IX. NOTE ON THE RÔLE OF THE ANTI-SCORBUTIC FACTOR IN NUTRITION.

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Considerable interest is focussed at the present time upon the antiscorbutic substance found in many natural foodstuffs, and the relationship of this substance to scurvy in man and to experimental scurvy in guinea-pigs and monkeys has been the subject of many investigations during the past few years. These researches have demonstrated that if individuals of these species are fed upon a dietary deficient in the antiscorbutic substance they will sooner or later exhibit the classical symptoms of scurvy. Other species, however, appear to be able to thrive for long periods of time upon similar dietaries, without showing apparent symptoms of ill-health, much less definite pathological lesions. Such a species is the rat. The researches upon the growth problem have been carried out very largely with this animal as an experimental subject, and they have yielded results which indicate that the rat requires for a satisfactory completion of its life cycle a diet containing not only adequately adjusted supplies of protein, fat, carbohydrate and inorganic salts, but also a sufficient supply of two accessory factors, which have been provisionally termed "fat-soluble *A*," and "water-soluble *B*." The general opinion has up to the present held that if the diet is adequate in these respects the rat will show a normal rate of growth and a normal standard of nutrition throughout the usual span. This has led to the assumption that the rat is a species representative of a type showing no susceptibility to scurvy, since to all intents and purposes it has been possible to obtain a normal standard of nutrition throughout its life period, although the diet has been seriously, if not totally, deficient in the antiscorbutic factor or "water-soluble *C*." The only alternative to such an assumption, as was pointed out by McCollum and Pitz [1917] is to conclude that scurvy is in reality not a deficiency disease in the sense in which the term has been employed during the past ten years.

Since this alternative has been shown to be unsatisfactory, and since it is now established without any doubt that scurvy is indeed a typical deficiency disease [Harden and Zilva 1918, 1], we are faced with the need for an explanation of the ability of the rat to grow and maintain apparently excellent health in the absence of the antiscorbutic substance.

Quite recently Harden and Zilva [1918, 2] have brought forward experimental evidence that the antiscorbutic factor does play a beneficial rôle in the nutrition of the rat. They state that rats subsisting on a diet containing the antiscorbutic substance as well as the water-soluble and fat-soluble factors grow better than rats from the diet of which the antiscorbutic factor is absent.

This, they point out, indicates that rats are susceptible to an antiscorbutic deficiency although they do not develop definite lesions of the disease. Some time prior to the publication of this paper the same point was under investigation in this laboratory, because some rough experiments had indicated that recovery from the pathological condition induced by a deficiency of fat-soluble *A* was in certain cases more rapid when a diet containing butter fat plus orange juice was given than when the ration contained butter fat but no fruit juice.

Two standard dietaries were made up as follows:

	Ration 1	Ration 2
Purified caseinogen	20 parts	20 parts
„ starch	50 „	50 „
Butter fat	20 „	20 „
Salt mixture	5 „	5 „
Yeast extract	5 „	5 „
Orange juice	0 „	10 „
Water	40 „	30 „

Several healthy litters of young stock rats of approximately the same age were selected and each litter was halved. Two batches were then made up of the halves of the divided litters, so that half of each litter would receive each dietary. At the commencement of the experiment the animals were about six weeks old and were all of very similar body weight. These two batches were fed, the one on the orange juice diet and the other on what may be termed the scorbutic ration.

Both lots grew well, and after maturity was reached breeding was permitted, and the growth and development of the second generation were also watched.

Throughout the experiment, more satisfactory development was shown by the batches receiving the orange juice addition to their diet. The difference was not marked until the animals approached maturity, and was not discernible to the eye, being only apparent in a study of the body weight.

Table I gives the average weights of male rats upon the two diets. All the animals in each batch showed body weights very close to the average, so that there was no case of one or two low weights causing an unfair reduction of the value.

Table I. *Average Weights of Male Rats in grams.*

Days	Ration 1 (6 animals)	Ration 2 (6 animals)	Donaldson [1915]
0	62	64	—
30	124	122	125
60	161	183	184
90	193	213	223
120	208	234	244
150	220	248	258
180	233	256	268
210	241	263	274
240	245	278	280
270	249	287	296

A similar observation was made in the case of the females, but in this case it is difficult to illustrate the fact clearly in tabular manner owing to the disturbances in the weight increments caused by pregnancies. In these two batches there was just as little to choose between the appearance of the animals as was observed in the case of the males. After maturity was reached the breeding propensities of both batches were good, although on the whole a larger number of litters was obtained from the females receiving the orange juice diet.

The representatives of the second generation nourished upon the two rations were in every case of good appearance, but Table II demonstrates that those receiving the orange juice supplement were able to grow at the more rapid rate. All litters were reduced to a uniform size (4) immediately after birth, so as to equalise the labour of rearing the young animals imposed upon the females of the two sets.

Table II.

	Males			Females		
Days	Ration 1 average of 9	Ration 2 average of 11	Standard value of Donaldson	Ration 1 average of 10	Ration 2 average of 18	Standard value of Donaldson
0 (birth)	5·7 g.	6·0 g.	—	5·7 g.	6·0 g.	—
7	14·5 „	15·0 „	—	14·0 „	14·6 „	—
14	23·5 „	23·5 „	—	22·6 „	22·6 „	—
21	34·2 „	36·0 „	30·0 g.	30·2 „	32·0 „	28·0 g.
28	48·0 „	52·0 „	48·5 „	48·0 „	50·0 „	41·0 „
56	122·0 „	146·0 „	110·0 „	102·0 „	105·0 „	100·0 „
84	165·0 „	204·3 „	173·0 „	132·0 „	146·0 „	143·0 „
112	197·0 „	226·4 „	213·0 „	146·0 „	159·0 „	166·0 „

Although these figures represent the averages of somewhat small numbers of animals, they may be taken as indicating that the rat requires the antiscorbutic factor in order to achieve a normal development, and that although the requirements of this species are of a very much smaller order than those exhibited by man, the monkey or the guinea-pig, they are sufficiently well-marked to dispel any idea that there exists a fundamental difference in the nutritive requirements of the two types of animal.

These results are in agreement with those published recently by Harden and Zilva [1918, 2].

It may therefore be accepted as experimentally proven that the dietary requirements of the higher animals include in addition to a satisfactorily balanced ration of protein, fats, carbohydrate and mineral salts, an adequate supply of three accessory food factors:

1. Fat-soluble *A*.
2. Water-soluble *B*, or antineuritic factor.
3. Water-soluble *C*, or antiscorbutic factor.

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