

between the level of plasma K or inorganic P and the occurrence of insulin convulsions. Glucose was the only blood constituent that appeared to be of significance in this connection.

10259 P

Mechanism of Insulin Convulsions. II. Effects of Varying Partial Pressures of Atmospheric O₂, N₂ and CO₂.

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In connection with a study on the relationship between the levels of potassium, inorganic phosphorus and glucose in the blood and the occurrence of insulin convulsions¹ dogs were subjected to atmospheres varying greatly in their partial pressures of O₂, N₂ and CO₂. The finding by Glickman and Gellhorn² that rats subjected to lowered O₂ tension (air in low pressure chamber at 460 mm Hg) became more sensitive to insulin and had convulsions sooner than they did in ordinary air, suggested the use of induced anoxic anoxia as an additional means of modifying our experimental conditions. The fact that the convulsions of epilepsy³ and those of hypoparathyroidism can not infrequently be prevented or aborted by the subject's breathing a gaseous mixture containing 10% CO₂ and 90% O₂ further suggested the desirability of investigating the influence of such alterations in the air breathed on the various constituents of the blood and on the occurrence of convulsions following the administration of insulin.

The method used was that of determining the effects of insulin administration, first, when the experimental animal was allowed to breath room air, and again, one week later when the same animal was kept in an ordinary oxygen tent containing O₂, N₂ and CO₂ at different partial pressures. The insulin was given subcutaneously in large single doses (10 to 25 units per kilo of body weight). In addition to the preliminary control experiments performed on all animals, the following studies were carried out: 17 experiments with low O₂ percentages; 4 with high O₂; 4 with high O₂ plus high CO₂; 4 with low O₂ plus high CO₂, and 10 with high CO₂ plus 20% O₂.

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

² Glickman, N., and Gellhorn, E., *Am. J. Physiol.*, 1938, **121**, 358.

³ Lennox, W. G., and Cobb, S., *Med.*, 1928, **7**, 105.

The specific effects of the various gaseous mixtures *per se* were determined before insulin was administered in some instances. The total pressure within the tent was always equal to the outside atmospheric pressure, variations in the partial pressures of the different gases being produced by admitting gas from special tanks. As a special check on the composition of the gaseous mixture within the tent, O₂ and CO₂ were determined at 30-minute intervals by the Orsat method. Blood samples were obtained at hourly or 2-hourly intervals without removing the animal from the tent. The technical procedures used for determination of the various blood constituents were the same as those referred to previously.¹

The results may be summarized as follows: Breathing an atmosphere with oxygen reduced to between 5% and 12% caused marked hyperglycemia and a simultaneous reduction in both the K and the inorganic P of the plasma without administration of insulin. Hemolysis frequently occurred after prolonged experiments involving the lower percentages of O₂. High CO₂ (15%) alone caused hyperglycemia accompanied by a significant increase in plasma inorganic P. The K of the plasma was little influenced by the animal's breathing a high percentage of CO₂. The effects of breathing the various gaseous mixtures used on the occurrence of insulin convulsions were as follows: Breathing high partial pressures of O₂ (60% to 76%) or partial pressures of CO₂ between 5% and 10% or a combination of these had no definite effect, convulsions occurring at approximately the same time after the insulin injection as they did in room air. Low O₂ pressures (4.5% to 9.2%), however, tended to prevent convulsions entirely or to greatly prolong the period between the time of insulin administration and the occurrence of convulsions. In a few instances reduction of the O₂ to only 12% had a similar inhibiting effect. Convulsions did not occur in many of the low-oxygen experiments, even when the degree of hypoglycemia was similar to that found to precede the onset of convulsions in the corresponding control tests in ordinary air. The plasma K and inorganic P were reduced to approximately the same degree when the animal was kept in the low O₂ atmosphere after receiving insulin as they were in ordinary air. The effect of breathing gaseous mixtures which were very low in O₂ and high in CO₂ was to inhibit the convulsive tendency. An atmosphere containing 15% CO₂ plus 20% O₂ had a similar effect even when the blood sugar was reduced well below the previously determined convulsive level. In the latter type of experiment, the inorganic P of the plasma was greatly elevated while the K was reduced along with the blood sugar. Convulsions occurred in spite of the 15% CO₂, when the O₂ in the

tent was increased to 80%. That the nervous system is not rendered entirely insensitive to convulsive agents by the low O₂, high CO₂ atmospheres is indicated by the fact that we were able to induce typical metrazol convulsions within the usual time under these conditions.

It may be concluded tentatively from the foregoing experiments that marked lowering of the O₂ content or marked increase in the CO₂ content of the respired air tends to inhibit rather than to accelerate insulin convulsions in the normal, fasting dog under the conditions described. While severe hypoglycemia appears to be the most important known causative factor, these experiments indicate that some additional physiological disturbance is involved in the mechanism of insulin convulsions.

10260 P

Inhibition of Growth of Rat by Oral Administration of Methylcholanthrene. Effects of Dietary Cystine and Methionine Supplements.*

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In the present communication it is desired to report preliminary results obtained in studies of the effects of certain carcinogenic substances on sulfur metabolism. The experimental approach employed in the first series of investigations is similar to that which has resulted in the demonstration that bromobenzene,¹ cholic acid,² naphthalene,³ and iodoacetic acid⁴ exert an inhibiting effect on the growth of the young white rat when any one of these compounds is incorporated into a basal diet of relatively low protein content. The addition of either l-cystine or dl-methionine to the basal diet containing either bromobenzene, cholic acid, naphthalene, or iodoacetic acid resulted in a prompt stimulation of growth, despite the continued presence of the foreign organic compound in the diet. It was sug-

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¹ White, A., and Jackson, R. W., *J. Biol. Chem.*, 1935, **111**, 507.

² White, A., *J. Biol. Chem.*, 1935, **112**, 503.

³ Stekol, J. A., *J. Biol. Chem.*, 1937, **121**, 87.

⁴ Simon, E. E., and White, A., *J. Biol. Chem.*, 1938, **123**, cix.