raised to maturity under cold room and room temperature conditions on purified rations differing only in the source of fat. The fats employed were cottonseed oil, corn oil, margarine fat, and butter fat. Gain in body weight was significantly reduced in all rats under cold room conditions. No significant difference was observed, however, either under cold room or room temperature conditions, in gain in body weight on the various diets employed.

16901

Central Inhibitory Effects of Carbon Dioxide. II. *Macacus rhesus*.

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Pollock's observation that carbon dioxide prevents electrically induced cortical seizures in cats suggested further study on primates.[1] Since the normal electroencephalograph of the *Macacus rhesus* is so well known, and it is not difficult to extrapolate from it to the human, this animal was chosen for the primate study.

Tracheal intubation, exposure of both femoral veins and of the calvarium were performed under ethyl ether anesthesia. Artificial respiration was started after an initial intravenous injection of 20 mg of dihydro-B-erythroidin hydrobromide and was maintained at 45 cc per stroke, 30 strokes per minute. 180 mg of dihydro-B-erythroidin hydrobromide in 300 cc of normal saline was administered as a slow drip throughout the experiment. Bilateral screw-in electrodes were placed 4 mm posterior to the coronal suture and 6 mm lateral to the sagittal suture. These electrodes were connected to a double-pole-double-throw switch allowing alternate connections to the input of a Goodwin non-blocking EEG amplifier with ink-writing oscillograph or to the output of a Lab-Tronics Stimulator (Model 3). The EEG was recorded concurrently with the EKG picked up from the right fore and left hind limbs.

Routinely the animals were ventilated with various concentrations of carbon dioxide in oxygen for intervals of 1 to 9 minutes and, on termination of each period of respiring carbon dioxide, stimulated with threshold and superthreshold voltages. A "saw-tooth" stimulating frequency of 60 impulses per second and a falling phase of 10 sigma were used throughout the experiment. It was found that concentrations of carbon dioxide below 15%, when administered for 3 minutes, would not prevent electrically-induced cortical seizures. When these concentrations were given for periods longer than 3 minutes, suppression of seizures occurred, which was more marked as the concentration of carbon dioxide approached 15%. Concentrations of carbon dioxide over 20% prevented the seizure response. Duration and intensity of the stimuli did not markedly affect the result. It appears that in *Rhesus macacus* the anticonvulsive level of carbon dioxide lies somewhere between 15% and 20%. The changes in the EEG and EKG found with carbon dioxide were similar to those found in cats by Pollock.[1]

Lorente de No' found that the rise of the membrane potential due to carbon dioxide is roughly proportional to the logarithm of its concentration, and this was accompanied not only by a decrease in fatiguability but also by a rise in threshold.[2] It is also known that carbon dioxide alters the pH, oxygen tension and blood flow of the brain.[3] Hence it is to be

[1] Pollock, G. H., Thesis, Univ. of Ill., College of Medicine, 1948.

[2] Lorente de No', R., Studies from the Rockefeller Institute for Medical Research, Vol. 131.

[3] Roseman, E., Goodwin, C. W., and McCulloch, W. S., unpublished data.

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.

16902

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 cats[1] 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 nonblocking 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 Gyarfas *et al.*[3]

Haldane and Smith[4] found that 10% CO_2 was the upper limit which man could breathe without becoming unconscious. Lennox and Cobb[5] stopped petit mal seizures by having patients breathe high concentrations of CO_2 in air. Both show the central depressant action of CO_2 in man. Heinbecker[6] and Bishop,[7] Necheles and Gerard,[8] Hettwer[9] 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 Gyarfas, 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.