

expected that with higher concentrations of carbon dioxide stronger stimuli would be required to evoke responses.

How these factors combine, and how carbon dioxide affects the action of other convulsants are being studied now.

Summary. Monkeys fitted with bilateral screw-in electrodes and immobilized with

dihydro-beta-erythroidine were artificially ventilated with various concentrations of carbon dioxide-oxygen for different periods of time. At the end of these periods they were stimulated with threshold and super-threshold voltages, and it was found that concentrations of carbon dioxide over 20% prevented seizures when inhaled for 3 minutes.

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Central Inhibitory Effects of Carbon Dioxide. III. Man.

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Previous investigations have shown that inhalation of carbon dioxide prevents electrically induced cortical seizures in cats¹ and monkeys.² This study was undertaken to note whether this phenomenon was also seen in man.

The subjects chosen were 18 carefully selected patients of varying ages. Fourteen were neurotics and the remaining 4, psychotics.* None had physical disability. The nature of the investigations were explained to them or their relatives prior to their volunteering for the test.

Each patient inhaled a commercially prepared mixture of known carbon dioxide concentration in oxygen for a definite period of time. At the end of this time an electrical stimulus sufficient to cause convulsion was given for 0.5 sec. from an Offner electroshock apparatus. As control, this same electrical stimulus was given after 5 minutes without carbon dioxide. Electroencephalograms were recorded with the Goodwin non-blocking EEG amplifier with ink-writing

oscillograph.

The electrical stimulus without carbon dioxide resulted in grand mal seizures. It was found that concentrations of carbon dioxide from 15% to 30% routinely prevented the electrically induced seizures. With 30% carbon dioxide in oxygen, 30 seconds of inhalation sufficed. Slightly longer periods were required with 15 and 20%. With these mixtures of carbon dioxide several cases had decerebrate seizures, which will be fully described by Gyarfás *et al.*³

Haldane and Smith⁴ found that 10% CO₂ was the upper limit which man could breathe without becoming unconscious. Lennox and Cobb⁵ stopped petit mal seizures by having patients breathe high concentrations of CO₂ in air. Both show the central depressant action of CO₂ in man. Heinbecker⁶ and Bishop,⁷ Necheles and Gerard,⁸ Hettwer⁹ and

¹ Pollock, G. H., Thesis, Univ. of Illinois College of Medicine, 1948.

² Stein, S. N., and Pollock, G. H., *PROC. SOC. EXP. BIOL. AND MED.*, in press.

* Thanks are due to the Chicago State Hospital for help with the selection of some of these patients and assistance in contacting relatives and arranging for voluntary transfers to Illinois Neuropsychiatric Institute.

³ Gyarfás, K., Pollock, G. H., and Stein, S. N., *PROC. SOC. EXP. BIOL. AND MED.*, in press.

⁴ Haldane, J., and Smith, J. L., *J. Path. and Bact.*, 1892, **1**, 168.

⁵ Lennox, W. G., and Cobb, S., *Medicine*, 1928, **7**, 105.

⁶ Heinbecker, P., *Am. J. Physiol.*, 1929, **89**, 58.

⁷ Heinbecker, P., and Bishop, G. H., *Am. J. Physiol.*, 1931, **96**, 613.

⁸ Necheles, H., and Gerard, R. W., *Am. J. Physiol.*, 1930, **93**, 318.

⁹ Hettwer, J. P., *Am. J. Physiol.*, 1938, **122**, 275.

Lorente de No¹⁰ found that CO₂ raised the threshold of axons of the somatic and the autonomic nervous systems. Lorente de No¹⁰ showed that the carbon dioxide raised the membrane potential and lengthened the refractory period of nerve. The central inhibitory effects of the carbon dioxide may well be due to the increase of membrane potential and threshold. Moreover, breathing carbon dioxide increases cerebral blood flow by dilating cerebral arterioles, increases respiratory rate and so the oxygenation of blood, shifts the hemoglobin dissociation curve so that the

blood releases more oxygen to the tissues and shifts cortical pH to the acid side. In the explanation of the central inhibitory action of the carbon dioxide these factors must all be considered.

Summary. Eighteen patients were ventilated with various concentrations of carbon dioxide-oxygen for varying lengths of time and then were stimulated with super-threshold shocking current. Concentrations of carbon dioxide from 15-30% routinely prevented electrically induced seizures; with 30% carbon dioxide, 30 seconds of inhalation sufficed; with 15-20% mixtures, slightly longer periods of time were required.

¹⁰ Lorente de No', Raphael, Studies of the Rockefeller Institute, vol. 131, 1937, New York.

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Central Inhibitory Effects of Carbon Dioxide. IV. Convulsive Phenomena.

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Convulsive phenomena produced by inhalation of carbon dioxide were first mentioned by Waters.¹ Meduna and Gyarfas² observed 3 types of convulsive manifestations. The first type is the so-called adersive seizure which consists of conjugate deviation, extension of the arm and flexion of the leg on the side toward which the eyes turn. These fits are not accompanied by any change in the peripheral reflexes and can be explained as tonic neck reflexes due to premotor release.

The second type consists of flexion in the upper with extension in the lower extremities and is accompanied by slight rhythmical twitching. No changes in the peripheral reflexes accompany this seizure. The third type consists of sudden dilation of the pupils, absence of any reaction to light, opisthotonus, extension of all extremities, and flexion of the

toes. This type of seizure was interpreted by Meduna and Gyarfas as a symptom of decortication.

Pollock,³ Stein and Pollock,⁴ Pollock *et al.*⁵ demonstrated that carbon dioxide in certain concentrations inhibits the action of cortical convulsants.

Pollock and Bain⁶ showed that changes in the metabolism of the brain produced by inhalation of carbon dioxide differ from those produced by cortical convulsants. In order to establish the anticonvulsant effect of carbon dioxide in man 92 experiments were carried out in 18 patients in the following way: First, the electro-shock dose of every patient was established, then carbon dioxide was adminis-

¹ Waters, R. M., *New Orleans Med. and Surg. J.*, 1937, **219**, 90.

² Meduna, L. J., and Gyarfas, K., *Diseases of the Nervous System*, in press.

³ Pollock, G. H., Thesis, Univ. of Illinois, College of Medicine, 1948.

⁴ Stein, S. N., and Pollock, G. H., *Proc. Soc. Exp. Biol. and Med.*, in press.

⁵ Pollock, G. H., Stein, S. N., and Gyarfas, K., *Proc. Soc. Exp. Biol. and Med.*, in press.

⁶ Pollock, G. H., and Bain, J. A., manuscript in preparation.