Original Articles

Rabies control and management

ERICK S. NICHOLLS,* MD, DPH
JOHN W. DAVIES,† MB, BS, DPH, M SC

Since the 1950s rabies has become a familiar threat in southern Canada. Periodic outbreaks remind us how slight our control over it is. Although new vaccines such as human diploid-cell rabies vaccine have greatly improved the management of rabies in humans, true control must be sought through knowledge of the disease in our wildlife. A guide to rabies prophylaxis in humans is presented, courtesy of the National Advisory Committee on Immunization.

Depuis les années 1950 la rage est devenue une menace familière dans le sud du Canada. Son apparition périodique vient nous rappeler la faiblesse de notre contrôle sur cette maladie. Bien que de nouveaux vaccins, tels que le vaccin rabique préparé sur cellules diploïdes humaines, aient considérablement amélioré le traitement de la rage chez l'humain, un contrôle véritable doit être recherché dans les connaissances que nous possédons sur la maladie dans notre faune. Avec la permission du Conseil consultatif national de l'immunisation un guide sur la prévention de la rage chez l'humain est proposé.

Although rabies in wildlife has long been prevalent above the Arctic Circle, in the more densely populated areas of southern Canada it once affected mainly domestic animals, such as dogs. Since the early '50s rabies in wildlife has spread southward to become enzootic in several provinces. Through contact and infection the epidemiologic characteristics of rabies in domestic animals have been affected as well.[1]

While control of the disease in wildlife is a major long-term objective, the current thrust of our effort is directed at vaccinating pets and protecting potentially exposed persons. Only 21 human deaths were attributed to rabies between 1924 and 1979, and 70% of them occurred before 1944. None the less, rabies prophylaxis in humans has been a complex, risky and often very painful procedure.[2,3]

The recent licensing of the human diploid-cell vaccine (HDCV) for use in Canada promises to simplify the management of persons exposed to rabies. HDCV is highly antigenic, requires fewer injections and causes side reactions less frequently than the older vaccines. While this constitutes a major advance in therapy, it does fail to deal with the source of the problem.

From the bureau of epidemiology, Laboratory Centre for Disease Control, Department of National Health and Welfare

*Medical officer
†Director

Reprint requests to: Dr. John W. Davies, Director, Bureau of epidemiology, Laboratory Centre for Disease Control, Department of National Health and Welfare, Tunney's Pasture, Ottawa, Ont. K1A 0L2

Rabies in animals

The statistics on rabies in animals are derived from the numbers of tissue specimens submitted and found positive by laboratory examination.[4] These constitute a minute and probably unrepresentative sample of the disease's occurrence in nature, yet provide the best available indication of recent trends and of human exposures.

The cumulative total of confirmed cases in animals during a 45-year period prior to the early 1950s came to less than 1000. A steady increase began in 1953, though, and reached a peak of more than 2000 cases in 1958. The situation has been relatively stable during the past two decades, with minor peaks every 3 or 4 years, each exceeding 1000 cases a year. The wildlife cases account for about two thirds of these.

The trend of rabies in domestic animals in Canada has closely paralleled that in wildlife since the early 1960s, in that 3-year peaks are also visible. Cattle are the most commonly affected, followed by dogs and cats. Horses, sheep and goats, among others, are seldom

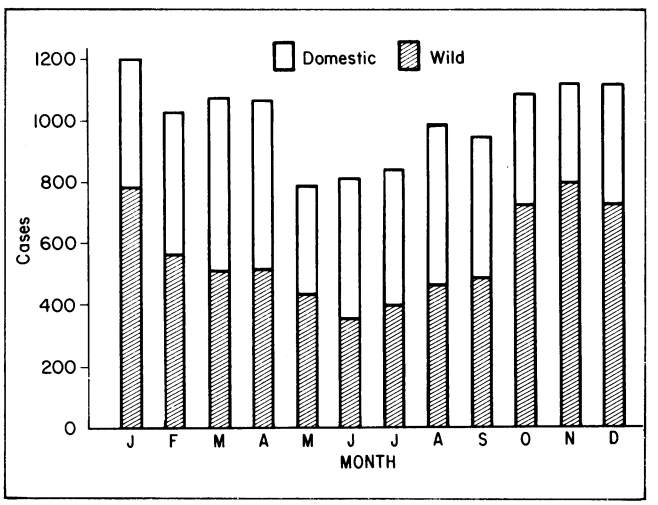

FIG. 1—Seasonal distribution of rabies in domestic and wild animals in Canada from 1968 through 1977. Source of data: Department of Agriculture.

affected. In the United States, by contrast, the trends for wild and domestic animals are quite divergent. The relation between the two groups there is neither clear nor close, and may reflect the success of aggressive prophylaxis programs in reducing the incidence of rabies in domestic animals.[5]

Between 1968 and 1977 inclusive rabies occurred more frequently in the winter months among both domestic and wild animals in Canada (Fig. 1). In 1976 the disease was more prevalent in central Canada and the central plains of the United States than elsewhere in North America, with a few additional foci in California, Florida and Georgia (Fig. 2). The occurrence of rabies is not necessarily associated with higher densities of human populations.

In Canada, between 1967 and 1980, foxes accounted for 62% and skunks for 32% of all cases of rabies reported in wildlife. Others that were occasionally infected included bats, raccoons, wolves and coyotes. In the same period, 80% of the cases in domestic animals and 86% of those in wild animals were in Ontario. Within that province certain areas — for instance, the counties bordering on Lake Huron and the southern part of Georgian Bay, and the eastern region — have persistently reported a high incidence of rabies in foxes. Almost 62% of the rabid skunks were reported in Ontario and 22% in Saskatchewan. Most of the infected bats, on the other hand, were found in the three western provinces as well as Ontario.

The seasonal and geographical distribution of rabies, and the 3-year cyclic trend, have been related to the life cycles of two kinds of wild animals, foxes and skunks. Their habitats, which are only slightly different, overlap throughout most of the central parts of North America.

In areas where there is a large fox population the incidence of rabies begins to rise in the autumn, just when the juvenile male foxes are dispersing and establishing new territories.[6-8] Male foxes have a significantly higher rate of physical conflict than females at this time, but after mating and close to the March parturition period such contact increases among the females too. Computer models simulating the annual rabies cycle that is observed in Ontario and in the United States[9] suggest that the longer, 3-year cycle may be the result of interaction between the fox's life cycle and the mechanisms of rabies transmission.

It is not clear whether transmission can occur in the absence of an epizootic, or if some other reservoir is required to maintain the chain of infection. Furthermore, the role of skunks in this ecologic situation has received little attention.

From this brief historical review of rabies in Canada

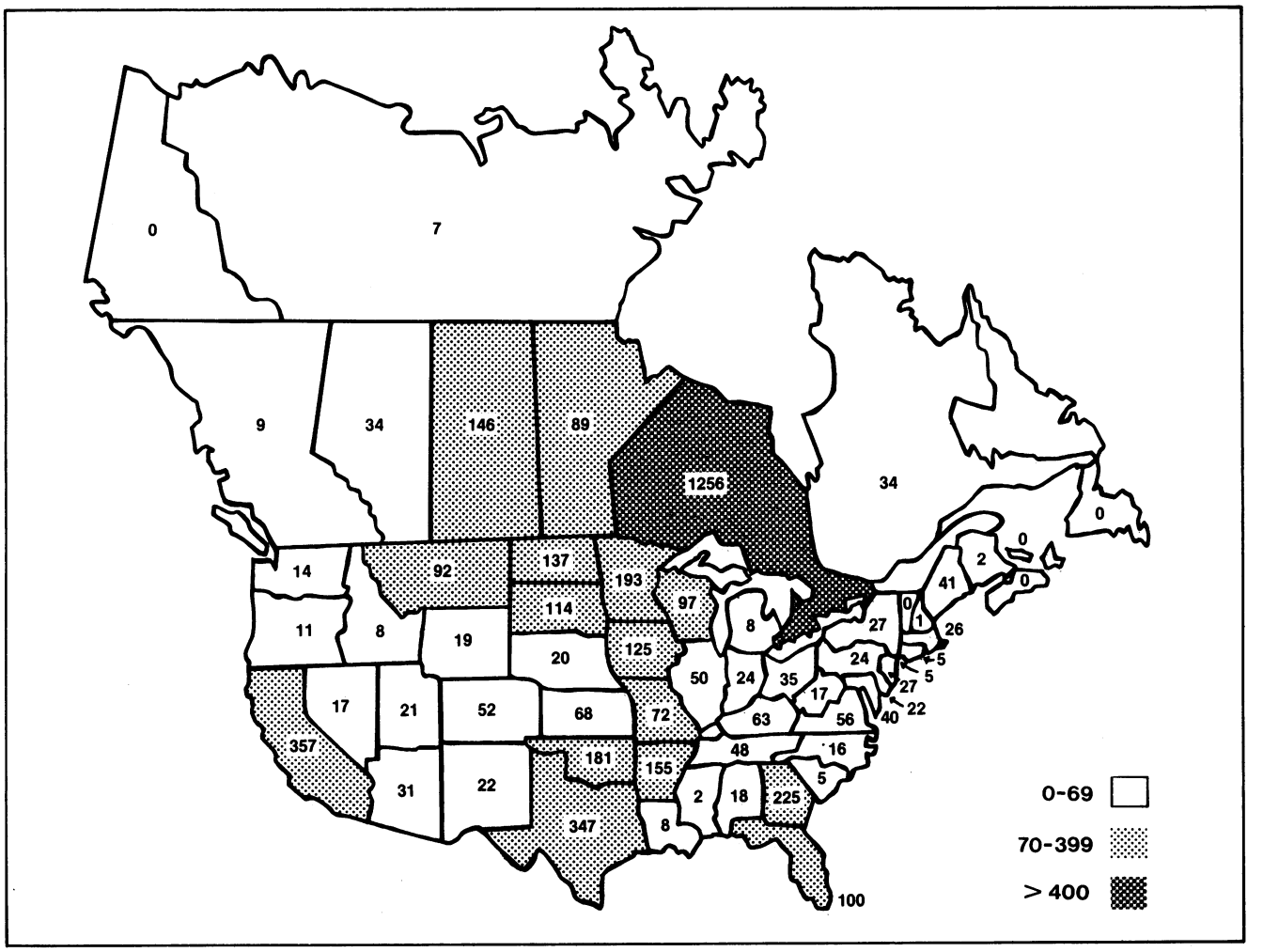

FIG. 2—Cases of rabies in animals in 1976. Source of data: Canadian Department of Agriculture and US Centers for Disease Control, Atlanta, Georgia.

it becomes apparent that the problem is not easing. On the contrary, the disease appears to have become firmly established in our wildlife.

Prospects for control

Several ecologic factors have been called upon in an attempt to explain why wildlife (and particularly fox) rabies became so predominant in Canada. It is generally assumed that the advent of conservation, the reduction in the populations of other wild predators, such as coyotes and wolves, and even changes in agricultural practices may have played a role. However, the most crucial issue involves the practical problem of rabies control.

Wildlife

In Canada it is the high density of fox and skunk populations that seems to be responsible for the perpetuation of the rabies enzootic. Control methods, therefore, are aimed either at reducing the populations to a level that will not support further spread of the disease or at preventing such dissemination through immunization of susceptible animals.[10,11]

Reduction of wild populations may serve to create either a buffer zone or a radial depopulation starting from the site of confirmed cases.[12] This has involved gassing, trapping, shooting and, more recently, the use of poison baits and hormonal sterilization. Oral immunization of wild foxes with ERA strains of rabies veterinary vaccines in baits is in the development stage.[13] Evaluation of the costs and effectiveness of these fundamentally different approaches awaits further study, particularly in view of the rapid turnover of wild populations.[13,14]

Rabies in bats is almost entirely confined to the three western provinces, where close to 50 cases are confirmed annually. Occasionally reports have come from other provinces. A chronic carrier state is found in some Canadian species, and there is potential for transmission of the virus to humans or to other animals by ingestion, bite or aerosol. There is, however, little evidence that terrestrial mammals are infected by bats. Accordingly, action is taken only when there is a definite risk of human exposure.

Domestic animals

Since the late '60s the incidence of rabies in cats and dogs has slowly declined. Presumably this is the result of widespread vaccination. In addition, stricter licensing, leashing requirements and regulations for international transfer together with the elimination of strays may have contributed to the partial control of the disease.[15]

Cattle are now the most frequently involved species owing to their exposure to wildlife in farming areas. This results in substantial economic loss, even though the farmers are compensated. The question of massive vaccination of cattle is not yet resolved, but vaccination does remain the cornerstone of rabies prevention in household animals.

Protection of humans

Humans can be best protected by elimination of the disease in the wildlife reservoirs, particularly foxes and skunks. In the meantime, maintenance of a protective barrier of immunized domestic animals reduces the risk. Even so, several hundred persons require prophylactic immunization every year following exposure to animals thought to be infected. Several groups of people who are at high risk by virtue of occupational exposure, such as animal handlers, veterinarians and certain laboratory workers, require specific protection. Detailed guidelines for rabies prophylaxis have recently been developed in Canada by the National Advisory Committee on Immunization[16] (Tables I and II) and in the United States by the Immunization Practices Advisory Committee.[17] Their recommendations in regard to the management of human rabies are briefly outlined below.

Management after exposure

Rabies prophylaxis must be considered in any biting or scratching incident in which the animal is suspected of being rabid. Contamination with saliva, body fluids or tissues is possible. Depending on the species involved and the circumstances of exposure, prophylaxis is indicated and should consist of two basic measures:

- Immediate and thorough washing of wounds and scratches with soap and water or detergent, this being the most effective procedure in the prevention of rabies. Antibacterial drugs and tetanus prophylaxis should be given as required and an antiseptic lotion (70% alcohol or tincture of iodine) applied to the wound.
- Concurrent immunization with both vaccine and rabies immune globulin for optimum prophylaxis.

The HDCV produced by Institut Mérieux, Lyon, France (M-HDCV) is the only licensed human tissue culture vaccine in Canada at present. It can be obtained on request from provincial health departments. It is safe, efficacious and capable of inducing an excellent antibody response, and is, therefore, the agent of choice for prophylaxis after exposure.[18-20] Few adverse reactions have been reported so far. A follow-up survey of some 2500 patients in the United States who received M-HDCV revealed that 4 (approximately 1 in 625) had had systemic allergic reactions verified by physicians. These ranged from hives to anaphylactic shock.[21] If HDCV is not available, duck embryo vaccine (DEV) should be given. It is now known that practically all vaccinees produce protective levels of antibody, so serologic tests are no longer required when HDCV is given as recommended.[22]

Rabies immune globulin (RIG), human, is recommended in a single dose of 20 IU/kg of body weight as soon as possible after exposure. If RIG is not available, antirabies serum (ARS), 40 IU/kg, may be used, but since ARS is an equine product it causes severe sickness in over 40% of adult recipients.

These treatments may be discontinued, of course, if fluorescent antibody tests of specimens from the animal are negative.

Management of the animals

Animals in Canada suspected of being rabid should be reported to the local medical officer of health and the Canadian Department of Agriculture. Stray domestic animals and those that are wild should be humanely

killed. Damage to the brain must be avoided, for the heads are to be submitted for laboratory examination. Clinically healthy domestic animals involved in biting or scratching should be confined and observed. If they remain well for 10 days the likelihood of their having been exposed to rabies virus is low. If, on the other hand, illness develops, the animals should be killed and their heads submitted immediately for laboratory examination.

Vaccination before exposure

Vaccine ought to be offered to those at high risk by virtue of occupational exposure. A course of three doses of HDCV, on days 0, 7 and any one of 21 to 28, followed by a booster dose every 2 years, or as needed, is recommended. The intradermal administration of HDCV has been shown to induce protective levels of neutralizing antibody and is recommended as an alternative to the intramuscular route for immunization before exposure. The dosage is 0.1 ml on days 0 and 7 and again in the 4th week, followed by a booster dose every 2 years.

When HDCV is unavailable, DEV or hamster kidney vaccine may be used, and then serologic testing is recommended for 2 to 3 weeks later. Rabies antibody determinations may be obtained from the Toronto laboratory of the Ontario Ministry of Health through referral by the appropriate provincial public health laboratory.

Conclusion

Since the abrupt increase and southward spread of rabies in wildlife during the 1950s, the situation in Canada has been fairly stable. Periodic outbreaks of the disease are associated with population peaks and seasonal mobility of the vectors, especially foxes. Through local reduction of their populations,

Table I—Guide to rabies prophylaxis after exposure*

Details of animal	Nature of exposure	Management of exposed person
Rabid Suspected to be rabid Wild animal in endemic area, particularly skunk, fox, coyote, raccoon or bat†	No skin or mucosal contact with animal or casual contact, such as petting, with no possible contamination of broken skin or a mucous membrane	No treatment
Escaped dog or cat in endemic area (unless clearly provoked)	Bite or contamination of scratch, abrasion, open wound or mucous membrane with saliva, body fluids or tissue	Local treatment of wound RIG injections (local and intramuscular) Full course of HDCV‡
Apparently healthy domestic dog or cat that can be held under observation for 14 days	Bite or contamination of scratch, abrasion, open wound or mucous membrane with saliva, body fluids or tissue	Local treatment of wound At first sign of rabies in the animal during holding period give RIG (locally and intramuscularly) and start full course of HDCV

*Source: National Advisory Committee on Immunization, Canada. RIG = rabies immune globulin (human); if unavailable, use antirabies serum (equine). HDCV = human diploid cell vaccine; if unavailable, use duck embryo vaccine (DEV).
†If available, the animal should be killed and tested as soon as possible; holding for observation is not recommended. Bites of squirrels, chipmunks, rats, mice, other rodents, rabbits and hares are seldom an indication for rabies prophylaxis.
‡Vaccine may be discontinued if fluorescent antibody tests of specimens from the animal killed at time of the attack give negative results.

Table II—Dosage regimens for rabies prophylaxis*

Rabies vaccine	No. of 1-ml doses	Schedule of doses	If no antibody response to primary series†
Before exposure‡			
HDCV (preferred)	3	Days 0, 7 and any one of 21 to 28¶	One booster dose¶
or			
HKV	4	Days 0, 28 and 56, and 3 to 6 months after third dose¶	Two additional booster doses of HDCV, each a week apart¶
or			
DEV	4	Days 0, 7 and 14, and 5 to 6 months after third dose¶	Two additional booster doses of HDCV, each a week apart¶
After exposure§			
HDCV (preferred)	5‖	Days 0, 3, 7, 14 and 28¶	An additional dose without delay
or			
DEV	23	Daily doses for 21 days, then one booster on days 31 and 41**	Additional doses, preferably three of HDCV at weekly intervals¶

*Source: National Advisory Committee on Immunization, Canada. HKV = hamster kidney vaccine.
†If no antibody response is demonstrated after the recommended additional booster dose(s) consult the provincial health department.
‡Indicated for persons at special risk of exposure to rabies, such as veterinarians, animal handlers, certain laboratory workers, spelunkers and forest rangers.
§Immediately administer RIG or antirabies serum, then initiate a course of either HDCV or DEV.
‖The World Health Organization recommends a sixth dose on day 90.
¶Collect blood for rabies antibody testing 2 to 3 weeks after the last dose.
**Collect blood for rabies antibody testing on day 61.

vaccination of pets and immunization of a small number of humans, a measure of control has been achieved. Recently the appearance of new immunizing agents has increased both the safety and the effectiveness of rabies prophylaxis in humans.

The basic problem of rabies in wildlife remains, though, and its solution depends on the development of more innovative methods aimed at breaking the chain of infection in free-roaming animals.

References

1. MOYNIHAN WA: Rabies in Canada. In *Proceedings of the National Rabies Symposium*, Center for Disease Control, US Dept of Health, Education, and Welfare, Atlanta, Ga, 1966
2. AOKI FY: Human diploid-cell-culture vaccine for rabies prophylaxis (E). *Can Med Assoc J* 1979; 120: 1044–1046
3. Rabies prevention program, 1972–1976 — Manitoba. *Can Dis Wkly Rep* 1977; 3: 177–180
4. BRADLEY JA: Laboratory diagnosis of rabies in western Canada (1968–1977). *Can Vet J* 1979; 20: 186–190
5. Center for Disease Control: *Rabies Surveillance Annual Summary 1977*, US Dept of Health, Education, and Welfare, Atlanta, Ga, 1977
6. JOHNSTON DH, BEAUREGARD M: Rabies epidemiology in Ontario. *Wildl Dis* 1969; 5: 357–370
7. Controlling wildlife rabies in Europe. *WHO Chron* 1976; 30: 250–251
8. SIKES RK: Pathogenesis of rabies in wildlife. I. Comparative effects of varying doses of rabies virus inoculated into foxes and skunks. *Am J Vet Res* 1962; 23: 1041–1047
9. PRESTON EM: Computer simulated dynamics of a rabies controlled fox population. *J Wildl Manage* 1973; 37: 501–512
10. WHO Expert Committee on Rabies: Sixth report. *WHO Tech Rep Ser* 1973; 523: 1–55
11. New prospects for rabies control. *WHO Chron* 1974; 28: 16–24
12. GURBA GB: Rabies vector control in Alberta. *Alberta Epidemiol Notes Rep* 1978; 2: 2–6
13. BLACK JG, LAWSON KF: The safety and efficacy of immunizing foxes (*Vulpes vulpes*) using bait containing attenuated rabies virus vaccine. *Can J Comp Med* 1980; 44: 169–176
14. KAHL W, QUANDER J, POSCH J, BÖGEL K: Cost analysis of wildlife rabies and its control in Europe. *Zentralbl Bakteriol [Orig A]* 1978; 240: 279–296
15. Rabies: controlling the spread in Europe. *WHO Chron* 1978; 32: 105–108
16. National Advisory Committee on Immunization: Statement on rabies prophylaxis. *Can Dis Wkly Rep* 1980; 6: 125–132
17. Recommendation of the Immunization Practices Advisory Committee (ACIP). Rabies prevention. *Morb Mortal Wkly Rep* 1980; 29: 265–272, 277–280
18. BAHMANYAR M, FAYAZ A, NOUR-SALEHI S, MOHAMMADI M, KOPIOWSKI H: Successful protection of humans exposed to rabies infection. Postexposure treatment with the new human diploid cell rabies vaccine and antirabies serum. *JAMA* 1976; 236: 2751–2754
19. DEMPSTER G, STEAD S, ZBITNEW A, RHODES AJ, ZALAN E: Management of 41 persons exposed to a rabid dog: unplanned experience with human diploid vaccine. *Can Med Assoc J* 1979; 120: 1069–1074
20. PLOTKIN SA, WIKTOR TJ, KOPROWSKI H, ROSANOFF EI, TINT H: Immunization schedule for the new human diploid cell vaccine against rabies. *Am J Epidemiol* 1976; 103: 75–80
21. Centers for Disease Control, US Dept of Health and Human Services: *Vet Public Health Notes* 1981; Jan
22. National Advisory Committee on Immunization: Supplementary statement on rabies prophylaxis. *Can Dis Wkly Rep* (in press)