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Effect of Continued Administration of Iodide on the Growth of the Albino Rat.*

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Early in the course of the attempts in this laboratory to prepare a mixture of inorganic salts that might be adequate as a source of the mineral nutrients in feeding experiments with purified food materials, the inclusion of small amounts of iodine was planned.[1] This is reflected in the widely used Osborne-Mendel (IV) salt mixture[2] that contains 0.0025% of iodine. The quantity of iodide thus included was somewhat arbitrarily chosen, because a suitable guide as to the precise needs of the animals (rats) under investigation was not available.

Hanzlik, Talbot and Gibson[3] published a report on the comparative effects of prolonged administration of iodide and of other salts on the growth and body weight of rats. They concluded that "the continued administration of iodide in small daily doses in food over long periods (covering from about one-seventh to seven-twelfths of the span of life) to rats caused moderate though variable increases in weight and growth of the body in the majority of animals on complete dietary." The effects of other salts—sulphocyanate, bromide, arsenite, etc.—"were found to be in marked contrast to those of the iodide, thus emphasizing the distinctiveness of iodide, which was found to be beneficial and at least not harmful."

Careful studies on growing chicks at the Illinois Agricultural Experiment Station[4] have failed to show "any apparent difference either in the health or rate of growth of the birds" when a good mixed grain ration was supplemented daily in the case of some of

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1 Osborne, T. B., and Mendel, L. B., *J. Biol. Chem.*, 1913, xv, 311.

2 Osborne, T. B., and Mendel, L. B., *J. Biol. Chem.*, 1918, xxxiv, 131.

3 Hanzlik, P. J., Talbot, E. P., and Gibson, E. E., *Arch. Int. Med.*, 1928, xlii, 579.

4 A Year's Progress in Solving Farm Problems of Illinois, 1927-28. Univ. of Ill. Agric. Expt. Station, 1928, p. 173.

the animals with 0.5 to 1 mg. of potassium iodide for each 100 gm. of body weight.

The subject is important not only pharmacologically but also in planning adequate rations for use under the restricted conditions of laboratory feeding tests or for nutrition of domestic animals in confined quarters. The necessity, or wisdom, of supplementing foods with iodine in goitrous or semi-goitrous regions is well known. There are claims, too, that iodide may improve the assimilation of nitrogen, phosphorus and possibly calcium in growing animals.[5] Chidester, Eaton and Thompson[6] have reported that "while thyroid extract and iodine will produce rapid metabolism resulting in small animals, minute doses of the iodides or desiccated thyroid prove beneficial to rats on a *normal* diet and induce bone growth and increased weight."

The experiments of Hanzlik, Talbot and Gibson attracted our attention because the iodide supplements that they fed were added to rations that already contained 4% of the Osborne-Mendel salt mixture with its 0.0032% of potassium iodide. On the assumption of an average daily food intake of 7 gm. per rat for the *unsupplemented* conventional food mixtures in which these proportions of the Osborne-Mendel salt mixture are included, the daily iodine intake will be about 0.007 mg. To this Hanzlik, Talbot and Gibson added sufficient sodium iodide to correspond to "about 1 mg. daily per rat or about 3.3 mg. daily per kg. throughout the major part of the life of the rats. This dosage of iodide would correspond to about 0.23 gm. (3½ grains) daily for an adult of 70 kg. and might represent the daily amount used during the course of medication with iodide for the prevention of simple goiter, and that used in the treatment for toxic goiter and for chronic inflammations such as bronchitis, asthma and arthritis, but would be several times greater than the daily dose of iodide used in the form of iodized table salt."

The somewhat augmented growth reported as the result of this greater iodine intake led us to investigate the possible desirability of improving the Osborne-Mendel salt mixture by increasing its content of iodide. Male albino rats in separate cages were fed from the time when they weighed about 60 gm. on a food mixture consisting of:

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[5] Kelly, F. C., *Biochem. J.*, 1925, xix, 559.

[6] Chidester, F. E., Eaton, A. G., and Thompson, G. P., *Science*, 1928, lxviii, 432.

	%	
Casein	35	
Cornstarch	37	plus 10 drops of cod liver oil and 0.2 or 0.3 gm. dried yeast (in tablet form) daily.
Lard	15	
Butter fat	9	
Osborne-Mendel salt mixture	4	

The daily dosage of yeast was increased from 0.2 gm. to 0.3 gm. after each rat had been on the diet 49 days (Series A) and 56 days (Series B) respectively. Some of the animals served as "controls" without supplementary iodide; others received a daily addition of 1.107 mg. of potassium iodide dropped, in solution, upon the yeast tablets. These were readily consumed so that a fixed dosage of iodide became possible. Series A included 3 "control" rats and 6 animals that received potassium iodide. All were kept on the diet more than 400 days, a considerable part of the animals' span of life. Series B included 6 rats in each of the 2 groups for comparison over a period of 200 days. The variations between the records of individual animals are not inconsiderable; but the graphs that represent the averaged rates of gain for the respective groups are, we think, too nearly alike to permit claims of superiority for either type of diet. Unfortunately the number of animals observed in each series is too small to offset the effects of variability due to unsatisfactory growth of a few individuals.

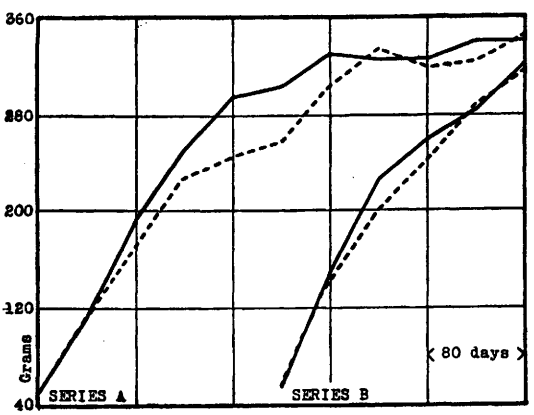

FIG. 1.

Graphs of the averaged rates of gain in body weight of comparable groups of rats. Those that received supplementary iodide are represented by the solid line; the control group by the broken line.

Whether differences between the iodine content of the water and of the "accessory" foods (yeast, alfalfa, cod liver oil) used in the two laboratories might explain the small differences in outcome is not apparent. One feature already emphasized by Hanzlik, Talbot and Gibson is particularly noteworthy, namely, the apparent harmlessness of very prolonged administration of iodide.

Mr. G. B. Moment of the Osborn Zoology Laboratory, Yale University, has kindly made histological examinations of the thyroids of all of the rats observed. He reported the absence of detectable differences in structure; on the other hand rats raised in our laboratory on diets without any additions of iodine other than that present in the natural foods and drinking water used showed somewhat defective thyroids.

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Vital Staining With Methyl Red.

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A generally accepted hypothesis advanced to explain the permeability of protoplasm to certain substances is that these substances penetrate because of the solubility of their associated molecules in the plasma-membrane of the living cell.

This hypothesis would account satisfactorily for the vital staining of the basic dye, neutral red, which is a chloride or iodide of a colored organic base. At the pH of the normal medium of living cells, viz., a pH greater than 7.0, this dye is presumably in its least dissociated state and it readily penetrates and accumulates within the cells. When the stained cells, e.g., marine ova, are placed in a medium having a pH of about 6.0 which is lower than that of the protoplasm[1, 2] the color quickly washes out. Moreover, vital staining with this dye does not occur when the outside medium is more acid than the protoplasm. Apparently, therefore, the dye passes readily through the plasma-membrane from a medium of a higher to that of a lower alkalinity.

An interesting case which is explicable on the same hypothesis of

[1] Needham, J., and D. M., *Proc. Roy. Soc., London*, 1926, xcix, 173.

[2] Chambers, R., and Pollack, H., *J. Gen. Physiol.*, 1927, x, 739.