

reaction stage. At this time the embryos when first stimulated almost always give a reaction toward the side stimulated and only exhibit the avoiding reaction after several responses of the more primitive type. This would seem to indicate that connections across the body occur only as a summation of stimuli.

In conclusion, it may be stated that the early tactile responses in the frog embryo are very similar to those of *Amblystoma* except that they are preceded by a constant response toward the side stimulated. The localization of the decussation in the cord seems to cover a wider region than that described by Coghill for the salamander and in this region to appear simultaneously over a length of one half to one millimeter.

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Permeability vs. tolerance of the kidneys for sugar in diabetes mellitus.

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In the study of the relation of hyperglycemia to glycosuria in diabetic and non-diabetic conditions, the following facts have been elicited:

1. In diabetic individuals possessing healthy kidneys the glycosuria bears a definite relationship to the hyperglycemia.¹
2. Cases of diabetes with definite renal disease, frequently show no relationship between the hyperglycemia and the glycosuria.² The hyperglycemia in such individuals is usually greater in proportion to the glycosuria than it is in those with normal kidneys. Means which promote renal secretion, increase the urinary output of sugar, with a consequent reduction of the hyperglycemia.
3. Acute impairment of renal function in clinical and experi-

¹ Epstein, Albert A., "Studies on Hyperglycemia in Relation to Glycosuria," Monograph, 1916, New York. PROC. SOC. EXPER. BIOL. AND MED., Vol. XIII, p. 67, 1916.

² Id.

mental diabetes leads to a diminution or cessation of the glycosuria with a progressive rise in the sugar content of the blood. The removal of both kidneys in animals, previously made diabetic by pancreatectomy, causes a progressive increase in the hyperglycemia.¹

4. Operative procedures in non-diabetic individuals, involving the use of anesthetics (nitrous oxid and ether) lead to the development of a hyperglycemia, and rarely a glycosuria.

5. Cases of diabetes are frequently encountered showing no evidence of renal disease, in which the glycosuria disappears spontaneously or as the result of treatment, but in which a hyperglycemia persists. The hyperglycemia may be of high degree, and show slight or no variation.

When tests to ascertain the functional activity of the kidneys are instituted on the different types of cases represented above, the following phenomena are observed:

1. In diabetic individuals in whom the glycosuria is proportionate to the hyperglycemia the response of the kidneys to the phenolsulfonephthalein test is normal.

2. That when the hyperglycemia and the glycosuria in diabetic individuals do not show any relationship (the hyperglycemia being greater than one would expect to find with a limited glycosuria) there is a delayed excretion of phenolsulfonephthalein. This group of cases, as stated above, is usually demonstrably nephritic.

3. Non-diabetic cases, subjected to surgical procedures (under anesthesia) which develop a hyperglycemia but no glycosuria, show a delayed elimination of phenolsulfonephthalein.²

4. Diabetic individuals, who lose their glycosuria spontaneously or as a result of treatment, but retain a hyperglycemia, show a normal excretion of the dye.

5. From the observations thus accumulated, the following deductions are made:

1. When a diabetic process is active (as a result of disease or experimental procedures) actual disease or defective function of

¹ Epstein, Albert A., and Baehr, George, *J. Biol. Chem.*, Vol. XXIV, p. 1, 1916.

² Epstein, A. A., Reiss, J., and Branower, J., Soon to be published. *Jour. Biol. Chem.*

the kidneys leads to diminution or cessation of the glycosuria with a "progressive" accumulation of sugar in the blood. The hyperglycemia in such instances does not remain stationary, but rises steadily—and often very rapidly.

2. Surgical procedures (under anesthesia) cause a disturbance in the carbohydrate metabolism, with the consequent accumulation of sugar in the blood (hyperglycemia). A glycosuria in such cases is usually absent, evidently because the function of the kidneys is impaired.

3. Cases of diabetes which become "a-glycosuric" spontaneously or following treatment, retaining a hyperglycemia, reveal the fact that disturbance of renal function has no part in the process. Diminution or cessation of glycosuria through impairment of renal function leads, as a rule, to a progressive increase in the sugar content of the blood; but the glycosuria in these cases is not "progressive." The hyperglycemia in such cases may be of high degree, and remains uninfluenced by starvation. Furthermore, such of the cases as are relieved of their glycosuria by treatment, may upon liberal administration of carbohydrate, develop a glycosuria, with further increase in the hyperglycemia, and show a definite relationship between the two.

These facts are interpreted as signifying that a shifting in the plane of carbohydrate metabolism may take place, in diabetes so that the utilization of sugar by the tissues proceeds at a higher level. Whereas there is no a priori reason to believe that the utilization of sugar in the kidney differs in any way from that of any other organ or tissue, it is concluded, that renal permeability for sugar, is constituted of two phases: (1) a negative phase, *i. e.*, diminished permeability due to impairment of renal function; and (2) a positive phase, diminished permeability due to increased tolerance of the kidney for sugar.¹

¹ Tests of renal function by means of lactose, according to Schlayer and Hedinger, are in progress, and the results will be reported later.