11131

Plasma Electrolytes as Affected by Insulin and by Varying Partial Pressures of Atmospheric Gases.

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In recent studies on the mechanism of insulin convulsions in which the decreases in plasma potassium and inorganic phosphorus, as well as the degree of hypoglycemia, were measured at regular intervals, it was found that the level of blood sugar alone bears a constant relationship to the convulsion.[1] Further experiments on the effects of varying partial pressures of atmospheric gases, O_2, N_2 and CO_2, showed that a drastic lowering of the O_2 content or a marked increase in the CO_2 of the respired air tended to prevent insulin convulsions entirely or greatly to delay their onset in the normal fasting dogs, even when the blood sugar was depressed to levels as low as or lower than those previously observed in the same animals before convulsions.[2] The latter finding indicates that some other factor in addition to hypoglycemia plays a rôle in the mechanism of insulin convulsions.

In the hope of obtaining further information on this phase of the problem, the present studies pertaining to changes in the plasma electrolyte patterns under the foregoing conditions were undertaken. The procedure followed was that of determining the various electrolytes of the plasma before and at regular intervals after administration of convulsive doses of insulin to fasting unanesthetized dogs, first in room air and subsequently in the various abnormal atmospheres referred to above. No 2 experiments on the same animal were carried out at intervals shorter than one week. The plasma electrolyte patterns were determined as follows: 12 times in 5 normal fasting dogs in room air; 3 times in 3 of the same dogs between 210 and 240 minutes after administering convulsive doses of insulin but before convulsions occurred; twice in 2 of the dogs 15 minutes following the insulin convulsion; 3 times in 3 of these animals after 150 minutes in a tent containing approximately 5% O_2 and 95% CO_2; twice under the latter conditions on 2 of the same dogs but with the administration of previously determined convulsive doses of insulin; twice in 2 dogs after 150 minutes in an atmosphere containing

1 Ziegler, Mildred R., and McQuarrie, Irvine, PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 142.

2 McQuarrie, Irvine, and Ziegler, Mildred R., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 525.

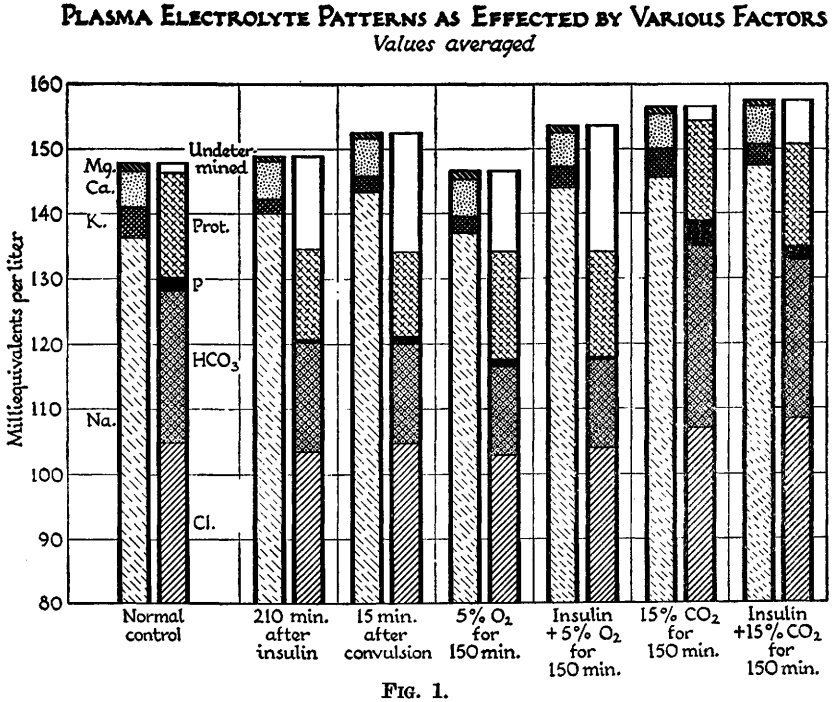

FIG. 1.

Plasma electrolyte patterns as affected by breathing atmospheres of various concentrations of O_2 and CO_2 with and without large doses of insulin.

approximately 15% CO_2, 20% O_2 and 65% N_2 and twice in the latter animals under the same conditions but with the administration of large doses of insulin. Convulsions did not occur during any of the experiments in which the animal was made to breathe the low O_2 or high CO_2 atmospheres.

For the sake of brevity and clearness the results are presented in graphic form in Fig. 1. Since the data from similar experiments were found to be consistent, average values obtained under the various conditions involved were employed in construction of the figure. Comparison of the different columns in the figure, which represent total values for the individual bases and acids of the plasma, shows the following changes, due to the various experimental conditions. Comparing the data for each of the experiments with those shown for the composite normal control shows that insulin in convulsive doses causes a fairly marked decrease in potassium and inorganic phosphorus and moderate decreases in plasma carbon dioxide content and protein. The sodium, calcium, magnesium and chloride remained practically unchanged, whereas the undetermined acid fraction is moderately increased. Fifteen minutes after the insulin con-

vulsion the inorganic phosphorus was found to have risen somewhat, the sodium was slightly increased over the preconvulsive level and the undetermined acid fraction increased still more. The most striking effect of breathing an atmosphere containing 5% O_2 was a fairly marked decrease in potassium, phosphorus and carbon dioxide content. The sodium, calcium, magnesium and protein were quite unaffected. The undetermined acid fraction was considerably increased. When insulin was given in large doses while the animals were left in the atmosphere containing 5% O_2 the sodium was increased by 8 milliequivalents per liter while both carbon dioxide content and the inorganic phosphorus were greatly decreased. The potassium showed a moderate decrease, also. The undetermined acid fraction was greatly increased above normal. The electrolyte pattern for this latter type of experiment in which the animal did not have a convulsion shows a striking resemblance to that found shortly after an insulin convulsion.

In contrast with the effects of anoxic anoxia the breathing of 15% CO_2 resulted in a slight increase in sodium, practically no change in potassium, calcium, magnesium, chloride and protein, but a significant increase in carbon dioxide content and a very marked rise in the inorganic phosphorus. The undetermined acid fraction remained essentially normal. Administration of insulin in large doses during the period of high CO_2 breathing caused but a slight increase in the undetermined acid fraction. The potassium and magnesium were moderately decreased. The sodium and phosphorus were moderately increased while the calcium, chloride, protein and carbon dioxide content remained unchanged.

Breathing an atmosphere containing approximately 5% O_2 and 95% N_2 or one containing 15% CO_2, 20% O_2 and 65% N_2 caused hyperglycemia in the normal animal. After adrenalectomy fairly marked hypoglycemia resulted from breathing the 5% O_2 atmosphere while slight hyperglycemia still resulted from breathing 15% CO_2. The effects of breathing an atmosphere containing but 5% O_2 on the plasma electrolyte pattern were found to be essentially the same in the adrenalectomized as in the normal animal.

It may be concluded that the results of this study do not indicate the existence of any definite relationship between changes in the electrolyte pattern and the occurrence of convulsions due to insulin.