Results. In the animals poisoned with phenol no consistent difference was noted between the fat and carbohydrate groups. The animals receiving protein showed a somewhat lower mortality. It is to be noted, however, that the animals fed high protein had not gained as much weight as the other groups, and, since the dose was based on body weight, these animals therefore received a somewhat smaller dose of phenol than the animals in the other groups of the same age.

With cyanide, we have tabulated separately the animals who were on the experimental diet only 10 to 14 days. Even in this group, however, it is noticeable that the mortality of animals on a high fat diet is distinctly less than on the high carbohydrate, high protein or stock diet. When the experimental diet was continued for 18 to 22 days this difference becomes very striking—the mortality in the high fat group being only 11% as contrasted with 56% for the high carbohydrate group and 44% for the high protein group. We have no explanation to offer for the marked protection against cyanide poisoning afforded by a high fat diet.

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Influence of Diet on Resistance to Diphtherial Toxin

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In order to investigate the influence of diet on the resistance of rats to diphtherial toxin, groups of rats were placed on diets rich in protein, carbohydrate, and fat respectively. The diets and conditions of the experiment were identical with those described in the preceding paper.[1] After 17 to 21 days on the experimental diet the rats were given a subcutaneous injection of diphtherial toxin* (7 m.l.d. per gram of rat). Relatively large doses of toxin are required to kill these highly resistant animals. According to Cobbet[2] and Ramon, *et al.*,[3] the rat requires from 1250 to 1750 times as much toxin per unit of animal weight as does the guinea pig. Preliminary experi-

[1] Meyer, A. R., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 402.

* The concentrated toxin used in these experiments was supplied by E. R. Squibb and Sons, through the courtesy of Dr. G. W. Rake.

[2] Cobbet (1899), quoted by Pettit, *Ann. de l'Inst. Pasteur*, 1919, **28**, 663.

[3] Ramon, Noureddine, and Erber, *Compt. Rendu Soc. de Biol.*, 1928, **99**, 562.

TABLE I.
Mortality of Rats Receiving Diphtherial Toxin* (7 m.l.d. per g).

Exp. No.	I	II	III	IV		Mortality
Days on exp. diet	17	18	20	21	Total	%
Mortality (deaths/total rats)						
High protein (avg wt = 83 g)	1/4	3/7	0/5	0/9	4/25	16
High carbohydrate (avg wt = 130 g)	4/4	5/6	3/5	5/10	17/25	68
High fat (avg wt = 124 g)	3/4	3/6	4/6	6/8	16/24	67
Stock (avg wt = 80 g)	3/4			2/4	5/8	63
Inanition 2-4 days (avg wt = 80 g)	1/5			1/6	2/11	18

ments with our rat colony indicated that the dose given above would kill 2 out of 3 rats in about 5 days. The mortality-data on the different diets are given in Table I. In fatal cases death occurred on an average about the fifth day in all groups of animals.

Results. An examination of Table I shows no difference in mortality between the high-fat and high-carbohydrate groups, but a very striking reduction of mortality in the case of the high-protein diet. One can not, however, conclude from this that protein is a superior food as far as increasing resistance to diphtherial toxin is concerned. Attention must be called to the fact that the high-protein animals had gained less weight than either the high-fat or the high-carbohydrate groups and that they consequently received a smaller absolute amount of toxin than either the high-fat or high-carbohydrate animals. Retardation in growth occurs inevitably when an animal's intake of protein is suddenly increased. The studies of Addis[4] and others have shown that under these conditions hypertrophy of various organs, particularly the liver, takes place, and time must be allowed for this adjustment to occur before the animal can thrive and grow on the new diet. In order to find out whether inanition could be playing a part in inducing the increased resistance of the high-protein-fed animals, it was decided to study the effect of acute inanition *per se*. Two groups of animals on stock diet were fasted 2 to 4 days and were then given doses of toxin based on body-weight as described above. The results are shown at the foot of Table I. It appears that acute inanition will cause a marked increase in resistance to diphtherial toxin when doses are based on body-weight.

It is possible that inanition played some part in increasing the resistance of our high-protein animals, but one is not justified in attributing their increased resistance to this alone, for at the time the high-protein animals were injected with toxin they were no longer suffering from inanition but were eating and gaining well.

[4] Addis, T., *J. Biol. Chem.*, 1936, **116**, 343.

TABLE II.
Mortality of Animals Receiving Diphtherial Toxin (900 m.l.d. per rat).

Exp. No. Days on experimental diet	V 21	Mortality %
Mortality (deaths/total rats)		
High fat (avg wt = 130 g)	5/8	63
High carbohydrate (avg wt = 132 g)	5/10	50
High protein (avg wt = 104 g)	2/8	25

The similarity of the results in the high-protein animals and the animals with acute inanition may have been due to the fact that the animals suffering from acute inanition were in reality living on a high-protein diet derived from their own body protein.

A further experiment was carried out to see if the increased resistance of the high-protein group—as contrasted with the high-carbohydrate and high-fat groups—would be evident if all animals were given the same absolute dose of toxin regardless of weight. The smaller protein-fed animals would then be receiving a larger per kilogram dose of toxin than the other groups. It was felt that if, under these circumstances, they still showed a higher resistance than the high-carbohydrate or high-fat groups, the conclusion would be justified that a high-protein diet really offered superior protection against the toxin. The results of this experiment are shown in Table II, in which animals in all groups received 900 m.l.d. of toxin.

It is apparent that even under these adverse conditions the high-protein-fed rats make the better showing.

Summary. 1. Rats fed on a diet rich in protein (casein) for 17 to 21 days showed a markedly higher resistance to diphtherial toxin than rats fed diets high in carbohydrate or fat. This could be demonstrated not only when the dose of toxin was based on the weight of the animals, but also when the dose was based on age. 2. Acute inanition caused an increased resistance to diphtherial toxin when the dose was based on the weight of the animal.