Protection against semicarbazide-induced convulsions in mice at a hypobaric pressure

Exposure to hyperbaric oxygen causes marked reduction of brain γ-aminobutyric acid (Wood, Watson & Ducker, 1967) and also convulsions in mice (Faiman & Hable, 1966). Although effects opposite to those of hyperbaric oxygen have been reported on brain γ-aminobutyric acid in mice after exposure to decompression hypoxia (Wood, Watson & Ducker, 1968) the relation of this environment to convulsions has not been investigated. We have found decompression hypoxia to antagonize the convulsant properties of semicarbazide.

Male, albino mice, random bred of the Swiss Webster strain (Charles River Farms), weighing 25–35 g, were injected intraperitoneally with a freshly prepared aqueous solution of semicarbazide (200 mg/kg). They were placed in pairs, in Plexiglass desiccators and either exposed to a hypobaric environment equivalent to an altitude of 19,000 ft (364 mm Hg; $pO_2 = 76$ mm Hg) for 5 h, the pressure being reduced at a rate of 50 mm Hg min^{-1}, or kept at room atmosphere (760 mm Hg; $pO_2 = 159$ mm Hg). Room air was used. Plexiglass desiccators had a height of 14 inches and inside diameter of 10 inches, they were connected in series to a vacuum pump (Baumel, Robinson & Blatt, 1967). Clonic or tonic convulsions were recorded in individual mice by two trained observers. The experiments were made at room temperature of 21–23°.

The incidence of convulsions and the course of their onset were altered markedly in the mice exposed to the hypobaric environment (Fig. 1).

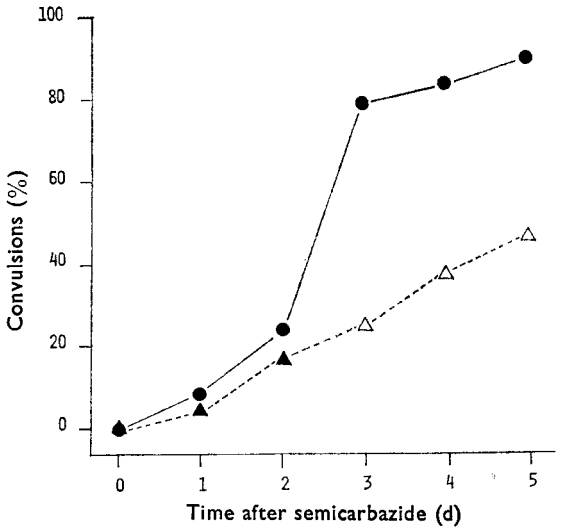

FIG. 1. Effect of exposure to hypobaric environment on convulsions due to semicarbazide. Each point represents % convulsed out of 24 mice. Differences between two groups indicated by open symbols are statistically significant ($P < 0.005$). Circles = 760 mm Hg. Triangles = 364 mm Hg.

Wood & others (1967) proposed that impairment of oxidative metabolism while breathing hypoxic air (Gurdjian, Webster & Stone, 1949) led to decreased use of γ-aminobutyric acid in the shunt pathway of the tricarboxylic acid cycle. Since convulsions produced by semicarbazide are associated with decreased levels of

γ-aminobutyric acid (Killam & Bain, 1957), the depleting action of semicarbazide on the level of the acid is likely to be compensated for by a decreased use of the acid during altitude exposure, resulting in an anticonvulsant effect.

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On the locus of the airway constricting effect of histamine in the dog

Although the ability of histamine to constrict the airway smooth musculature of a variety of animal species (including man) has been recognized for a number of years, little evidence has appeared in the literature concerning the precise location within the tracheobronchial tree at which this effect of histamine manifests itself. We now report the results of experiments which shed light on the problem.

The experiments were made on five mongrel dogs (6 to 10 kg) anaesthetized with a solution containing 100 mg of allobarbitone, 400 mg of urethane and 400 mg of monoethylurea in each ml (0·6 ml/kg i.p.). The animals were intubated with a cuffed Murphy endotracheal tube and their interpleural spaces were cannulated. Airflow was measured with a Fleisch pneumotachograph in conjunction with a differential strain gauge (Sanborn 270). A volume signal was obtained by electrical integration of the flow signal. Transpulmonary pressure was measured with a differential pressure transducer (Sanborn 267B), one side being connected to the interpleural cannula and the other side to an opening in the endotracheal tube. Individual parameters of airflow, volume and transpulmonary pressure were recorded simultaneously on a Sanborn multi-channel recorder and from these tracings values for total lung resistance were obtained by the method of Amdur & Mead (1958).

Constriction of airway smooth muscle was induced by administering five inhalations of a 2% solution of histamine base from a DeVilbiss No. 42 nebulizer. Arterial blood samples were collected anaerobically via a polyethylene cannula inserted into a femoral artery. The oxygen tension (pO_2) of the arterial blood was determined with a Radiometer oxygen microelectrode. The pH of each blood sample was measured as drawn at 38° with a Radiometer ultra-micro capillary electrode unit and again after the blood was equilibrated with two different known CO_2 mixtures. The nomogram of Siggaard Andersen & Engel (1960) was then used to determine the carbon dioxide tension (pCO_2) of each sample.

The results of a typical experiment are presented in Table 1. Intrapulmonic administration of the histamine solution evoked a rapid increase in respiratory minute volume and total lung resistance. The increased minute volume was the