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Wildlife rabies in perspective

ALEXANDER I. WANDELER

Rabies Unit, Animal Diseases Research Institute, Agriculture Canada
3851 Chemin Fallowfield Road, Nepean, Ontario, K2H 8P9, Canada

ABSTRACT

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Populations of a number of species of the orders *Carnivora* and *Chiroptera* maintain independent rabies epidemics in different parts of the world. However, in large parts of Africa, Asia, and Latin America, rabid dogs outnumber diagnosed wildlife cases. Rabies virus variants circulating in different host populations can be distinguished by the use of monoclonal antibodies and by genomic analysis. Rabies virus strains and their hosts have to be co-adapted in order to allow their prolonged co-existence.

INTRODUCTION

Rabies in wildlife occurs on all continents except Australia and Antarctica. However the areas for which the association of lyssaviruses with wildlife populations is well documented are limited to North America, Europe, and parts of southern Africa. This brief review will allude to a limited number of considerations related to wildlife rabies epidemiology and public health aspects.

WILDLIFE RABIES–DOG RABIES

One can readily distinguish between areas in which dogs are the main hosts and areas where rabies is maintained by wild animals. The latter situation is found in America north of Mexico, in Europe, and in parts of southern Africa. In these areas a majority of the rabies cases reported are in wild animals and usually only 0,1–5 % in dogs (Tabel, Corner, Webster & Casey 1974; Steck & Wandeler 1980). Three factors may account for the low prevalence of rabies in dogs: most dogs are restricted in their movements; they are kept indoors or in enclosures and leashed when outside; dog vaccination is strongly recommended and practiced, or is even compulsory. It may also be that virus strains adapted to wild species are not very well suited for propagation within dog populations.

In large parts of Asia, Africa, and Latin America, the bulk of diagnosed rabies cases is seen in dogs (Fekadu 1991). Even though dog rabies is often termed "urban rabies", it is clearly a rural problem in many developing countries. Dogs are kept and/or tolerated at very high numbers in most human societies. Their abundance is not explained by their limited economic usefulness. Cultural practices determine the level of supervision of their social interactions and access to resources (food, water, shelter, mates). It is assumed that high density dog populations permit the occurrence of enzootic canine rabies, but this is not very well documented. Despite the easy access to dog populations for data collection, not much is known about dog rabies epidemiology. From accounts given by Glosser, Hutchinson, Rich, Huffaker & Parker (1970), Beran, Nocete, Elvina, Gregorio, Moreno, Nakao, Burchett, Canizares & Macasaet (1972), Belcher, Wurapa & Atuora (1976), Fekadu (1982), and others, one gets the impression that dog rabies is

highly enzootic with only moderate fluctuations in prevalence. There is some speculation that the virus could be excreted by dogs with no apparent infection for prolonged periods, and that these dogs would transmit the virus during the assumed frequent biting. These speculations need confirmation, or at least some quantitative indication of their epidemiological importance. On rare occasions, experimentally infected dogs become sick yet recover from the disease (Fekadu 1991). In some areas, rabies in dogs may not be independent of rabies in jackals, mongooses, or other wildlife; however, there are also situations where a dog population alone maintains endemic rabies.

WILDLIFE RABIES–HUMAN RABIES

Direct human exposure to rabid wildlife is relatively rare. There is however, no doubt that rabid dogs are the major source of human infection. 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/year (Bögel & Motschwiller 1986; Bögel & Meslin 1990). Almost all human rabies deaths and the vast majority of treated bite exposures occur in developing countries (Acha & 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, Matter, Kappeler & Budde 1993).

EPIDEMIOLOGY OF WILDLIFE RABIES

Populations of a number of species of Carnivora and Chiroptera maintain independent rabies epidemics in different parts of the world. The principal rabies hosts of the order Carnivora are all small to medium size (0,4–20 kg) omnivores, scavenging, and foraging on small vertebrates, invertebrates, fruit, and refuse produced by humans. They reach highest population densities in and near human settlements. High intrinsic population growth rates allow rapid recovery of populations decimated by persecution or disease. Chiropteran rabies hosts have quite different life history traits: they are small, long lived, have a low intrinsic population growth rate, and are ecological specialists. 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. For detailed information on epidemiological features of rabies in different host species, see articles published in Baer's "*Natural history of rabies*" (1991). The disease occurs regularly in a number of other mammalian species in addition to the species recognized as principal host (Carey 1985). 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. While a variety of theoretical models mimic the epizootiological behaviour of rabies within carnivore populations (Bacon 1985a), little has been done to understand the population biology of bat rabies.

With the development of monoclonal antibody technology it became possible to demonstrate that antigenically distinct variants circulate in different host populations (Rupprecht, Dietzschold, Wunner & Koprowski 1991). More recently these epizootic variants can now also be characterized on the basis of virus genome structure (Sacramento, Bourhy & Tordo 1991; Bourhy, Kissi, Lafon, Sacramento & Tordo 1992; Smith, Orciari, Yager, Seidel & Warner 1992).

Each principal host population has its special life history pattern and specific means of social interaction. These host qualities determine what virus variants are capable of survival. We assume that each principal host has its own virus variants adapted for persistence in its populations. It is essential for rabies survival 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 1985b; 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). That distinct rabies virus strains circulate in different principal hosts and in separate geographic areas may be considered as support for the hypothesis. However, there is no proof that the observed virus strain differences are specific adaptations. How a virus manages to induce a specific disease syndrome in a particular host is largely unknown. Proper adjustment to a particular host species is constraining virus variability and impeding adaptation to new hosts. This notion is supported by the observation that virus variation in nature is not as prominent as one might expect from an RNA virus. During host passage from the site of entry through the central nervous system to the salivary glands, viruses may also experience a number of population bottlenecks and subsequent clonal growth under different selective constraints. During this process they must maintain their genetic

integrity and overall adaptation to their host's biology.

WILDLIFE 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.

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 carnivores, 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.

The most important conclusion to be drawn from the field application of oral immunization with live attenuated and live recombinant vaccines in Europe and in Canada is that it is possible to immunize enough foxes by bait in order to stop the spread of the disease into rabies-free areas and to eliminate the disease from enzootic areas. In areas freed of fox rabies the disease also disappeared from all other terrestrial species although not from bats. The disease did not re-appear spontaneously from an undetected reservoir after fox vaccination campaigns were discontinued, but rabies was occasionally able to re-invade a fox population from infected contiguous areas (Wandeler 1991b).

WILDLIFE RABIES: QUESTIONS AND CONCLUSIONS

Adaptation of a particular virus variant to its principal host is indicated by the high frequency and magnitude of its excretion on one hand and by the host's high susceptibility to it on the other. These properties allow for transmission from an infective to a susceptible individual in the case of a biting incident. Viruses must either take advantage of normal mechanisms of social interaction or they must promote infectious contacts by altering host physiology and behaviour. However, susceptibility, aggressiveness, and virus excretion are insufficient attributes for ensuring a prolonged persistence of the virus in a host population. Other significant aspects of viral host adaptations are more difficult to explore experimentally. Encounters between infective and susceptible individuals leading to transmission must occur at the correct frequency. How often an infective individual meets a susceptible one may depend on the duration of the infective phase, on its social status and behaviour, the social organization in the population surrounding it, social sequestration of diseased animals, population density, and population dynamics. The molecular biology of the postulated and observed viral adaptations to specific hosts are not yet understood.

An infectious pathogen circulating in a host population promotes the evolution of mechanisms for evading and fighting it, but it also has other consequences. By altering the mortality pattern the disease affects life history evolution. Current life history theory views growth, fecundity, mating success, length of life etc. as coadapted traits or "fitness components" that allow trade-offs between them. These traits have physiological reaction norms. They evolve by natural selection. Potential longevity and senescence are also results of natural selection; however, realised longevity is dependent on the changing prevalence of numerous mortality factors. These "epidemiological terms" were largely forgotten when dividing the "fitness pie" into components (Wandeler 1991a). When searching natural populations for evolutionary effects of rabies, one may have difficulty finding them. Life history traits and disease defense mechanisms effective in a population affected by rabies may not

be perceptibly different from those in a population governed by other mortality factors. Changes may not occur for several reasons: there are too many constraints (fitness-related costs exceed benefits); expected changes are not adaptive, and/or adaptive traits were prevalent before the incursion of rabies. A large fraction of the mechanisms for evading the consequences of rabies are quite nonspecific, and are operative against other diseases that take advantage of the host population.

Enormous progress has been made in recent decades in our understanding of rabies virus biology, pathogenesis, prevention and epidemiology. The dreams of controlling rabies in wildlife through vaccination have become a reality. Molecular biology has led us to the threshold of a new disease prevention era, but the number of human rabies deaths in the world has not diminished accordingly. No doubt, progress in our understanding of the natural history of lyssaviruses will allow us to approach more efficiently some of the problems associated with rabies control. However, there is also little doubt that the major obstacles to rabies prevention in humans are of economic and cultural nature. Dialogue with other disciplines is necessary.

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