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The acid base ratio of the diet in rickets production.

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The results of the work on experimental rickets in rats have shown that rickets can be produced by diets which are poor in phosphorus and rich in calcium or diets which are poor in calcium and rich in phosphorus. A condition produced in that manner can be prevented or restored to normal by exposing the animals to a sufficient amount of light of certain wave lengths or by administering cod liver oil which contains a substance that affects the calcium and phosphorus metabolism. There is no evidence at present that this substance regularly occurs in natural foodstuffs, and, therefore, there seems no valid reason to put it into the class of vitamins. Until it has been shown that the curative agent in cod liver oil is a component of normal foods, we cannot assume that rickets is due to a vitamin deficiency. This, then, leaves us, in spite of the accumulated data on experimental rickets in animals, without any definite information as to the physiological changes which lead to rickets in children since children will develop rickets on diets well balanced with regard to calcium and phosphorus. It is important, therefore, to learn more concerning other factors which influence rickets-production, in order to gain an understanding of the possible causes of human rickets when it is produced under conditions where dietary factors cannot be held responsible. We believe that we have obtained evidence of a factor not taken into consideration in the recent work on experimental rickets. Ernst Schloss[1] in one of his monographic papers on rickets has called attention to the fact that contrary to the hypothesis held at one time, according to which rickets is due to an acidosis, it is found that rickets seems to develop more frequently under conditions rather the opposite of an acidosis. There are also certain indications that during cure of rickets a relative acidosis develops. Schloss, however, had no very def-

[1] Schloss, Ernst, *Ergebn. inn. Med. u. Kinderh.*, 1917, xv, 95.

inite data on which to base this assumption. Furthermore, Schabad[2] has shown that in active rickets the distribution of calcium and phosphorus between urine and feces is such as we now know will occur with insufficient acidity of intestinal contents. We believe that in some of our rat experiments we have supplied evidence pointing in the direction of Schloss's hypothesis. On a diet consisting of flour, casein, calcium lactate, sodium chloride, and a trace of ferric citrate, rats will regularly develop a rather marked rickets as shown by X-ray and microscopic sections of ribs. This diet, like practically all diets used in rickets production, contains a large excess of base-ion over acid-ion, the lactic acid of the calcium lactate being a weak acid, while calcium is a strong base. When we substitute, in this diet, calcium chloride for calcium lactate in equivalent quantities, we markedly increase the acidity. Such a diet, when fed to rats, resulted in bone growth so nearly normal that it could not be called more than minimal rickets, while the control rats getting calcium lactate developed a very marked rickets. In another set of experiments, we made the rickets producing diet mentioned above more acid by addition of 2 per cent. of ammonium chloride. The rats receiving ammonium chloride developed no rickets, while those on the control diet showed, as always, perfectly definite rickets. We think, therefore, that without modifying any of the factors discussed heretofore, we can change a rachitic into a non-rachitic diet.

The reverse of the above experiments was obtained on certain diets made up of flour and egg albumen together with a suitable salt mixture. The control rats were given an egg albumen-flour diet to which enough potassium phosphate had been added to prevent development of rickets. To this diet was added 2 per cent. of sodium carbonate making the diet extremely alkaline. On the latter diet rats developed a very marked rickets. Thus we have changed a non-rachitic diet into a rachitic diet without changing the calcium or phosphorus intake in the food or any of the other known factors which affect rickets. The growth curves of these rats were all approximately the same, thus ruling out the question of total food intake.

If we consider that the digestive tract is capable of a good deal

[2] Schabad, *Ztschr, f. klin. Med.*, 1909, lxviii, 94.

of variation in hydrogen ion concentration through the varying growth, we will see what the significance of these experiments may be. In the first place, it is well known that the hydrogen ion secretion of digestive juices and also possibly through bacterial concentration of the gastric juice of infants on a milk diet is only a small fraction of that of older children and adults on mixed diet. Therefore, it is quite possible that through a still further reduction of acid in the digestive tract a significant lack of absorption of calcium and phosphorus may take place. We reported experiments in these Proceedings[3] some time ago on the effect of varying intake of acid and base on the partition of calcium and phosphorus between urine and feces, and interpreted the effect of greater urinary excretion under a more acid regime as a greater absorption from the intestine. Data supplied by Scheer[4] in the meantime further substantiate this, and show that in children there is concomitant with a greater absorption under the influence of acid, also a greater retention of calcium and phosphorus.

We come to the conclusion, therefore, that on a diet which from the point of view of balance between calcium and phosphorus should not lead to rickets, it may be possible that with a change in the intestinal tract in the sense of a lessening acidity, rickets may be produced. Here we have, then, a factor which resides in the individual and not in the diet, and may lead to at least a partial explanation of the occurrence of rickets in infants on a diet which is perfect from a dietetic point of view.

In the course of this winter we are planning to investigate the application of this hypothesis to infantile rickets.

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[3] Zucker, T. F., PROC. SOC. EXP. BIOL. AND MED., 1921, xviii, 272.

[4] Scheer, *Jahrb. f. Kinderh.*, 1922, xcvii.