electronarcosis. Fig. 1, C, shows the results of such an experiment. The mean increase of 4 experiments was 6 gamma/100 cc. In the blood of animals killed by asphyxiation the level rises even more, up to 38 gamma/100 cc has been observed.

Discussion and Summary. There is reason to believe that when asphyxiation is prevented electronarcosis causes only small increases of the level of adrenalin-like compounds in blood. It had been found previously[11] when one of two rabbits connected by a double carotid-jugular anastomosis was given an asphyxia-free electronarcosis, that the blood pressure in the other showed a slight increase. This was believed to be due to a release of adrenalin, which in the present experiments may cause the slight rise in the level of "adrenalin-like" compounds during asphyxia-free electronarcosis. It seems likely that the much larger increase of these compounds which is always present in animals subjected to electronarcosis without further precautions, is caused by asphyxiation.

Kobro[12] did not observe any effect of respiratory impairment (letting the animal breathe through a tightly woven cloth) on the adrenalin level. The impairment employed in the present experiments, though of shorter duration, was more severe (clamping of the trachea), which may account for the difference in the results obtained.

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16971

Obesity in Albino Mice Due to Single Injections of Goldthioglucose.

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During a toxicological study of goldthioglucose, it was noted that a number of albino mice receiving this compound showed a marked increase in size. This response occurred in animals which had been injected with a single dose of this drug. The present investigation was undertaken in an attempt to define the conditions under which these gains in weight occur.

Experimental. Goldthioglucose is an unstable compound of gold and thioglucose, containing 50% gold. It dissociates in the presence of water. The compound is hygroscopic and is therefore utilized as a suspension in sesame oil. The concentration of the suspension used in these experiments was 100 mg of goldthioglucose in 1 cc of the oil (supplied by Schering Corporation, Bloomfield, N.J.). The route of administration was by intraperitoneal or intramuscular injection.

Stock male and female mice were used. The animals were kept on a pellet diet, and fed *ad lib.* In some of these studies the animals were kept in individual cages and the food intake determined. All animals were weighed at weekly intervals.

The LD_{50} of goldthioglucose was 40-50 mg intraperitoneally for mice weighing 20 g. Fifty to 70% of the animals survived doses of 35 mg of goldthioglucose, and 90% survived doses of 25 mg. All animals survived the intraperitoneal injection of 12 mg of the compound. Fatalities from the administration of goldthioglucose generally occurred within the first 3 to 4 days. There was no further mortality due to the toxicity of the drug among those animals which survived one week.

In one representative experiment, animals weighing 18-23 g were given single injections

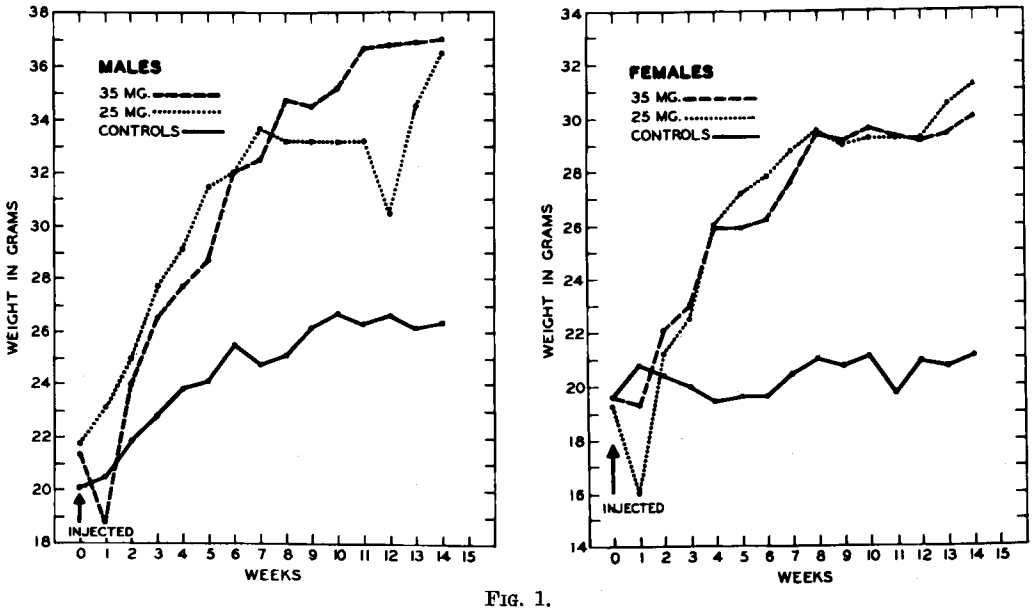

FIG. 1.
Average weights of male and female mice injected with goldthioglucose (25 and 35 mg), compared with controls.

of goldthioglucose intraperitoneally. Thirty males and 30 females were given 35 mg of the compound, and 5 males and 5 females were given 25 mg of the compound. Of the animals injected with 35 mg of goldthioglucose, 15 males and 24 females survived. Of the animals injected with 25 mg of the compound, 4 males and 4 females survived. The average weight of these survivors and of the controls is represented in Fig. 1. The differences in weight gains between treated and untreated animals were statistically significant in both males and females.

In another experiment, some of the control mice were injected with 0.5 cc of sesame oil. This was done to exclude the possibility that the oil of sesame used as the vehicle for goldthioglucose may have an effect on body weight. Out of a group of 25 male mice, 15 were injected intraperitoneally with 25 mg in 0.25 sesame oil. Seven of these survived. Four animals received 0.5 cc sesame oil intraperitoneally, and 5 animals were left untreated. Fig. 2 shows the individual weights of these animals at weekly intervals. The difference in weights of untreated controls and those injected with sesame oil were not statistically significant, while the animals given goldthioglucose in sesame oil showed significantly greater weight gains. An identical experiment with female mice showed similar results.

In order to test the possible influence of the route of administration, one group of mice was given a single dose of 25 mg of goldthioglucose intramuscularly. Because of the small muscle mass available, the dose was split and 12.5 mg of goldthioglucose was given in each thigh. The weight curves of these animals were in all respects similar to those of the intraperitoneally injected animals. Weight increases in the injected group were again significantly higher than in the controls.

In all these experiments only one-third to one-half of the injected animals showed unusual weight gains. This is well shown in Fig. 2, in which the individual weights of animals surviving the injection of 25 mg goldthioglucose are recorded at weekly intervals. In several experiments animals that failed to show significant weight gains by the eighth week were given another 25- or 35-mg dose of goldthioglucose. Significant weight gains were subsequently observed in a number of re-injected animals.

Animals injected with 12 mg of goldthio-

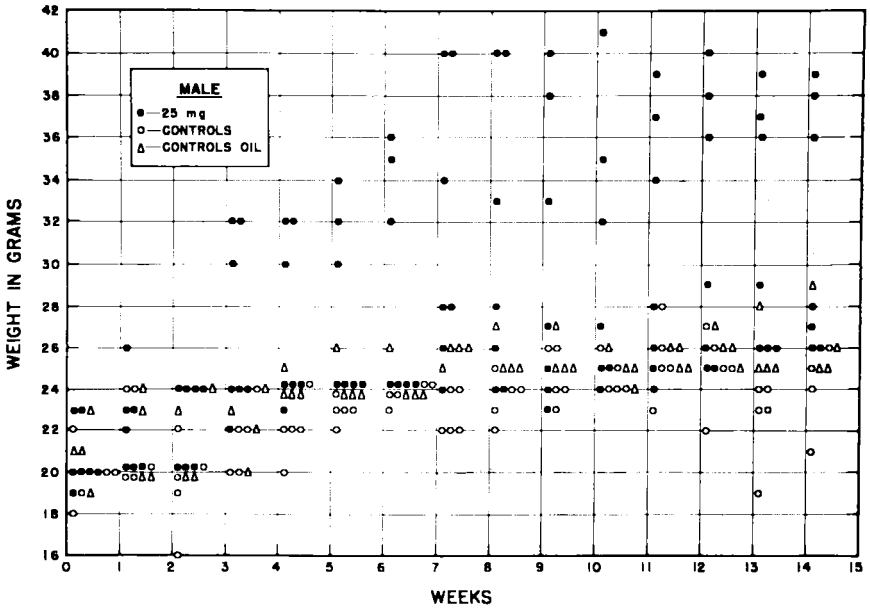

FIG. 2.

Comparison of individual weights of male mice injected with goldthioglucose, sesame oil, and controls.

glucose intraperitoneally showed no significant weight increases as compared with the control animals. Animals given injections of 5 mg of goldthioglucose intraperitoneally twice a week until a total of 150 mg was given, failed to show any significant weight gains.

All animals used in the above experiments were killed at the end of 14 weeks. There was marked increase in intra-abdominal fat and some increase in intrathoracic fat in the heavy animals. There was also a moderate increase in subcutaneous fat in the pelvic region and the region of the shoulder girdle. The viscera and the brain of both injected and control animals were examined microscopically. Mild inflammatory reactions at the site of injection and histochemically demonstrable gold in reticulo-endothial cells of various organs were present in all injected animals. There was mild to moderate centrolobular fatty infiltration of the liver in obese animals. This fatty infiltration ran roughly parallel with the weight of the animals. No other lesions were found in the liver, spleen, pancreas, kidney, adrenal, genital organs, heart, lung, lymph nodes, brain, hypophysis, thyroid, parathyroids, and adipose tissue.

Autopsy findings indicated that the abnormal amount of adipose tissue in injected mice might account for most of their weight gain. To verify this observation, the total body fat content was determined by the gravimetric method, using acid hydrolysis and ether extraction. Nitrogen, water, and ash were determined on aliquots from the same animals. Untreated controls selected at random were used for these determinations and compared with a group of injected animals showing marked weight gains. The weight of the injected animals so selected ranged from 38 to 60 g, and that of the controls from 18 to 25 g. The mean values and standard errors of the analytical determinations in the two groups are given in Table I. These analyses showed that the weight difference between injected heavy animals and non-injected controls could be primarily accounted for by the marked increase in adipose tissue in the injected animals.

Roentgenological examinations of the skeleton of obese and normal animals showed no recognizable difference in size, shape, or density of bones.

Summary. Marked weight gains were produced in stock albino mice by single injec-

TABLE I.
Total Lipids, Protein, Water, and Ash.

	Normal mice (7 animals)					Injected mice showing marked wt gains (7 animals)				
	Wt, g	Lipids g	Protein g	Water g	Ash g	Wt, g	Lipids g	Protein g	Water g	Ash g
Mean	22.1	2.42	3.65	16.2	.74	45.6	18.07	5.55	20.0	.72
Stand. error	.9	.33	.12	.7	.05	2.4	1.94	.26	.9	.09

tions of goldthioglucose. Analysis of total body lipids, protein, water, and ash showed these weight gains to be primarily due to an increase in adipose tissue. This obesity occurred in approximately one-third of the survivors of sublethal doses of goldthioglucose. Except for centrolubular fatty infiltration of the liver in obese animals, no anatomic lesions were found in the organs examined.

16972

Effect of Aminophylline on Plasma Prothrombin and Ac-Globulin in Dogs.

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Several conflicting reports have appeared in recent literature concerning the effect of the administration of methylxanthines on prothrombin activity. Field and coworkers[1] reported a hyperprothrombinemia following oral administration of these drugs to experimental animals in doses ranging from 10-400 mg/kg body wt. Scherf and Schlachman[2] also reported a shortening of prothrombin time in human subjects given therapeutic doses of aminophylline and theophylline with sodium acetate either orally or intravenously. However, a number of investigators have been unable to confirm these results. Quick[3] noted no increase in the prothrombin level of dogs and rabbits fed large doses (100-200 mg/kg) of methylxanthines. In a careful study, Holland and Gross[4] reported that methylxanthines, when given to dogs either in single intravenous doses of 25-50 mg/kg, or in daily oral doses of 20 mg/kg, produced no shortening in prothrombin time. Furthermore, single intravenous doses of 0.5 g of aminophylline failed to shorten the prothrombin time of human subjects. Several other studies[5-8] with human subjects failed to demonstrate significant changes in prothrombin time after oral or intravenous administration of aminophylline. All studies reviewed above were done by using only one-stage methods for the determination of prothrombin. Either Quick's original technique or one of its numerous modifications were utilized.

Because of recent advances in the under-

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