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Fragility of Erythrocytes as Affected by Anoxia, CO_2 Inhalation and Insulin Hypoglycemia.

MARGUERITE BOOTH. (Introduced by Irvine McQuarrie.)

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In the course of studies on the mechanism of insulin convulsions, McQuarrie and Ziegler[1] frequently observed marked hemolysis in blood samples drawn during the later stages of experiments involving severe anoxia or hypoglycemia. The present investigation was undertaken in an attempt to determine the nature of the hemolytic mechanism responsible for this effect. The current tendency to widespread use of insulin shock and anoxia in the treatment of schizophrenia and certain other neuropsychiatric disorders lends added significance to the problem. While other hematological changes were also investigated, alterations in the fragility of the erythrocytes alone are considered here.

Most of the experiments were carried out on full-grown normal dogs. A number of these were repeated, however, after bilateral adrenalectomy had been performed on the animals to render them more sensitive to insulin. The adrenalectomized animals were kept in comparatively good condition by daily injections of cortin and by use of a diet of low potassium and high sodium content. All dogs were fasted for at least 18 hours before experiments were begun. Erythrocyte fragility tests were made on freshly drawn venous blood by the method of Todd and Sanford[2] immediately before and at intervals of 30 to 60 minutes during prolonged periods of exposure to atmospheres varying widely in their partial pressures of O_2, N_2, and CO_2. When gaseous mixtures, other than room air, were used, they were mixed and adjusted at atmospheric pressure in an ordinary oxygen tent connected with separate tanks of N_2, O_2, and CO_2. As an added check on the partial pressures of the gases in the tent, rough analyses were made at 30-minute intervals throughout each experiment.

Thirty-one experiments were carried out on 9 dogs as follows: Twelve with a gaseous mixture of 5% O_2 and 95% N_2 (3 after adrenalectomy); 2 (lasting but 2 minutes) with 1% O_2 and 99%

[1] McQuarrie, I., and Ziegler, M. R., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 525.

[2] Todd, J. C., and Sanford, A. H., *Clinical Diagnosis by Laboratory Methods*, 8th ed., revised, Saunders, Philadelphia, 1937.

N_2; 5 with 15% CO_2, 20% O_2, and 65% N_2 (3 in normal and 2 in adrenalectomized animals); 3 with 90% O_2 and 10% N_2; 1 with 15% CO_2, 70% O_2, and 15% N_2; 7 involving marked insulin hypoglycemia (in room air) and 1 involving both anoxia (5% O_2) and insulin hypoglycemia. These experiments were controlled by blood sampling at similar intervals in room air. To ascertain the range of erythrocyte fragility for normal dogs breathing room air, 48 determinations were carried out in 19 different animals. The initial hemolysis in the latter series of dogs varied from 0.40% to 0.58% of NaCl solution, and complete hemolysis from 0.26% to 0.42%. None of the dogs used in the experiments showed hemolysis at these higher concentrations while breathing room air.

Breathing atmospheres containing high percentages of O_2 had no measurable influence on the fragility of the erythrocytes. Adrenalectomy *per se* likewise had no effect. However, breathing an atmosphere containing but 5% O_2 over a period of several hours produced a marked increase in fragility in all animals so exposed. Initial hemolysis occurred at concentrations of NaCl solution as high as 0.70% in some animals and well above 0.60% in the majority. An atmosphere containing 15% CO_2 increased the fragility of the red blood cells by 0.04 to 0.10% in normal and also in adrenalectomized dogs. Prolonged, severe insulin hypoglycemia increased the fragility of the erythrocytes by 0.04 to 0.08% saline solution. This effect was accentuated by simultaneous exposure of the animal to an atmosphere containing but 5% O_2

Conclusion. From the foregoing results it is concluded that the erythrocytes are severely injured, as evidenced by their increased fragility, by prolonged anoxia, by exposure to a high CO_2 atmosphere and to a less degree by long periods of insulin hypoglycemia.