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CARNIVORE RABIES: ECOLOGICAL AND EVOLUTIONARY ASPECTS

LA RABBIA NEI CARNIVORI: ASPETTI ECOLOGICI ED EVOLUTIVI

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ABSTRACT

Populations of a number of species of the order Carnivora sustain independent rabies epidemics in different parts of the world. These main hosts 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 recoveries of populations decimated by persecution or disease. The rabies virus is very uniform, so strains circulating in different host populations can be distinguished by the use of monoclonal antibodies. Rabies virus strains and their hosts have to be coadapted in order to allow their prolonged coexistence. The coadapted (or coevolved?) traits are pathogenicity, cell specificity (including species specificity), length of incubation period, duration and magnitude of virus excretion, duration and symptoms of clinical illness, per capita population growth rate of the host, its use of resources (habitat use), social organization and behaviour, and mortality factors other than rabies. These virus and host properties determine rates of infectious contacts and all other epidemiological parameters such as incidence, prevalence, morbidity, and mortality rates.

Key words: Rabies, Ecology, Coevolution, Carnivora.

RIASSUNTO

Diverse specie di Carnivori mantengono indipendentemente epidemie di rabbia in varie parti del mondo. Questi Carnivori sono tutti di piccola o media taglia (0,4 - 20 kg); sono onnivori, spazzini, e si alimentano di piccoli vertebrati, invertebrati, frutti e di vari rifiuti antropici. Essi raggiungono le densità più elevate nelle aree ubane e suburbane. Il loro elevato tasso di crescita consente una rapida ripresa deiie popolazioni decimate dagli abbattimenti o dalle malattie. Il virus deila rabbia è molto uniforme, così che i diversi ceppi presenti nelle popolazioni ospite, possono essere distinti con l'impiego degli anticorpi monoclonali. I diversi ceppi di virus della rabbia ed i rispettivi ospiti si sono coadattati, al fine di consentire la loro prolungata coesistenza. I caratteri che hanno subito un coadattamento (o una coevoluzione?) sono la patogenità, la specificità cellulare (compresa la specificità speciiica), la durata del periodo di incubazione, la durata e l'intensità della escrezione virale, la durata e i sintomi delle manifestazioni cliche, il tasso di crescita pro capite dell'ospite, il suo utilizzo delle risorse (uso dell'habitat), l'organizzazione sociale e il comportamento, e i fattori di mortalità diversi da quelli riconducibili alla rabbia. Tutte queste proprietà dei virus e dell'ospite determinano l'andamento dei contatti infettanti e di tutti gli altri parametri epidemiologici quali l'incidenza, la prevalenza, la morbosità e la mortalità.

Parole chiave: Rabbia, Ecologia, Coevoluzione, Carnivora.

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INTRODUCTION

Ecological and evolutionary questions associated with parasite-host interactions are of great interest to several branches of biology. The behaviour of diseases within populations, communities and ecosystems is a topic of population biology, ecology and evolutionary biology. Unfortunately, most textbooks on these subjects give very limited information on morbidity and mortality due to parasites. Most of them are limited to Lotka-Volterra formulas describing the dynamic nature of host-parasite systems, and to some general remarks on the inevitability of an evolution towards higher degrees of attenuation of parasites. Nevertheless, epidemiology has become a topic of theoretical biology (Anderson, 1981; Anderson and May, 1982) and interest in the evolutionary aspects of parasitism is continuously growing (Barnard, 1984). Models have proven extremely useful in elucidating evolutionary mechanisms (Bacon, 1985). In this paper I shall try to describe some of the unresolved problems as they might occur in rabies-carnivore associations integrated in an ecosystem (Fig. 1).

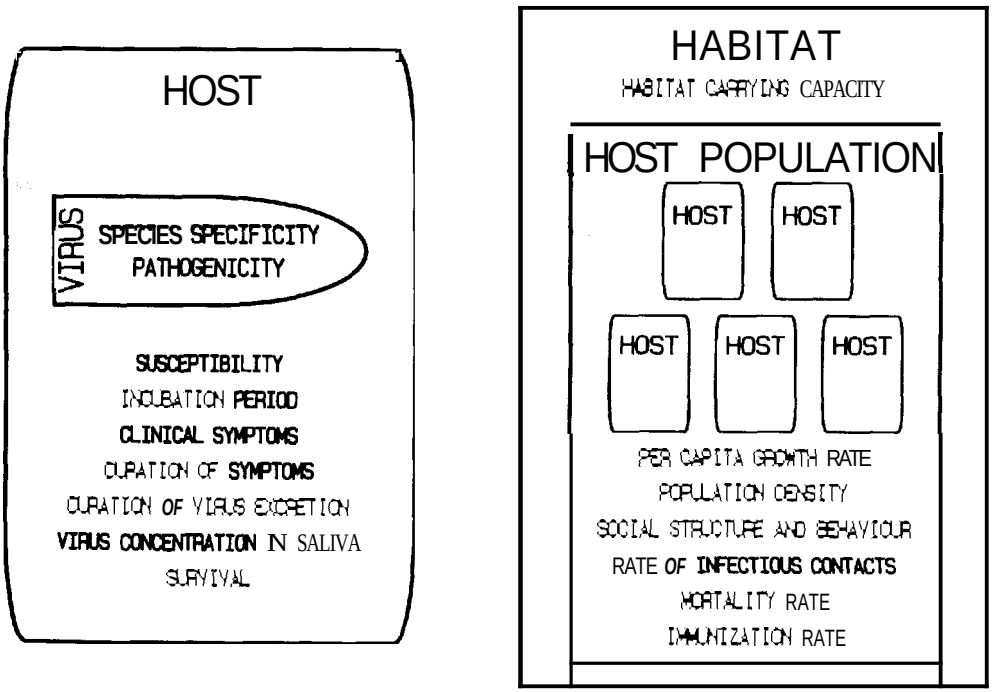

Fig. 1 – Schematic representation of habitat, host population, host individual, and pathogen characteristics and their importance for host-pathogen interactions.

EPIDEMIOLOGY OF RABIES IN CARNIVORE POPULATIONS

Our knowledge of the mechanisms leading to the spread and maintenance of rabies in carnivore populations is still quite incomplete. Nevertheless, careful surveillance of an epidemic reveals important information. Fox rabies in Central Europe is probably the best surveyed epidemic. Here, rabies disappeared for unknown reasons around the turn of the century. A new epidemic in foxes originated in Eastern Europe during World War II. Its frontwave progressed slowly, but rather continuously toward the west and southwest, until it came to standstill in the middle of France and in northern Italy. The features of this epidemic in Europe have been described and analysed by numerous authors (Wandeler et al., 1974; Bogel et al., 1976; Toma and Andral, 1977; Macdonald, 1980; Steck and Wandeler, 1980; Blancou, 1988). The progress of epidemic waves is stopped within zones of low fox density (Wandeler et al., 1974) and within areas where more than 60% of the fox population is immunized through oral vaccination (Steck et al., 1982; Wandeler et al., 1988). Where rabies itself and fox control reduce the fox population below a certain level, rabies disappears not only in foxes, but also in all other terrestrial mammal species (except bats). This is a further indication that foxes are not only the victims, but also the only important terrestrial vectors of present-day rabies in Europe.

The survival of rabies depends on the virus being transmitted by an infected fox to enough other susceptible individuals during the short period of virus excretion. The rate of infective contacts is density dependent; rabies transmission ceases when population density drops below a certain level. In summer and autumn only a small proportion of juvenile foxes are found rabid reaching adult level of infection only during winter (Wandeler et al., 1974). This temporal pattern of the incidence of rabies in different age groups is certainly not the result of differences in susceptibility, but of the different social behaviour of juveniles and adults. It seems probable that adults attack sick disoriented foxes intruding into their territory, while juveniles avoid outsiders. It should be remembered that for rabies transmission to occur, the participation of both a sick and a healthy fox is required. A sick aggressive fox may bite a healthy individual only if the latter responds to the challenge. The willingness to respond may depend on age, sex and social status, and may also vary in a yearly cycle linked with the establishment of territories and mating. Fox rabies spreads through a landscape from territory to territory, and only rarely over larger distances. This is also suggested by the observation of radiotagged infected foxes (Andral et al., 1982) dying from rabies within or close to their original home range. Only occasionally is rabies brought into a new area by an infected subadult animal dispersing during its incubation period.

Table 1 lists the most important species of the order "Carnivora" recognized as main hosts of rabies in different parts of the world. They are ail able to support initial epidemics of high case density and thereafter an oscillating prevalence over many years. They are all small to medium-size (0.4 - 20 kg) omnivores, scavenging, and preying on rodents, other small vertebrates, and invertebrates. When available,

they also collect cultivated fruit and corn crops, and they profit from garbage and refuse produced by humans. Their generalist foraging behaviour enables them to reach highest population densities in and near human settlements. The available information on reproduction suggests high intrinsic population growth rates, allowing a rapid recovery of populations decimated by persecution or disease.

Several other carnivore species besides those listed in Tab. 1 may also function as principal hosts of rabies. Gray foxes (*Urocyon cinereoargenteus*) in some North American areas (Winkler, 1975; Carey et **al.,** 1978), and introduced raccoon dogs

Tab. 1 – Main hosts of rabies.

SPECIES	GEOGRAPHY OF HOST FUNCTION	SOCIAL ORGANIZATION	ECOLOGY, FOOD RESOURCES	r*	REFERENCES ON RABIES EPIDEMIOLOGY
Canis familiaris (domestic dog)	Africa Asia Latin America	hierachical	generalist refuse by owners	2 - 4 partial control	I
Canis aureus *Canis mesomelas* (jackals)	Asia, Africa Africa	territoriai	generalist refuse, fruit, carrion, inverte-brates, small mammals	2.5	2
Vulpes vulpes (red fox)	Northern Asia Europe NE North America	territorial	generalist refuse, fruit, carrion, inverte-brates, small mammals	2.5	see text
Mephitis mephitis (striped skunk)	American Midwest California	hierachical	generalist refuse, fruit, carrion, inverte-brates, small mammals	2.5	3
Procyon lotor (raccoon)	Southeast and Midatlantic USA	hierachical	generalist refuse, fruit carrion, inverte-brates, small mammals	2	4
Herpestes sp. (mongooses)	Carribean Islands South East Asia?	hierachical	generalist refuse, fruit, carrion, inverte-brates, small mammals	2	5

* estimated number of young born per adult per year

References: 1 = Baer and Wandeler, 1987, Wandeler et al., 1988; 2 = Foggin, 1985; 3 = Parker, 1975, Charlton et al., 1988; 4 = Burridge et al., 1986, Jenkins et al., 1988; 5 = Everard and Everard, 1988; for references on host species biology see Eisenberg, 1981.

(*Nyctereutes procyonides*) in Eastern and subarctic Europe (Cherkasskiy, 1988) are sometimes suspected of supporting independent epidemics. Arctic rabies is not well understood, it may differ considerably from the general picture of carnivore rabies described above. *Also* not very clear is the role played by other small to medium-size wild carnivores in Africa, Asia, and South America. It is important to note that a particular species may serve as a main host only in a limited part of its distributional range, while in other sections other species are responsible for the maintenance and spread of rabies. This is especially obvious with North American carnivora.

The epidemiological features of rabies in other carnivore hosts are not too different from what has been described for fox rabies. But besides common denominators there are also differences between the main host carnivores. In most areas studied, red fox and blackbacked jackal appear to occupy relatively small and distinct family territories. But the other species serving as principal hosts are usually nonterritorial. The home ranges of a large number of individuals may be overlapping. In these species territorial defense cannot be the mechanism driving a healthy individual to fight with an abnormally behaving animal. Other aspects of their social organisations must allow for infectious contacts, e.g. dominance hierarchies during the concurrent use of foraging sites or shelter by many individuals. It is also possible that during such gatherings an aggressive rabid animal succeeds in attacking conspecifics by surprise. But as hypothesized for the territorial red fox, a normal individual must usually answer the challenge of a diseased one in order to receive an infective bite.

Populations of a number of bat species also maintain independent epidemics. These chiropteran species do not fit the above characteristics of carnivore rabies hosts. All of them are ecological specialists and have very low intrinsic population growth rates. Properties of lyssaviruses adapted to bats must therefore be different from those of carnivore rabies.

During an epidemic in the principal host, rabies cases in nearly all other species of mammals occur with different frequencies. But these are more sporadic, being spatially and temporally isolated. Short chains of intraspecific transmission are rare in species other than the principal hosts, e.g. in badgers (*Meles meles*) in Central Europe. Here the population densities of both foxes and badgers, but no other species, are perceptibly reduced by a rabies epidemic. Badger populations, however, recover so slowly that they would not be able to support rabies in an area over a prolonged period. Other carnivores reaching considerable population densities in Central Europe are listed in Tab. 2. None of them support independent rabies epidemics. Patterns of spatial distribution and low per capita growth rates may have precluded the adaptation of the virus to some of these potential hosts. The reasons for the lack of adaptation are not so obvious with other species, e.g. the domestic cat. But a sudden access to a new host species may occasionally occur. The appearance of a rabies epidemic in raccoons in Florida, **USA,** in the early 1950s may reflect such an event (Burridge et al., 1986). Thereafter, raccoon rabies became well established in south-eastern and mid-atlantic United States (Jenkins et al., 1988). The virus that spreads among raccoons is an antigenic variant distinct from other carnivore rabies viruses on the continent (Smith et al., 1984).

LYSSAVIRUSES

Rabies and other bullet-shaped viruses found in plants, arthropods and vertebrates are assigned to the family Rhabdoviridae (Knudson, **1973).** Some members of this family have very wide host ranges; others infect just one species. They can be grouped in genera of serologically related viruses (Tesh et al., **1983).** Most of the mammal rhabdoviruses belong to two closely related genera, the genus *Vesiculovirus* and the genus *Lyssavirus* (Matthews, **1982).** Rabies virus **is** the type species of the genus *Lyssavirus*. Other members of this genus are Lagos bat virus, isolated from bats in several African countries; *Mokolavirus* from shrews, humans, and **cats,** also in several countries in Africa; Duvenhage virus from bats and from a man bitten by a bat in South Africa. Obodhiang and Kotonkan viruses, two rabies-related insect viruses, also originate in Africa. The fact that almost all the isolations of rabies-related viruses were made in Africa once suggested that this continent of high *Lyssavirus* diversity is also the cradle of the species rabies (Shope,

Tab. 2 – Characteristcs of some free ranging carnivores in rural zones of the Midlands and prealpine area **of** Switzerland

SPECIES	ECOLOGY FOOD RESOURCES	r*	DENSITY INDIVIDUALS /KM^2	DISTRIBUTION	CAUSE OF MORTALITY	REFERENCES
Canis familiaris (domestic dog)	generalist refuse	0,2**	8	uniform	distemper parvovirus age	1
Meles meles (badger)	generalist invertebrates grain, fruit	**0,3**	0,5	uniform	? rabies hunting	**2;6**
Vulpes vulpes (red **fox)**	generalist refuse rodents invertebrates	2,6	6	uniform	rabies sarcoptic mange hunting	3;6
Felis catus (domestic cat)	generalist refuse rodents	1,7	*22*	uniform	FIP leucosis culling	4;6
Martes foina (beech marten)	generalist refuse rodents	0,7	5	unifrom	distemper arnyloidosis	5;6
Mustela erminea (stoat)	specialist *Microtus Arvicola*	**3**	0,5	patchy	?	6

* estimated number **of** young born per adult per year in examined arca
** reproduction controlled by owners
References: **1** = Matter, 1985; *2* = Graf, 1988; 3 = Capt und Stalder, 1988; **4** = Reist und Moser, 1987; *5* = Blaser, 1984; 6 = **Swiss** Rabies Centre, unpublished data.

1982). But the recent discovery of the widespread occurrence of other "rabies-like" viruses in bats in the palaearctic may challenge this statement (King and Crick, 1988).

Each rabies virion contains one molecule of linear, negative-sense single stranded **RNA** of about 10,000 nucleotides. The virions are built of five structural proteins: L, N and NS ($=M_1$) are associated with the nucleocapsid, M ($=M2$) and G with the envelope (Cox, 1982). The glycoprotein G forms the surface spikes. It is the only rabies protein inducing neutralizing antibodies (Cox et al., 1977). G protein is also the rabies virus hemagglutinin. It probably has an important function during the adsorption and penetration of viral material into a cell and bears at least one virulence determinant.

Variations of antigenicity of the rabies are not so obvious. The antibodies of mammals immunized with rabies virus of different origin usually do not discriminate between different strains in ordinary cross neutralization tests. Furthermore, rabies strains so far analysed display between 90% and 98% amino acid sequence identity (Tordo and Poch, 1988). Only monoclonal antibodies produced by cloned hybridoma cells distinguish clearly between strains with different passage histories (Wiktor and Koprowski, 1978, Flamand et al., 1980), isolates of different geographic origin (Sureau et al., 1983), and between rabies viruses circulating in different host populations (Smith et al., 1984, 1988; Smith and Baer, 1988). Within an area of predominant fox, skunk, or raccoon rabies there is very little virus variation. ***An*** occasional rabid skunk or raccoon in a fox rabies area yields virus with fox rabies characteristics, and vice versa.

When comparing virus isolates of different origin, as we have done by looking at epitopes of the capsid protein N with monoclonal antibodies (Fig. 2), one rapidly realizes a number of interesting facts. European carnivore viruses resemble the carnivore isolates from other parts of the world, but the differences among wild carnivore strains are greater than those among the dog isolates from different continents, The American bat strains bear more resemblances to carnivore viruses than do the European chiropteran viruses. One could note in addition that the label "Duvenhage" for the European bat isolates was probably a mistake.

Adaptations to different hosts have been documented to some extent by in vivo experiments. Sikes (1962, 1966) demonstrated marked differences between species in susceptibility to intramuscular injection of American street rabies isolates. The calculated virus doses necessary to successfully infect 50% of the inoculated animals was as follows: less than 5 M.i.c.LD_{50} for foxes, 500 M.i.c.LD_{50} for skunks, 1000 M.i.c.LD50 for raccoons, and more than 80,000 M.i.c.LD_{50} for opossums. The extremely high susceptibility of red foxes (*Vulpes vulpes*) was confirmed by several authors using American and European fox rabies isolates (Parker and Wilsnack, 1966, Black and Lawson, 1970, Winkler et al., 1975, Blancou et al., 1979; Steck and Wandeler, 1980). Parker and Wilsnack (1966) used a skunk isolate and they found that foxes and skunks are equally susceptible to it. Foxes were suceptible to low doses of a canine rabies virus from North Africa, but they resisted the injection of higher doses and became immune in experiments conducted by Blancou et al. (1983). This may be taken as an indication that virus strains circulating in different main hosts also bear a variety of adaptations to them.

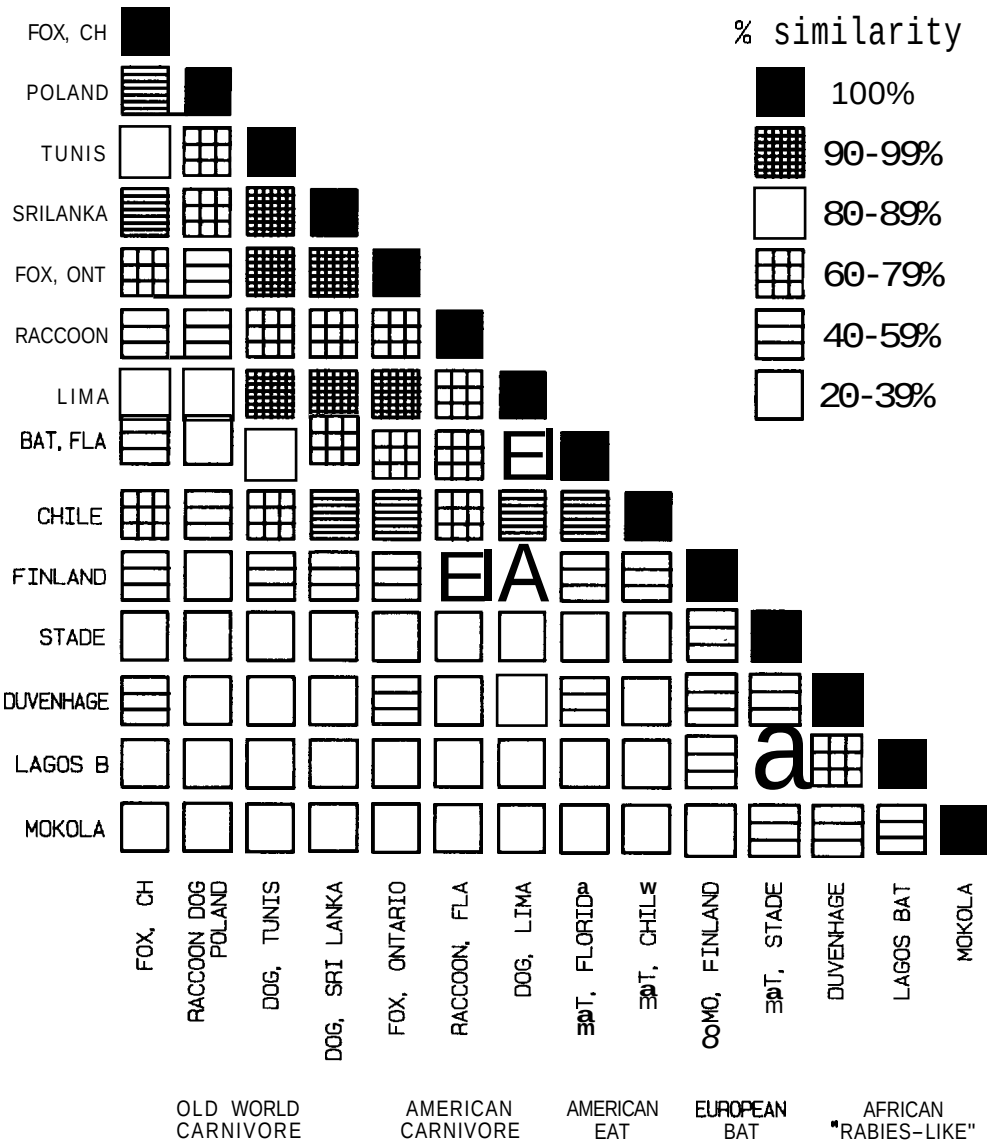

Fig. 2 – Similarity of lyssaviruses and rabies virus strains as determined with monoclonal antibodies directed against N-protein (data: H.Gerber, A.I. Wandeler, Swiss Rabies Centre).

Present day lyssavirus classification is unsatisfactory and it is unfortunate that modern techniques such as genome sequencing and epitope comparisons are not yet used for more appropriate classifications. Nevertheless, the extraordinary similarity of large parts of the genome (Tordo and Poch, 1988) and of many epitopes (King and Crick, 1988) among ail examined lyssaviruses suggests a common origin. There arises a series of interesting questions concerning the phylogeny of rabies viruses. Did the neurotropic lyssaviruses evolve from epitheliotropic vertebrate rhabdoviruses (such as vesicular stomatitis virus) or was it arthropod rhabdovirus acquired by insect eating mammals (e.g. bats); Was rabies from the beginning a virus adapted to carnivores, or was it a bat virus first? A transfer from bat to terrestrial mammals seems to be more likely. Looking at the features of carnivore rabies today one wonders where rabies was before man helped to develop dense and continuous populations of the actual host species by creating and providing the necessary resources. But lyssavirus adaptations to low density hosts are not necessarily impossible; they may even exist today (arctic rabies?), we do not understand them yet. Particular speculations may carry more weight when they receive support from cladistic approaches to virus classification.

Rabies virus strains and their hosts have to be coadapted in order to allow their prolonged coexistence. Coadapted (or coevolved?) traits are pathogenicity, cell specificity (including species specificiiy), length of incubation period, duration and magnitude of virus excretion, duration and symptoms of clinical illness, per capita population growth rate of the host, its use of resources (habitat use), social organization and behaviour, and mortality factors other than rabies. These virus and host properties determine rates of infectious contacts and all other epidemiological parameters such as incidence, prevalence, morbidity, and mortality rates. As a concequence, each host species has to have its own adapted virus, This seems to be the case, as suggested by susceptibility and epitope studies. But one should keep in mind that the differences in virus strains recognized by monoclonal antibodies do not necessarily reflect adaptations; they could also document random genetic drift in ecologically isolated virus clones.

The terms coevolution and coadaptation may be somewhat misleading. The features of the virus-host associations as we observe them today are the actual outcome of arms races; arms races between the hosts defending themselves against exploitation by the viruses, and the viruses finding counteradaptations for circumventing host defenses.

A mammalian organism has numerous possibilities to defend itself against an infectious agent. They may be classified as follows:

1. Antigen recognition and immune responses are very well explored, so the number of recognized factors controlling, contributing and modifying them is continuously increasing. The role of naturally acquired immunity in rabies pathogenesis and epidemiology is somewhat controversial (see Wandeler, 1987, for discussion). In most cases, rabies virus does not induce efficient immune responses and/or is capable of escaping its effects (Murphy, 1977). But one would expect that

mechanisms and behaviours leading to immunisation (e.g. by cannibalism of infected conspecifics) should spread in a population in the presence of rabies.

2. Resistance not directly dependent on immunity and not due to interferon is less well understood. Since there are species differences in susceptibility (or resistance), one may well consider individual differences also, e.g. due to histocompatibility complexes. Such strain differences in susceptibility to rabies are known from laboratory rodents (Lodmell, 1988). Whether they play any role in the association of a particular virus strain with its main host remains questionable. Bremermann (1980, 1981) and Hamilton (1982) suggested that frequency variations of alleles for resistance to parasites are of considerable importance for the evolution of sexual reproduction. It seems obvious that the intensity of selection for host protein variability varies with the parasite. It might be low with enteric helminths and high with parasites living exclusively on host proteins. Rabies, like many other viruses, interacts with host molecules (receptors), whose variation is limited by physiological constraints. The hypothesis has received very little consideration in either theoretical or empirical studies, with the exception of the inferences drawn on mate choice.

3. An animal's ability to recognize the health status of a social partner especially of a potential mate, has received some attention in recent years. Hamilton (1982) and Hamilton and Zuk (1982) suggested that bright male sexual characters might allow females to assess the genetic resistance of their mates to parasites. Looking through the 1986 Dahlem Workshop Report on "Sexual Selection" (Bradbury and Andersson, 1987) one does not find too much support for this hypothesis. As Kirkpatrick (1987) points out, variation in male performances may simply reflect magnitudes of parasite loads or severity of infection, and not necessarily genetic resistance to parasites. It seems clear that the recognition of an infectious social partner is as advantageous as the recognition of any other potentially hazardous situation. Viability indicators (good genes) of a partner and the avoidance of an infectious situation both have fitness consequences. An experimental distinction may not be simple.

4. Trying to generalize point 3 gives rise to a very unsatisfactory situation. Today, behavioural ecology favours resource availability patterns as ultimate causes for the evolution of foraging and social behaviour. Resource distribution was also declared responsible for the social organization of different species of carnivora (Macdonald, 1983). Unfortunately, the evolution of behaviour under the selective influence of infectious agents is today virtually unexplored. One notable exception is Freeland's paper on "pathogens and the evolution of primate sociality" (1976). Freeland attributes .fitness consequences to pathogen transmission during nearly every aspect of social behaviour. In dividing the fitness "pie" into pieces (Vehrencamp and Bradbury, 1984) one important component has been overlooked; it may be named "epidemiological terms".

5. Soma defense mechanisms are costly. These mechanisms should, in relation to cost and benefit, not be maintained forever, but only for the time span during which they bring a relevant increase in fitness. One would therefore expect a number of potentially lethal conditions to occur predominantly in older individuals. This argument is taken from Kirkwood's (1977) disposable soma

theory (see also Kirkwood and Holliday, 1979). To my mind, similar reasoning could be applied to any host defense mechanism, whether structural, physiological or behavioural.

One example may illustrate some aspects. If our interpretation of rabies transmission within a fox society is correct, then every animal not participating in territory defense increases its life expectancy considerably. Not helping to defend the parents' territory, and engaging in territorial behaviour only as an adult, still increases the chances of reaching reproductive age. That this is only an expression of a more general parent-offspring conflict does not depreciate the value of postponing risky behaviour as long as possible.

The tricks played by parasites for avoiding the negative effects of host defense mechanisms are well described (Bloom, 1979; Kennedy, 1984). Rabies virus, spreading its genome inside neurons within an organism, is thereby avoiding contacts with immunocompetent cells. As important as avoiding being eliminated too quickly are mechanisms for tricking an infected host into transmitting parasite progeny to susceptible ones. The rabies virus genome manipulates the host organism on every possible level. It first obtains admission into cells surreptitiously by binding to membrane receptors, then it usurps cellular mechanisms for making viral proteins and genome copies, then it takes advantage of the host physiology in order to spread in the organism and be excreted, and it finally abuses the interactions of individuals in a population for transmission to other hosts/victims.

The arms races between rabies viruses and their carnivore hosts are asymmetrical, so Dawkins' life/dinner principle and rare-enemy effect (Dawkins, 1982) both apply only partially. The hosts have every interest in eliminating the viruses, the viruses have no interest in eliminating host populations. The first statement is clear, the second is problematic. The viruses (a virus clone) in a host individual are bound to act in their own selfish interest to be transmitted. The need for transmission hinders an evolution towards attenuation (Anderson and May, 1982). Could it be that virus variants causing too heavy losses in the host population bring themselves to extinction before they completely eliminate the host species? These questions are only partially solved by theoretical models of coevolution, none of them holding all the answers (see Levin, 1983 for discussion and references).

Very important differences between the contestants are represented by the potential rates of evolution (Hamilton, 1982). The generation times of the hosts are on the order of twelve months, those of the viruses on the order of a day (they may be considerably longer during the latent phase of incubation). There are millions of descendants of a single infecting particle in one host individual, and the number inoculated by bite into the next victim may still be many thousands. In addition, the mutation rate of the genomes of RNA viruses is very high, a thousand to a millionfold higher than that of DNA genomes (Holland et al., 1982). This might in part be due to the fact that DNA replication is checked by exonucleases, while there is no proof-reading enzyme for RNA replication. The variability allows rapid evolutionary changes. One wonders that host species have any chance to survive. I doubt that survival of hosts is fully explained by their flexibility in resistance. Why is adaptive radiation not more common among the lyssaviruses? If

we look at the consequences of possible changes of rabies virus properties (Tab. 3), then we may feel that this virus is trapped in its ecological niche. Adaptations to new hosts or the adoption of other transmission strategies may both be difficult due to structural and functional constraints or may need too many simultaneous coadapted changes. That there are such constraints is indicated by the fact thay many epitopes recognized by monoclonal antibodies are conserved over a wide range of lyssaviruses and rabies strains. No doubt there are also constraints making it difficult for the hosts to win the race against the virus, e.g. physiological necessities of receptors usurped by viruses.

Some of the above puzzles may be relatively easy to solve. Important circumstantial evidence can be gathered by a more rational approach to virus classification and phylogeny. There is in addition an urgent need for exploring the fitness consequences of host behaviours abused by parasites. Other problems are

Tab.3 – Alternative strategies of rabies viruses and of carnivore hosts: consequences and constraints.

STRATEGY	CONSEQUENCES + CONSTRAINTS
RABIES VIRUS:	
change of receptor (cell) specificity	loss of easy access to central nervous system (as in some attenuated virus strains)
change of host specificity	loss of epidemiological correlation with parameters of the host population
change in pathogenicity	loss of bchavioral mechanisms of virus transmission
CARNIVORE RABIES HOST:	
improvement of peripheral immune surveillance for an early virus recognition and immune response	increase in number of allergic responses (?)
increase in number of molecular sites functioning as virus receptors on peripheral cells (increased peripheral virus replication, earlier immune response)	loss of physiological function of receptors
structural change of molecular sites functioning as virus receptors (reduction in susceptibility)	loss of physiological function of receptors
avoidance of all contacts with potentially infectious conspecifics	abstinence from competition (resource defense), cooperation, mating, etc.
recognition of infective animals (avoidance of contacts with infective animals)	no constraints (?)

more complicated. Some of the present contradictions may be solved when ecologists **and** ethologists complement the too comfortable optimality reasoning with ideas of "equilibria" and "gene selfishness".

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