# 17188. Effect of Isuprel Upon Tolerance of the Eviscerate Rat for Glucose.

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Epinephrine[1] and posterior pituitary extracts[2] have similar effects upon the tolerance of the eviscerate rat for glucose. When a solution of glucose without insulin is administered to the eviscerate rat, the addition of epinephrine or posterior pituitary extract to the solution has little or no effect upon the level of blood glucose during the first 2 hours but over a period of 24 hours there is an increase in glucose tolerance. When insulin is given with glucose, the addition of either epinephrine or posterior pituitary extract caused a rapid decrease in glucose tolerance.

It was proposed to extend these studies by testing a derivative of epinephrine having a depressor action upon blood pressure. In the present study, isuprel (isopropylepinephrine) was found to behave as epinephrine and the pressor principle of the posterior pituitary in causing a striking decrease in the glucose tolerance of the eviscerate rat given glucose and insulin.

*Methods.* The two-stage procedure of evisceration has been described.[3] When male rats of the Sprague-Dawley strain reached 250 ± 2 g, they were anesthetized (cyclopal) and subjected to the second stage of evisceration. Intravenous infusions of solutions containing glucose (C.P. Dextrose, Merck) and insulin (Regular Insulin, Lilly) were made by a continuous injection machine which delivered fluid into the saphenous vein of the right hind leg at the rate of 20 cc per 24 hours for each of 6 rats simultaneously. The glucose load was 64 mg per 100 g of rat per hour and the insulin dose was 4 units per 24 hours per rat. The temperature was constant at 26.5 ± 0.5°C. At the end of 2 hours, jugular vein blood was analyzed for glucose by the method of Miller and Van Slyke.[4]

*Experiments and results.* In Experiment 1, isuprel was administered to one rat of each of 12 pairs by adding it to the infusion fluid in a concentration of 1:25,000. In Exp. 2, isuprel was administered to one rat of each of 12 pairs by adding it to the infusion fluid in the concentration of 1:10,000. As shown in Table I, the addition of isuprel caused a striking decrease in glucose tolerance in both experiments.

*Discussion.* The effects of isuprel upon blood pressure were not studied under these experimental conditions. Although this compound has been described[5] as having a vasodepressor action in experimental animals, it would be unsafe to assume that its vasomotor effects are dissimilar from those of epinephrine and posterior pituitary extracts in the eviscerate rat. It was noted that isuprel caused the skin to become pink, suggesting peripheral vasodilatation, in contrast to the pallor caused by the peripheral vasoconstriction which occurs during the administration of epinephrine or of posterior pituitary extract under identical conditions. The mechanism whereby these drugs affect glucose tolerance in the eviscerate rat is not known but the possibility that it is secondary to circulatory changes must be considered.

*Summary.* Eviscerate rats (250 g) were given continuous intravenous infusions of glucose and insulin during a period of 2 hours. The glucose load was 64 mg of glucose per 100 g of rat per hour and insulin was given at the rate of 4 units per rat per 24 hours. The solution of glucose and insulin was infused at the rate of 20 cc per 24 hours. The addition

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TABLE I.
Effect of Isuprel upon Level of Blood Glucose at the End of 2 Hours in Eviscerate Rats Given Glucose and Insulin by Constant Injection.

| Exp. | Conc. isuprel | No. rats | Avg blood glucose | Avg* | Diff. in avg | Diff.* | Diff. / diff.* |
|---|---|---|---|---|---|---|---|
| 1 | 1:25,000 | 12 | 161 | 7.9 | | | |
| | 0 | 12 | 84 | 6.9 | 77 | 10.5 | 7.3 |
| 2 | 1:10,000 | 12 | 185 | 9.1 | | | |
| | 0 | 12 | 84 | 5.2 | 101 | 10.5 | 9.6 |

* Standard deviation.

of isuprel in concentrations of 1:10,000 and 1:25,000 caused a marked decrease in the glucose tolerance of the eviscerate rats.

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## 17189. Effect of Testosterone Propionate on Phosphatases in the Seminal Vesicle and Prostate of the Rat.*

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The discovery by Kutscher and Wolbergs[1] that the human prostate gland and ejaculum contain high concentrations of acid phosphatase provided the stimulus for a series of investigations of this enzyme in the tissues and secretions of the male reproductive tract.

Gutman and Gutman[2] showed that the high level of acid phosphatase (AcP-ase) as well as alkaline phosphatase (Alp-ase) in the prostatic tissue of the adult rhesus monkey is not present in the prepubertal animal, but that these enzymes can be raised to the adult level by the injection of androgen.

Pazos and Huggins[3] found that administration of androgen to starving, castrate immature dogs caused an 8 to 11-fold increase in AcP-ase activity of the prostate gland over that of a control animal. The Alp-ase in the glands of these dogs decreased 15-45%.

When Gutman and Gutman[4] studied the rat, however, they found that the levels of both AcP-ase and AlP-ase in the prostate gland were extremely low compared to levels in the primates studied. Administration of testosterone to normal adult male rats produced no change in the activity of either enzyme.

Atkinson[5] has shown histochemically that the AlP-ase in the stromal elements of the mouse seminal vesicle diminishes after castration and returns to normal after androgen treatment. Dempsey, Greep, and Deane[6] recently demonstrated the same phenomenon in the rat, also by histochemical means.

It was decided to conduct investigations to (1) determine whether an enzymatic response to testosterone could be obtained in the

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