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THE EPIZOOTIOLOGY OF RABIES

An inter-disciplinary working party has recently discussed the use of quantitative methods in studying the transmission of rabies. Mathematical models may help to identify control measures necessary to prevent spread if the disease were introduced to Britain, but many biological problems need further research.

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1. Introduction

In 1977 a Working Party on Quantitative Studies in the Epidemiology of Rabies was formed on the initiative of the Royal Statistical Society. The Working Party, which now receives financial support from the Institute of Terrestrial Ecology, brings together workers from different disciplines (including animal disease control, ecology, virology, statistics and data processing) and different institutions (universities, research institutes and government departments) to discuss the use of quantitative methods in the study of the transmission of rabies. These include the collection of quantitative data and the use of mathematical and computer-based modelling. Apart from encouraging collaboration between biologists and specialists in numerical sciences on specific research projects, the Working Party was held two meetings, the latter of which was at the Institute of Terrestrial Ecology, Merlewood on 9-12 April, 1979. The aim of this meeting was to emphasize and consider the feasibility of a systems approach to the study of the transmission and control of the disease. The attendance was enlarged to include a number of additional workers with varied experience of rabies studies, notably L. Andral and J. F. Boisvieux from France, J. Berger from Germany and C. O. R. Everard with recent experience of mongoose rabies in Grenada.

In the present article we summarize the general trend of the presentations and discussions and indicate some of the problems left for further study.

2. A Systems Approach

An attempt was made to consider the complete epizootic process without concentrating unduly on any one scientific discipline. It seemed particularly important to identify -

(i) which host species needed to be included,

(ii) which processes e.g. transmission, mortality, dispersal, should and could be modelled in detail, and

(iii) what factors determined the outcomes of these processes.

The discussion concentrated in turn on four key aspects of rabies epizootiology; virology; host ecology; control methods, and modelling. We discuss each of these below.

In practice it is difficult to determine the causative factors for many processes. For example, is the frequency distribution of incubation times an attribute of the host, of the virus or of an interaction between them? On evolutionary grounds, using game theory, we can argue that selection on the virus might have produced the observed distribution of incubation times to permit virus survival under a wide range of host densities. A similar argument could explain the 'dumb' and 'furious' forms of rabies, the former being selected to promote persistence within groups, the latter to allow spread between groups of hosts.

Rabies control techniques should be designed to exploit appropriate aspects of the situation, and integrated to give maximal overall effect. Practical and financial constraints may, of course, prevent the use of the optimal combination of methods. If control using immunization were possible, natural selection would operate in favour, not (as usual) against it, since foxes not taking vaccine would probably die from rabies. In such circumstances, long-term control policies might succeed, particularly if immunization is combined with the use of temporary sterilants to prevent immunized individuals producing susceptible offspring.

3. Virus Biology

The clinical aspects of the disease and its basic development within the host are well documented but poorly understood. In general the causes of particular effects are too poorly known to be modelled. Research could provide answers to some of these questions, for example the effects of different virus strains on different host species: such work would be costly but worthwhile.

The participants agreed that there were insufficient data to justify the construction of detailed models of rabies virology, (e.g. virus proliferation within the host and its effects on the host) or for describing in quantitative terms the effects of the virus on its host. The curcial persistence of rabies virus at low fox densities could be attributed to long incubation times, latency, temporary reservoirs of virus in other species or protracted survival of a few infective individuals. Data are currently quite inadequate to distinguish between these possibilities; accordingly, low-density aspects of wildlife epizootics cannot be accurately modelled.

There are many imperfectly understood aspects of behaviour of animals with rabies. 'Dumb' and 'furious' rabies are to some extent misleading terms since most rabid carnivores display both types of symptoms to some degree. All rabid individuals can transmit the disease. There are considerable differences between and within species in the distances moved by 'furiously' rabid individuals.

Another important question is the nature of the infectious period. If 'furiously' rabid animals are infective mainly before symptoms appear, as some think may be the case, their 'furious' movements may be largely irrelevant. Much basic research on rabies virology is needed, and should be undertaken. For example, it would be useful to know whether British and continental foxes are similar in their susceptibility to current strains of virus. Models are needed to highlight the virological aspects which need most urgent study.

4. Host Ecology

The principal host in Europe is undoubtedly the red fox, and discussions of possible epizootics in this country naturally focus on the same species. Many important aspects of fox ecology are adequately documented. However, there are some key areas of fox population dynamics and social behaviour which are poorly understood and for which existing data are quite inadequate for modelling purposes. Further ecological research could largely fill these gaps and such work should be undertaken. There was general agreement that efforts should be made to relate the characteristics of rabies epizootics to the habitats through which they spread and to investigate whether variations in fox densities between such habitats could account for the different characteristics of spread. Some work has been done, and more is feasible, to study these questions using field data from Europe. Special effort should be made to analyse the spread of rabies among foxes when rabies is diagnosed in only a few animals located in isolation in a rabies-free area.

The discussants agreed that models of rabies spread in fox and other populations were both feasible and desirable and that the relationships between habitat, population density and structure and the characteristics of rabies epizootics should be investigated. In view of the possibility, already mentioned, of virus transmission in a pre-symptomatic infective period, interactions between apparently normal foxes are highly relevant and may be over-riding. Detailed studies of the behaviour of normal foxes need to be continued and developed.

There was less agreement on the form that the models should take. Models of homogeneous populations are easier to build and understand, but there was considerable support for the view that habitat heterogeneity could easily be of over-riding importance.

A distinction was made between the requirements of models for Britain and Europe. Throughout much of central Europe rabies is spreading among foxes and from them to domestic animals and thence to man; other species may be involved. If the disease enters Britain it is most likely to start in domestic dogs or cats, possibly smuggled, and a model of the interactions of these (and other species) is needed to evaluate the probability of spread to, and persistence in, British foxes. Outbreaks in Britain are more likely in urban and suburban areas where fox densities are often high, interactions between species quite frequent and control measures difficult to implement effectively.

5. Control Methods

It is important to distinguish between control to eliminate rabies from a small localised area, control to prevent the spread of rabies to, or elimination of rabies from, wide geographic areas and measures appropriate for islands which are free from the threat of continuous re-invection. Strict quarantine procedures are by far the most effective preventive control option for Britain.

In rabies endemic areas immunization of wildlife is a very attractive potential means of control, but at present there is some doubt about the safety of vaccines available for use in the field. Furthermore, undesirable features associated with the use of attenuated oral vaccines * preclude their use in Britain although a much stronger case could be made for their use in countries where rabies was already established. The combined use of immunization and sterilisation might well lead to more effective control than the separate use of these measures. Currently, control methods rely on the reduction of fox population densities to levels below the thresholds at which epizootics

* The attenuated vaccines could give rise to virulent mutant strains that would cause rabies rather than prevent it.

can persist (usually about 0.2 foxes Km^{-2}). A similar effect could be produced by suppression of breeding, but this technique could only be effectively implemented at some seasons. In the interests of non-target species one could only advocate the use of temporary sterilants The effectiveness of methods of population reduction vary with season and habitat: a control scheme must be flexible, adaptable to circumstances and logistically practicable.

It was emphasised that public awareness and cooperation in rabies exclusion and control were vital: information and correct reaction protects people more effectively than vaccination. Concern was expressed that the publicity campaign in Britain was occasionally mis-interpreted: some people erroneously thought, as a result of publicity, that rabies was already present in Britain and hence believed the disease unimportant and that the continued quarantine regulations were unnecessary. Appropriate publicity should enhance the acceptance of control measures. Official attempts to reduce fox numbers prior to rabies entering Britain would be pointless. However the public might usefully be informed that foxes visiting dustbins and compost heaps could, in the event of a rabies outbreak, provide the most direct link with domestic animals and thence man. Encouragement of more sanitary garbage disposal would be a useful step in reducing the proximity of foxes with man and domestic animals.

Concern was expressed that control measures involving widespread reduction of the fox population had largely failed on the continent; on occasions severe public opposition to such control has been encountered. It was recognised, however, that containment of an isolated outbreak such as might arise in Britain was much easier than stopping the spread of a well-developed epizootic wave or eradicating enzootic rabies. There are examples of the successful containment of isolated outbreaks. However, owing to the high densities of urban and suburban foxes in many areas of Britain, acceptable control schemes appropriate to serious local outbreaks are necessary and are being developed.

6. <u>Modelling</u>

A number of mathematical and computational techniques were described and discussed. These had three basic aims. First to analyse the data on rabies spread and remove random 'noise' and thereby obtain a better picture of the underlying course of events; second, to build 'simulation' models based on known parameters of rabies epizootics with the aim of identifying the key aspects of the process (including habit effects); third, to assess the effectiveness of control programmes and their consequential effects on the populations being controlled.

It was agreed that all three approaches had merit and should be followed up by small groups of ecologists and modellers, each group keeping in close touch with the other groups.

It is too early to point to any clear inferences to be drawn from existing models of rabies epizootics, except that their development serves as a spur to biologists to identify the crucial aspects of transmission and to highlight those features which are inadequately understood. Most published models have been stimulated by problems arising in countries where rabies is enzootic; such models aim primarily to simulate the transmission process and to identify control measures which may affect the extent and speed of transmission without exterminating the disease. In the United Kingdom interest focusses on the conditions under which the disease could infect wild animals and would or would not spread if it were introduced. In terms of epidemic theory the aim is to ensure, by local control measures, that the net reproduction rate of the disease is sufficiently low to ensure that any case produces on the average less than one new case. Modelling in isolation cannot answer this question, but it may be able to indicate to the biologists and disease control authorities which parameters of the transmission process need to be determined by field studies before a clear answer can become available.

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The following are listed to provide a general background for readers wishing to pursue this topic in greater depth: these references are NOT specifically cited in the text NOR are they a comprehensive list of background references.

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