

Gastric juice volume and gastric juice volume/100 g^{10,11} are indicated in Figure 1. Peak responses were obtained with 1000.0 µg/kg doses of ICI-50123 and are significantly different from injected control rats ($p < 0.001$). Increasing the dose 3-fold did not increase the response. Acidity, total acidity and acid output are indicated in Figure 2. Peak responses were obtained for these 3 parameters with doses of 1000.0 µg/kg and are significantly different from injected control rats ($p < 0.001$). Increasing the dose 3-fold depressed slightly acid production. Gastric juice pH (Figure 2) in control rats was 1.67 U. This fell to pH 1.35 at a dose of 1000.0 µg/kg ICI-50123 ($p < 0.05$). Increasing the dose 3-fold did not statistically increase the response.

The data presented in this report indicate that ICI-50123 is a powerful stimulant of Shay rat gastric secretion producing maximal volume and acid outputs with a dose of 1000.0 µg/kg s.c. This dose is far greater than that required to produce maximal stimulation in man¹, dog³ and cat², and is roughly parallel to the response to histamine⁹. Maximal gastric juice volume, volume/100 g and acid output induced by ICI-50123 (Figures 1 and 2) are approximately similar to data obtained in Shay rats under maximal stimulation with histamine and insulin-induced hypoglycemia^{9,12}.

Large doses of hog gastrin given i.v. have been shown to depress acid gastric secretion¹³. As can be seen from this report supramaximal doses of ICI-50123 although not influencing gastric juice volume (Figure 1), minimally depress acidity, total acidity and acid output (Figure 2); p values are not significant¹⁴.

Zusammenfassung. An männlichen Ratten wurden nach 2 h Pylorusligatur Magensaftmenge, Volumen/100 g Körpergewicht, pH, Azidität, gesamte Azidität und Säureproduktion bestimmt und als Funktion von ICI-50123 studiert. Eine maximale Stimulation erfolgte bei einer Dosierung von 1000.0 g/kg s.c. Eine Abnahme der Säureproduktion zeigte sich bei supramaximaler Dosis.

J. H. THOMPSON

*Department of Pharmacology
and Experimental Therapeutics
University of California School of Medicine,
Los Angeles (California 90024, USA), 30 September 1968.*

¹⁰ R. J. MADDEN, H. H. RAMSBURG and J. M. HUNDLEY, *Gastroenterology* 18, 119 (1951).

¹¹ S. P. BRALOW and S. A. KOMAROV, *Am. J. Physiol.* 203, 550 (1962).

¹² Y. H. LEE and J. H. THOMPSON, *Experientia* 23, 300 (1967).

¹³ I. E. GILLESPIE and M. I. GROSSMAN, *Gastroenterology* 44, 301 (1963).

¹⁴ Acknowledgments. This research was supported in part by grants from the National Science Foundation (No. GB 6105) and American Medical Association Education and Research Foundation to J. H. THOMPSON. The expert technical assistance of JOAN ELM-LINGER is gratefully acknowledged. Dr. T. ROBISCHER of Ayerst Pharmaceuticals Inc., generously supplied the ICI-50123.

Body Weight and Organ Sizes in Warmth-Adapted and in Cold-Adapted, Hibernating Golden Hamsters

When investigating hibernation under laboratory conditions, one should realize that the animals studied are not only prepared for and changed by the lethargy, but that they are also adapted to cold and to the prevailing light-dark rhythm as well as being subjected to seasonal fluctuations. The influence of the light-dark rhythm and of the season can be eliminated by the introduction of strictly paired observations on hibernating and control individuals. A subtraction of the results obtained in both animals of a pair will yield information pertaining directly to cold adaptation-hibernation, presuming that season and light-dark rhythm influence the hibernating hamster and its control in the same way.

Here, the observations will be reported, done on body weight and organ sizes in golden hamsters which were kept on hibernation in a long-term experiment. These data were compared with those obtained in adequate controls.

Material and methods. The material and the procedure have already been published previously (SMIT-VIS and AKKERMAN-BELLAART¹). Measurements of the following organ weights were performed: testes, kidneys, adrenals, spleen, pancreas (after fixation in Bouin for 24 h), liver, heart (opened, rinsed and blotted), lungs, interscapular brown adipose tissue, skin and femora. The femora were included because they constitute a part of the body bearing no relation to thermoregulatory processes. The results of the weighings are listed in Table I. In order to study the adrenal cortex and medulla separately, their

proportions in the total adrenal weight have been approximated by determining histometrically their respective volumes, assuming that the 2 tissues do not differ in specific gravity. The volume measurements of the 2 adrenals have been treated separately, because they had been fixed in different fixatives: left gland in Susa and right gland in Orth's, and, therefore, a different shrinkage may take place. The average quotient weight/volume amounted to 2.06 for the left and 2.45 for the right adrenal, demonstrating a higher degree of shrinkage in the Orth fixative. The results of the volume measurements are given in Table I.

With regard to the evaluation of the data, it is of importance that ROBINSON and WILBER² found a close correlation between the body weight on the one hand and the weights of some organs on the other. Based on this observation the assumption may be made that if there had been differences between the weights of the various organs of one hamster pair at the start of the experiment (both having the same body weight then!), these differences can be considered to be samples of a distribution with a mean value of zero. If, at the end of the experiment, such a distribution of differences in

¹ J. H. SMIT-VIS and M. A. AKKERMAN-BELLAART, *Experientia* 23, 844 (1967).

² P. F. ROBINSON and C. G. WILBER, *Anat. Rec.* 141, 1 (1961).

Table I. Mean values of the absolute body weights and the absolute organ weights and/or volumes of the cold-exposed golden hamsters and their warmth-adapted controls

	Weight (mg)		Volume (μ^3)	
	Hibernating	Control	Hibernating	Control
Body	75.5 \pm 2.0	74.2 \pm 2.2		
Liver	3,180 \pm 106	2,838 \pm 103		
Lungs	668 \pm 24	484 \pm 16		
Kidneys	1,023 \pm 20	783 \pm 21		
Heart	482 \pm 15	418 \pm 11		
Pancreas	396 \pm 13	340 \pm 9		
Brown adipose tissue	233 \pm 11	181 \pm 8		
Skin	13,016 \pm 445	12,732 \pm 404		
Testes	768 \pm 92	743 \pm 67		
Spleen	87.8 \pm 3.4	69.5 \pm 4.2		
Femora	580 \pm 18	560 \pm 19		
Adrenals	18.4 \pm 0.9	16.7 \pm 0.6		
Left adrenal	9.78 \pm 0.50	8.99 \pm 0.38	4.92 \pm 0.23	4.22 \pm 0.12
Right adrenal	8.60 \pm 0.39	7.74 \pm 0.29	3.37 \pm 0.10	3.17 \pm 0.10
Left adrenal cortex			4.46 \pm 0.22	3.78 \pm 0.12
Right adrenal cortex			3.06 \pm 0.09	2.86 \pm 0.10
Left adrenal medulla			0.46 \pm 0.02	0.44 \pm 0.01
Right adrenal medulla			0.31 \pm 0.01	0.31 \pm 0.01

Table II. Mean differences between the cold-exposed, hibernating hamsters, expressed as percentages of the mean values in the warmth-adapted hamsters

	Weight		Volume	
	% difference	significance	% difference	significance
Body	+ 2	—		
Liver	+ 12	0.01		
Lungs	+ 38	0.001		
Kidneys	+ 31	0.001		
Heart	+ 15	0.001		
Pancreas	+ 16	0.001		
Brown adipose tissue	+ 29	0.001		
Skin	+ 2	—		
Testes	+ 3	—		
Spleen	+ 26	0.01		
Femora	+ 3	—		
Adrenals	+ 10	0.01		
Left adrenal	+ 9	0.01	+ 17	0.01
Right adrenal	+ 11	0.01	+ 6	0.10
Left adrenal cortex			+ 18	0.01
Right adrenal cortex			+ 7	0.10
Left adrenal medulla			+ 5	—
Right adrenal medulla			+ 1	—

+ means increase in the cold-exposed hamsters.

organ weights of a hamster pair is not found, this must be due to cold- and/or hibernation-adaptation. The differences in organ weights pro hamster pair were statistically evaluated by calculating the $(100 - \alpha)$ confidence interval of the mean of these differences for each parameter investigated, using the Student distribution. Table II gives the mean differences, expressed as percentages of the mean values in the warmth-adapted hamsters.

Results and discussion. The consensus is that the golden hamster shows a decrease in body weight in the period prior to hibernation. Rather unexpectedly, however, the

control hamsters also showed a decrease in body weight that was, on average, equal to the observed drop in body weight in the cold-exposed hamsters. This similarity may be due to adaptation to the same light-dark circumstances and/or seasonal influences and can, therefore, no longer be considered as a response specific to cold.

With regard to the weights of the testes, skin and femora, no significant differences were found between the 2 series of animals. The absence of differences between cold- and warmth-exposed hamsters, in the weight of the femora which — as has already been noted — do not bear any relationship to thermoregulatory processes, is understandable. For the skin, however, this result is rather surprising. The observations on the skin corroborate the findings of HALE et al.³ in temperature studies on rats. The results of the testes measurements and their histology have already been commented elsewhere (SMIT-VIS and AKKERMAN-BELLAART¹).

With regard to the other organ weights, always a statistically significant increase was found in the hibernating animals. The increase in weight of the lungs and heart and the heavier kidneys illustrate the trophic response to cold. The hypertrophy of the pancreas can also be considered as part of this adaptation syndrome, although the weight increase may, at least partially, also be due to retention and accumulation of secretion products, which is usually observed in hibernating animals. The increase of the liver certainly has a multifactorial cause, because the liver participates in many metabolic processes and is, simultaneously, a store of carbohydrates that are accumulated in the beginning of a hibernation period (SMIT and SMIT-VIS⁴). Liver, heart and kidneys also increased in size in rats exposed to cold for 24 weeks (HALE et al.³).

The adrenals were significantly heavier in the cold-exposed hamsters. This was also true for the left and the right adrenals separately. A significant difference

³ H. B. HALE, R. B. MEFFERD JR., G. VAWTER, G. E. FOERSTER and D. CRISCUOLO, *Am. J. Physiol.* 196, 520 (1959).

⁴ G. J. SMIT and J. H. SMIT-VIS, *Archs néerl. Zool.* 16, 453 (1966).

($p < 0.01$) in volume of the total gland and of its cortex was present only in the case of the left adrenal. For the right adrenal a less distinct difference ($p < 0.10$) existed. This discrepancy between the results of the volume measurements on the 2 sides can be explained by the right gland being much more severely shrunk. Nevertheless, because in the right adrenal gland at least the same tendencies are manifest, the results of the measurements in the left gland may be considered to be representative for both glands. The measurements show further that the medullae in both series of hamsters are of about the same size, but that the cortices in the hibernating, cold-exposed animals are significantly larger ($p < 0.01$) than those in the warmth-adapted individuals. Evidently, the adrenal cortex has been stimulated by the low environmental temperature; a phenomenon that is already well-known in cold-exposed, nonhibernating mammals such as the rat (cf. SMITH and HOIJER⁵).

It should be stipulated that changes in weights and/or volumes are only rough indications of changes in functions: Even the absence of such changes does not imply an unaltered function. This was clearly illustrated by the results of our previous histological studies on the testes. Nevertheless, from the results presented here the following conclusions can be drawn. The changes in organ size observed in the cold-adapted, hibernating hamsters must be attributed to cold-adaptation; this is in accordance with the findings in cold-adapted, homoiothermic mammals such as the rat. This means that our findings illustrate that the golden hamster

behaves as a homoiothermic mammal, even when it shows hibernation; a conclusion similar to that of POHL⁶ and POHL and HART⁷, though with quite different argumentation. The preparation for hibernation occurs simultaneously with the trophic responses of the tissues to the stimulus to augmented heat generation.

Zusammenfassung. Von Dezember bis März wurden bei Goldhamstern im Winterschlaf und gleichzeitig bei wachen Kontrolltieren, die bei Zimmertemperatur gehalten wurden, Veränderungen von Organgewichten untersucht. Eine signifikante Zunahme des Gewichtes wurde bei Leber, Nieren, Herz, Pankreas, braunem Fettgewebe, Milz, Nebennieren und Nebennierenrinde der Winterschläfer gefunden. Bei Körpergewicht, Haut, Testes, Femora und Nebennierenmark waren keine Unterschiede zwischen beiden Tiergruppen festzustellen.

J. H. SMIT-VIS and G. J. SMIT

*Anatomical-Embryological Laboratory,
University of Amsterdam and
Central Institute for Brain Research,
Amsterdam (Netherlands), 4 September 1968.*

⁵ R. E. SMITH and D. J. HOIJER, *Physiol. Rev.* 42, 60 (1962).

⁶ H. POHL, *Z. vergl. Physiol.* 45, 109 (1961).

⁷ H. POHL and J. S. HART, *J. appl. Physiol.* 20, 398 (1965).

The Excitation by Suxamethonium of Non-Proprioceptive Afferents from the Caudal Muscles in the Rat

The excitatory effect of suxamethonium on the muscle spindle is well known¹, but no attempt has been made to determine its action on unencapsulated muscle receptors. A possible sensitivity to suxamethonium of the free nerve endings is suggested by the response of some myelinated cutaneous fibres to related agents^{2,3}. The problem has importance since suxamethonium evoked discharge from muscle spindles has been used as a form of selective input to the central nervous system^{4,5}.

Materials and methods. Adult male rats were anaesthetized with urethane (170 mg/100 g body weight) and the intertransverse caudal muscle, which comprises a number of small slips, was exposed and stretched over a light source which formed the bottom of a pool filled with Krebs' solution⁶. The spinal cord was exposed by laminectomy and the dorsal and ventral roots of the second and third caudal segments were cut, protected and prepared for electrical recording, or stimulation, under liquid paraffin.

The muscle selected for the experiments is the most distal of the group since it is usually innervated by a single branch from the lateral caudal nerve and contains between 4–8 receptors. The description of the afferent innervation is supported by Figure a. Before obtaining that record, neuromuscular transmission in the slip was blocked by addition of tubocurarine chloride (Tubarine, Burroughs Wellcome 1:10⁶) to the muscle pool to ensure that confusing action potentials were not generated as a result of contraction of skeletomotor or fusimotor units in the muscle.

Results and discussion. Action potentials evoked by a single stimulus to the muscle nerve branch fall into 2 groups: those conducting at velocities between 25 m/sec and 11 m/sec which serve spindles and tendon organs, and slowly conducting afferents (7–4 m/sec), the majority of which do not respond to stretch. None of the slowly conducting afferents we used responded to stretch. When a suitable nerve branch was obtained, all others adjacent were cut, so the dorsal root used carried effective afferents only from the slip being studied.

Figure b was obtained from a dorsal root filament with 2 effective afferents, and their conduction velocities (19 m/sec and 6.3 m/sec) indicate that they are the first and fourth potentials of the compound of Figure a. When such a convenient filament had been obtained the tubocurarine was removed and the muscle was washed with Krebs' solution until neuromuscular transmission reappeared. 30 min later the action of suxamethonium on the afferents was investigated.

¹ C. M. SMITH, *A. Rev. Pharmac.* 3, 223 (1963).

² W. W. DOUGLAS and J. M. RITCHIE, *Physiol. Rev.* 42, 297 (1962).

³ W. FJÄLLBRANT and A. ICGO, *J. Physiol.* 156 (1961).

⁴ H. D. HENATSCH, *Symposium on Muscle Receptors* (Ed. D. BARKER; Hong Kong U. P., Hong Kong 1962).

⁵ N. GAUTIER, A. LAICAISSÉ, P. PASQUIS and P. DEJOUR, *J. Physiol.*, Paris 56, 560 (1964).

⁶ M. H. GLADDEN and G. L. KIDD, in press (1969).