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Mechanism of Insulin Convulsions. III. Effects of Varying Partial Pressures of Atmospheric Gases After Adrenalectomy.

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In a previous communication[1] on the effects of varying partial pressures of atmospheric O_2, N_2, and CO_2 on the blood sugar and serum electrolytes in the normal fasting dog, it was reported that breathing atmospheres containing between 5% and 12% O_2 caused marked hyperglycemia and a simultaneous reduction in the plasma K and inorganic P. Breathing a gaseous mixture containing 15% CO_2, 20% O_2, and 65% N_2 caused hyperglycemia accompanied by a marked rise in inorganic P but only a slight rise or no change in the K of the plasma. Convulsions either did not occur or their occurrence was greatly delayed when insulin was administered subcutaneously in doses of from 10 to 25 units per kilo of body weight (sufficient to cause convulsions in ordinary room air), if the animal was kept in the low O_2 or the high CO_2 atmospheres far beyond the periods previously found to be required for convulsions to occur. This effect was observed even when the blood sugar fell to levels well below those at which convulsions had occurred in room air. Breathing atmospheres containing from 60% to 80% O_2 had no detectable influence on the occurrence of insulin convulsions. Breathing an atmosphere of N_2 alone without administration of insulin caused convulsions within 2 minutes accompanied by a rise in K.

The present study was undertaken as an extension of the foregoing. A hope was entertained that any relationship that might exist between plasma electrolyte and blood sugar changes on the one hand and occurrence of convulsions on the other would be brought out more clearly in animals made highly sensitive to insulin by complete adrenalectomy. The effects of low O_2 (5% to 9%) and of high CO_2 (15%) were determined with and without administration of insulin. Methods used were the same as those described in the previous report. The effects of breathing low O_2 for from 2 to 3 hours were determined 6 times in 2 adrenalectomized dogs without administration of insulin. The response to breathing

[1] McQuarrie, Irvine, and Ziegler, Mildred R., PROC. SOC. EXP. BIOL. AND MED., 1939, **39**, 525.

atmospheres containing 15% CO_2, 20% O_2, and 65% N_2 was determined 4 times in 2 adrenalectomized dogs before insulin was given. The effects of breathing an atmosphere of 5% O_2 and 95% N_2 on the response to insulin were determined 9 times in 5 adrenalectomized dogs.

The results may be summarized as follows: Whereas breathing 5% O_2 plus 95% N_2 was found to cause a prompt and often fairly marked hyperglycemia in normal dogs, it was found to produce an equally prompt and sustained fall in the blood sugar in totally adrenalectomized animals. In contrast to the latter results, it was found that breathing a mixture of 15% CO_2, 20% O_2, and 65% N_2 caused a slight but significant rise of the blood sugar of the adrenalectomized dogs. While the anoxic anoxia of the first type of experiment caused definite decreases in the inorganic P and K, breathing 15% CO_2 resulted in a fairly marked increase in the P and a slight rise or no change at all in the K of the plasma.

As was to be expected, all of the dogs showed a marked increase in sensitivity to insulin following adrenalectomy, having convulsions after as little as 1% of the insulin dosages used before operation. The effect of breathing 5% O_2 plus 95% N_2 was to prevent the occurrence of convulsions completely in spite of the fact that the dose of insulin used was between 4 and 8 times the previously determined convulsive dose for a given adrenalectomized animal. The periods of observation under the low-O_2 experiments were approximately double those required to induce convulsions in room air. The degree of hypoglycemia was as great or greater at the end of the anoxic experiments as at the time of the convulsion in the control experiments. Blood glucose values as low as 9 to 14 mg % were recorded without the animal having convulsions. Breathing 15% CO_2, 20% O_2, and 65% N_2 had a similar effect so far as preventing convulsions was concerned. Blood sugar values decreased somewhat more slowly under the conditions of this experiment than under the previously described conditions, but fell to the previously determined level without the occurrence of a convulsion.

Conclusions. Anoxic anoxia (breathing 5% O_2 plus 95% N_2) causes hypoglycemia in adrenalectomized dogs without insulin in contrast to the hyperglycemia observed in normal animals. Insulin convulsions are prevented by anoxia of this degree even when the fall in blood sugar is maximal. Breathing 15% CO_2 likewise tends to prevent insulin convulsions from occurring.