13. Mackaness, G. B., J. Path. and Bact., 1952, v64, 429.
14. Batson, H. C., An Introduction to Statistics in Medical Sciences, Burgess Publ. Co., 1963, p22.
15. Youmans, G. P., J. Chron. Dis., 1957, v6, 606.
16. Dubos, R., Am. Rev. Resp. Dis., 1964, v90, 505.
17. Elberg, S. S., Bact. Rev., 1960, v24, 67.
18. Jenkin, C. R., Rowley, D., ibid., 1963, v27, 391.
19. Kochan, I., Smith, L., J. Immunol., 1965, v94, 220.
20. Suter, E., J. Exp. Med., 1953, v97, 235.

Received June 28, 1965. P.S.E.B.M., 1965, v120.

Responses of Xeric-Adapted Rodents to Waterloading.* (30529)

ROBERT M. CHEW AND ORMOND G. MITCHELL† (Introduced by Paul R. Saunders)
Department of Biological Sciences, University of Southern California, Los Angeles

Several studies have indicated that desert-inhabiting rodents have "difficulty" in eliminating a water load, presumably because of factors associated with their adaptation to conservation of water. Hofmann(1) found that Merriam's kangaroo rat, *Dipodomys merriami*, "excreted the load only with the greatest difficulty." *D. merriami* given 5 ml/100 g of distilled water by stomach tube eliminated 40% of the load only after 367 minutes, while Long-Evans white rats did so in 84 minutes. *D. merriami* loaded intraperitoneally showed a still more pronounced water retention(2). The banner-tailed kangaroo rat, *D. spectabilis*, excreted the same percentage (85-88%) of a water load within 6 hours as did white rats, but only after a diuretic lag of 3 hours(3). A gerbil, *Meriones shawii*, "cannot excrete orally administered tap water by means of a hypotonic diuresis," when kept on a dry diet(4).

We have compared *D. merriami, D. agilis* and *M. unguiculatus* in order to check and extended these observations. The genus *Dipodomys* has had its center of evolution in the deserts of southwestern North America. *D. merriami* is one of the most ubiquitous species in these deserts; a few species such as the nimble kangaroo rat, *D. agilis*, have dispersed into semiarid habitats adjacent to deserts. Species of *Meriones* inhabit deserts and semiarid regions of the Old World. The Mongolian gerbil, *M. unguiculatus*, is found in semiarid areas of Mongolia, northern Korea and the Necca Province of China.

Materials and methods. *D. merriami* were live-trapped in the desert near Pearblossom, Calif., and *D. agilis* in chaparral near Etiwanda, Calif. *M. unguiculatus* were bred from stock from Tumblebrook Farms, Brant Lake, N. Y. Body weights of the animals were: *D. merriami*, 32-40 g, *D. agilis*, 60-70 g, *M. unguiculatus*, 63-72 g.

In all cases the water load was 5 ml/100 g of body weight of warm distilled water, given in one dose by stomach tube. Animals were stimulated to empty their bladders before intubation; they were weighed before and after loading to determine the absolute amount received. After loading, animals were placed on wire mesh over mineral oil in tared beakers. Urine excretion was measured by weighing the beakers at half-hour intervals for 6 hours; weights were corrected for any feces present. Urine output was plotted against time, and time for excretion of 40% of the load was estimated from the plot. Rate of excretion was measured after the first water load, and again after a second loading the same day or the next day, or after a third load the next day.

Results. Measurements are summarized in Table I.

Discussion. There are numerous observations of instances in which the abilities of different species of mammals to conserve body water have evolved in direct relationship to the average aridity of their habitats(5). The water conservation of such species often per-

* Supported by NSF Grant G19446.
† Present address: New York Univ., College of Dentistry, N.Y.C.

TABLE I. Rate of Excretion of Water Load.

Prior feeding regimen	Species	No. of animals	Load	Time to excrete 40% of load, min
Air-dry grain only	*merriami*	5	1st	—*
		3	3rd	158 (145–180)
	unguiculatus	4	1st	—†
		4	3rd	120 (95–150)
Air-dry grain and lettuce	*merriami*	7	1st	405 (280–720)
		6	2nd‡	194 (150–225)
	agilis	6	1st	285 (227–360)
		3	2nd‡	162 (125–186)
	unguiculatus§	13	1st	123 (95–152)
		3	2nd‡	98 (73–120)

* No urine in 360 min.
† 3.8% (0–6.3%) of load excreted in 360 min.
‡ *merriami* and *agilis* were given 2nd load 24 hr after first; *unguiculatus* was given 2nd load 8 hr after first.
§ 7 control animals (*i.e.*, no load) excreted urine equal to 0-1.3% of a load in 6 hr.

sists in captivity although water or succulent food is provided. An obvious degree of conservation may remain after generations of domestication, as in white mice(6). Therefore, the rate of elimination of a water load (as a measure of the failure to conserve the water) can be expected to be inversely related to an animal's "chronic level" of water conservation, as adapted to the "chronic level" of aridity of its habitat. This seems to be true of the present species. When they were given an opportunity to be hydrated by eating lettuce, they showed a rate of excretion of a water load inversely related to the subjectively ranked aridity of their natural habitats: *D. merriami* (desert) < *D. agilis* (chaparral) < *M. unguiculatus* (semiarid grassland). Measurements for the white rat(1) put it well at the end of this sequence. The sequence of conservatism was also reflected in the behavior of the species towards their lettuce ration. *D. merriami* usually ignored the lettuce, *D. agilis* usually ate part, while *M. unguiculatus* ate it "avidly."

When water is available in captivity, a species may function at only a fraction of its potential for conservation, as in the present case of *M. unguiculatus versus D. merriami*. When they were dehydrated by 6-10 days on an air-dry grain diet, both were anuric, or almost so, during the 6 hours after an initial water load; however, they were very different when allowed lettuce prior to loading. The gerbil showed other characteristics which are at least equal to the exceptional abilities of *D. merriami*(5). Adult *M. unguiculatus* maintained normal weight for 40 days on dry grain and a 1 M NaCl drinking solution; young animals grew well on only air-dry grain for at least 4 months (unpublished results). In these equipotent species, the chronic conservatism of *D merriami vs* the facultative conservatism of *M. unguiculatus* may be the result of natural selection for adaptation to chronic water shortage as compared to only occasional severe shortage. Or, it may reflect an adaptation to normal diets of different water contents: predominantly air-dry seeds for *D. merriami vs* more succulent leaves, stems and roots for *M. unguiculatus*. The facultative conservatism of *Meriones* is also shown in the work of Hummel(4) on *M. shawii*, which inhabits semiarid areas of North Africa. These gerbils failed to develop diuresis when water loaded after being kept on dry diets, but when allowed lettuce beforehand, they excreted a load "as well as the white rat."

In the present study, repetition of water loading always resulted in a decrease in time for excretion of 40% of the water load. One loading conditioned the shifting from water retention to diuresis. Rollason(2) found pronounced retention by *D. merriami* after 3 intraperitoneal loadings within 96 hours; slow absorption through the peritoneum may explain the failure of diuresis in his animals. The factors involved in the shift from retention to diuresis present the opportunity for an interesting study. This has been begun by Cole *et al*(3).

After 3 loadings, the present species still had a "residue" of water conservation in comparison to white rats. Reloaded *Dipodomys* were slower in excretion than *Meriones*. Only *Meriones* that were *reloaded* within 8 hours approached the rate of diuresis of white rats after their *first* load. This "residue" of conservation might have disappeared after further loading, or it may be an irreducible minimum dependent upon the morphological and functional characteristics of the kidneys of these species. All 3 species were able to "cope with" water loads. A "difficulty in excretion" is a possible interpretation only for the first loading of dehydrated animals. Only 2 animals, *D. agilis* that had been accidentally overloaded beyond 5% of their body weight, showed obvious hematuria; this contrasts with a 50% incidence of hematuria observed by Hofmann(1).

Summary. *Dipodomys merriami*, *D. agilis* and *Meriones unguiculatus* excreted orally administered water loads at rates slower than those reported for white rats. Dehydrated animals retained all, or almost all, of an initial load of 5 ml/100 g for at least 6 hours. Animals fed lettuce before loading excreted 40% of the load in 123 to 504 minutes; rate of excretion was inverse to the aridity of the species' habitats. The rate of diuresis doubled or tripled after a second or third loading, but a residue of conservation remained. None of the species showed "difficulty in excretion" after being conditioned by the first loading.

1. Hofmann, F. G., in Hormonal Control of Water and Salt-electrolyte Metabolism in Vertebrates, I. Chester-Jones, P. Eckstein, Eds., Mem. Soc. Endocrinol., 1956, No. 5, p38.

2. Rollason, H. D., Am. Zoologist, 1964, v4, 305.

3. Cole, P. M., Chester-Jones, I., Bellamy, D., J. Cell. Comp. Physiol., 1963, v38, 165.

4. Hummel, V. R., Helv. Physiol. Acta, 1963, Suppl. XIV, 1.

5. Chew, R. M., in Physiological Mammalogy, W. V. Mayer, R. Van Gelder, Eds., Academic Press, New York, 1964, v2, 43.

6. Silverstein, E., J. Appl. Physiol., 1961, v16, 194.

Received June 28, 1965. P.S.E.B.M., 1965, v120.

Circadian Variations in Sensitivity to Glucocorticoid Evaluated by Urinary Trypsin Inhibitor Excretion. (30530)

HANS J. FAARVANG AND OVE S. LAURITSEN (Introduced by Tage Astrup)
Biological Institute, Carlsberg Foundation, and University Hospital, Medical Department A and Dermatology Department H, Copenhagen, Denmark

Excretion of the urinary trypsin inhibitor (TI) in man is regulated by pituitary-adrenal hormones(1,2) and is increased in pregnancy (3) and during stress(1,2). Excretion of TI parallels in the individual the 17-ketosteroid and 17-ketogenic steroid excretion(1,4). In different individuals there is a correlation between cortisol production, or amount of exogenously administered glucocorticoid, and the diurnal excretion of TI(5,6), but the quantitative response, in terms of TI excretion, to a given amount of glucocorticoid, (*i.e.*, the sensitivity to this function of the hormone) varies individually(2,5).

The purpose of the present note is to show that there is a circadian rhythm in the individual in sensitivity to glucocorticoids. The quantitative response, assayed as excretion of TI, to a given amount of glucocorticoid is usually much lower during the night than during the day.

Materials and methods. Six persons were examined, most of them more than once. Two suffered from collagenoses (scleroderma and disseminated lupus erythematosus); 2 had dermatological diseases; and 2 were Addison patients. All patients were under treatment with glucocorticoids. On the days of this investigation, their usual treatment was replaced by 2 daily doses of steroid (cortisone