The initial weight is weight immediately before first injection of antigen. Final weight is weight immediately before toxin injection. Weights were carefully watched to make certain that resistance to toxin was measured only in apparently normal healthy animals.

The above results are similar to those obtained by Cowie and Kempton[4] and by Kolle and Schlossberger.[5] They found that injecting guinea pigs with typhoid organisms or horse serum did not protect against small doses of diphtheria toxin, (3 mld.). That three guinea pigs receiving 100 times the fatal dose of diphtheria toxin were saved with normal horse serum as reported by Kastenmeyer,[6] is extremely doubtful.

Data on the non specific resistance of guinea pigs to several organisms are omitted. The difficulty of accurately determining the minimal lethal dose of a live culture obscured the results. Non specific agglutinins were looked for but not found. The methods of calculating and preparing the doses of standard antitoxins, together with several useful modifications of the standard or Hygienic Laboratory technic have already been described by Berg.[7]

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The antiketogenic influence of insulin in diabetes.

By JOHN A. KILLIAN.

[*From the Department of Biochemistry, New York Post-Graduate Medical School and Hospital, New York.*]

The object of this study was to determine the action of insulin upon the production and excretion of ketone bodies and upon the acid-base equilibrium of the blood of human cases of diabetes mellitus. This report presents the results of seventeen

4 Cowie, D. M., and Kempton, R. M., *J. Med. Research*, 1921, xlii, 227.
5 Kolle, W., and Schlossberger, H., *Med. Klin.*, 1919, 1, 83.
6 Kastenmeyer, B., *Deutsch. med. Woch.*, 1919, xlv, 1338.
7 Berg, W. N., *J. Infect. Dis.*, 1921. xxix, 86.

observations upon fourteen patients. The only therapeutic agent employed was insulin.

To avoid the necessity of utilizing other agents such as alkalies or glucose, it was essential to grade the dose of the insulin so as to secure the maximum beneficial effect without producing untoward results. In a series of preliminary experiments it was demonstrated that for individuals weighing from 50 to 70 kg. one unit of insulin decreased the blood sugar about 0.008 per cent in from 4 to 6 hours. The doses of insulin employed in the present studies were calculated as the quantity required to decrease the initial blood sugar to 0.130 per cent.

Previous to the administration of the insulin the patients had been starved overnight for 12-14 hours, and during the period of observation lasting from 8 to 10 hours, no food was taken. However, water by mouth was permitted *ad libidum*. As a control on the factor of starvation in 5 cases, two series of curves were obtained representing changes in the blood sugar and carbon dioxide combining power of the plasma with and without insulin. It was noted that the starvation alone continuously decreased the blood sugar about 0.04 per cent, but this drop is insignificant in comparison with the fall after insulin. In three instances the carbon dioxide combining power rose steadily during starvation, but in the 2 remaining cases a fall of 5 vol. per cent was noted.

The insulin used in these experiments was the product of the Eli Lilly Co. The subjects were all patients of Dr. H. O. Mosenthal of the Department of Medicine. Before the administration of the insulin a control specimen of blood was obtained, and a specimen of urine collected over one or two hour periods. After the subcutaneous injection of the insulin, specimens of blood and urine were secured every hour or two hours. The sugar, ketone bodies and carbon dioxide combining power of the blood were determined, and in the urine the concentration and the actual excretion in grams per hour of the sugar and ketone bodies were studied. The total ketone bodies were estimated as acetone in the blood and urine by Van Slyke's gravimetric method. The specimens of blood were analyzed immediately after withdrawal by venipuncture to obviate any source of error due to glucolysis or the production of fixed acid bodies in the blood upon standing.

In three cases analyses were confined to the blood since it was

impossible to obtain simultaneous urine collections from these patients who at the outset were in a coma. It was observed that following the administration of the insulin the blood sugar decreased, the decline reaching the maximum 4 to 6 hours. The total fall in blood sugar was from 50 to 60 per cent of the control. The lowest figure obtained was 0.104 per cent. The drop in blood sugar was accompanied by a corresponding diminution of the urine sugar, both in per cent and in grams per hour.

The rise in the carbon dioxide combining power was very striking, from 8 to 20 vol. per cent. The highest values obtained were noted 4 to 6 hours after the insulin. All of the cases studied showed in the control specimens of blood a marked increase in the concentration of ketone bodies in the blood and urine. After the insulin a decrease to 40 to 16 per cent of the original concentration in the blood was found, the fall closely paralleling the rise in the carbon dioxide combining power. A corresponding drop in the excretion of the ketone bodies of the urine was also noted. A rise of the blood and urine sugar and of the blood and urine ketone bodies and a decrease of the carbon dioxide combining power of the plasma were observed 8 to 10 hours after the insulin injection.

In six instances determinations of the blood pH were made by the Myers' method simultaneously with the carbon dioxide combining power or content of the blood. A rise in the pH was observed corresponding to the rise in the combining power or of the content of carbon dioxide. It is evident from the results obtained that in diabetes mellitus insulin inhibits for a short period the production of ketone bodies, and in this manner readjusts the acid-base equilibrium of the blood.