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Blood Regeneration in Severe Anemia—Influence of Inorganic Ash of Liver, Kidney and Apricots.

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In some of the early anemia work at the University of California Robscheit-Robbins and Whipple observed an unusually favorable reaction to the feeding of dried peaches in short term anemia experiments in dogs. Repetition of this apricot and peach diet in severe anemia in dogs shows clearly that the original observations were correct.¹ The addition of 200 gm. of this cooked fruit to the daily standard diet may cause an average output of 40 to 45 gm. hemoglobin per 2-week period over and above the standard control period. All of this work indicated clearly that the inorganic elements of this fruit should be tested. We have recently reported^{2, 3} experiments dealing with various fractions of extracts of beef liver.

It is to be kept clearly in mind that our experiments deal with the simplest form of anemia, due to withdrawal of blood. One must be cautious in comparing simple anemias of this sort with fasting or nutritional anemias. Different animals may react quite differently to various diets—for example, the herbivora may utilize the chlorophyll of green vegetables to build hemoglobin whereas dogs cannot do so.⁴ We are greatly interested in a recent preliminary report of Waddell, Elvehjem, Steenbock and Hart⁵ which indicates that the ash of beef liver has a favorable effect upon certain nutritional anemia of rats. It is probable that some differences will come out as we learn more about this nutritional anemia as compared with simple anemia due to hemorrhage.

The various samples of inorganic ash were prepared in the following manner: Fresh beef liver, pig kidney, or dried apricots are weighed and placed in a large fire brick container. Free flames from several blow-torches are played on this material until it is reduced to a black carbon mass. At this point a stream of oxygen is directed into the hot material burning it down to a white, gray, or bluish brown, glassy ash. This is then ground in a mortar, passed through a 40 mesh sieve, weighed and fed in doses equivalent to the original fresh material. The material used in these experiments contained 4 to 8% of carbon but it is reasonably certain that all organic com-

pounds are broken down. In liver and kidney ash experiments we used the ash equivalent to 500 to 600 gm. fresh material which varied from 2 to 5 gm. in weight. In the apricot ash experiments the ash equivalent of 200 gm. dried fruits was used—this also varied from 2 to 6 gm. in weight.

Of this fine gray ash 2 to 6 gm. corresponding to a known amount of fresh material were added to the standard basal bread ration⁶ of the experimental animal. There was a surprisingly uniform reaction to the various ash samples whether from liver, kidney or apricots. One might suspect the presence of some common substance or group of substances in the material. In fact we are testing various elements and simple compounds which are present in these inorganic mixtures.

We have completed 6 experiments with *liver ash* added to the standard bread ration of these anemic dogs. During the usual 2-week period these dogs averaged 40 to 50 gm. hemoglobin production over and above the control periods. Liver ash corresponding to 500 to 600 gm. fresh beef liver was added daily to the bread ration. These same dogs during a 2 weeks period on 300 to 400 gm. cooked liver, equivalent to 450 to 600 gm. fresh liver, would produce 60 to 100 gm. hemoglobin over control periods.² These same dogs on a large excess of ferric citrate (0.2 gm.) or chloride (0.06 gm.) daily during 2 weeks would average about 20 to 25 gm. hemoglobin production over and above the control periods.

We have completed 6 experiments with *kidney ash* using the same amounts as in the liver ash experiments. We may say that the hemoglobin production observed is exactly similar to the liver ash experiments. It may be recalled that cooked pig kidney feeding is about as potent as liver feeding.

We have completed 5 experiments with *apricot ash* which corresponds very closely to those with liver and kidney ash. The average values for the hemoglobin production per 2-week period are 35 to 45 gm. over the control periods. It may be recalled that apricots as fresh cooked moist sauce (200 gm. daily) added to this bread ration produces 40 to 45 gm. hemoglobin over and above the control period. Perhaps one may generalize to the extent of stating that the apricot ash seems to contain about one-half of the potent material in whole apricots favorable to new hemoglobin production.

It would seem that *iron* as the essential factor responsible for the entire reaction could be ruled out on a number of counts. For example, among the fruits tested raspberries were inert, yet they contain as much iron as do apricots which are so active.

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.

⁴ Robscheit-Robbins, F. S., and Whipple, G. H., *Am. J. Phys.*, 1925, lxxii, 431.

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

⁶ Whipple, G. H., and Robscheit-Robbins, F. S., *Am. J. Phys.*, 1925, lxxii, 395.

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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 communication¹ 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