

Relation of Adrenal Glands to Experimental Pancreatic Diabetes.

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It was reported^{1, 2} that unilateral adrenalectomy or interference with epinephrine secretion (by adrenal denervation, etc.), ameliorates diabetes in depancreatized dogs. It was stated that in animals already diabetic the adrenal operations diminished the glycosuria; also, that in dogs previously subjected to these operations, pancreatectomy either failed to cause or caused only a mild degree of glycosuria. Insulin requirement (on a constant diet) for controlling the glycosuria was reported to be decidedly less as the result of the adrenal operations which also were said to render animals more sensitive to insulin. In general, these statements agree with conclusions previously reported by others.

We find it necessary to revise the interpretations made from the earlier experiments and published in preliminary reports. More extensive investigation, under better conditions, and quantitative studies of the rate of epinephrine output (by the method employed by Stewart and Rogoff), on an adequate series of control animals, indicate that we were misled in the previous evaluation of our experimental data. Indeed, we are now convinced that satisfactory experiments lead to the conclusion that partial adrenalectomy, or operations for suppressing epinephrine secretion (adrenal denervation, with or without mechanical destruction of medulla), do not prevent or diminish the experimental diabetes produced by total pancreatectomy in dogs.

Although quantitative determinations demonstrated marked reduction or suppression of epinephrine output, in some of the preliminary experiments on depancreatized animals subjected to the adrenal operations, the assumption that this is responsible for reduced insulin requirement proved to be incorrect when a sufficient number of satisfactory control experiments became available. It is not significant that animals surviving only a short time after

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¹ Barnes, Scott, Ferrill and Rogoff, *Proc. Soc. Exp. Biol. and Med.*, 1934, **31**, 524; *Am. J. Physiol. (proc.)*, 1934, **109**, 35, 89, 95.

² Ferrill, Rogoff and Barnes, *Am. J. Physiol. (proc.)*, 1935, **113**, 41.

operation required less insulin, sometimes little or none, since it is known that hyperglycemia and glycosuria may be low or may fail to develop if the post-operative condition of the animal is not good. Of those surviving much longer, the insulin requirement usually was decidedly less after a few weeks than shortly after pancreatectomy.

That reduction of epinephrine output is not responsible for the diminution in insulin requirement, when it occurs, is obvious from the following experimental observations: (1) under identical conditions (diet, etc.), control depancreatized dogs require the same relative amounts of insulin, at various periods of survival, as those subjected to adrenal operations in addition to pancreatectomy; (2) ordinary insulin requirement may be associated with a normal average epinephrine secretion (for animals under usual experimental conditions) or with a reduced or suppressed output of epinephrine from the adrenals; (3) low insulin requirement may be associated with either normal, reduced or suppressed epinephrine output; (4) insulin requirement may vary between relatively wide limits during the survival of depancreatized dogs, kept on a constant diet, regardless of the epinephrine output of the adrenal glands and it may vary in different animals, under the same conditions.

Finally, we have made the interesting observation that in depancreatized dogs, not subjected to interference with the adrenal glands but kept on a constant diet and insulin, sooner or later there is a definite reduction or suppression of epinephrine secretion. Whether this occurs in pancreatectomized animals that are not treated with insulin, and whether other possible factors may be responsible for the reduced or suppressed epinephrine output, are under investigation. This observation has an important clinical significance. It indicates that treatment of diabetes by X-ray irradiation or surgical denervation of the adrenals is not fundamentally sound, since it might be responsible for aggravating a pathologic condition already present.