It is not easy to understand the mechanism by which inorganic material may so profoundly influence the production of blood hemoglobin. We may recall a few observations which may have some bearing on this puzzle. Fasting dogs usually produce more hemoglobin in anemia than dogs given a liberal amount of carbohydrate, which we believe indicates a careful conservation of intermediates derived from body protein breakdown to be used for construction of new hemoglobin. Further we recall that during a period of rapid gain in weight on a meat diet the dog will not form the expected amount of new hemoglobin. Evidently material suitable for tissue growth has been diverted from new hemoglobin construction. There is probably a certain give and take within the body of essential amino acids and other elements suitable either for tissue growth or repair as well as for new hemoglobin production. It is possible that certain salts and inorganic elements have an influence upon internal protein metabolism and may in some measure determine the direction of the flow of these building stones—now for tissue growth or repair—now for body fluid protein maintenance—now for emergency new hemoglobin and red cell production.

[1] Robscheit-Robbins, F. S., and Whipple, G. H., *Am. J. Phys.*, 1927, lxxx, 400.

[2] Robscheit-Robbins, F. S., and Whipple, G. H., *Am. J. Phys.*, 1925, lxxii, 408; *ibid.*, 1927, lxxix, 271.

[3] Whipple, G. H., and Robscheit-Robbins, F. S., PROC. SOC. EXP. BIOL. AND MED., 1927, xxiv, 86.

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[5] Waddell, J., Elvehjem, C. A., Steenbock, H., and Hart, E. B., *Science*, 1928, lxvii, 139.

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Influence of Acid-Forming and Base-Forming Constituents of Ketogenic Diet Used in Treatment of Idiopathic Epilepsy.

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In a previous communication[1] data were presented to show the relationship between variations in the degree of ketosis and the occurrence of convulsions in certain epileptic children on ketogenic diets. The convulsions were found to occur practically always during the periods of minimum ketosis as measured by the urinary and

blood acetone bodies. However, during the past 12 months, we have repeatedly made the observation recently reported by Lennox,[2] that administration of considerable quantities of sodium bicarbonate to patients under this form of treatment causes temporary recurrence of the convulsions in spite of the diet. This suggested to us the importance of determining the relative efficiency of ketogenic diets having an acid-ash and those containing an excess of base-forming over acid-forming elements.

Observations were made over a total period of 60 days in the case of a 13-year-old patient suffering from severe idiopathic epilepsy. This time was subdivided into periods in which the test diets were given alternately. Except for one period in which a non-ketogenic diet with a very highly acid ash was given, the diets throughout were strongly ketogenic, varying only in their ash content. The most notable fact observed from the study was that the convulsive seizures, which practically ceased to occur during the acid-ash, ketogenic diet periods, promptly recurred in alarming numbers when a diet, containing the same amounts of protein, fat and carbohydrate but with a predominantly basic ash, was given. During the relatively long subperiod, when a non-ketogenic diet with a strongly acid ash was given, the patient had from 2 to 12 grand-mal attacks daily, in spite of the fact that the diet contained in its ash, according to calculation, an excess of acid equivalent to 1110 cc. of 0.1 N solution.

Data derived from a fairly comprehensive study of the factors concerned in the maintenance of the acid-base equilibrium of this patient were found to lend support to the theory that there is a fundamental disturbance in the acid-base metabolism in this form of epilepsy. The ineffectiveness of the ketogenic, alkaline-ash diet in controlling the convulsions is, therefore, probably best explained by assuming that the diet tends to accentuate the abnormal tendency already present. Most of the blood pH values recorded for the periods in which frequent convulsions occurred were found to be definitely above those obtained during the periods characterized by relative freedom from seizures. Three slight convulsions occurred during the first acid-ash period of 11 days, but these were associated in each instance with a marked diminution in the degree of ketosis, following the inadvertent giving of anti-ketogenic material. The time of their occurrence, which was from 1 to 2 hours after meals, and the finding of higher blood pH as well as higher acetone values after meals than before, suggest the possibility of a relationship of these convulsions to the "alkaline tide". This is being investigated

further as a possible explanation for the greater frequency of epileptic convulsions at or near the time of meals.

The fact that the non-ketogenic diet with the excessively acid-ash failed to have any influence on the number of convulsions and failed to sustain the hydrogen-ion concentration of the blood within normal limits, indicates a more or less specific value of the ketogenic diet in this respect so far as its effect on the epileptic subject is concerned. Since the concentrations of acetone bodies in the blood and the urine were found to be elevated during the alkaline-ash period very distinctly above the levels for the acid-ash periods, it is evident that the relationship between the degree of ketosis and the frequency of convulsions previously reported holds only when the ketogenic diet is one with an acid or neutral ash. Finally, it may be tentatively concluded from the foregoing results that the ketogenic diet with an acid-ash is the most efficient so far studied in controlling convulsions in that group of epileptic subjects who respond at all to the dietary form of therapy.

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Expulsion of its Contents as a Function of the Gall Bladder.

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Since the introduction of methods that visualize the gall bladder, many opinions have been expressed as to the mechanism of its emptying. These can be divided into 2 groups: (a) that the gall bladder has a passive rôle in this process, and (b) that the gall bladder empties due to the contraction of its own musculature. We wish to present further evidence that expulsion of its contents is an inherent function of the gall bladder and acts independently of purely mechanical factors.

The chief extrinsic agencies suggested as causing the discharge of bile from the gall bladder are: (1) variations in intra-abdominal pressure, (2) intestinal peristalsis, (3) elastic recoil following relaxation of the common-duct sphincter, and (4) the washing out of the gall bladder by hepatic bile.