blood sugar levels are approximately the same. Thus, both sets of animals have a low initial blood sugar level before nephrectomy, and rise to a level somewhat higher than that observed in normal animals after nephrectomy. This post-nephrectomy blood sugar level is maintained constant over the period of time studied. Hence, it is probable that the blood sugar *per se* is not the factor responsible for the stimulation of the thyroid gland.

Summary and Conclusions. The administration of phlorhizin results in a stimulation of the thyroid gland which in turn is responsible for part of the increased protein metabolism observed in phlorhizin diabetes. Since this increased protein metabolism of the phlorhizinized animal continues even after the removal of the kidneys, but does not occur when phlorhizin is administered to previously nephrectomized animals,[2] it is probable that this drug exerts some specific effect on the kidney, which is in turn responsible for the thyroid stimulation. Our observations do not offer evidence for the possibility that the blood sugar level is the responsible factor in the increased activity of the thyroid but suggest some primary renal factor.

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Deleterious Effects of Insulin Shock.

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The effects of a hypoglycemia of long duration on the various tissues and the organism as a whole are of fundamental importance. On the practical side the possibility of the use of excessive doses of the new slow acting protamine insulin by untrained individuals, because of the lack of immediate results or the accidental administration of the concentrated precipitate from a vial which has not been agitated, make essential a knowledge of the effects of hypoglycemia due to insulin shock.

In experiments on dogs we have found that when a state of insulin shock is maintained for 24 hours or longer with protamine zinc insulin it is apparently impossible to resuscitate the animal and death always ensues. Often this result follows when the period is shorter. A typical protocol follows: A male dog weighing 29 kg., last fed the day before the experiment started, was given 40 units (1 cc.)

of protamine zinc insulin,* and 23 hours later 20 units more. Five hundred cc. of fluid were given by stomach tube at 23, 30, 38, 50, 57, and 71 hours. With the exception of the first dose this was 10% sucrose and at 38 and 57 hours 5 gm. of sodium chloride were also administered. The blood sugar concentration was 61 mg. % at 0 hours and 22 at 6.5, 36 at 23, 28 at 25, 22 at 30, 28 at 38, 73 at 47, 52 at 50, 67 at 56, 41 at 71, and 67 mg. % at 73 hours respectively. At this time the dog died, apparently of circulatory failure. The animal had his first convulsion 7 hours after the first dose of insulin and became unconscious within 13 hours. He never came out of this coma which after 40 hours could have had no relation to the blood sugar concentration at the moment. In other experiments milk or milk and sugar has been given with the same result. In many of our experiments death has resulted from hypoglycemia before sufficient sugar was administered. So far we have had seven animals in which death ensued long after the blood sugar level had been returned to normal. Fat and well nourished dogs appear to suffer less from the hypoglycemia than thin ones.

Experiments are being carried out in an attempt to determine the relation of the undesirable effects of insulin shock to the hypoglycemia itself and to the secondary effects on the circulation and other body mechanisms. An important point is the length of the shocking period which is necessary to produce such damage that recovery does not occur. Grossly the brains do not appear particularly abnormal, but it seems possible that damage to the brain, analogous to that due to anoxemia, may explain the untoward effects of hypoglycemia. Insulin shock is being purposely used in schizophrenia therapy[1, 2] and Steinfeld[3] has reported that circulatory collapse or epileptiform convulsions are serious side reactions which may occur even when the blood sugar has again been raised to a normal level. We have seen this happen in our experiments and hypoglycemia is obviously not the immediate cause of the death of our animals.

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