct isolates is still good for surprises.

Chiroptera have life history traits that are quite different from those of carnivoran rabies hosts: they are small, long lived, have low intrinsic population growth rates, and are ecological specialists. Properties of lyssaviruses adapted to bats must therefore be different from those of Carnivora rabies. This statement remains a hypothesis since the population biology and epidemiology of bat rabies is insufficiently explored.

An interesting feature of bat rabies is the large diversity of isolates. In Canada alone, 7 distinct variants of serotype 1 are recognized with monoclonal antibodies. Several variants occur in a single species, and geographical distribution of variants are overlapping. This is in sharp contrast to the pattern of rabies in Carnivora, where very little epitope variation is recognized over very large areas, so synonymous base replacements in the viral RNA lead to geographical patterns of genome variants (Nadin-Davis et al., 1993).

4 DOG RABIES.

In large parts of Asia, Africa, and Latin America, the bulk of diagnosed rabies cases is seen in dogs (Baer and Wandeler 1987). For a brief overview see Wandeler on "Canine Rabies" in these Proceedings.

The rabies viruses isolated from wild Carnivora of a particular location all resemble the isolates from wild Carnivora from other parts of the world, but the differences among strains from wild Carnivora are greater than those among the isolates from dogs from different continents. This has been recognized previously with monoclonal antibodies (e.g. Wandeler, 1991a), and has now been confirmed by genome analysis (Smith et al., 1992). Similarities may indicate a common origin (transport of infected dogs), however they may also be the consequence of selective constraints imposed by the host.

5 HUMAN RABIES.

Worldwide about 35 000 people die from rabies every year. The number of people receiving postexposure treatment - mostly after dog bites - is about 3.5 million per year (Bögel and Motschwiller, 1986; Bögel and Meslin, 1990). Almost all human rabies deaths and the vast majority of treated bite exposures occur in developing countries (Acha and Arambulo, 1985). This may in part be due to a high rate of exposure to biting rabid dogs, but even if this assumption is correct, it does not fully explain the high number of rabies casualties. In view of the high efficacy of modern postexposure treatment, nearly all human rabies cases must be considered as failures of the medical system; the correct treatment was not applied, or not applied in time. The appropriate treatment may not be universally available (spatially, temporally, socially, economically), or the appropriate treatment is not in compliance with traditional (religious) beliefs. It is also possible that the necessity of the appropriate treatment is not recognized because other treatments are considered equivalent or superior, or because the disease entity is not recognised (Wandeler et al., 1993).

6 RABIES CONTROL.

The ultimate purpose of rabies control is the protection of man from both infection and economic loss. The occurrence of rabies in man can be controlled by prophylactic vaccination and post-exposure treatment, by reducing the risk of human exposure, or conclusively, by disease elimination. The easiest way to reduce the incidence of human infection is by prophylactic immunization of those domestic
animals which are the most common source of human exposure. A far more ambitious task is the elimination of rabies in its main host.

For a brief review of dog rabies control see Wandeler on "Canine Rabies" in these Proceedings.

Wildlife rabies control by decimating host populations has been attempted in nearly all recognized major terrestrial hosts. However, the resilience of these opportunistic Carnivora to persecution and their reproductive potential, together with high carrying capacities of rural and urban habitats, often render control efforts unavailing. A more promising approach is mass vaccination of the main hosts, although immunization of free-living wild animals is not an easy task. The wild mammal has to be lured by some trick into vaccinating itself. This is possible when oral vaccines are included in baits targeted at the principal rabies host species. The methods have to be simple and efficient, so that it becomes technically and economically possible to establish the level and distribution of herd immunity required to eliminate rabies.

A vaccine to be used for oral immunization of free-living wild animals should comply with a number of requirements (WANDELER 1991b). If a safe, efficacious, and sufficiently thermostable vaccine is available, then a suitable bait needs to be selected. Efficacy and safety of candidate vaccines has been properly tested for only a limited number of target situations. The most important qualities of baits for proper vaccine delivery are that they should be attractive for the target species, and that they should be avoided by other species. All baits tested so far have been picked up not only by various domestic and wild Carnivora, but have been taken up by ruminants and rodents as well. In the event that vaccine and bait are found to be suitable, then the next goal is a vaccine delivery system that assures mass immunization of target species. This requires temporal and spatial bait distribution strategies. When deciding on these strategies it is important to take into consideration technical resources, administrative structures, and manpower needs, as well as constraints imposed by safety requirements, terrain, climate, etc.

BIBLIOGRAPHY.


