Adaptation of Hypophysectomized Rat to Fasting. (19631)

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Since the hypophysectomized rat in several instances had been found to a tendency to develop hypoglycemia during fasting(1-4), it seemed likely that it would succumb readily to fasting. The present study was undertaken because it had been observed that hypophysectomized rats whose nutrition had been maintained by stomach tube feeding seemed to survive fasting rather better than had been expected. Inasmuch as it appeared that the maintenance of nutrition by such feeding was the explanation, the study was arranged to check on this possibility.

Procedure. Male albino rats obtained from Sprague-Dawley and of the same age were sorted into groups of similar average weight. The animals were hypophysectomized or sham operated by a parapharyngeal approach. The pituitary was exposed but not otherwise disturbed in those sham operated. At the end of the experiment, the completeness of the removal of the pituitary was checked by serially sectioning a block of tissue including the base of the skull and the overlying brain. Every tenth section was mounted and stained. The sections were cut 10 μ thick. In all the hypophysectomized animals from which data are reported there was no trace of pituitary within the dural capsule which normally contains it, nor were any implants found along the operative path. The stalk lying between the infundibulum and dural capsule always remained intact, for care was taken at the time of the operation not to rupture the dorsal layer of the capsule. The animals were allowed to fast for the 2 days following the operation. They were then given a liquid diet in which 20% of the calories were from protein and 40% each from carbohydrate and fat. Those fed by stomach tube were given 2 or 3 feedings per day of sufficient quantities to induce a gain in weight(5). The amounts given the hypophysectomized rats and their sham operated controls were identical. After 19 days of feeding, the animals were allowed to fast until they died. During the period of fasting they were kept in a laboratory temperature of approximately 25-27°C. They were housed in cages with screen bottoms, but because it was expected that at least those hypophysectomized rats which had been allowed to feed *ad libitum* would promptly succumb to fasting and thus terminate the experiment, several animals were placed in each cage. Consequently their oral intake may have included more hair and debris such as rats get in grooming each other as well as more feces due to coprophagia than if they had been caged singly. In addition a few grams of tissues were eaten from each of 2 animals, one dying on the 11th and the other on the 12th day of fasting. The fasting conditions, therefore, were not absolute; but it seems reasonable to describe them as severe. Furthermore, there is no reason to suspect that they favored the hypophysectomized animals as compared with their controls. Tap water was offered *ad libitum.* Blood sugar was determined by a modification of the Folin-Malmros ferricyanide method on samples taken from the tip of the tail(6).

The data from 3 force fed hypophysectomized rats dying on the 2nd, 3rd and 11th day of fasting and from one hypophysectomized rat fed *ad libitum* dying on the 12th day of fasting were discarded. The animals dying on the 2nd and 3rd days were found to have multiple pulmonary abscesses at postmortem.

Results and discussion. The average body weight and blood sugar concentration of the groups are shown in Fig. 1. The numerical data at selected points on these curves are given in Table I together with the data for the postmortem weight of the body, liver and testes and the number of days the animals survived fasting. It appears that a number of hypophysectomized rats which had been allowed to feed *ad libitum* as well as many of those which had been force fed survived

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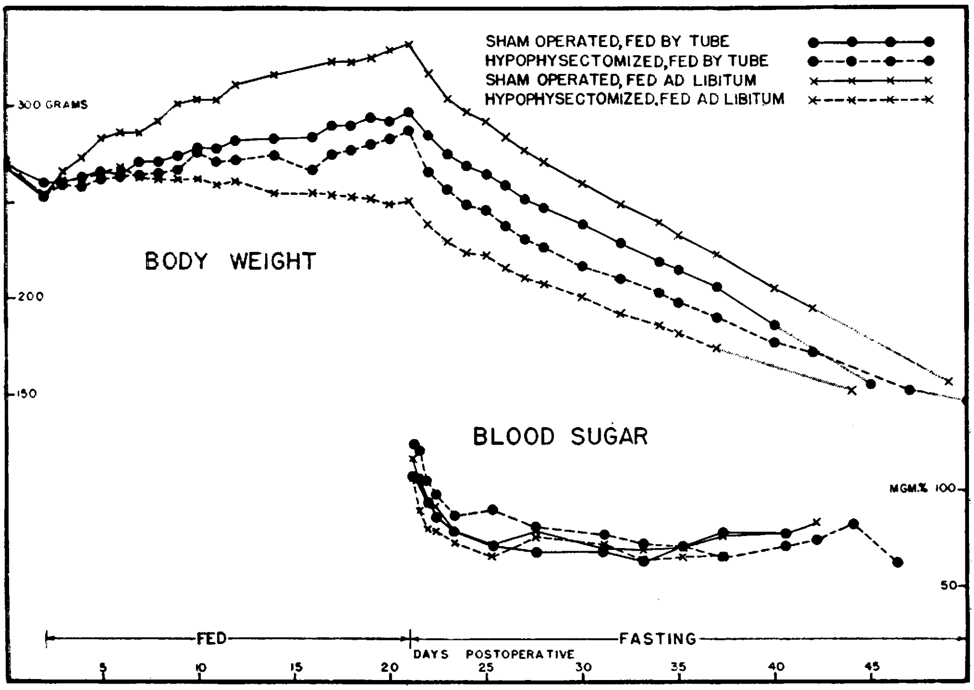

FIG. 1. Avg body wt and blood sugar concentrations. The final points on the body wt curves show avg body wt and avg day of death for respective groups.

fasting about as long as their controls. It further seems that these hypophysectomized animals which survived fasting well on the average were able to maintain their blood sugars at values not differing greatly from those of their controls. At times the hypophysectomized rats fed *ad libitum* did have a lower average blood sugar concentration than their controls in agreement with the findings in previous studies. When the averages over a longer period are considered, however, the differences are not impressive. It also may be noted that at death from inanition the controls had smaller livers and larger testes. While the hypophysectomized animals fed *ad libitum* apparently gained less weight during the period of feeding, yet they seem to have compensated for this deficit by consuming their weight more slowly during fasting. It may be pertinent that the hypophysectomized animal tends to have a higher percentage of body fat and that smaller weight changes are involved in either storing or consuming a calory in the form of fat rather than protein(7).

It is evident that the prior maintenance of its nutrition by stomach tube feeding is not essential for the fasting hypophysectomized rat to maintain its blood sugar concentration above that at which the symptoms of hypoglycemia appear and to survive for about as long as its control.

Evidence has been offered that suggests that the hypophysectomized rat suffers defects both in removing an excess of sugar from its blood and in supplying sugar to prevent or overcome low blood concentrations(9,10). The findings of the present study do not indicate that such defects are absent, but merely that if they are present they do not necessarily lead to hypoglycemia and an early death during fasting.

Summary. It was found that in a group of hypophysectomized rats allowed to feed *ad libitum* as well as in a group force fed by stomach tube some animals subsequently survived fasting about at long as their non-hypophysectomized controls. These hypophysectomized animals which survived fasting well also maintained blood sugar concentrations

TABLE I. Numerical Data, Averages and Ranges (in Parentheses) for Groups.

	Sham operated, fed by stomach tube	Hypophysectomized, fed by stomach tube	Sham operated, fed *ad lib.*	Hypophysectomized, fed *ad lib.*
No. of animals	7	5	7	9
Body wt, g				
Day of operation	270(258–283)	272(262–287)	268(261–282)	269(260–285)
Beginning of fast	297(282–314)	287(280–293)	332(298–353)	251(237–266)
16th day of fast	209(193–215)	190(182–197)	223(199–234)	174(161–187)
Day animal died	155(148–172)	146(138–153)	156(150–174)	152(135–170)
Blood sugar, mg %				
Beginning of fast	108 (94–116)	124(101–147)	117(101–134)	107 (93–114)
2nd day " "	78 (72–84)	87 (78–96)	79 (71–95)	73 (62–84)
16th " " "	78 (65–102)	65 (46–72)	76 (64–98)	66 (54–84)
Survival after beginning of fast in days	24 (19–28)	29 (27–31)	28 (23–31)	23 (18–29)
Organ wt at death, g				
Testes	1.96(1.76–2.20)	.35(.28– .42)	1.93(1.60–2.38)	.37(.29– .44)
Liver	2.1 (1.8 –2.3)	3.3 (3 –3.6)	2.2 (1.9 –2.6)	3.6 (3 –5)

during fasting which were comparable to those of their controls.

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Spermicidal Effect of Certain Physiologically Active Substances. (19632)

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A great number of compounds have been tested to determine their action on spermatozoa. Among those which have been found to be toxic are alkyl hydrocupreidine derivatives(1), metabolites such as indole, maleate, and glyceraldehyde(2), and long chain compounds such as sulfo-dioctylsuccinate(3). Ketone reagents have also been reported to be toxic(4), as have known enzyme inhibitors like fluoride and iodoacetate(5). Heavy metal salts, like phenylmercuric acetate(6,7), wetting agents, such as Duponol(8), and quinones(9) have been found to have toxic properties.

It is apparent that a large number of compounds of widely varying chemical structure have in common the property of toxicity toward spermatozoa. For this reason the possibility is relatively high that a given compound may have some spermatocidal effect. The ever increasing number and variety of chemical compounds in clinical use suggested that it might be of value to determine whether such substances would have a deleterious effect on spermatozoa, since this might affect their utility as therapeutic agents. In addition it was felt that the possibility of discovering one or more spermatocidal agents in types of