7977 P

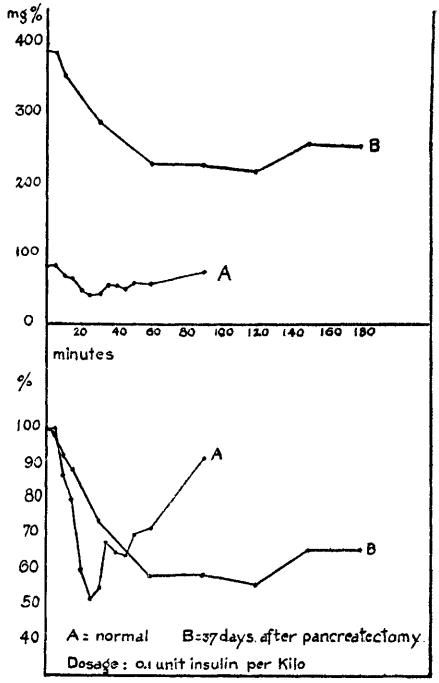
Blood Sugar Curves in Normal and Diabetic Dogs After Intravenous Injection of Insulin.*

B. N. BERG, J. GROSS, J. McAFEE, AND T. F. ZUCKER.

From the Department of Pathology, College of Physicians and Surgeons, Columbia University.

The following report deals with the blood sugar curve after the intravenous injection of insulin into normal and depancreatized dogs. The study includes over 50 observations upon normal and 350 observations upon diabetic animals.

Experiments on blood sugar lowering were performed on male dogs weighing 12 to 18 kilos, 18 hours after the last (afternoon) feeding and routine insulin injection. Doses from .02 to 1.0 units of insulin (Lilly) per kilo given in a volume of 1 cc. were injected into the jugular vein. Glucose determinations on tungstic acid filtrates were made by the Shaffer-Hartman method. The time intervals shown in the chart were found to bring out most clearly the differences in the 2 types of curves.



*This work was aided by a grant from the Eli Lilly Company and we also wish to acknowledge their liberal supplies of insulin.

The chart gives typical examples of time curves after the injection of 0.1 unit of insulin per kilo intravenously before and after removal of the pancreas. The upper curves show the results expressed in mg. % of blood sugar. The striking change in amount of sugar transported from blood to tissues by a given dose of insulin is apparent. The conclusion that in the diabetic the activity of insulin is enhanced is shown to be erroneous when we compare relative blood sugar lowering on the basis of the fraction removed, assigning the value of 100% to each initial blood sugar level (Scott[1]). This is shown in the lower set of curves.

In the normal dog the blood sugar falls rapidly, reaching its lowest level within 20 to 30 minutes after the injection of insulin. This is followed by an abrupt rise and then restoration to approximately the original value within 90 minutes. The return phase is usually represented by a broken curve frequently giving several maxima and minima. Duration of action, varying with the dose of insulin, reflects itself in the return phase but never in the initial drop which terminates sharply at about 25 minutes with all doses so far observed.

In the diabetic animal, although the fraction of blood sugar removed may be about the same, the rate of initial action is distinctly less than in the normal. In the smaller dose range (up to about 0.3 units per kg.) there is an uninterrupted drop lasting one hour or more and according to the condition of the animal, reaching levels of 40 to 80% of the initial value. This is followed by a gradual return to the original level occupying at least another hour. With larger doses the continuous blood sugar lowering may be extended for over 2 hours, coming within range of the level of non-fermentable reducing substance, and followed by a correspondingly slow recovery. With no dose and at no time is there any evidence of the sharp upturn which is characteristic of the insulin response in the normal. The "diabetic type" of curve persists in animals examined up to one year after pancreatectomy. The character of the response is unaffected by the level of the initial blood sugar.

Instances of similar characteristic curves after intravenous administration of insulin in normal and diabetic man have been reported.[2-7] Bøggild[8] has also described the course of action of intravenous insulin in normal dogs.

---

[1] Scott, E. L., and Dotti, L. B., *Arch. Int. Med.*, 1932, **50**, 511.

[2] Lyman, R. S., Nicholls, E., and McCann, W. S., *J. Pharm. and Exp. Therap.*, 1923, **21**, 343.

[3] Raab, W., *Z. f. d. ges. exp. med.*, 1924, **42**, 723.

In order to determine how soon after removal of the pancreas the change from the normal to the diabetic type of curve occurs the following experiment was performed. After establishing the normal response of the blood sugar to the intravenous injection of insulin the pancreas was removed from a dog and observations were made at the following intervals after pancreatectomy: 18, 42, 66, 90, 138 hours and 14 days. The dose of insulin was 0.1 unit per kilo.

Eighteen hours after removal of the pancreas the blood sugar was 311 mg. %. The shape of the blood sugar curve deviated markedly from the normal and had many of the characteristics of the diabetic. Compared with the curves obtained before pancreatectomy, the initial rate of decrease in blood sugar was diminished, minimum sugar values were reached later than in the normal, and the abrupt upturn was largely lost, its place being taken by a slow gradual return. However, the curve did not assume the form of an uninterrupted drop until 138 hours after pancreatectomy. The deviations at 25 minutes decreased gradually in consecutive observations. Comparison of the percentage reduction of blood sugar after 14 days with the results obtained at 138 hours showed a marked increase in sensitivity to insulin.

Apparently a number of factors are affected by the removal of the pancreas. Although the blood sugar level indicates a fully developed diabetes soon after removal of the pancreas, the adjustment of the diabetic response to insulin is not completed until several days later. Experiments on a number of animals with varying time intervals have concordantly shown the transition from the normal to the diabetic type of curve as outlined above.

---

[4] Bodansky, A., and Simpson, S., *Quart. J. Exp. Physiol.*, 1927, **17**, 57.

[5] Csépai, K., and Ernst, Z., *Wien. Klin. Wchnschr.*, 1928, **41**, 25.

[6] Norgaard, A., and Thaysen, T. E. H., *Act. Med. Scand.*, 1929, **72**, 492; Thaysen, T. E. H., *Act. Med. Scand.*, 1930, **73**, 408.

[7] Collens, W. J., and Grayzel, H. G., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 487.

[8] Bøggild, D. H., *Acta Med. Scand.*, 1933, **79**, 458.