warn physicians of the possibility of rabies infections in horses and to alert them about its possible public-health consequences.

On October 29, 1983, a 14-month-old male horse was brought to a local veterinary hospital with a "vague neurological disorder." The yearling had been vaccinated for rabies at two months of age by its owner. When seen, it stood with its head down and was noted to have tremors, exaggerated startle responses, and excessive salivation. Radiographs of the neck were suggestive of a fracture of the first cervical vertebra. The animal was humanely destroyed. The brain was sent to the State Laboratory in Concord for examination. On November 3, 1983, our health center received a report of a positive immunofluorescence test for rabies, which was confirmed the next day by the Centers for Disease Control in Atlanta. An effort to coordinate the identification of contacts and the administration of human rabies immunoglobulin was initiated. Because local supplies of rabies immunoglobulin were found to be inadequate for our anticipated needs, a special shipment was arranged by Cutter Laboratory in New Jersey. Officials from the State Department of Public Health, including the state epidemiologist and the state veterinarian, were on hand to supervise the epidemiologic investigation and to help formulate recommendations regarding prophylaxis. On the basis of standard criteria for rabies exposure, 15 persons were considered at risk and were offered prophylaxis with human rabies immunoglobulin (20 mg per kilogram of body weight, administered intramuscularly) and the human-diploid-cell vaccine series (1 ml given intramuscularly on Days 0, 3, 7, 14, and 28). Two patients with equivocal exposure, in whom the determination of risk was less certain, were offered the same prophylaxis.

Bat rabies is known to be present at a low endemic level in New Hampshire, and a rabid fox was reported in Rye, some 30 km (20 miles) away, in September. It may be of interest that the owner of the infected horse has noted an unusual number of foxes on her property during daylight hours within the past two months; bats are known to occupy the building where the horse was stabled.

This report is submitted to alert physicians and other health-care professionals to the possibility of equine rabies, especially in areas adjacent to southeastern New Hampshire. In addition, this communication should serve as a timely reminder of the constant threat of spillover from the sylvatic reservoir to the domestic animal population.

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A LONG-ACTING BENZODIAZEPINE IS MORE EFFECTIVE IN DIVIDED DOSES

To the Editor: On a pharmacokinetic basis and as a function of their plasma half-lives, benzodiazepines have been divided into two groups: short-acting (such as oxazepam, lorazepam, temazepam, and triazolam) and long-acting (such as chlordiazepoxide, diazepam, clorazepate, and medazepam).[1] Short-acting benzodiazepines are frequently recommended in the treatment of insomnia, whereas long-acting compounds are thought to be preferable for the treatment of chronic anxiety, with the possibility of once-a-day administration.

Actually, no study has proved that daily administration of a single dose of a long-acting benzodiazepine is as effective as divided doses in the treatment of anxiety disorders. Therefore, we performed a controlled study with prazepam, a long-acting benzodiazepine, the "prodrug" of desmethyldiazepam, which possesses a plasma half-life ranging from 30 to 120 hours.[2] Two groups of 10 inpatients each were selected according to Research Diagnostic Criteria for "generalized anxiety disorder."[3] In addition, patients had chronic and steady symptomatology, with at least a one-year history of regular daily intake of benzodiazepines in high doses (at least 20 mg of diazepam or equivalent), and a high level of severity (minimal score of 25 on the Hamilton Anxiety Scale[4] at the end of a one-week washout period). Patients received prazepam (40 mg a day) according to one of two different dosage schedules: either 10 mg in the morning and at noon and 20 mg in the evening or a single 40-mg dose in the evening. The study was performed in double-blind, randomized fashion, with each patient receiving three identical tablets a day, in order to control for any placebo effects of multiple doses.

Table 1. Changes over Time in Mean Scores for Patients on a Divided-Dose (DD) or Single-Dose (SD) Regimen.

	Regimen	Week 0	Week 1	Week 2	Week 3	P Value
Hamilton anxiety scale	DD	32.9	20.1	12.4	10.5	<0.0005
	SD	31.4	22.2	17.1	16.1	
Morning drowsiness	DD	0.0	0.2	0.2	0.3	<0.0001
	SD	0.0	2.2	1.4	1.4	
Evening worsening of symptoms	DD	0.2	0.3	0.1	0.0	<0.0001
	SD	0.0	1.8	1.9	1.8	
Visual Analogue Scale						
Morning	DD	94.1	61.0	28.8	27.4	<0.01
	SD	92.9	57.0	41.3	45.7	
Afternoon	DD	92.6	64.5	33.0	30.3	<0.0002
	SD	91.3	79.7	67.6	61.1	
Difference between a.m. & p.m.	DD	1.5	−3.5	−4.2	−2.9	<0.005
	SD	1.6	−22.7	−26.3	−15.4	

The three weeks of therapy were preceded and followed by one week of washout. Patients were evaluated at the end of each week by means of the Hamilton Anxiety Scale. Two additional factors were also rated from 0 (absent) to 4 (severe): worsening of symptoms in the evening and drowsiness in the morning (hangover). The assessment was always performed at 10 a.m. (±30 minutes). On the same days, patients completed the Visual Analogue Scale[5] in the morning (at 10 a.m. ±30 minutes) and in the afternoon (at 5 p.m. ±30 minutes), characterizing themselves between two limits: "extremely relaxed" and "extremely anxious."

The significance of the data was determined by means of an analysis of variance with repeated measures.

The results (Table 1) show that the anxiolytic effect obtained with divided doses was significantly better than the one obtained with a single dose. Tolerance was also clearly better when divided doses were given, and the anxiolytic effect was steadier.

These results suggest that in some cases of generalized anxiety disorders, anxiolytic pharmacotherapy administered in divided daily doses may be more effective overall, without diurnal variation, and may be better tolerated than the administration of a single dose in the evening. The findings also suggest that plasma pharmacokinetics alone may not be sufficient to explain the duration of the clinical activity.

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