IX. A NOTE CONCERNING THE INFLUENCE OF DIETS UPON GROWTH.

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In a recent paper Osborne and Mendel [1912, 1] have described certain experiments which seem to show that young animals (rats) can grow when fed upon artificial diets consisting of "purified" constituents alone.

These experiments would therefore indicate that the accessory factors of uncertain nature (complex lipoids or "vitamines" or "hormones") which others have believed to be necessary are not, as a matter of fact, indispensable. Such experimental results must give pause to those who like ourselves are engaged in an endeavour to separate, and identify more closely, the accessory substances referred to. But they are results which contradict what is now a considerable body of experience, and the experiments which yielded them seem to call for repetition.

These particular experiments were in a sense merely incidental to a wide enquiry, on the part of the authors quoted, into the nutritive efficiency of various proteins; and those which are of significance to the matter at issue (those, namely, which showed actual growth, and not maintenance alone) concerned only three animals [1912, 1, pp. 356, 358]. In a later paper [Osborne and Mendel, 1912, 2] the authors again refer incidentally to the subject and speak of having obtained "a considerable degree of success" by feeding in the absence of "the hypothetical organic hormones," etc. [1912, 2, p. 242].

But the weight-curves given in this paper show little more than maintenance of the animal, without growth; while, for some reason, the three experiments of the earlier paper which showed complete success in the promotion of vigorous growth are not further quoted. This success the authors attributed in the main to the fact that, in this dietary, salts were

supplied in a mixture made to imitate as exactly as possible the salts of milk ; but it is difficult to understand how animals so omnivorous as rats can depend for normal growth upon a very exact balance of particular acid and basic ions. In the experiments described by one of us in an earlier paper [Hopkins, 1912] the salts administered were obtained by carefully ashing a normal food mixture of proved efficiency. Upon an artificial diet containing these salts the animals did not grow ; but they grew at once when certain substances were added to the diet, some of these addenda being certainly incapable of supplying any deficiencies in the inorganic constituents of the original diet.

We have now fed a large number of rats upon the diet employed by Osborne and Mendel. The salt mixture as described by them was made with the greatest care, and all their directions for the preparation of the food mixture were exactly followed. But the protein and starch were thoroughly extracted with alcohol, and the lactose used was several times precipitated from its aqueous solution by the addition of alcohol. The methods of feeding were exactly those used in the paper by one of us already referred to, except that the food, being more fatty and coherent, was not mixed with water.

Twenty-four rats from various sources, of weights from 50 to 60 grms., were placed upon the mixture. Although the consumption of food was satisfactory, every rat, without exception, rapidly ceased to grow. In the greater number growth ceased as early as the sixth day, in some on the ninth, and in all before the fifteenth day. A comparatively brief period of maintained weight was then followed by a steady decline. In the case of eighteen of the animals the diet was administered up to the time of death, which, in all but four cases, occurred before the fortieth day.

To six of the above set of rats, after the decline in their weight had begun, 2 c.c. of milk per diem were given. An immediate betterment of the general condition of the animals followed ; growth was re-established and the health then maintained. In another experiment six rats were put upon Osborne and Mendel's diet, but were given milk from the first. In each case the animal grew.

We have spoken of the food consumption (which was carefully determined each day) as being satisfactory. It was smaller however than the consumption of the animals upon a somewhat different artificial dietary in the experiments described earlier by one of us. Its energy value, during the period which preceded actual loss of weight, was just under 40 calories per 100 grms. live weight, instead of over 50 calories. That the former value is nevertheless well in excess of the amount required for maintenance is shown by some, as

yet unpublished, experiments upon comparable animals made in the Cambridge Physiological Laboratory by Miss Hill.

When the small ration of milk was given each day in advance of feeding with the Osborne and Mendel diet the food consumption remained of the same order, and did not rise to the amount consumed by the rats in Hopkins' earlier experiments [1912]. The resulting growth though quite definite and steady was distinctly slower than in the experiments mentioned.

Our rats clearly behaved very differently from the three animals fed upon a similar diet by Osborne and Mendel. The difference we are unable to explain. Realising from previous experience how very small a remainder of the substances which are extracted by alcohol may leave an artificial dietary with some power of maintaining growth, and knowing that ether is a greatly inferior solvent for them, we fed rats upon the Osborne and Mendel mixture in which the protein (commercial casein) was extracted with ether only (as in one of Osborne and Mendel's experiments [1912, 1]; Curve 58, p. 358) and the lactose not crystallised from alcohol. We were unable to obtain growth however, though even this small difference in the diet appreciably lengthened the period during which the animals remained in health.

We do not in this note propose to publish the schedules of weights, etc. They will be given elsewhere at a later date. The purpose of the present note is to indicate that there is still reason for a continuance of the search for special accessory substances of potent influence upon growth. It should be pointed out that Osborne and Mendel themselves admit that such substances may exist.

REFERENCES.

- Hopkins, F. G. (1912), *J. Physiol.* **44**, 425.
Osborne and Mendel (1912, 1), *Zeitsch. physiol. Chem.* **80**, 307.
Osborne and Mendel (1912, 2) *J. Biol. Chem.* **13**, 233.