

tropic drugs also resulted in a considerable elevation in the plasma levels of H<sup>3</sup>-norepinephrine for the first 5 minutes after the injection of the hormone. Fig. 1 includes the plasma concentrations of the hormone after 2 minutes. No significant differences in the plasma concentration of the catecholamine in the control and drug-treated groups were found after 5 minutes.

Other psychotropic drugs such as sodium pentobarbital and J-B 516, a monoamine oxidase inhibitor, had no effect on the tissue and plasma concentration of norepinephrine. The monoamine oxidase inhibitor, however, raised the tissue and plasma levels of H<sup>3</sup>-normetanephrine.

The psychotropic drugs might reduce the tissue levels of noradrenaline by speeding its passage across membranes to the site of intracellular transformation, by increasing the rate of enzymatic destruction, or by interfering with its binding. If the transfer of norepinephrine across cell membrane were to be enhanced, plasma as well as tissue concentrations of the hormone would be reduced. In connection with the second proposal, it is unlikely that these drugs act by increasing enzymatic destruction since we have found that they do not activate catechol-O-methyl transferase, the enzyme primarily concerned with the metabolism of circulating catecholamines (3). However, it is possible that these drugs are producing their effects of catecholamine metabolism by influencing the binding mechanism. Interference with binding would affect the uptake of circulating norepinephrine and consequently lower the tissue concentration and elevate the plasma levels of the catecholamine. We have recently shown that the uptake of circulating norepinephrine by tissues is dependent upon the intact sympathetic nerve endings (4). The present finding indicates that psychotropic drugs may exert their effect on the disposition of catecholamines by altering the binding sites at the nerve endings.

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## Evaporative Water Loss of Small Vertebrates, as Measured with an Infrared Analyzer

**Abstract.** Evaporation is linearly and inversely related to absolute humidity at 26° to 27°C. The relative rate of loss in desert reptiles, rodents, and anurans is about 1:10:40. The maximum rate of water loss is about 2.5 and 5 times the basal rate, respectively, in pocket mice and sand lizards. The ratio of loss from lung to loss from skin is about 84:16 in kangaroo rats and 70:30 in rattlesnakes.

Although evaporative water loss is an important item in the water balance of vertebrates, it has been difficult to measure directly under biologically meaningful conditions. Direct measurements made to date on small mammals (1, 2) and lizards (3) are of limited value because they involve exposure of the animals to dry air, an unusual biological condition. Almost all measurements on larger mammals (4) have been made indirectly.

The modern infrared gas analyzer provides a means of easily making accurate measurements of evaporative water loss over a complete range of ambient humidities. Prototype analyzers were used to study insensible water loss in human beings (5). The recent work of Decker (6), who used an infrared analyzer to study plant transpiration, was the stimulus for the work reported here (7).

In the method discussed here, animals that had been without food 12 to 24 hours were individually placed within a cylindrical glass chamber of 400-ml volume, and air of controlled humidity was drawn through the cham-

ber and then through a Beckman 15A infrared analyzer. Air could also be drawn directly through the analyzer via a by-pass. It was thus possible to change quickly from monitoring the water content of the air leaving the chamber to monitoring the content of the air entering it.

Constant, known humidities were obtained by passing room air through drying tubes of Anhydrone, or by bubbling it through saturated potassium acetate solution, saturated sodium acetate, or distilled water, kept at 20.0° ± 0.1°C. The humidities thus obtained, for animal-chamber temperatures of 26° to 27°C, were 0.0, 3.3, 10.0, and 12.3 mg of water, respectively, per liter of air (15.6 mg/lit. = saturation).

When recording over the humidity range of 0.0 to 15.0 mg/lit., with an air flow of 423 ml/min, it was possible to measure water-vapor loss to ± 0.04 mg/min. For animals that had a rate of loss near this value, measurements were made by sealing the animal in the chamber without air flow for 15 to 30 minutes and then flushing out and recording the amount of water vapor accumulated. The responsiveness of the instrument is such that the water expired with individual breaths of slow-breathing vertebrates, such as rattlesnakes, can be recorded. Recording was continued at a particular humidity until a minimum rate of loss was maintained for 15 to 30 minutes while the animal was sleeping (mammals) or remaining quiet (others).

Some measurements were made with animals that had been deliberately excited. Other measurements were made

Table 1. Evaporative water loss of a series of small vertebrates, measured at 26° to 27°C and at four different absolute humidities (in milligrams of water per liter of air).

Species	Measurements (No.)	Wt. (g)	Av. water loss from evaporation (mg/g hr)			
			Absolute humidity			
			0.0 mg/lit.	3.3 mg/lit.	10.0 mg/lit.	12.3 mg/lit.
<i>Mus musculus</i> (white mouse)	6	9.0-23.9	3.92 ± 0.90*	3.61 ± 0.70	2.30 ± 0.69	1.36 ± 0.64
<i>Dipodomys merriami</i> (kangaroo rat)	6	30.1-37.4	1.46 ± 0.27	1.14 ± 0.21	0.94 ± 0.22	0.51 ± 0.14
<i>Perognathus baileyi</i> and <i>P. intermedius</i> (pocket mice)	8†	12.2-29.2	2.47 ± 1.02	2.18 ± 0.89	1.34 ± 0.43	0.95 ± 0.43
<i>Uma notata</i> (sand lizard)	3	15.5-16.0	0.361	0.327	0.120	
<i>Dipsosaurus dorsalis</i> (desert iguana)	1	32.0	0.197	0.159	0.0363	0.0329
<i>Phrynosoma solare</i> (horned lizard)	1	35.1	0.218			
<i>Crotalus atrox</i> (western diamond-back)	1	123	0.175			
<i>Crotalus scutellatus</i> (Mojave rattlesnake)	1	278	0.177	0.126		
<i>Scaphiopus couchi</i> (spadefoot toad)	1	24.4		6.07	3.40	

\* One standard deviation. † Two measurements were made on *P. baileyi*, six on *P. intermedius*.

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 cardiovascular 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.