with animals in a double chamber (of 1300-ml volume), with the head protruding on one side of a rubber diaphragm and the body on the other side.

The data for measurements on ten species of small vertebrates are summarized in Table 1. The inverse relationship between water loss and absolute humidity is relatively linear, indicating that a diffusion process is involved, as was previously concluded for dogs and human beings (*4*). In white mice and kangaroo rats, water loss at each measured humidity is significantly different from that at other humidities. As expected, the water loss in white mice is significantly higher than that in the desert rodents, *Dipodomys* and *Perognathus*. This finding confirms earlier measurements (*1*). Species differences are not significant above a humidity of 10.0 mg/lit.

Also, as was expected from indirect evidence (see *8* for a summary), the rate of water loss in desert-inhabiting reptiles is considerably less than that in rodents, by a factor of about 10. Evaporation from a terrestrial anuran, *Scaphiopus couchi,* is only about 2 times that from white mice and 4 times that from desert rodents.

The rate of water loss is very sensitive to changes in degree of activity of the animal. When *Perognathus intermedius* were caused to run in place for 5 to 10 minutes, they maintained a maximum rate of water loss 200 to 290 percent of their rate when sleeping. The maximal rate of loss in *Uma notata* was 413 percent of their rate when resting.

In kangaroo rats, water loss from the head averaged 87.7 percent of the total water loss, and that from the body, only 12.3 percent. These averages are only for rats whose total loss was within the range expected for sleeping, nonpartitioned individuals. The head-to-body ratio did not vary significantly with ambient humidity. Assuming that the skin of the head loses water at the same rate as that of the body, we find the ratio of water loss from respiratory organs to water loss from skin to be about 84:16. This finding supports the conclusion of the Schmidt-Nielsens (*1*) that the kangaroo rat has a rather insignificant loss of water through its skin. *Dipodomys merriami* is importantly different in this regard from another common desert-inhabiting rodent, *Peromyscus maniculatus,* in which loss of water from skin is about 46 percent of the total water loss (*9*).

The ratio of water loss from the head to water loss from the body in rattlesnakes was 70.1:29.9 for both species at humidity of 0.0 mg/lit. and 68.2:31.8 for *Crotalus scutellatus* at humidity of 3.3 mg/lit. Since the head surface is quite small in relation to the body surface in snakes, these ratios are essentially ratios of water loss from respiratory organs to water loss from skin. As has been often contended (*8*), the skin of at least certain reptiles is indeed nearly waterproof.

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Electrocardiographic and Behavioral Effects of Emetine

Abstract. The effects of subacute emetine poisoning on conditioning, spontaneous behavior, and the electrocardiogram of the guinea pig are reported and compared. The depression in spontaneous behavior shown by the animals does not seem to be dependent upon any psychogenic action of emetine; there appears to be a correlation between the cardiac damage and the depression caused by the drug.

Previous research by my co-workers and me has demonstrated that emetine is a drug with specific cardiotoxicity (*1*). Subacute emetine poisoning provides a useful method for producing a pathological condition of the heart of the guinea pig and may be used in evaluating the cardiac effects of drugs and other factors (*1*). The electrocardiographic changes observed in over 200 guinea pigs so poisoned, together with histologic studies, have suggested that emetine is able to evoke generalized myocardial damage, which spreads to the specific conduction tissue in the terminal stage of treatment (*1*).

Along with electrocardiographic changes, a marked behavioral depression is seen in all guinea pigs, from the first days of subacute poisoning until the death of the animals from cardiac failure, which occurs, in general, 6 to 7 days after the beginning of treatment. The onset and course of this depression seem to be closely connected with the signs of cardiac disturbance evoked by emetine. However, there are no data which permit the exclusion of interference of nervous or psychological factors in the pathogenesis of the emetine depression. Moreover, cases of polyneuritis and other nervous manifestations after emetine intoxication in man have been reported in the clinical literature (*2*), and many authors have reported that they obtained good results with emetine in the treatment of some neurological syndromes, such as herpes zoster (*3*) and alcoholic neuritis (*4*).

These clinical data suggest that emetine, under certain conditions, may produce neurotropic as well as cardiological effects. However, prior to our study there had been no experimental or clinical data on psychological effects or mental disturbance attributable to emetine in therapeutic or toxic doses (*1, 2*). To discriminate between myocardial and psychological factors in the pathogenesis of the emetine depression, in the research reported here (*5*) the effects of subacute emetine poisoning on the behavior and the electrocardiogram of the guinea pig were studied and compared.

Six female guinea pigs were condi-

Table 1. Effects of subacute emetine poisoning in six guinea pigs.

Days from beginning of treatment	Animals (No.)*	Reduction of body wt. (mean %)	Electrocardiographic changes (intensity)	Depression (intensity)†	Motor disability (intensity)‡	Reduction of conditioned avoidance (intensity)‡
2	6	−3.6	+	+		
3	6	−9.3	++	++		
4	6	−12.6	+++	+++	++	++
5	6	−19.5	+++	+++	+++	+++
6	2	−23.0	+++	+++	+	+
7	2	−27.5	+++	+++	++	++
8	2	−30.5	+++	+++	+++	+++

* Four animals died on the fifth day of treatment, after body weight and spontaneous and conditioned behavior had been checked and electrocardiograms had been made. The two remaining animals died on the eighth day, after the tests had been made. † On the second day only four animals manifested depression of spontaneous behavior. ‡ No animals manifested motor disability or reduction of conditioned avoidance on the second and third days, only two on the fourth day, and only four on the fifth day.

tioned to an avoidance situation, by the method described by Mowrer (*6*). The unconditioned stimulus was a mild electric shock. The conditioned stimulus was a combination of a steady light and a noise. The animals were conditioned to avoid the shock by crossing a barrier from a lighted into a dark compartment of the cage. They reached the maximum percentage of positive responses—that is, conditioned avoidance—in from seven to 11 training sessions, each session comprising 20 presentations of the conditioned stimulus. After this maximum had been maintained for more than three sequential sessions, the emetine treatment, as described previously (*1*) was begun, and it was continued until the animals died. The animals were given 5 mg of emetine per kilogram of body weight, per day, subcutaneously. During the treatment the animals were regularly subjected to the conditioning sessions (*7*).

Conditioning alone did not cause reduction in body weight or any adverse symptoms (*8*). Electrocardiographic records made 15 minutes after the training sessions showed only a slight tachycardia. The six animals died 102, 107, 111, 116, 170, and 180 hours, respectively, after the beginning of emetine treatment (*8*). During this period the guinea pigs showed a progressive reduction of body weight, together with electrocardiographic changes such as depression or inversion of the T wave and tachycardia in the first days, prolongation of the PR interval and widening of the QRS complex, and, in the terminal stage, bradycardia and intra- or atrio-ventricular blocks.

By the third day of treatment, all the animals showed depression of spontaneous behavior, but no significant changes in conditioned avoidance were observed. Only in the terminal stage of treatment, when the animals were almost completely incapable of moving or crossing the barrier to avoid the shock, was there a marked reduction in conditioned avoidance. The mean values for conditioned avoidance in the six animals during the conditioning sessions immediately prior to emetine treatment, during the emetine depression, and during the terminal stages were, respectively, 90, 92, and 24 percent. Similarly, the other parameters of conditioning, such as the duration of each session, the number of shocks, and the number of spontaneous crossings during each session, were not significantly influenced by the emetine treatment except in the terminal stage, when the duration of each session and the number of shocks were increased as a consequence of the animals' impaired movements.

From these results, which are summarized in Table 1, it seems that a reduction in conditioned avoidance occurs only when the animals are physically incapable of moving and is not associated with the early depression produced by emetine. Since emetine is a drug specifically toxic to the heart (*1*), and since it does not influence the conditioning even when spontaneous behavior is depressed, it seems more likely that the depression is correlated with the heart disturbance caused by emetine than with a possible psychogenic action of this drug.

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1. An extensive bibliography on emetine cardiotoxicity is to be found in previous papers by my co-workers and me. The most recent of these are: A. Marino and E. Miele, *Boll. soc. ital. biol. sper.* **35**, 749 (1959); A. Marino and E. Russo, *ibid.* **35**, 1244 (1959); A. Marino and S. Magliulo, in preparation; A. Marino, *Pharmacologist* **2**, 73 (1960).
2. The bibliography on cases of polyneuritis and nervous involvement during emetine intoxication in man can be found in various textbooks of toxicology, such as those of C. H. Thienes and T. J. Haley [*Clinical Toxicology* (Lea and Febiger, Philadelphia, ed. 3, 1955), p. 148], W. F. von Oettigen [*Poisoning: A Guide to Clinical Diagnosis and Treatment* (Saunders, Philadelphia, ed. 2, 1958), p. 348], S. Locket [*Clinical Toxicology* (Kimpton, London, 1957), p. 429], and S. Moeschlin [*Klinik und Therapie der Vergiftungen* (Thieme, Stuttgart, ed. 3, 1959), p. 484], and in the reports of F. J. Leibly [*Am. J. Med. Sci.* **179**, 834 (1930)] and F. Vizioli [*Fühner-Wieland's Samml. Vergiftungsfällen* **9**, 5117 (1938)].
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6. For details of the conditioning method, see O. H. Mowrer, *J. Exptl. Psychol.* **27**, 497 (1940); ——— and R. R. Lamoreaux, *Psychol. Monogr.* **54**, No. 5 (1942).
7. Control animals maintained the maximum conditioned avoidance for at least ten sequential sessions—that is, more than the period of subacute emetine poisoning.
8. In earlier research [*Pharmacologist* **2**, 73 (1960)], I found that conditioning did not significantly potentiate emetine cardiotoxicity.

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