plasma tocopherol concentration and permanent plaster casts prepared of the affected hands in maximal passive dorsal flexion. 2. The alpha-tocopherol administration resulted in a slow but steady rise of the mean plasma tocopherol level from 0.55 to 1.37 mg %; after discontinuation of the treatment the concentration again fell to the original level. A moderate, but statistically certain effect of the therapy was observed on the condition of the hands. Thus, during the treatment the volume of the palmar concavity decreased from 18.2 to 13.2 ml, and the angle between the fifth finger and the palmar surface increased by 14.7°. The improvement continued for some time after discontinuation of the therapy, but some regression had taken place on examination 350 days after the end of the alpha-tocopherol treatment.

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Effects of Potassium on the Guinea Pig after Barbiturate Administration. (19693)

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Lamson and coworkers(1) have demonstrated that glucose and other organic substances can modify the anesthesia produced by barbiturates in various animal species. The well-known relation of potassium to glucose in the movements of the latter in and out of cells, and the implication of this cation in carbohydrate metabolism and neuromuscular processes(2) suggested a trial of potassium under conditions similar to those described for glucose. Preliminary work indicated that potassium could reinduce deep levels of anesthesia in guinea pigs recovering from hexobarbital anesthesia. The results of the investigation which followed are the subject of this report.

Methods. Guinea pigs were used throughout the study. Hexobarbital sodium† was used as the anesthetic agent, fresh solutions being made up for each experiment. Potassium chloride (KCl) and sodium chloride (NaCl) were administered as isotonic solutions (1% and 0.85% respectively). All doses of anesthetic or inorganic salt were injected intraperitoneally.

Results. The first experiments were attempts to reinduce deep anesthesia in guinea

TABLE I. Effect of KCl on Guinea Pigs Recovering from Barbiturate Anesthesia.

Guinea pig	Hexobarbital, mg/kg	Duration of anesthesia, min	KCl, mg/kg	Additional anesthesia, min
1	60	32	100	7
2	60	35	100	6
3	60	31	200	8
4	60	33	200	7
5	40	13	20	2
6	40	9	25	3½
7	40	14	50	5
8	40	15	50	5
9	40	26	400	13
10	40	20	400	10

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TABLE II. Effect of NaCl on Guinea Pigs Recovering from Barbiturate Anesthesia.

Guinea pig	Hexobarbital, mg/kg	Duration of anesthesia, min	NaCl, mg/kg	Additional anesthesia, min
1	60	34	170	
2	60	33	170	
3	40	24	50	
4	40	24	200	0
5	40	10	200	
6	40	19	400	
7	40	11	400	

pigs recovering from the narcosis produced by 40 to 60 mg of hexobarbital per kg. KCl was injected when the pig showed spontaneous activity or would squeal and make definite running movements if picked up by the skin over the back. In 10 experiments in 10 pigs, the injection of KCl was followed by an apparent return to deeper anesthetic levels (limpness, failure to move when placed on side or back) in all cases. Table I shows the time required to recover to the point described above following hexobarbital and then KCl. Depicted in Table II is the failure to affect the course of recovery with injections of NaCl in 7 animals.

The next step was to investigate the effects of potassium on the unanesthetized guinea pig. Forty-two experiments were performed in 13 guinea pigs. KCl produced apparent excitement, with scurrying, twitching, and nodding movements,‡ followed by a disturbance of the righting reflex lasting about 30 to 120 seconds, and a suggestion of slight muscular weakness, for the same period of time, following the larger doses. Some animals required 25, others as much as 200 mg per kg, to produce these effects. In all instances, the pigs were capable of standing and moving about if placed on their feet. In addition, 6 of the animals were given 800 mg per kg, with similar results, except that after 20 to 45 minutes, having apparently recovered from the acute effects of the injected potassium, the animals showed respiratory difficulties, weakness, occasionally convulsive movements, and death. Respirations were noted to cease before cardiac standstill, as described by Amberg and Helmholz(3). Except for the situation immediately before death, there was never observed any relaxation of the type seen in the barbiturate-KCl treated animals described above.

‡ These symptoms were also observed (prior to the onset of anesthesia) after KCl in the first group of experiments described.

In the next group of experiments, attempts were made to obtain deep anesthesia by combining large doses of KCl with doses of hexobarbital which either had no effect on the pigs or produced only a disturbance of the righting reflex. Eight experiments were performed in 8 animals. Doses of 20 mg per kg of hexobarbital were injected, followed in 4-5 minutes by doses of 100 to 400 mg of KCl. In 7 out of the 8 experiments, the period of "excitement" was immediately followed by a state indistinguishable from moderately deep stages of anesthesia (flaccidity, inability to rise when placed on their backs or sides, or to stand when put on their feet). A number of animals exhibited roving uncoordinated movements of their eyeballs, and inability to respond to pinprick. The data, with duration of effects noted, are shown in Table III. In no case was there seen quite the degree of narcosis or duration of effect that could be obtained with large doses of hexobarbital.

The last group of experiments comprised a study of the ability of hexobarbital to alter the response to potassium when the drugs were employed together in doses that were fractions of the amounts required to produce effects when either drug was administered alone. The method utilized was the following: First, a group of 13 pigs was injected intraperitoneally with successively increasing doses of hexobarbital, starting with 10 mg per kg and doubling the dose until an effect was produced. In all cases, at least 24 hr elapsed between administration of individual doses. As a measure of effect, abolition of the righting reflex was chosen. All untreated pigs invariably righted themselves when placed on their backs, so that abolition of this reflex was a reliable indication of definite effect. Also, this relatively clear-cut endpoint eliminated the subjective element in the evaluation of response. The results were as follows: no pig showed any effect from 10 mg per kg, 3 pigs showed disturbance of righting reflex from 20 mg per kg,

TABLE III. Effects Produced by KCl in Guinea Pigs Given Non-Anesthetic Doses of Barbiturate.

Guinea pig	Hexobarbital, mg/kg	KCl, mg/kg	Duration of anesthesia, min	Effects noted: Loss of righting reflex	Flaccidity	Loss of response to pin prick	Roving pupils
1	20	100	6	+	+		
2	20	200	19	+	+	+	+
3	20	200	6	+	+		
4	20	400	12	+	+		+
5	20	400	15	+	+	+	+
6	20	400	13	+	+		
7	20	400	15	+	+	+	+
8	20	400	3	+	Slight		

and 10 pigs required 40 mg per kg. In most instances this latter dose produced rather deep anesthesia.

This same procedure was then followed for KCl, starting with 25 mg per kg. One pig showed disturbance of the righting reflex with 25 mg per kg (and not with 15), 5 with 50 mg per kg, 4 with 100 mg per kg, and 3 required 200 mg per kg to show an effect.

The last step was to use the barbiturate and inorganic salt together. For this study, each pig was given a dose of hexobarbital which was 1/4 of the smallest dose required to produce a disturbance of the righting reflex. After 4-5 minutes (the maximal time required for definite evidence of onset of anesthesia when effective doses of hexobarbital were used) the pig was injected with a fraction of the minimal dose of KCl needed to produce an effect when injected alone. With this technic, abolition of the righting reflex was obtained with the following fractions of the "minimal effective dose" of KCl: 1/2 in 2 pigs, 1/4 in 4 pigs, 1/5 in 2 pigs, 1/10 in 4 pigs, and 1/40 in 1 pig. These results confirm the other studies in demonstrating an unmistakable modification of the response to KCl by the previous administration of hexobarbital. This alteration of response can thus be shown both with anesthetic doses of barbiturate and with doses of barbiturate which have no demonstrable effect.

Discussion. Although this study was initiated by theoretical considerations of the glucose effect of Lamson *et al.*(1), the results described in this paper are in no way offered as an explanation of this effect. The widespread participation of potassium in such diverse processes as nerve impulse formation, acetylcholine formation, carbohydrate metabolism, electrolyte transfer, etc.(2,4) makes extremely difficult the interpretation of such simple experiments as those described here. The report of Stewart(5) on the ability of barbiturate anesthesia to increase markedly the blood concentrations of potassium achieved in the rabbit after intraperitoneal injection of KCl is of considerable interest in regard to the work being reported. The results obtained in the studies on the righting reflex could be explained by a similar effect in the guinea pig. However, the relegation of hexobarbital to the role of a mere elevator of the blood potassium concentrations achieved after injection of potassium salts leaves some observations unexplained, such as the ability of potassium to reinduce, in a pig recovering from anesthesia, or to induce, in a pig given ineffective doses of anesthesia, a state indistinguishable from that obtained with anesthetic doses of barbiturate. The essential absence of signs of anesthesia in pigs given sublethal or even lethal doses of potassium suggests qualitative differences which require the postulation of a more complex joint action of barbiturate and potassium.

Summary. A study of the effect of hexobarbital on the response of the guinea pig to injected potassium has revealed the following: 1) Potassium, even in maximally tolerated doses, is incapable of producing anesthesia when injected alone. 2) Potassium is capable of inducing a state indistinguishable from deep narcosis in pigs recovering from hexobarbital anesthesia. 3) Potassium can produce moderately deep narcosis in guinea pigs

given subanesthetic doses of hexobarbital. 4) Following the injection of small doses of hexobarbital, potassium can abolish the righting reflex in a fraction of the dose required when injected alone.

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Effect of Cortisone on Lipids of Serum, Liver and Testes in Intact and Adrenalectomized Rats.*† (19694)

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Cortisone therapy in man increased the serum concentration of cholesterol and phospholipid, and decreased serum neutral fat (1,2). The increase of serum cholesterol, total and esterified, has been reported in rats treated with cortisone(3). In rabbits, adrenal extract and cortisone administration also increased cholesterol, lipid phosphorus and total fatty acids of serum(4-6). ACTH was shown to cause fatty infiltration of the liver in the rabbit(6,7) and rat(8). Adrenalectomy prevented fat mobilization into the liver in mice given ACTH(9). Cortisone caused no fatty infiltration of the liver in intact or adrenalectomized mice(10). However, lipid granules were found in hepatic cells of intact rabbits treated with cortisone(6). Cortisone was not found to cause a severe involution of testis in rats(3,11). ACTH was found to cause a slight reduction in the weight of rat testes with atrophy of the Leydig cells(12).

This study reports the effect of cortisone administration on total cholesterol and lipid phosphorus concentration of serum, liver and testes in adrenalectomized rats maintained with desoxycorticosterone pellets, as compared with the effects of the hormone in intact rats.

Experimental. The animals used in this study were 56 adult male rats of the Sprague-Dawley strain, selected for uniformity and with a weight range of 270 to 320 g. They received Rockland Rat diet and tap water *ad libitum*. Vit. A (200 I.U.) and vit. D (100 I.U.) were given orally once a week.

The experimental groups are shown in Table I. Adrenalectomy was performed through a flank approach. Each rat was maintained with a 15 mg pellet of desoxycorticosterone acetate (DCA).§ For the first 2 days following operation, the animals received by mouth 5% glucose in 0.3% saline, after which they were kept on the same diet as the other rats. Cortisone acetate¶ was given subcutaneously, 4 mg every day (0.5 ml in 0.9% saline) for 28 days. The rats were weighed twice weekly. The cortisone-treated rats lost about 50 g. At different times, daily food intake was weighed in each group. Blood was drawn under ether

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