The findings discussed here are typical of experiments on 5 subjects. It is possible that the red cell-plasma K exchanges may have occurred *in vitro* in spite of our care. Such an effect could not, however, have masked any appreciable true gain of "foreign" potassium.

There is another possibility—new red cells low in potassium could have been added to the blood stream from the spleen or some other reservoir. It can be calculated that these "new" red cells would have to contain the extraordinarily low concentration of 105 m.eq. K/kg H_2O to account for the red cell values found.

There is no doubt that potassium enters the blood from the muscles when longer periods of exercise are used. It may be that even in these short periods of exercise K enters the blood from the muscle, but if so it must be removed elsewhere, perhaps in the liver, at an equal rate.

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Prevention of Histamine and Surgical Shock by Cortical Hormone (Desoxycorticosterone Acetate and Cortin) and Saline.

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It is well established from pathological and experimental studies that the suprarenal cortex plays a significant rôle in the mechanism of natural resistance to intoxications, poisons, shock and bacterial and protozoan infections.* The similarity between adrenal insufficiency and the condition of secondary shock has been emphasized by many investigators.[3, 4, 5] The therapeutic effect of cortical hormone in the prevention of anaphylactic shock in guinea pigs[6] and in shock due to intestinal obstruction in dogs[7] has been reported.

It was observed that parenteral administration of large amounts of physiological saline given some hours prior to the production of

* This subject is reviewed by Perla and Marmorston.[1,2]

1 Perla, D. and Marmorston, J., *Arch. Path.*, 1933, **16**, 379.

2 Perla, D., and Marmorston, J., *Natural Resistance and Clinical Medicine*, Little, Brown and Co., Boston, Mass., 1940, in press.

3 Sweet, J., *Am. J. M. Sc.*, 1918, **155**, 627.

4 Swingle, W. W., Pfiffner, J. J., Vars, H. M., Bott, P. A., and Parkins, W. M., *Science*, 1933, **77**, 58 (includes review of literature).

5 Zwemer, R. L., and Scudder, J., *Surgery*, 1938, **4**, 510.

6 Wolfram, J., and Zwemer, R. L., *J. Exp. Med.*, 1935, **61**, 9.

7 Heuer, G. J., and Andrus, W. de W., *Ann. Surg.*, 1934, **100**, 734.

severe shock (by histamine) enhanced resistance in rats, enabling them to withstand about twice the lethal dose of histamine for normal animals (Perla[8]). In the present study the effect, both prophylactically and therapeutically, of the suprarenal cortical hormone with and without saline on resistance to shock was determined.

Treatment of histamine shock in rats and mice with saline and cortin. A number of normal adult rats were each given an amount of histamine (1200 mg per kg of body weight) above the minimal lethal dose of this poison for our strain of rats (1000-1100 mg). Immediately thereafter they were divided into 4 groups. One group was given repeated injections of 5 cc of physiological saline intraperitoneally at short intervals, as indicated in Table I. A second group received adrenal cortical extract (Wilson) in 5 repeated doses at similar intervals of 15 to 30 minutes. A third group received both saline and adrenal cortical extract combined in a total amount of 5 cc at the same intervals. A fourth group was untreated. The results indicate that combined treatment was more beneficial than the use of saline or cortical extract alone (Table I). The experiment was repeated using a slightly higher amount of histamine (1300 mg per kg of body weight) with similar results.

A similar experiment was performed using young adult mice. In preliminary studies the minimal lethal dose of histamine for our strain was found to be about 400 mg per kg. Therefore, a series of mice were each given subcutaneously 600 mg of histamine per kg.

TABLE I.
Therapeutic Effect of Parenteral Saline and of Cortical Extract in Rats* on Histamine Poisoning. (Combined results of several experiments.)

Amt histamine acid phosphate per kg body wt	Untreated Rats		Saline† treated		Cortin‡ treated		Saline and§ Cortin treated	
	Total No.	No. survived	Total No.	No. survived	Total No.	No. survived	Total No.	No. survived
1200	10	4 (40%)	11	6 (55%)	12	9 (75%)	7	7 (100%)
1300	3	0 (all died within 15 min)	4	2 (2 died in 2 to 4 hr)	4	1 (3 died within 1 hr)	4	3 (1 died in 4 hr)

* The rats were of an inbred strain of Bartonella-free stock, 3 to 4 months of age.

† Physiological saline in amounts of 5 cc was given at intervals of 1, 15, 30, 45 and 75 minutes.

‡ Cortical extract (Wilson) in amounts of 2 cc was given at once and in 15 minutes, then 1 cc was administered at intervals of 30, 45, and 75 minutes.

§ The cortical extract as above was brought up to a total volume of 5 cc with saline and injected at the same intervals as in the other groups.

8 Perla, D., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 234.

They were divided into 4 groups. One group was repeatedly treated with parenteral saline, a second with cortin, a third with both saline and cortin, and a fourth was untreated. Details are given in Table II. Of mice treated with saline 23% survived; of those given cortin 30%. Of mice given both cortin and saline 71% survived. Only one of 14 untreated mice survived this dose of histamine.

Prophylactic effect of saline and desoxycorticosterone (Table III).

TABLE II.

Therapeutic Effect of Parenteral Saline and of Cortical Extract in Mice* on Histamine Poisoning. (Combined results of two experiments.) (All mice were given 600 mg of histamine acid phosphate per kg body weight subcutaneously.)

Untreated		Cortin treated†		Saline treated‡		Cortin and Saline§ treated	
Total No.	No. survived	Total No.	No. survived	Total No.	No. survived	Total No.	No. survived
14	1 (7%)	13	4 (30%)	13	3 (23%)	14	10 (71%)

* The mice were of a special uniform "Swiss strain" inbred for susceptibility to viral and bacterial infection at the Rockefeller Institute by Dr. Webster and raised on the Carworth Farms. They were 20 to 22 g in weight.

† The adrenal cortical extract (Wilson) was given in amounts of 0.2 cc at intervals of 1 and 15 minutes; then 0.1 cc at intervals of 30, 45 and 75 minutes intraperitoneally.

‡ The physiological saline was given in amounts of 0.5 cc at the same intervals as in †.

§ The cortical extract as above was brought up to a total volume of 0.5 cc with saline and given at the same intervals as in †.

TABLE III

Prophylactic Effect of Parenteral Saline and Desoxycorticosterone on Resistance to Histamine in Rats*. (Combined data of several experiments.)

Amt of histamine acid phosphate per kg body wt	Untreated		Treated with Desoxycorticosterone†		Treated with Saline‡		Treated with Saline and Desoxy.§	
	Total No.	No. survived	Total No.	No. survived	Total No.	No. survived	Total No.	No. survived
1200	8	0	4	1	—	—	—	—
1300	2	0	—	—	—	—	—	—
1400	2	0	4	0	2	1	2	2
1600	—	—	2	0	2	1	2	1
1800	—	—	—	—	4	2	2	2
2000	—	—	—	—	5	1	5	3
2200	—	—	—	—	2	1	4	1
2400	—	—	—	—	—	—	4	1‖
2600	—	—	—	—	—	—	2	0

* The rats were 3 to 4 months old, of Bartonella-free stock.-

† The desoxycorticosterone acetate in oil was given subcutaneously in amounts of 5 mg 24 hours before the test and 3 mg 4 hours before the test.

‡ The physiological saline was given 24 hours and 4 hours before the test intraperitoneally in amounts of 15 to 20 cc.

§ In amounts as in † and ‡.

‖ A second animal survived 6 hours. The animals that succumbed died within one to 2 hours.

In these experiments 4 groups of young adult rats were used. In one group each rat received desoxycorticosterone acetate subcutaneously† 24 hours and again 4 hours before the test. In a second group each rat received saline intraperitoneally at the same intervals. In a third group each received both desoxycorticosterone acetate subcutaneously and saline intraperitoneally. In a fourth group the rats were unprepared. Four hours after the last injection, the animals were given histamine in amounts varying from 1200 to 2600 mg per kg. Desoxycorticosterone acetate alone afforded only slight protection. As previously demonstrated[8] the prophylactic administration of saline alone greatly enhanced resistance. More pronounced protection, however, was observed in the group of rats prepared both with saline and desoxycorticosterone acetate (an occasional animal surviving 2400 mg per kg).

The results were even more striking in mice (Table IV). Though saline alone was slightly more effective than desoxycorticosterone alone, the use of both protected the mice against histamine to a greater degree than either and raised their resistance to a level more than 5 times that of untreated mice.

Prevention of surgical shock in man. On the basis of these experiments a plan for the prevention of surgical shock was carried out in the preparation of a series of chronically ill patients for severe

TABLE IV.
Prophylactic Effect of Parenteral Saline and of Desoxycorticosterone on Resistance to Histamine in Mice.* (Combined data of 2 experiments.)

Amt of histamine acid phosphate per kg body wt	Untreated		Treated with Desoxycorticosterone†		Treated with Saline‡		Treated with Saline and Desoxycorticosterone§	
	Total No.	No. survived	Total No.	No. survived	Total No.	No. survived	Total No.	No. survived
750	5	0	—	—	—	—	—	—
1000	5	0	6	5	6	2	6	5
1200	—	—	6	4	6	2	6	5
1500	—	—	6	1	5	4	6	5
2000	—	—	3	1	6	1	6	3
2400	—	—	—	—	3	0	6	4

* The mice were of the same strain as in the previous experiments reported in this communication.

† The desoxycorticosterone acetate in oil was given subcutaneously in amounts of 1.5 mg 24 hours and 4 hours before the test.

‡ The saline was given 24 hours and 4 hours before the test in amounts of 1 and 1.5 cc respectively, intraperitoneally.

§ In amounts as in † and ‡.

† In the therapeutic experiments desoxycorticosterone could not be used because it is absorbed too slowly and at present is not available in a solvent permitting rapid absorption.

surgical procedures. From the fifth to the second day before operation, patients received daily 8 to 10 g of salt in divided doses in water, 3 liters of fluid by mouth, and 5 mg of desoxycorticosterone acetate intramuscularly. Two days prior to, on the day of, and on the day after operation intravenously 1000 to 1500 cc of physiological saline daily and 10 mg of desoxycorticosterone intramuscularly were given.‡ During 2 weeks after operation patients were given 5 mg of desoxycorticosterone daily for 5 days, then 5 mg every second day, as well as salt and high fluid intake by mouth. (General supportive measures such as a high protein, high vitamin diet with supplements of vitamin C were given where possible during the entire period.)

Table V shows the results in 12 consecutive instances in patients with chronic diseases in whom such operative procedures were performed as resection of colon or stomach, thoracoplasty and the like. None of these patients had any evidence of Addison's syndrome as determined by serum sodium, potassium and hematocrit determinations. In all instances the patients were strikingly benefited; there was no objective evidence of shock, blood pressure was maintained or elevated from 10 to 30 mm, the temperature in general returned to normal within 24 to 48 hours, post-operative exhaustion and toxemia were definitely lessened, complications did not occur and operative recovery appeared, to the surgeons concerned, to be more rapid than in their preceding surgical experience with similar conditions in our hospital.§ On the chest service the procedure has been adopted as a routine.

It is fully appreciated that this series of cases is in itself inadequate and that with further work our impressions may be modified.‖ However, the clinical results have been so striking that in view of the preceding experimental evidence we believe it justifiable to make a report as this time¶

Summary. In the prevention and treatment of histamine shock in rats and mice, parenteral saline combined with cortical hormone is

‡ Where only a short period of preoperative preparation is possible the desoxycorticosterone is increased up to 20 or 30 mg within 24 hours or cortical extract may be given intravenously in amounts up to 30 cc within this period in divided doses.

§ The only contraindications to the use of this treatment would appear to be cardiac decompensation, nephritis, and severe hypertensive states.

‖ The method is now being tried in two other large hospitals in the metropolitan area in addition to its continued use at Montefiore.

¶ We are indebted to Dr. Schwenk and Dr. Gilbert of Schering, to Dr. Oppenheimer of Ciba for supplying us with desoxycorticosterone acetate and to Dr. Klein of the Wilson Laboratory for the adrenal cortical extract.

TABLE V.

Use of Desoxycorticosterone Acetate and Saline in Prevention of Surgical Shock in Humans.

	Pre-operative				Operative						Post-operative				
Case	Diagnosis	Duration in yrs	Blood pressure	Condition	Type of operation	Anesthesia	Duration of operation	Pulse	Respiration	Blood pres.	Condition	Temperature	Pulse	Respiration	Blood pres.	Condition
V.M. 39 yr	1. Tbc. lung 2. Tbc. Osteomyel.	7 1	120 — 88	Poor; anemic; bronchial stenosis, bronchiectasis; poor surg. risk	Spinal fusion (L_2-S_1) with tibial bone graft.	Gas—O_2 Ether	1½-2 hr	90-96	20-24	130/68	Excellent; no evidence of shock.	100.2-100.8	98-112	No change	108-140 — 86 - 90	Excellent; No asthenia Appetite good; Gained weight.
E.S. 49 yr	Ca. of rectum	2	108 — 60	Fair; toxic, 1st stage Lahey 1 mo previously; did poorly	Resection of rectum	Spinal	1-1½ hr	100-112	20	116/70	Excellent	(2 day 103) 100-101	110-96	No change	130-112 — 78 - 64	Good; asthenia less; appetite increased.
L.H. 25 yr	Pulm. tbc.	3	140 — 90	Good; rapid prep. within 2 hrs [Cortin (20cc) and 500 cc saline]	1st stage thoracoplasty	Gas—O_2	1 hr	80-118	18-24	130/68	Alert, with sense of well-being	99-100.8	106-80	24-18	152-130 — 100- 70	Excellent; 2nd stage done in 3 weeks
,, ,,	,, ,,	,,	,,	Good	2nd stage thoracoplasty	Gas—O_2	1 hr	112	24	168/88	Excellent	99.0-99.2	120-80	24-18	142-170 — 86 - 90	Rapid recovery; discharge in 2 weeks
S.W. 23 yr	Pulm. tbc. (bilat.)	3	102 — 68	Fair; status post-pnthx. left Oleothx; left tbc. empyema. 1st stage—2 mo prev.; did poorly; needed transfusion	2nd stage thoracoplasty	Gas—O_2	1 hr	100	24	104/68	Same. Sense of well-being.	98-99	88-96	18-22	130-120 — 80 - 76	Excellent course in contrast to unprepared 1st stage

A.K. 20 yr	Extensive unilat. bronchiectasis	19	120 — 76	Fair; toxic	Attempted pneumonectomy.	Avertin Gas O_2	1½-2 hr?	106	18-36	142/90	Op. not completed; mediastinal adhes.	100-102	112-128	24-36	112-146	80 - 96	Patient did well; temperature rise due to sputum retention
F.S. 43 yr	Ca. of colon (Splenic flexus)	3	122 — 64	Poor; anemia; marked asthenia and wt loss; febrile; diarrhœa 8 mos.	Resection with side to side anastomosis	Avertin plus inhalation anes.	2-3 hr	96-100	120/68	22	No signs of shock, Felt well. (transfusion-hgb-48).	99.2-102	94-100	18-24	120	70	Retention of purulent matter in wound. Temp. normal after release. Out of bed in 2 weeks.
H.C. 39 yr	Pulm. tbc.	8	128 — 86	Fair; 1st stage done 5 weeks prev. with slow recovery and marked asthenia. (bl. pr.—96/30).	2nd stage thoracoplasty.	Gas—O_2	1 hr	104	118/86	20	Good	98.4-100.2	110-88	18-22	126-132	88 - 90	Little asthenia compared with 1st stage. No shock; rapid healing and recovery.
S.G. 55 yr	Cholelithiasis	1	140 — 80	Fair; prep. with vit. K. Also coronary dis. and mild hypertension.	Cholecystectomy	Spinal procain	1-1½ hr	84	134/68	26	Good	102-99.6	96-88	28-22	140-110	100- 68	For 5 days condition excellent. Evisceration with peritonitis (sutures removed too early). Rapid recovery.
H.B. 35 yr	Pulm. tbc. (bilateral)	11	104 — 68	Fair; (Gynecomastia and small testes). Low vital capacity. Marked fibrothorax.	1st stage thoracoplasty	Gas—O_2	1 hr	96	118/88	28	No shock	98.6-99.2	96-88	28-20	140-112	100- 84	Patient felt well; appetite good; rapid recovery and healing.
J.T. 49 yr	Carcinoma of stomach	5	148 — 86	Fair; fibroid tbc. and arterioscl. heart disease	Partial gastric resection	Spinal	2½ hr	100	142/82	22	Temp. 100.6 After 3rd day normal	101-98	104-72	24-20	150	74	Excellent.
L.S. 26 yr	Pulm. tbc. (bilateral)	7	130 — 80	Fair; 1st stage 3 mos. prev. Became toxic, febrile and did poorly.	2nd stage thoracoplasty	Gas—O_2	1-1½ hr	88	134/92	22	Excellent	101-99.8	104-84	32-20	134-126	92 - 70	Excellent.

more effective than either alone. The prophylactic effect of this combined treatment in raising resistance of rats and mice to histamine shock is much more pronounced than the therapeutic effect after histamine is administered. Application of these experimental observations to the prevention of surgical shock in human beings is reported.

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Are Gonadotropic Hormones Destroyed While They Exert Their Action on the Ovary?

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The question whether hormones are inactivated by the organs on which they act is of fundamental importance for the interpretation of hormone action in general. Some authors regard hormones as catalysts, which would imply that they are not used up during their activity, while others believe that they are destroyed while they exert their action. This latter view appears to receive some support from observations showing that if hormone preparations are administered parenterally only a fraction if any of the injected material may be recovered from the excretions. The fact that removal of one ovary causes compensatory hypertrophy of the remaining gonad has likewise been looked upon as "an expression of the effect of the total amount of anterior pituitary hormone being available for one ovary."[1] However, neither one of these arguments is conclusive and little effort has been made, up to the present, to solve this problem by experimental investigation.

It is doubtless true that hormones are destroyed in the organism but this does not prove that they are used up by the organs upon which they act. Furthermore, the compensatory hypertrophy of an organ such as the ovary may not only be explained by assuming that more gonadotropic hormone is available for the ovarian remnant but might also be looked upon as resulting from increased gonadotropic hormone secretion by the hypophysis of the partially spayed animal.

In order to elucidate this problem, the following experiment was

[1] Adams, A. Elizabeth, *Proceedings of the Second International Congress for Sex Research*, 1930, p. 190.