Failure to Produce Obesity in the Rat Following Gold Thioglucose Injection.* (21104)

GEORGE B. TALBERT AND JAMES B. HAMILTON.

From the Department of Anatomy, College of Medicine, State University of New York, Brooklyn.

Brecher, Waxler and co-workers(1-3) have shown that extreme obesity can be induced in one-third or more of C_3H and albino mice by an injection of gold thioglucose. These findings have been confirmed by others in albino mice(4), Swiss mice(5,6), and non-obese littermates of a strain of mice genetically-susceptible to obesity(6). The following data show that rats do not become obese after injections of gold thioglucose in dosages which are, respectively, less than, comparable to, or in excess of those which produce obesity in mice.

Materials and methods. Three groups of rats of Wistar stock, raised in our laboratory were used in this study: 1) 41 immature males, 2) 36 young adult males, and 3) 38 male and 18 female castrated animals. In the first group the experimental animals received a single intraperitoneal injection of gold thioglucose.† The remaining animals were untreated. In the second group half the number of animals which received each of the 2 doses of gold thioglucose were injected intramuscularly and half intraperitoneally. Ten animals were given amounts of sesame oil equivalent to those employed as the vehicle in the rats receiving the gold preparation. Half of this group were injected intraperitoneally and half intramuscularly. Six animals served as uninjected controls. The animals in the third group were castrated when they were 30 days old. The experimental animals were initially given a single intraperitoneal injection of gold thioglucose. Thirty-five days later 6 of the previously injected males were given a second dose and their weight followed for an additional 21 days.

Fifty-eight young adult male C_3H mice‡ were employed to obtain data for comparison with the results obtained with the rats. The experimental mice received a single intraperitoneal injection of the gold preparation while the control animals were untreated. The treatment of the rats or mice in each group and the dose of gold thioglucose given to each group is shown in Table I. All animals were weighed at weekly intervals throughout the experimental period.

Results in rats. Group 1. No animal became obese (Table I) and at no time did the body weight of any experimental animal equal that of several of the control animals.

Group 2. Death occurred in all adult male rats which received 1 mg of gold thioglucose per g of body weight. Of those given 0.75 mg per g of body weight, 50% survived in both the intramuscularly- and intraperitoneally-injected groups. The experimental animals which survived treatment lost considerable weight initially, but regained their former status about 3 weeks later. By 60 days following the injection the average gain of the gold-injected animals was still 27 g less than in either control group. The data from intramuscularly and intraperitoneally injected animals are combined in Table I since the results were similar. The sesame oil vehicle exerted no detectable influence upon weight.

Group 3. In neither sex did the average body weight of the experimental animals surpass that of the control rats during a 10-week period following the injections. In none of the injected animals did the body weight exceed the range found in control rats. A second injection of gold thioglucose also failed to initiate the development of obesity. As might be anticipated from the results obtained in

* This investigation was supported in part by research grant A-89 from the National Institute for Arthritis and Metabolic Diseases of the National Institutes of Health, Public Health Service.

† Gold thioglucose, prepared as 50 or 100 mg/cc of sesame oil, was obtained through the courtesy of Dr. Edward Henderson of the Schering Corp., Bloomfield, N. J. Gold thioglucose is stated to be stable and to be 50% gold.

‡ Obtained from Jackson Memorial Laboratory, Bar Harbor, Me.

TABLE I. Gain in Weight of Rats and Mice following Injection of Gold Thioglucose.

Group	Age (days) Body wt	Treatment	Dose gold thioglucose, mg/g body wt	No. of animals	No. surviving	Avg total gain in body wt	Duration (days)
Rats	18-26	G*	.5 to 1.6	32	12	230	60
(1)	30-60 g	0	—	9	9	254	
"	90	G	.75	12	6	51	60
(2)	225-386 g	G	1.0	8	0	—	
		Sesame 0.1	—	10	10	78	
		0	—	6	6	78	
"	80	G (1 inj.)	.6 to 1.4				70
(3)	140-310 g	♂		8	6	84	
		♀		7	4	72	
		G (2 inj.) ♂	.6 to 1.4 and .9 to 1.3	6	5	53	
		0	—				
		♂		24	24	110	
		♀		11	11	102	
Mice	50-60	G	.8	48			38
	13-27 g	Obese			10	11	
		Non-obese			9	2	
		0	—	10	10	2	

* G = Gold thioglucose.

these three groups of rats we have found in a subsequent experiment that rats which have been injected with gold thioglucose do not consume more food than uninjected control animals.

Results in mice. Table I shows the rate of growth in mice which became obese as compared with uninjected controls and with injected animals which did not develop obesity. The weight increased at a much quicker rate in obese than in control mice and the obese animals were still gaining weight rapidly at the termination of the experiment.

Discussion. The experimental procedures which did not produce overweight rats appear to be essentially similar to those which resulted in obesity in mice. The gold thioglucose was prepared in the same way by the same company. That the dosages were not too small in rats is indicated by the fact that only 41% of the immature animals in Group 1 survived, and that all of the rats in Group 2 which received 1 mg of the gold preparation per g of body weight died. This compares with 90% survival in the mice in the study of Waxler and Brecher(1) and 40% survival in our mice, after receipt of 0.8 mg per g of body weight. The period of observation far exceeded that necessary to detect the development of obesity in the mice. Mice given gold thioglucose exhibited accelerated gains in weight within 2 to 3 weeks in our study and in that of others(1-4).

Age, sex, and reproductive status are probably not factors in the difference between the results obtained in rats and mice. The span of age employed in these studies included those successful in studies of mice. Immature males and adult rats of both sexes were utilized; neither sex became obese in rats, but both did so in mice(1-4). Even castrated rats did not become obese as a result of the gold thioglucose, although castration increases the tendency to obesity in many species(7-10).

In the light of available information a genetic difference seems to be the most likely explanation for the failure of rats, and for the ability of mice, to develop obesity following injections of gold thioglucose. In this connection it should be noted that the white rat appears to have little tendency to develop obesity under ordinary circumstances(5), although a special strain which is prone to obesity has been reported(11).

Summary. White rats, originating from the Wistar strain, did not become obese following injections of gold thioglucose under experimental conditions that have resulted in obesity

in 4 strains of mice studied. It is possible that genetic factors influence the capacity to develop obesity after injection of gold thioglucose.

1. Brecher, G., and Waxler, S., PROC. SOC. EXP. BIOL. AND MED., 1949, v70, 498.

2. Waxler, S., and Brecher, G., *Am. J. Physiol.*, 1950, v162, 428.

3. Waxler, S., Tabar, P., and Melcher, L., *Cancer Res.*, 1953, v13, 276.

4. Anderson, A. B., *J. Endocrinology*, 1953, v9, xxxv.

5. Mayer, J., *Physiol. Rev.*, 1953, v33, 472.

6. Mayer, J., and Zighera, C., *Science*, 1954, v119, 96.

7. Sellheim, H., *Z. f. Geburtsh. u. Gynäk.*, 1913, v74, 362.

8. Fish, P., PROC. SOC. EXP. BIOL. AND MED, 1925, v22, 248.

9. Holt, H., Kecton, R., and Vennesland, B., *Am. J. Physiol.*, 1936, v114, 515.

10. Hamilton, J. B., *Recent Progress Hormone Research*, 1948, v3, 257.

11. Palmer, L., Kennedy, C., Calverley, C., Lohn, C., and Weswig, P., *Tech. Bull.*, Agric. Exp. Sta., Univ. Minn., 1946, No. 176, p54.

Received May 27, 1954. P.S.E.B.M., 1954, v86.

Apparatus for Continuous Infusion of Microvolumes of Solution into Organs and Tissues.* (21105)

MARCUS SINGER.† (Introduced by Samuel L. Leonard.)

From the Department of Zoology, Cornell University, Ithaca, N. Y.

An apparatus has been devised for continuous infusion of microvolumes of solutions over long periods of time directly into tissues. It has been used successfully to infuse chemical substances into small regenerating limbs of salamanders(1-4), but it could be adapted for use in fields of study other than that for which it was designed. In comparison to other devices for perfusion into blood vessels (5-7), the apparatus has the advantages of non-interrupted flow, of delivering volumes of the order of 0.001 cc or less per hour, and of simplicity in construction, operation and performance. It utilizes the principle of the hand-driven micrometer screws that are employed in microchemical analyses(8,9).

Three models demonstrate the essential mechanism which may be modified for specific needs. In each, the rotary movement of a clock motor (Telechron) is translated into the forward movement of a screw device which advances, directly or indirectly, the plunger of a small hypodermic syringe. The syringe in turn delivers solution into fine polyethylene tubing and thence into a glass capillary needle which is inserted into the tissue. In experiments on the salamander, clocks with a speed of one revolution in 4 hours are most useful. In the simplest model (Fig. 1) a mounted micrometer caliper, in which a screw clamp is substituted for the anvil to accommodate the syringe, serves as the advancing mechanism. The mechanism to couple the clock and micrometer consists of a metal tube attached to the shaft of the clock and slit along its length to engage the pins of an extension shaft connected to the barrel of the micrometer. The motor, revolving counter-clockwise, is supported by an angle plate mounted between 2 rails of the stand so that the clock and micrometer can be engaged or disengaged. A thumb screw passing through a slit in the plate locks the plate in a selected position. The coupling constitutes an automatic shut-off device since, with forward movement of the

*Supported in part by a grant from the American Cancer Society on the recommendation of the Committee on Growth of the National Research Council.

† I wish to acknowledge with gratitude the work of Mr. John Fitzgerald, supervising mechanician of the Department of Physics, Cornell University, in construction of the apparatus and introduction of his original ideas in redesigning later models; and to my former students, Dr. Ned Fader and Dr. Richard Sidman, for suggestions in elaborating and testing the early model.