type. It is probable that more frequent observations would have shown a brief rise in the curve at first as in O. The steady decrease in the blood sugar for the last three hours is striking. During this period there was marked hunger, relieved for only a few minutes by water-drinking. The most obvious explanation for these observations seems to be the following. The hyperglycemia during food absorption acts as a physiological stimulus to insulin production by the pancreas. The immediate result is glycogen storage and glucose utilization. The insulin thus produced outlasts the need for it. Its presence in greater amount than previous to breakfast leads to the typical hypoglycemia when artificially administered. The hunger is a consequence of the hypoglycemia. The hypoglycemia acts as a physiological stimulus to the glycogenolytic mechanism and the blood sugar returns to the normal "fasting level."[2] This latter level is an optimum operating level for the body in the post-absorptive equilibrium. In some individuals the glycogenolysis may occur at such a slight hypoglycemia that the curve shows it only when frequent observations are made. In others, such as subject O, a definite diphasic curve is found. In still others, such as subject N, the glycogenolysis is a poor response, and hunger gets worse until another meal is taken. N stated that he was not hungry during the morning when he ate no breakfast, but always hungry when he did eat. The reports of Harris[3] seem to be of such individuals.

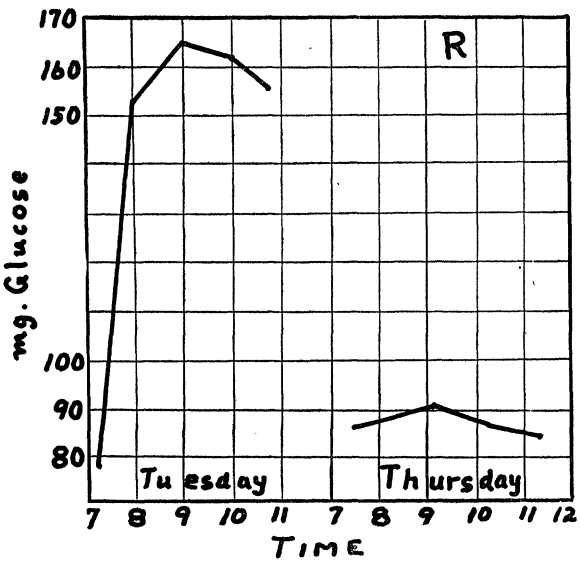

FIG. 2

[2] Cannon, W. B., McIver, M. A., and Bliss, S. W., *Am. J. Physiol.*, 1924, lxix, 46.

[3] Harris, S., *J. Am. Med. Assn.*, 1924, lxxxiii, 729.

In Fig. 2 are shown the results of a somewhat different type of study. R was one of the three students who went on a voluntary three day fast. Blood sugar determinations were made twice on the first and third days. There was a gradual decline in the sugar concentration from 92 mg the first morning to 77 mg the fourth morning. This was not associated with marked hunger. The fast was broken on the fourth morning by a breakfast rich in carbohydrates, including fruit. The blood sugar curve marked "Tuesday" was obtained during this morning. There was a notable lack of satisfaction from the meal until after about two hours afterward. This is to be correlated with the unusually high curve and the marked delay in the return to a normal level. The urine of the last fasting day showed ketosis. Two days later, after meals had been taken as usual, the Tuesday breakfast was repeated exactly, and the blood again analyzed. The curve marked "Thursday" shows a marked contrast to that of the morning after the fast. The Thursday breakfast gave satisfaction subjectively. The two other students studied reacted in this same fashion throughout, except for no evidence of ketonuria. We propose as rapidly as possible to extend these observations and to verify the extent of ketosis. It may be that there is contained here some hint of the nature of the apparently vicious cycle of vomiting and starvation which occurs in pregnancy and after surgical procedures. Insulin has repeatedly been found efficacious in breaking this cycle and restoring normal oxidation without ketosis, when glucose alone failed. These observations may help to explain why in the presence of ketosis it is necessary to use such large doses of insulin to render the diabetic free from glycosuria.

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THE EFFECT OF FLUORINE AS SODIUM FLUORIDE ON THE GROWTH AND REPRODUCTION OF ALBINO RATS

IT has long been known that fluorine is present in the bones and teeth of mammals, and fluorine was used by Osborne and Mendel[1] in one of their salt mixtures for rats more than a decade ago. It is quite generally considered as being one of the inorganic elements essential in nutrition, which is necessary in small amounts only, although there is no evidence of its necessity except its occurrence in the animal body.

[1] Osborne and Mendel, *Journal of Biological Chemistry*, Vol. 15, 317, 1913.

Since rock phosphate generally contains considerable amounts of fluorine, the unfavorable results obtained by Forbes and collaborators[2] at the Ohio station when feeding raw rock phosphate "floats" to swine in comparison with bone products directed suspicion to the fluorine content of the rock phosphate. While some of the unfavorable results obtained in their work may have been due to the considerable magnesium content of the rock phosphate, the occurrence of fluorine in commercial ground phosphate rock adds considerable interest to the results described below, which were obtained in the course of our work on certain inorganic elements in the nutrition of rats.

The toxicity of fluorides has also been studied by several investigators from a pharmacological point of view, using mainly rabbits and dogs. More recently, Sollman, Schettler and Wetzel[3] have fed sodium fluoride to rats in varying amounts, causing progressive impairment of growth and food consumption. Their results agree with those reported here insofar as they are comparable.

The basal ration used in our work was one which was being used in the comparison of other mineral supplements. It consisted of yellow corn 76 parts, meat meal tankage 10 parts, linseed oil meal 10 parts, bone meal 2.5 parts and common salt 0.5 parts. On this basal ration with wood shavings litter the control groups of rats grew at a normal rate and reproduced normally. Sodium fluoride was fed to other groups of rats in the following amounts, mixed thoroughly and ground with the ration: 0.05 per cent., 0.10 per cent., 0.15 per cent. and 0.25 per cent. of the ration.

The rate of growth of the rats in the first fluorine group was normal or better and the animals in this lot remained in good condition after nine months on the ration. There were only two females in this group, but each one successfully produced and reared two litters of young in that time.

The rats in the second group, which received 0.10 per cent. of sodium fluoride, did not grow as well or as rapidly as the first group. The rate of growth of most of the rats in this group was slightly below the normal. Out of six litters of young in this lot four were reared, but these grew at a very slow rate. Both old and young in this lot showed a quite unthrifty appearance, even though the growth of the first generation was nearly at the normal rate. Both the first and second groups produced a third generation, but in the second group the number of young reared was much below the average performance of the controls.

The rats in the third lot, which received 0.15 per cent. sodium fluoride, grew at approximately the same rate as the second group, but out of four litters produced, only two litters lived, to grow at a slow rate. In this lot as in all the sodium fluoride lots, the rats which had been on the ration longest presented the most unthrifty appearance.

In the fourth group, which received 0.25 per cent. sodium fluoride, all the seven rats in the lot died after 8 to 14 weeks on the ration. None of them reached a weight of 100 grams.

The data on the first group, which received 0.05 per cent. sodium fluoride, do not show a performance varying much from the controls on this basal ration, but the observations of the writers lead them to suspect that there was some stimulating effect due to the fluoride, and also that the amount fed was at or very near the maximum possible without showing the ill effects observed in the other groups. Smaller allowances of sodium fluoride have since been tested on the same basal ration.

Amounts of sodium fluoride varying from 0.001 per cent. to 0.25 per cent. of the ration were fed in the second series, with results which corroborate the results just described. No ill effects on growth and well-being are observed until 0.10 per cent. or more of sodium fluoride is fed. A very marked toxic effect is observed when 0.15 per cent. to 0.25 per cent. is allowed in the above-mentioned basal ration. It appears that an unfavorable effect on reproduction begins at a level of about 0.025 per cent. sodium fluoride in the ration. We also have evidence that the toxic effect on growth begins at a lower level of fluorine when a purified basal ration is used.

A remarkable effect of the fluorine on the growth of the teeth of these rats was observed. The upper incisors of the second and third groups grew to a length of about 15 mm, curving upward until they began to pierce the cheeks of the animals. At this time they were clipped, but the teeth continued to grow at the same rapid rate. The first group reported above which received only 0.05 per cent. sodium fluoride, presented teeth which were somewhat longer than the normal, but not so long as the teeth of the groups receiving more fluoride. The average length of the upper incisors of the mature rats observed in our colony is 5 mm. The lower incisors are normally about twice as long. In the fluoride rats, however, it was only the upper ones which showed an excessive growth.

This study of fluorine and its function in nutrition is being continued.

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[2] Forbes, *et al.*, Ohio Agr. Exp. Sta., Bulletin 347, 1921.

[3] Sollman, Schettler and Wetzel, *Journal of Pharmacology and Experimental Therapeutics*, Vol. 17, 197, 1921.