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The Cost of Rabies Postexposure Prophylaxis: One State's Experience

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SYNOPSIS

Objective. This study was undertaken to evaluate trends in the use of rabies postexposure prophylaxis (PEP) before, during, and following an epidemic of raccoon rabies in Massachusetts.

Methods. The authors reviewed initiation of PEP as reported to the Massachusetts Department of Public Health (MDPH) from August 1994 to December 1995 and surveyed hospital pharmacies to determine the number of vials of Human Rabies Immune Globulin (HRIG) dispensed from 1991 through 1995 and charges to patients per vial.

Results. PEP use increased dramatically, from 1.7 per 100,000 population in 1991 (pre-epidemic) to 45 per 100,000 in 1995 (after the first stages of the epidemic). The median costs per patient for biologics was \$1646 (range: \$632-\$3435). Including physician and emergency room charges, per-patient median costs were \$2376 (range: \$1038-\$4447). Total health care charges for PEP in Massachusetts in 1995 were estimated at \$2.4 million to \$6.4 million.

Conclusions. Given the rapid increase in use of PEP, further studies should be undertaken to determine the appropriateness of use, and other alternatives, such as oral wildlife vaccines, should be considered.

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The Middle Atlantic raccoon rabies epidemic began in West Virginia in the late 1970s and has spread inexorably north and south to encompass all states on the Atlantic coast as well as Alabama, Ohio, Pennsylvania, and Vermont. Raccoon strain rabies is spread primarily by raccoons, although spillover infection to other species occurs.

While bat rabies has been endemic at least since testing began in the early 1950s, there is very little spillover from bats to terrestrial animals and thus little cause for alarm. But because raccoons live in such close proximity to humans, and encounters between raccoons and domestic animals are common, raccoon rabies has heightened public concern about human and domestic animal exposure to rabies.

Rabies control measures include vaccination of domestic animals to create a barrier between raccoon and humans; postexposure prophylaxis (PEP) for exposed humans; and, experimentally, oral rabies vaccination of wild animals, which has been tested in several states, including Massachusetts,¹ the site of this study.

There have been few human deaths from rabies in the United States, and none reported due to raccoon strain rabies.² However, rabies remains a significant public health concern due to the number of human and domestic animal exposures and the costs associated with rabies PEP. The decision to provide PEP is based on guidelines developed by the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC).³ Under these guidelines: (a) for previously unvaccinated people exposed to a rabid or potentially rabid animal, PEP consists of the administration of one dose of human rabies immune globulin (HRIG) and five doses of Human Diploid Cell Vaccine (HDCV); (b) for previously vaccinated people exposed to a rabid or potentially rabid animal, PEP consists of the administration of two doses of HDCV.

Overuse and inappropriate use of PEP by medical providers has been identified as a major problem by state and Federal public health agencies.⁴ Although precise national data are not available, CDC estimates that more than 40,000 courses of PEP may be given annually in the United States.² Several states have reported the effect of the spread of raccoon rabies on PEP use.⁵⁻⁷ For example, in 1994, potential exposure to a single rabid kitten infected with the raccoon rabies virus variant led to treatment of 665 people in New Hampshire at an estimated total cost of \$1.5 million.⁸ The national Healthy People 2000 goals include a 50% reduction in the number of people undergoing rabies PEP;⁹ however, since the num-

ber of people receiving rabies PEP is increasing, the achievement of this goal is highly unlikely. Oral wildlife vaccination could potentially decrease the cost associated with rabies prevention by reducing the number of exposures of both domestic animals and people to potentially rabid animals and reducing the need for PEP.

We undertook this study to: (a) evaluate trends in the use of rabies PEP initiated before, during, and after the raccoon rabies epidemic in Massachusetts and (b) evaluate some of the direct costs associated with PEP.

In September 1992, Massachusetts reported its first case of raccoon rabies. Since then, approximately 90% of the 351 Massachusetts cities and towns have had one or more raccoon rabies cases, with only Cape Cod and the islands of Nantucket and Martha's Vineyard remaining unaffected to date. As of December 1996, the Massachusetts State Laboratory had detected raccoon rabies virus in over 1900 animals, including raccoons, skunks, foxes, woodchucks, cats, cattle, coyotes, horses, a pig, a beaver, an otter, a fisher, and a dog.

METHODS

We collected two kinds of data on the incidence of rabies PEP treatment in Massachusetts: (a) the number of mandated reports of PEP use and (b) the amount of HRIG distributed and associated costs.

Reports of PEP use. Since August 1994, medical personnel in Massachusetts have been required to report initiation of PEP to the Massachusetts Department of Public Health (MDPH). We used reports of rabies PEP received by MDPH between August 1994 and December 1995 ($N=1255$) to derive population-based incidence rates of PEP use for that period. In calculating the number of reports per month per 100,000 population, we used 1990 U.S. Census figures for the denominators.¹⁰

Survey of hospital pharmacies. We collected data on the amount of HRIG used in the state over a five-year period and the associated costs. In May 1996, we mailed a questionnaire to the pharmacies of all 105 hospitals in the state licensed by MDPH. (Because PEP is an emergency treatment, patients are typically treated in hospital emergency departments. Although some patients may be seen first in other settings, HRIG is very expensive, and physicians do not generally keep a supply on hand. According to the mandatory reports received by MDPH, fewer than 2% of treatments in 1997 were administered in physicians' offices.)

“We estimated the total median direct costs to patients and insurers associated with rabies PEP...in Massachusetts to be between \$2.4 million and \$6.4 million in 1995.”

The survey instrument, based on one used by the Connecticut Department of Health,⁵ asked for the number of HRIG vials (either the 2 ml or the 10 ml size) dispensed during the calendar years 1991 through 1995 and the amount charged per vial. Because most of the cost of PEP is due to the administration of HRIG, and we wanted to make it easy for pharmacies to complete a short survey, we asked if they dispensed HDCV or RVA (Rabies Vaccine Absorbed) and the cost of HDCV and RVA per vial but not the quantity dispensed.

Since HRIG is administered only once, we were able to estimate the incidence of rabies PEP based on the total amount of HRIG dispensed by hospital pharmacies. We first collected information on the amount of HRIG administered to a sample of patients and from this estimated an average dose per patient. Then, to obtain the total number of treatments in Massachusetts per year, we divided the total amount of HRIG dispensed per year by the average dose per patient. We used the total number of treatments per year as the numerator for incidence rates; the denominator was the Massachusetts population according to the U.S. Census.¹⁰ Incidence rates were calculated for each year from 1991 through 1995.

We first reviewed medical records of patients seen by the emergency or ambulatory care services of 10 acute care hospitals located in the city of Boston and surrounding suburbs from 1991 to 1995 with diagnosis codes for rabies, rabies exposure, and rabies inoculation (*International Classification of Diseases, Ninth Revision (ICD-9)* codes 071, V01.5 and V04.5).¹¹ These hospitals were selected to represent areas in Massachusetts with and without raccoon rabies: six were in areas with raccoon rabies, and four were in areas that had not experienced raccoon rabies.

From these medical records, we collected information on the age and weight and amount of HRIG administered on 120 patients for whom data were available out of 418 hospital records of people receiving any type of rabies treatment from 1991 to 1995. Data unavailable for the other people were weight and other specific information about treatment (such as site of administrations of HRIG or HDCV).

We calculated an average per-patient dose of 6.3 ml or 945 IU (median = 5.9 ml or 885 IU) based on the amount of HRIG administered to these 120 patients. Then, based on the total amount of HRIG dispensed by the responding pharmacies from 1991 through 1995, we estimated the total number of treatments in Massachusetts by dividing the total quantity dispensed by the average estimated dose. We then calculated the incidence rate of PEP use for 1991–1995 with the 1990 population of Massachusetts as the denominator.¹⁰

Cost data. We obtained hospital and physician charges from a sample of six hospitals located in the Boston suburbs. From these, we estimated two components of the cost of PEP treatment: charges for use of the emergency room and physicians' charges. Using the cost data obtained from the pharmacy survey, we estimated the average charge per vial of HRIG and HDCV.

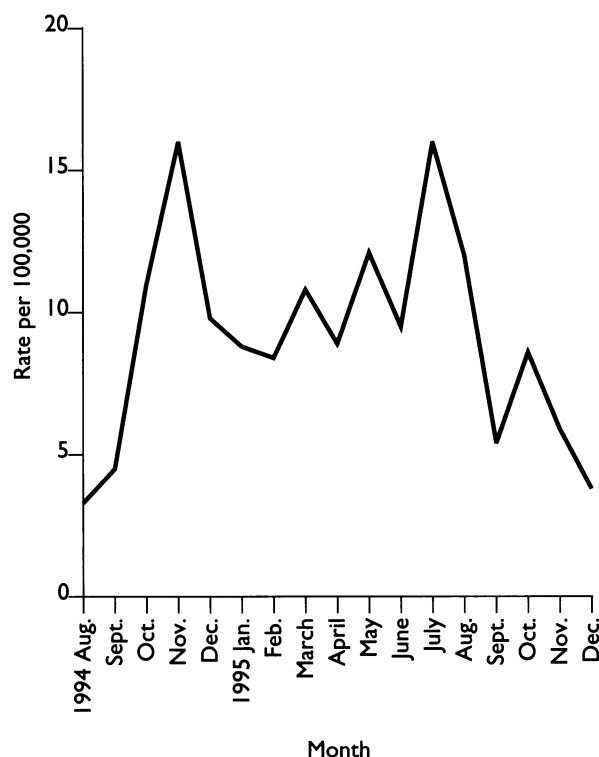
We derived estimates of the total cost of PEP in Massachusetts for 1991 through 1995 by adding the average cost of each component of the treatment (use of emergency room, physician charges, one dose of HRIG, one or more doses of HDCV) and multiplying it by the overall incidence rate for those years. To derive a lower limit, we calculated the cost for only one visit to the hospital (one-time use of emergency room, one doctor's visit, an average dose of HRIG, and one dose of HDCV). The upper limit represented the complete treatment (five visits to the emergency room, physician's charges for the initial visit and four return visits, an average dose of HRIG, and five doses of HDCV).

Descriptive statistics were generated using EpiInfo 6.2.¹³

RESULTS

The monthly incidence of PEP use, as reported to MDPH from August 1994 to December 1995, varied from 3.3 per 100,000 population to 16 per 100,000. As seen in the Figure, there was an increase in the reported incidence of PEP use in October to November 1994, which coincided with publicity about the mass exposure

Figure. Incidence of use of rabies postexposure prophylaxis in Massachusetts as reported to the Massachusetts Department of Health, August 1994 to December 1995



The graph shows an increase in the reported incidence of PEP use in October to November 1994, which coincided with publicity about mass exposure to rabies in New Hampshire. Another peak predictably occurred in the summer months of July and August 1995.

to rabies in New Hampshire.⁷ Another peak predictably occurred in the summer months of July and August 1995.

We received completed questionnaires from 96 (91.4%) of 105 hospital pharmacies; 28 (30%) of responding pharmacies reported that they did not dispense any rabies PEP between 1991 and 1995. From 1991 to 1995, there was both an increase in the number of hospitals dispensing HRIG and an increase in the total volume dispensed. A 25.6-fold increase in the amount of HRIG dispensed by 68 hospital pharmacies occurred concomitant with the appearance of raccoon rabies in Massachusetts: from 0.66 liters in 1991 to 16.88 liters in 1995. It should be noted, however, that pharmacy records were not consistent before 1993 due to the lack of computer systems in many hospitals and may not be very reliable.

The Table shows our estimates of the incidence rates

of rabies PEP use according to the number of doses of HRIG administered.

Charges to patients for biologics ranged widely across the hospitals. Charges for a 10-ml vial of HRIG ranged from \$369 to \$1619, with a median of \$859. Assuming that each patient would be charged for a 6.3 ml dose, we estimated an average per-patient charge of \$541 for HRIG alone (range \$232 to \$1020). The charge for one dose of HDCV ranged from \$80 to \$483, with a median of \$221. Thus using the average charge for HRIG and the median charge for five doses of HDCV, we calculated the total cost for biologics to be \$1646 (range: \$632 to \$3435).

The median emergency room charge for the first visit was \$87 (range \$69 to \$111), and the median emergency room charge for a return visit was \$71 (range \$34 to \$111). Thus the charge for five visits (first visit and four return visits) ranged from \$205 to \$555; we added the median charges for an estimate of \$371 for the cost of five visits. The median physician's charge for emergency treatment was \$75 (range: \$42 to \$89), and the median physician's charge for follow-up visits was \$71 (range \$40 to \$92).

The total estimated charge for initial treatment and biologics (excluding hospital and physician costs for follow-up visits) was \$1808 (range: \$743 to \$3635). This included the emergency room charge for the first visit, the physician's charge for the first visit, and the cost of one dose of HRIG and five doses of HDCV. Assuming charges of \$284 (range \$136 to \$444) for return emergency room visits for completion of treatment and \$284 (range \$160 to \$368) for return physician visits, the total estimated charge for the complete PEP treatment was \$2376 (range: \$1039 to \$4447).

Since completion rates of PEP could not be estimated, we also estimated the cost of one visit to the emergency room in which the patient was administered

Table. Estimated incidence of use of post-exposure prophylaxis based on pharmacy survey, Massachusetts, 1991-1995

Year	Estimated total doses administered	Estimated rate per 100,000 population
1991	105	1.7
1992	634	10.5
1993	1141	19.0
1994	2172	36.1
1995	2680	44.6

one dose of HRIG and one dose of HDCV; this estimate was \$924.

Thus we estimated the total direct costs to patients and insurers associated with rabies PEP (emergency room, physician, biologics) in Massachusetts to be between \$2.4 million and \$6.4 million in 1995 based on 2680 cases.

CONCLUSIONS

Use of rabies PEP increased dramatically after raccoon rabies was first observed in Massachusetts. Using estimates based on the amount of rabies HRIG dispensed by hospital pharmacies, we found that the use of rabies PEP increased more than 26-fold, from 1.7 per 100,000 in 1991 (pre-epidemic) to 45 per 100,000 in 1995 (following the first stages of the epidemic).

This study has several important limitations. We relied on data returned by hospital pharmacies, some of which were just initiating computerized inventory systems during the same period. In addition, although the response rate to the survey was high, it was not 100% so we may have slightly underestimated the total incidence and total costs. However, for the period studied, there was both an increase in the number of hospitals dispensing HRIG as well as an increase in the total volume dispensed. A comparison of our estimates based on the

pharmacy survey with our analysis of the passive surveillance system reveals that passive reporting underestimated actual treatment.

Previous studies have suggested that approximately 20% of people undergoing PEP do not receive HRIG^{4,12,14} and are treated with the vaccine alone; thus our estimates may overestimate statewide treatment costs. On the other hand, since HRIG is distributed only in 2 ml and 10 ml vials, there is also some wastage so the total of HRIG dispensed is probably higher than the amount actually administered to patients. These two issues may balance each other in the end.

There is general agreement on the part of state and Federal public health agencies that a large amount of PEP is administered inappropriately, although objective data on inappropriate use are limited. The fact that data from Massachusetts and other states shows a high level of PEP use suggests that interventions such as education of the public and health care providers might be more cost-effective than the use of wildlife oral vaccination in reducing PEP. In some geographic areas, oral rabies vaccination may not be appropriate and education may be the more feasible option.

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