

## ADRENALIN IN SCURVY

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It was reported earlier (1) that there was a significant increase in the adrenalin content of the adrenal glands of scorbutic guinea pigs. Unfortunately the paired feeding technique was not then employed. As inanition is always associated with the onset and development of scurvy, it might be argued that the results obtained were due to inanition alone and not to the specific effect of vitamin C deficiency. In the present investigation, therefore, an attempt was made to study the relation of scurvy to the adrenalin content of the adrenal glands of guinea pigs by the use of the paired feeding technique.

We observed a diabetic type of glucose tolerance curve in scorbutic guinea pigs (2) and pointed out that the lowered glucose tolerance of the scorbutic guinea pigs compared with that of normal animals might be partly due to an increased action of adrenalin (1) in the absence of the opposing action of insulin (3). The rôle of the adrenal medulla on the glucose tolerance test was, therefore, studied in guinea pigs in which the medulla had been removed; a scorbutic diet with or without the supplement of ascorbic acid and the paired feeding technique were employed.

### EXPERIMENTAL

#### *Relation of Scurvy to Adrenalin Content of Adrenal Glands of Guinea Pigs*

Young male guinea pigs with an average weight of 225 gm. were fed *ad libitum*, for 1 week, a scorbutic diet (1) with a daily supplement of 5 mg. of ascorbic acid. Those animals which were growing on this diet were selected. They were divided into two groups, housed in individual cages, and paired evenly so that the weights of the animals in each pair, one from each of the groups, were about the same. One of the groups was fed *ad libitum* the scorbutic diet without any supplement of ascorbic acid for 20 days. The daily food consumption of each animal of this group was measured and an equivalent amount of the scorbutic diet was given to the corresponding animal of the second group which received in addition a daily oral supplement of 5 mg. of ascorbic acid. All the animals were fed 2 drops of a concentrate of vitamins A and D twice a week. In the evening of the 20th day the food was removed from the cages of all the animals. The next morning, the animals were sacrificed by a blow on the

head, the neck veins cut, the adrenals removed and transferred to a weighed tube containing normal saline and a few drops of 10 per cent trichloroacetic acid, and the whole weighed again. Adrenalin was determined by the method previously described (1). The results are shown in Table I.

TABLE I  
*Determination of Adrenalin in Normal and Scorbutic Guinea Pigs*

Pair No.	Weight at death		Weight of adrenals		Weight of adrenals per 100 gm. body weight		Adrenalin per 1 gm. adrenal	
	Normal	Scorbutic	Normal	Scorbutic	Normal	Scorbutic	Normal	Scorbutic
	gm.	gm.	mg.	mg.	mg.	mg.	$\gamma$	$\gamma$
1	308	286	132.6	153.2	43	54	233	515
2	250	220	Lost	106.8		49		731
3	270	252	111.6	115.8	41	46	202	604
4	260	220	137.6	186.8	53	85	210	437
5	238	230	121.4	161.8	51	70	186	449
6	258	242	111.8	146.2	43	60	238	510
7	238	215	123.0	124.8	52	58	234	577
8	296	258	134.4	216.0	45	84	169	371
9	335	240	136.0	159.0	41	66	220	478
10	227	189	82.4	106.4	36	56	297	670
11	228	186	126.6	139.4	55	75	173	503
12	304	292	167.8	182.6	55	62	120	447
13	266	226	167.4	190.0	63	84	137	418
14	297	265	143.2	207.6	48	78	144	344
15	165	155	75.4	118.6	46	77	286	444
16	330	272	168.6	193.2	51	71	123	433
17	240	209	111.2	155.6	46	74	258	427
18	225	211	103.2	170.2	46	81	135	335
Average.....			127.2	157.4	48	68	198	483
Difference of means.....					20		285	
Standard error of difference.....					3.65		28.01	
$t^*$ .....					5.48		10.17	

\* All values of  $t$  are highly significant.

*Relation of Adrenal Medulla to Glucose Tolerance Test in Normal and Scorbutic Guinea Pigs*

Three groups of guinea pigs, each containing three animals, were housed in separate cages and fed *ad libitum* the scorbutic diet with daily oral supplements of 5 mg. of ascorbic acid. Two animals from each group were selected. They were fasted overnight and on the 6th day adrenal enucleation was performed under ether anesthesia according to the method, slightly modified, described by Evans for rats (4). After the operation,

the animals were allowed to drink a 1 per cent solution of sodium chloride. On the 22nd day after demedullation, by which time the cortex is completely regenerated, the ascorbic acid supplement was withdrawn from one of the demedullated animals in each group. The daily consumption of the diet of the animal receiving no ascorbic acid was measured and an equivalent amount of the diet was given separately to the other two of the group.

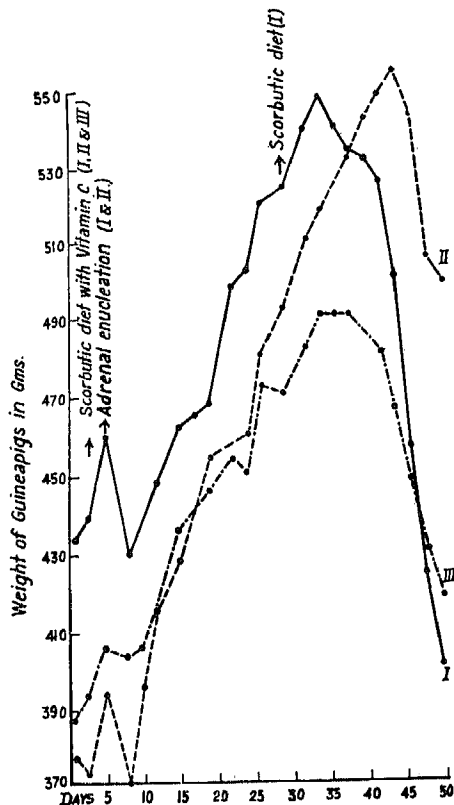


FIG. 1. Growth curves of guinea pigs. Curve I shows the growth of the scorbutic guinea pig with demedullated adrenals; Curve II, the demedullated guinea pig receiving vitamin C; Curve III, the guinea pig with intact adrenals receiving vitamin C.

Thus, in each group, one demedullated animal received the scorbutic diet only, while the other demedullated guinea pig and also the animal with intact adrenals received an equivalent amount of the scorbutic diet with a daily oral supplement of 5 mg. of ascorbic acid. All the animals were fed 2 drops of a concentrate of vitamins A and D twice a week during the experimental period. In the evening of the 49th day of the experiment, 21 days after the withdrawal of ascorbic acid from one of the demedullated

guinea pigs of each group, food was withdrawn from the cages of all the animals. The glucose tolerance test was performed the next morning. After a fasting blood specimen had been taken from the heart, each guinea pig was fed 0.2 gm. of glucose per 100 gm. of body weight in a 50 per cent solution. Blood samples were taken from the heart at intervals of 45 minutes up to 280 minutes after the administration of glucose. The blood sugar was estimated according to the method of Hagedorn and Jensen (5).

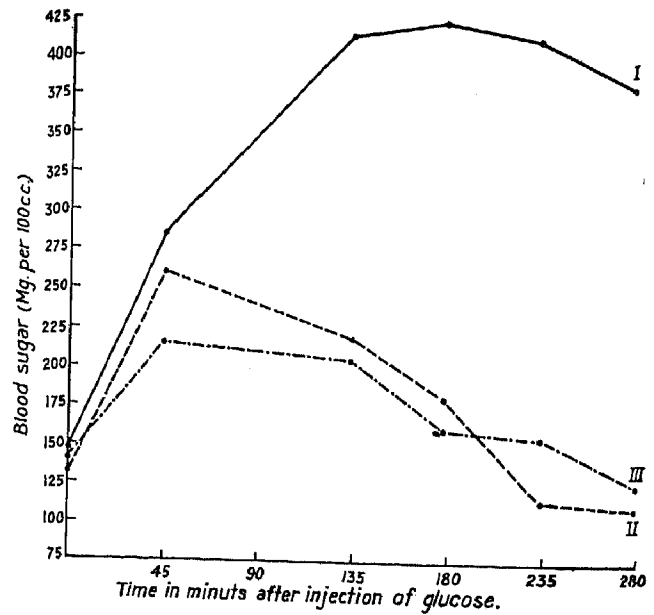


Fig. 2. Glucose tolerance curves of guinea pigs. Curve I represents the results on the scorbutic guinea pig with demedullated adrenals; Curve II, the demedullated guinea pig receiving vitamin C; Curve III, the guinea pig with intact adrenals receiving vitamin C.

Curves for growth and glucose tolerance of one of the groups of guinea pigs are shown in Figs. 1 and 2.

#### DISCUSSION

Both the size and the adrenalin content of the adrenal glands of scorbutic guinea pigs were significantly increased when compared with those of the pair-fed normal control animals (Table I). In our previous report (1), in which the normal control animals received the diet *ad libitum*, both the size and the adrenalin content of the adrenal glands were relatively higher. Inanition, therefore, slightly affects the above findings. The increase in the size and the adrenalin content of the adrenals in scurvy is therefore mainly due to the effect of vitamin C deficiency. In the present investi-

gation all the scorbutic animals were fed *ad libitum* the scorbutic diet for 20 days, when they were sacrificed. Unlike the scorbutic animals of the previous report (1), which received the scorbutic diet up to 25 days, the animals of the present experiment were in the early stage of scurvy and the size and adrenalin content of the adrenal glands were at a relatively lower level. It seems, therefore, that the size of the adrenal glands and the adrenalin content increase gradually with the progress of scurvy.

Fig. 1 shows that the normal control animals, fed the same amount of diet as the animal of the scorbutic group, lose weight similar to the scorbutic animals, but the effect is delayed. The loss in weight with the progress of scurvy is therefore mainly due to inanition. The demedullated scorbutic guinea pig gave a diabetic type of glucose tolerance curve like that observed in scorbutic guinea pigs (2). The demedullated guinea pig and the control with intact adrenals, which received the same amounts of diet consumed by the scorbutic animal in addition to the supplement of vitamin C, gave normal glucose tolerance curves. This indicates that neither adrenalin nor inanition is responsible for the lowered glucose tolerance as observed in scurvy. The disturbed carbohydrate metabolism in scurvy seems more likely to be due to diminished insulin secretion by the pancreas of the scorbutic guinea pigs (3).

#### SUMMARY

1. The effect of scurvy on the adrenalin content of the adrenals of guinea pigs was studied by a paired feeding technique.
2. There was significant increase in the size and also in the adrenalin content of the adrenals of scorbutic guinea pigs.
3. The glucose tolerance tests were performed on scorbutic guinea pigs with demedullated adrenals, on demedullated guinea pigs receiving vitamin C, and on guinea pigs with intact adrenals receiving vitamin C.
4. The demedullated scorbutic guinea pigs gave a diabetic type of glucose tolerance curve, whereas the others showed a normal tolerance to glucose.
5. Neither adrenalin nor inanition was responsible for the lowered glucose tolerance observed in scurvy.

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