prolongation of anesthesia, but if enough pitressin is added to produce a local anesthesia equal to that with procaine-epinephrine, the intravenous toxicity is increased, and to the same extent as with epinephrine (Table II).

TABLE II.
Intravenous toxicity of procaine, procaine-pitressin, and procaine-epinephrine. Mortality Ratio: No. of animals dying/No. of animals used.

mg./kg.	Procaine	Procaine+1-200 Pitressin	Procaine+1-100 Pitressin	Procaine+1-50,000 Epinephrine
20	—	—	0/3	0/2
25	0/5	—	2/5	1/3
30	1/5	0/1	2/5	3/5
35	3/5	1/3	3/4	—
40	4/5	3/3	—	—

Furthermore, pitressin does not delay absorption sufficiently to reduce the subcutaneous toxicity of a local anesthetic. Pantocain (courtesy Winthrop Chemical Co.), a local anesthetic resembling procaine, in a subcutaneous dose of 25 mg./kg. kills 6 of 8 rabbits. The same dose killed 2 of 3 rabbits although pitressin 1-100 was present, it serving only to delay the onset of symptoms. In a solution of 1-50,000 epinephrine, the same dose of pantocain produced no intoxication in 3 rabbits.

Summary. The addition of pitressin to a solution of a local anesthetic agent prolongs anesthesia on intradermal injection, and permits of sterilization. Both pitressin and epinephrine increase the intravenous toxicity of a local anesthetic. While epinephrine by delaying absorption reduces the subcutaneous toxicity, pitressin does not.

6442

Effect of Suprarenalectomy on Sugar Tolerance.

ELSIE HILL AND ALFRED E. KOEHLER.

From the Potter Metabolic Clinic, Santa Barbara Cottage Hospital.

The rabbit adapts itself well for the determination of sugar tolerance because of the convenience with which sugar can be given in the ear vein and the ease with which the blood can be withdrawn without excitement. Bilateral suprarenalectomy can readily be performed in 2 stages with good recovery of the animal but with a

variable survival period.[1] The rabbits in these experiments were all of a uniform inbred stock free of any parasitic infections. They were kept on an alfalfa-barley diet. The right gland, which was always removed at the first stage operation, lies so closely against the vena cava that its removal with its capsule intact is difficult without injury to the vessel. To overcome this difficulty, a curved clamp was applied between the gland and the vena cava including a part of the vessel. A crescent shaped portion of the vessel wall was then removed together with the gland which had previously been freed. The vena cava was then ligated by placing the ligature behind the convex portion of the clamp. This technic assured the complete removal of the right gland and caused only a slight constriction in the vena cava. The left gland was removed 7 to 10 days after the first operation.

Of 18 rabbits only 4 survived over a 60-day period; the other 14 succumbed within 20 days, with an average survival period of 14 days. The rabbits made a quick recovery from the second stage operation and the incisions were well healed without infection in a week. There was, however, a gradual weight loss for practically all the rabbits, particularly during the second week after operation, except for those rabbits which survived longer than 20 days.

To determine the sugar tolerance, 1.0 gm. of glucose per kilo was given as a 50% solution in the median ear vein of the rabbit after a 24-hour fast. The duration of injection was approximately 1 minute. In both the unilateral and bilateral suprarenalectomized rabbits the sugar tolerance was determined 7 to 10 days after operation. The average blood sugar values of 8 unilaterally operated animals (Figure 1) was practically the same before and after glucose injection as the average for normal rabbits as shown in Figure 2 and also indicated by squares in Figure 1.

The blood sugar level averages in bilaterally suprarenalectomized rabbits were practically the same before glucose injection but remained distinctly higher after glucose (Fig. 1). One bilaterally suprarenalectomized rabbit had an unusually high blood sugar 30 and 50 minutes after glucose injection which greatly increases the average value. If a weighed average is taken, the 30 and 50 minute points for the bilateral curve are materially lowered and consequently depress the slope of this curve.

These experiments indicate that the suprarenalectomized rabbit has a poorer sugar tolerance than the normal rabbit. In interpret-

[1] Marine, D., and Baumann, E. J., *Am. J. Physiol.*, 1921, **57**, 135.

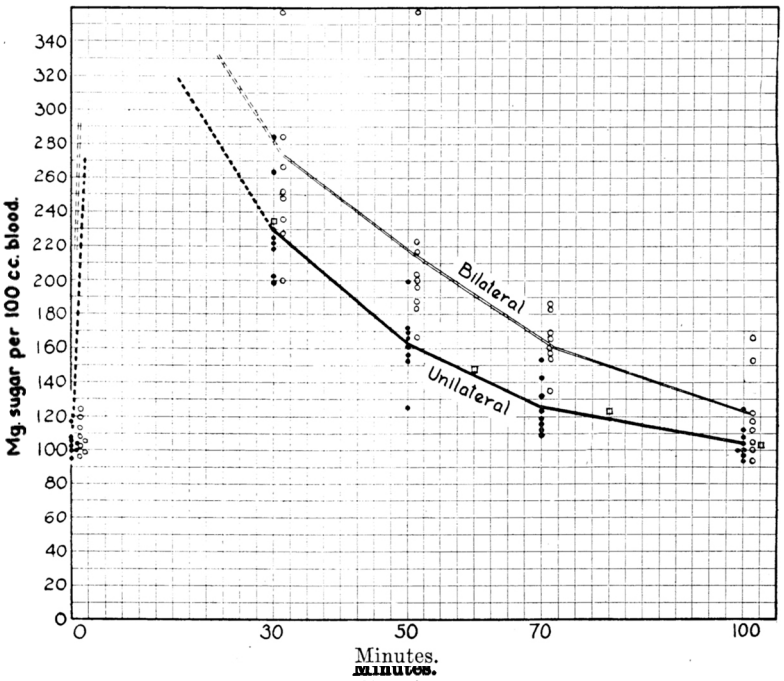
Mg. sugar per 100 cc. blood.
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
0
30
50
70
100
Minutes.
Bilateral
Unilateral

FIG. 1.

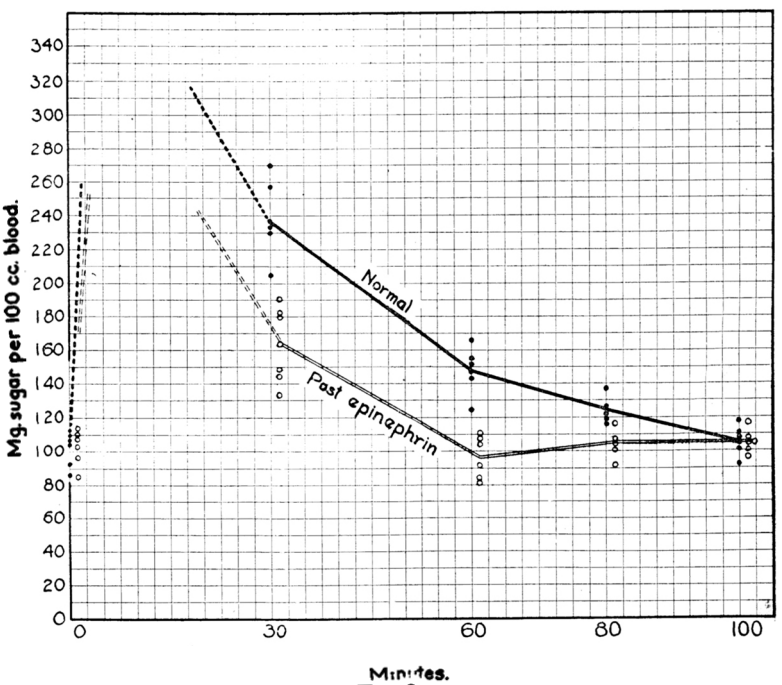
Mg. sugar per 100 cc. blood.
340
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
0
30
60
80
100
Minutes.
Normal
Past epinephrin

FIG. 2.

ing the significance of these findings, consideration must be given to (1) rate of diffusion of sugar into the tissues, (2) rate of glycogen and fat formation, (3) rate of sugar oxidation, and (4) state of nutrition previous to the test.

If epinephrin depresses sugar utilization directly, or if it depresses insulin formation, then suprarenalectomy, considered from the epinephrin standpoint alone, might well improve the sugar tolerance. If the diminished sugar tolerance after suprarenalectomy is due to decreased tissue utilization of sugar then it is possible that the suprarenal glands contain a substance other than epinephrin or possess a function favorable to carbohydrate consumption. Such a conclusion is not justified from these experiments at present because of the possibility that the decreased tolerance after suprarenalectomy may be related to the nutritional disturbances associated with diminished food intake and weight loss.

Effect of previous epinephrin administration on sugar tolerance. Sahyun and Blatherwick[2] have shown that epinephrin injection 24 hours previous to the administration of insulin greatly increases the sensitivity of rabbits to insulin. Figure 2 shows the normal fasting sugar tolerance of 6 rabbits and also 24 hours after the administration of 0.1 mg. of epinephrin per kilo. Three of the rabbits received the epinephrin daily for a week and 3 received it twice during the 12 hours preceding the 24-hour fast before the sugar tolerance. Practically no sugar was excreted in the urine (occasionally traces) after the epinephrin, so the improved sugar tolerance was not due to sugar loss. The improved tolerance and increased insulin sensitivity may be related to (1) increased insulin secretion secondary to its depression by epinephrin, (2) changes in the mobilization of carbohydrate induced by the epinephrin such as deglycogenation of muscle, and (3) increased utilization of carbohydrate or increase in its conversion to fat. Other possibilities such as the sensitization by epinephrin of nerve structures instrumental in carbohydrate metabolism must be considered.

[2] Sahyun, M., and Blatherwick, N. R., *J. Biol. Chem.*, 1928, **79**, 443.