showed a minimum count of 2,644,000. This destruction was compensated, however, in a considerable measure before the next injection, the lowest count observed immediately before injection being 3,220,000. Anisocytosis and polychromatophilia became marked on the 17th day. Erythroblasts appeared on the 12th day, numbering 124 per cu. mm. The loss of weight was 36 per cent.

The production of more or less severe experimental anemia in animals by injections of bacterial toxin only verifies generally accepted clinical experience on human beings that such poisons play a very important part in the more chronic types of anemia of man, but it is evident that further observations will be required before one can justly designate such experimental anemias, even when they are very severe or fatal, as presenting the counterpart of so called pernicious anemia in man.[1, 2]

## 2881

### Lactic acid and inorganic phosphorus of normals and diabetics after glucose, with and without insulin.

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Briggs, Koechig, Doisy and Weber[1] have observed a decrease in sugar, inorganic phosphorus, and potassium of the blood of normal dogs after insulin. There was a parallel increase in the lactic acid apparently formed from the glucose under the influence of insulin. The animals were not anesthetized, but the authors believe that the increased muscular activity played no part in the observed production of lactic acid. Best and Ridout[2] state that the blood lactic acid of dogs does not significantly increase during

[1] Cornell, Beaumont S., *J. Infect. Dis.*, 1925, vi, 508.

[2] Kahn and Torrey, PROC. SOC. EXP. BIOL. AND MED., 1925, xxii, 8-13.

[1] Briggs, A. P., Koechig, I., Doisy, C. A., and Weber, C. J., *J. Biol. Chem.*, 1924, lviii, 721.

[2] Best, C. H., and Ridout, J. H., *J. Biol. Chem.*, 1925, lxiii, 197.

insulin hypoglycemia, when this condition is uncomplicated by extreme asthenia or by marked hyperirritability. Moreover Cori[3] has found that insulin hypoglycemia produced no definite change in the lactic acid content of the blood of either fasting rabbits or cats. Nor did the insulin have any effect on the blood lactic acid of phlorizinized rabbits or depancreatized cats, but the insulin convulsions lead to a strong increase in the lactic acid concentration of the blood. Blatherwick, Bell and Hill[4] observed in normal individuals a marked decrease of the inorganic phosphorus of blood plasma accompanied by a lessened excretion of phosphorus in the urine after the administration of insulin to normal individuals. These changes occur during the period of hypoglycemia. A comparison of *in vitro*-glycolysis with the hypoglycemia after insulin has been made by Morgulis and Barkus.[5] These authors state that *in vitro*-glycolysis is different from the hypoglycemia caused by insulin in that the disappearance of the glucose in the former is parallel with the formation of lactic acid, but the insulin hypoglycemia is not necessarily associated with a production of lactic acid.

This brief survey of the literature reveals an apparent contradiction in reported data on changes in the blood lactic acid associated with insulin hypoglycemia. With the object of determining the relation of changes in the lactic acid concentration of the blood to the oxidation or storage of glucose, the sugar and lactic acid of blood of rabbits were studied before and after insulin administration. In these experiments eight rabbits were used (average weight, 2 kilograms). One animal was given 10 units of insulin, and two hours later the blood sugar was reduced to 0.047 per cent, and the lactic acid rose to 300 per cent of the control concentration. These changes accompanied convulsions, during which the animal died. The administration of strychnine sulphate produced convulsions in a second animal resulting in death. In this instance the blood lactic acid was increased at the time of the convulsions to 200 per cent of the control figure. Here, however, the hyperglycemia was observed at the time of convulsions. The six remaining rabbits received sufficient of a 50 per cent urethane solution to produce complete muscular relaxation

[3] Cori, C. F., *J. Biol. Chem.*, 1925, lxiii, 253.

[4] Blatherwick, N. R., Bell, M., and Hill, E., *J. Biol. Chem.*, 1924, lxi, 241.

[5] Morgulis, S., and Barkus, O., *J. Biol. Chem.*, 1925, lxv, 1.

of the extremities. Control specimens of blood were obtained and then insulin administered. The dose of insulin used varied from 2 to 40 units. Hypoglycemia resulted in all cases sufficient to cause death, but no convulsions were observed. The changes in the blood lactic acid were insignificant.

Although Mendel, Engel and Goldscheider[6] report that the usual rise and fall in the blood sugar after the ingestion of 100 grams of glucose occurs independently of any alteration in the blood lactic acid, it has been found that the administration of 1.75 grams of glucose per kilogram of body weight results in an increase in the blood lactic acid in normals, hyperthyroids and diabetics. However, the changes in the inorganic phosphorus, either of the blood or urine were not uniform. Changes in the sugar, lactic acid and inorganic phosphorus of the blood after glucose and insulin have been studied in four normal individuals and six cases of diabetes mellitus. Clausen's method has been utilized for the determination of the lactic acid of the blood. With this method in 78 individuals representing normals and pathological conditions showing no disturbance of carbohydrate metabolism, the maximum concentration of lactic acid was 18 mg. per 100 cc. of blood, the minimum 11 mg., the majority varied from 13 to 15 mg. Venous blood was drawn from the arm without stasis, after the subject lay at rest for one hour in the fasting state. Specimens were analyzed immediately after withdrawal.

The observations were made on the subjects after a night's fast of 12 to 14 hours. For an hour preceding and throughout the entire period of the observations, the subjects were maintained in a state of complete rest in bed. At end of the first hour a control specimen of blood was obtained. Then glucose was given by mouth, 1.75 grams per kilogram of body weight. Specimens of blood were drawn at hourly intervals for 2 or 3 hours, then insulin was given. In the normal cases 10 units of insulin were given, with about 50 grams of glucose by mouth. After the ingestion of the glucose by the normal individuals, the lactic acid rose to 2 to 3 times the concentration of the control blood. The maximum concentration was observed after the blood sugar had begun its return to normal. However, following the administra-

[6] Mendel, B., Engel, W., and Goldscheider, I., *Klin. Woch.*, 1925, iv, 306 and 542.

tion of insulin the lactic acid of the blood rose to 4 to 10 times the control concentration. The rise in the lactic acid paralleled the drop in sugar.

In the diabetic subjects the ingestion of glucose produced an increase in the blood lactic acid of from 50 to 100 per cent of the control concentration. The administration of the insulin resulted in a rise in the lactic acid, paralleling the decrease in the blood sugar. In the cases of diabetes the dosage of insulin was based upon the level of blood sugar. The response of the blood lactic acid to the insulin in diabetes was much less pronounced than in the normal subjects. In both the normals and diabetics, the insulin administration produced a decrease of the inorganic phosphorus of the blood and urine, with a subsequent return to normal. Glycolysis *in vitro* was accompanied by a rise in the blood lactic acid; however this increase is not as great as the rise associated with insulin hypoglycemia. The increase in the lactic acid does not account for the entire loss in blood sugar in either case.

## 2882

### The development of cutaneous hypersensitiveness following the intestinal absorption of antigenic protein.

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It has been shown by Schloss and Anderson,[1] and Anderson and Schloss[2] that marasmic infants frequently absorb antigenic protein from the intestinal tract in amounts sufficient to cause the appearance of specific precipitin in the blood. In many instances also, the blood has the power passively to sensitize guinea pigs to

[1] Schloss, O. M., and Anderson, A. F., Allergy to Cow's Milk in Infants with Severe Malnutrition, PROC. SOC. EXP. BIOL. AND MED., 1922, xx, 5.

[2] Anderson, A. F., and Schloss, O. M., Allergy to Cow's Milk in Infants with Nutritional Disorders, *Am. J. Dis. Child.*, 1923, xxvi, 341.