creased kidney NPSH. No change was observed in the chlorpromazine and thiamylal groups, but a slight increase in kidney NPSH occurred in the thiopental group. The possible relationship of anesthetics on tissue NPSH and metabolism is discussed.

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Effect of Administered Ascorbic Acid on Nitrogen Metabolic Response to Thermal Trauma. (22078)

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Numerous investigators have confirmed Cuthbertson's(1) observations of an increase in urinary nitrogen excretion by injured patients and animals. Lowered excretion of ascorbic acid, decreased adrenal and plasma ascorbic acid content, and decreased tissue ascorbic acid "saturation" as judged by load tests have also been observed during the period of increased urinary nitrogen excretion (2-5). These changes in ascorbic acid and nitrogen metabolism may be interrelated; ascorbic acid may be important in adrenal cortical function, and there is evidence to indicate that the nitrogen metabolic changes after injury are dependent, in part, on the level of adrenal activity. Ascorbic acid administered subcutaneously to normal rats was shown by Noble and Toby(6) to reduce urinary nitrogen excretion for at least 34 hours, the period of their observations. Further, rats traumatized by leg clamping and given ascorbic acid, either subcutaneously or orally, excreted less nitrogen in the first 34 hours after injury, the period of their observations, than rats similarly injured but not given ascorbic acid.

Accordingly, we have investigated the effects on nitrogen excretion of supplemental ascorbic acid given to rats with severe thermal injury throughout the period of negative nitrogen balance (2½ weeks following injury).

Methods. Thirteen male young adult albino rats of the Wistar strain were adapted over a period of 6 days to the force-feeding of a liquid diet(7,8). From the end of the adaptation period to the end of the experiment, each of the animals was given 10 cc of the diet 2 times daily. According to chemical analysis, each animal received 640 mg of nitrogen every 2 days. By calculation, this diet yielded about 0.2 calorie per gram of body weight per day and was made up, on a caloric basis, of 18% protein, 63% carbohydrate, and 19% fat. Six days after rats reached full feeding, they were placed in metabolism cages from which acidified urine and feces were collected every 2 days. Total nitrogen in urine, feces, and diet was determined by micro-Kjeldahl analysis(9). Urinary amino nitrogen was estimated by the colorimetric ninhydrin technic(10); no correction was made for urea which reacts with ninhydrin to the extent of 3%. Rats were weighed every other day. After a 12-day control period, all rats were lightly etherized and deep thermal injuries produced over 30-35% of their body surfaces by dipping their clipped backs into hot water (73°C) for 30 seconds

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TABLE I. Nitrogen Metabolism in Thermally Injured Rats: Effect of supplemental ascorbic acid.

Day of study	Body wt (g)		Urinary amino N (mg/48°)†		Urinary total N (mg/48°)†	
	Controls	Ascorbic acid supplemented	Controls	Ascorbic acid supplemented	Controls	Ascorbic acid supplemented
1- 2	295 ± 6*	278 ± 9	29.9 ± 2.1	30.7 ± 3.9	534 ± 48	504 ± 34
3- 4	286 ± 8	271 ± 8	32.5 ± 2.0	31.1 ± 4.1	515 ± 46	499 ± 43
5- 6	287 ± 8	274 ± 8	31.8 ± 1.7	29.3 ± 1.3	502 ± 24	491 ± 32
7- 8	293 ± 7	278 ± 7	29.7 ± 4.1	31.5 ± 4.1	500 ± 23	482 ± 48
9-10	293 ± 6	279 ± 8	(lost)	(lost)	513 ± 60	475 ± 28
11-12	296 ± 5	282 ± 7	31.6 ± 3.7	34.9 ± 2.6	506 ± 56	519 ± 52
13-14‡	296 ± 5	283 ± 7	37.5 ± 2.6	41.3 ±10.8	700 ± 98	702 ± 102
15-16	307 ± 9	297 ± 13	34.0 ± 4.7	37.2 ± 6.2	704 ± 88	718 ± 106
17-18	298 ± 11	279 ± 10	40.8 ± 2.8	40.8 ± 2.1	741 ± 43	746 ± 48
19-20	287 ± 10	267 ± 7	39.3 ± 3.8	43.5 ± 5.0	698 ± 77	725 ± 74
21-22	282 ± 9	261 ± 9	37.1 ± 3.1	41.3 ± 4.1	678 ± 35	733 ± 81
23-24	276 ± 11	260 ± 9	39.3 ± 6.3	42.7 ± 6.9	633 ± 75	624 ± 91
25-26	272 ± 12	254 ± 11	44.3 ± 6.9	38.4 ± 7.2	716 ± 102	609 ± 101
27-28	270 ± 19	245 ± 22	41.0 ± 4.9	47.1 ± 6.5	697 ± 107	695 ± 58
29-30	260 ± 11	250 ± 14	35.4 ± 8.9	37.1 ± 5.9	603 ± 117	581 ± 32

* Stand. dev. † 48° intake, 640 mg N (constant). ‡ All rats thermally injured on day 13.

according to the method of McCarthy(11). All rats were maintained on the constant tube-fed diet. Seven of the 13 animals received supplemental ascorbic acid; the first dose (25 mg) was given intramuscularly 1½ hours after injury. Thereafter, 25 mg of ascorbic acid were given twice a day, orally, to each of these 7 rats. Ascorbic acid was added to their food just prior to each tube feeding. The study was conducted for 18 days after injury, by which time the nitrogen excretion in both groups had returned close to the pre-injury levels. At this time the injured skin of the back was in the form of a dried eschar; epithelization was slowly taking place at the periphery of the injured area.

Results. During the control period, all rats were in slight positive nitrogen balance. Their body weights were stable. The thermal injury was followed by a loss in body weight (after a transient gain due to edema in the injured area) and prompt and prolonged increase in urinary nitrogen excretion, total and amino. These changes were uninfluenced by the administration of ascorbic acid (Tables I and II; Fig. 1). (The data were analyzed

TABLE II. Nitrogen Metabolism in Thermally Injured Rats: Effect of supplemental ascorbic acid.

Day of study	Urinary + fecal total N (mg/48°)†		N balance (mg/100 g body wt/48°)†	
	Controls	Ascorbic acid supplemented	Controls	Ascorbic acid supplemented
1- 2	594 ± 45*	557 ± 40	+16 ± 15	+30 ± 14
3- 4	576 ± 35	551 ± 43	+23 ± 12	+33 ± 15
5- 6	552 ± 29	541 ± 38	+30 ± 10	+36 ± 13
7- 8	550 ± 16	547 ± 42	+31 ± 6	+33 ± 14
9-10	560 ± 26	524 ± 32	+27 ± 8	+42 ± 12
11-12	561 ± 50	568 ± 50	+27 ± 16	+26 ± 16
13-14‡	746 ± 108	749 ± 101	−36 ± 36	−39 ± 33
15-16	750 ± 93	766 ± 106	−36 ± 31	−42 ± 35
17-18	797 ± 47	811 ± 52	−53 ± 15	−61 ± 16
19-20	754 ± 105	789 ± 76	−40 ± 35	−56 ± 25
21-22	750 ± 25	799 ± 85	−39 ± 9	−61 ± 28
23-24	672 ± 67	690 ± 90	−12 ± 22	−19 ± 30
25-26	751 ± 98	669 ± 110	−41 ± 33	−11 ± 36
27-28	757 ± 103	761 ± 56	−43 ± 34	−49 ± 18
29-30	623 ± 95	636 ± 32	+ 7 ± 32	+ 2 ± 11

* Stand. dev. † 48° intake, 640 mg N (constant). ‡ All rats thermally injured on day 13

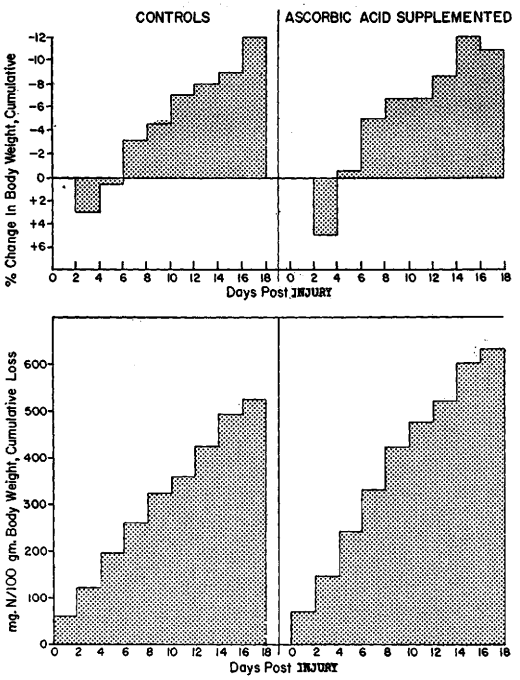

FIG. 1. Cumulative nitrogen balances and changes in body wt in thermally injured rats.

by the Fisher t test).

Prior to injury, the rats which were later to receive ascorbic acid were slightly lighter, about 5% on the average, than the controls. The rats in both groups lost about 12% of their pre-injury control weights during the 18-day period of increased urinary nitrogen excretion. About half of this weight loss can be accounted for by the observed increase in nitrogen excretion—if one assumes that the extra-urinary nitrogen was derived from tissue with approximately normal protein and water contents.

Lack of effect of ascorbic acid on the increase in urinary nitrogen excretion in this study is in apparent contradiction to the observation of Noble and Toby. However, the trauma employed in their study was leg crushing and their observations were limited to a brief (34-hour) period after injury; our observations were made in thermally injured rats and continued over a period of 18 days.

The rat, unlike man, does not require exogenous ascorbic acid for his daily normal requirements. Whether any supplemental ascorbic acid is needed by the rat following severe stress is not known. Ralli *et al.*(12) have recently studied the effect of the surgical removal of about 15% of the skin on the urinary ascorbic acid excretion by female rats. Ralli and her coworkers noted an increase in ascorbic acid excretion during the first 2 days after wounding, followed by a decrease to below the preoperative level for the next 2 weeks.

Conclusion. Loss of weight and increase in urinary nitrogen excretion, total and amino, by rats with severe thermal injury were unaffected by large doses of ascorbic acid begun shortly after injury and continued throughout the period of negative nitrogen balance (18 days). That these findings may be applicable to those species (man, monkey, and guinea pig) which depend on exogenous ascorbic acid for their normal requirements, unlike the rat, is suggested by the observations that marked increases in urinary nitrogen excretion following severe injury occur in patients receiving up to one g of vit. C daily(13).

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