

Effect of Oestrin Injections upon Experimental Pancreatic Diabetes in the Monkey.*

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The anterior hypophysis has been shown to be related to carbohydrate metabolism by the studies of Houssay and Biasotti¹ in which the acute diabetes induced by pancreatectomy, in the dog, was relieved by removal of the anterior hypophysis. In a study based on the recognized action of oestrin in suppressing the anterior lobe it was shown by one of us² that administration of oestrin in depancreatized dogs had much the same effect as removal of the hypophysis.

Repetition and extension of this work on a form more closely related to man was believed to be of some importance. Accordingly we have employed the rhesus monkey in a series of experiments designed not only to repeat the studies on the dog, but also to gather data concerning the physiological mechanisms involved, and to determine the effect of continued oestrin administration, in depancreatized animals, upon certain other organs. At this time we are reporting the results of experiments conducted on 6 immature female monkeys (3 to 3.5 kg. in weight).

In 2 animals the injection of an acid extract of beef hypophyses² has induced hyperglycemia and glycosuria. We have used, uniformly, the Shaffer-Somogyi³ method for sugar determination and have determined the true sugar as well as total reducing substances in both blood and urine. Twenty-four hour collections of urine were made regularly.

Four animals have been depancreatized. In 2 cases a small fragment of pancreas was not removed. In the remaining 2 animals pancreatectomy is believed to have been complete.

Two animals were treated with 100 R. U. oestrin (Theelin†)

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¹ Houssay, B. A., and Biasotti, A., *Endocrinology*, 1931, **15**, 511.

² Barnes, B. O., Reagan, J. F., and Nelson, W. O., *J. Am. Med. Assn.*, 1933, **101**, 926.

³ Shaffer, P. A., and Somogyi, M., *J. Biol. Chem.*, 1933, **100**, 695.

† The pituitary extract was supplied through the kindness of Dr. Oliver Kamm and Dr. D. A. McGinty of Parke, Davis and Company. The Theelin used in this experiment was an oil solution, also supplied by Dr. Kamm.

daily for 2 weeks previous to and for 6 days following pancreatectomy. There was no appreciable glycosuria (.3 to .5 gm.) during the period following operation. However, when oestrin injections were suspended the urine sugar increased to 11 gm. When oestrin injections were resumed the urine sugar gradually decreased. In one animal the administration of 200 R. U. daily resulted in the total disappearance of sugar. Two animals received no oestrin prior to operation and were allowed to develop a glycosuria before injections were initiated. The injection of 100 R. U. daily resulted in the complete disappearance of sugar. Alternate periods of injections and withdrawal of injections resulted in corresponding fluctuations in the urine sugar. During one of the periods of treatment the animals also received injections of the pituitary extract. As a result sugar reappeared in the urine and persisted for several days. At the present time, over 5 months after operation, 3 of the 4 operated animals are alive and in good condition. The weight lost during periods when no oestrin was given has been more than compensated for under oestrin treatment. One monkey died 72 days after pancreatectomy. Her diabetes had been well-controlled according to blood and urine sugar findings. Autopsy showed the probable cause of death to be numerous metastatic abscesses in the liver and lungs from a pyogenic blood stream infection originating in an abdominal abscess present prior to operation. This abscess failed to respond to treatment and probably was chiefly responsible for the animal's death.

Blood sugar tests on normal fasting monkeys have shown a considerable range (55 to 125 mg. per 100 cc.). Following pancreatectomy it has risen as high as 550 mg. per 100 cc. and has been regularly decreased by the administration of oestrin. However, in the 2 totally pancreatectomized animals we have been unable to lower the blood sugar level to the normal level. For example monkey 17 had a normal level of 125 mg., a diabetic level of 550 mg., and a level after oestrin treatment of 185 mg.

It is believed that the evidence presented here may be interpreted as evidence that oestrin has suppressed the diabetogenic activity of the anterior lobe. These studies are being continued and extended.