Anticonvulsant Threshold of CO_2 in Oxygen under High Pressure. (22129)

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Taylor(1) found that addition of small amounts of CO_2 to the breathing mixture hastened the onset of convulsions under high oxygen pressure. Chapin(2) in determining CO_2 toxicity under OHP found no convulsions when mice were subjected to 304 mm Hg $^{P_I}CO_2$ and 2890 mm or 6080 mm PO_2. This disparity suggested that CO_2 may enhance convulsions only in low concentrations. If this is true it should be possible to determine that tension at which CO_2 becomes anti-convulsant.

Method. A high pressure gas chamber with volume about 1.2 liters was constructed from heavy 4 inch pipe closed at one end. The other end contained a thick lucite window and screwed onto the nipple. A heavy rubber gasket sealed the chamber when tight. Two ports were fitted into the nipple to facilitate introduction and expulsion of gas. Test animals were placed in the chamber which was then closed and ventilated with the test gas. When air had been expelled, exit port was closed and pressure increased to desired value.

Mice were exposed to gas mixtures containing 27, 61, 69, 97, 101, 120, 125, 132, and 165 mm $^{P}CO_2$ each in 3800 mm PO_2 Exposure time to onset of first convulsion was recorded in those cases where a full tonic convulsion occurred.

Results. These experiments confirm the reported enhancement of onset of convulsions by low CO_2, but in addition shows that the time by which convulsions are hastened is about the same when the $^{P}CO_2$ is between 27 mm and 120 mm Hg.

The tension at which only half of the mice convulse and the other half goes on to die without convulsion is about 120 mm $^{P}CO_2$. Table I shows the tabulated results of these experiments.

TABLE I. Influence of CO_2 on OHP Convulsions and Convulsion Time. $PO_2 = 3800$.

$^{P}CO_2$	No. used	No. convulsing	Min. exposure before convulsions
0	15	15	21 (10-35)
27	4	4	8 (6- 9)
61	15	15	8 (6-11)
97	3	3	12 (10-14)
101	4	4	9 (8-11)
120	10	5	9 (8-10)
125	4	0	—
132	4	0	—
165	9	1	10

Discussion. This study confirms Taylor's (1) findings that: 1) Carbon dioxide hastens onset of OHP convulsions, 2) within certain limits tension of CO_2 used to shorten convulsion time, appears to be immaterial.

It further appears that CO_2 hastens onset of OHP convulsions in one range and inhibits them in another. The division between these ranges appears to be about 120 mm $^{P}CO_2$. This value falls slightly below that found by Chapin(4) to produce maximal ventilatory response in the hamster and may be related to CO_2 tension at which anesthetic effects are first manifested.

Taylor did not mention failure to convulse in any of his 20 trials although he exposed one cat to 12.2% CO_2 at 55 lb pressure. (He did not specify whether this is gauge or total pressure. Neither did he specify whether this was the pressure due to O_2 and CO_2 together or O_2 alone. If it is total pressure and due to both gases, the $^{P}CO_2$ was 347 mm. If it is gauge pressure and due to both gases, the $^{P}CO_2$ was 439 mm.) This is well within the range for which CO_2 was found by this study to be anticonvulsant.

Stein and Sonnenschein(3) contended that they were unable to confirm the potentiating action of CO_2 on OHP convulsions in cats even though they used CO_2 as low as 1%. Their gauge pressure appears to have been either 75 or 90 lb. The $^{P}CO_2$ at which they failed to get convulsions but only depression

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may be calculated at 46 or 54 mm. This is far below the anti-convulsant threshold determined in mice by this study.

Summary. 1. A series of 68 mice was exposed to 5 atmospheres of oxygen in a small pressure chamber. Some of these received pure oxygen while others received mixtures of oxygen diluted with varying quantities of CO_2. All mice receiving only pure oxygen convulsed. All mice receiving less than 120 mm $^{P}CO_2$ in OHP convulsed. One half of the mice receiving 120 mm $^{P}CO_2$ in OHP convulsed. The other half went on to die without convulsions. Only one out of 17 mice receiving over 120 mm $^{P}CO_2$ convulsed. 2. Mice receiving oxygen diluted with CO_2 convulsed sooner than mice receiving pure oxygen. Amount of shortening of convulsion time did not appear to be dependent upon amount of CO_2 diluting the oxygen as long as $^{P}CO_2$ lay in the range of 27-120 mm. Both of these findings confirm those of Taylor(1). The tension at which CO_2 becomes anticonvulsant appears to be about 120 mm. or about 16% of 1 atmosphere.

1. Taylor, H. J., *J. Physiol.*, 1949, v109, 272.
2. Chapin, J. L., AF Tech Rep., in press.
3. Stein, S. M., and Sonnenschein, R. R., *J. Aviation Med.*, 1950, v21, 401.
4. Chapin, J. L., *Am. J. Physiol.*, 1954, v179, 146.

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Effects of Altitude, Acidosis, and Alkalosis upon Hypoxic Threshold.* (22130)

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Hoff and Breckenridge(1) have contended since acclimatized subjects exhibit hyperventilation at all altitudes above sea level that in acclimatized breathing there is no anoxic threshold. Rahn and Otis(2) on the other hand suggest that the alveolar $^{P}CO_2$ begins to fall (and the ventilation begins to rise) in all residents of altitude when the $^{P_A}O_2$ is lowered to about 100 mm Hg.

This study was undertaken to determine whether there was or was not a hypoxic threshold for altitude dwellers, if so where it was, and whether it was the same no matter what altitude was represented.

Method. Experiments were carried out on 6 subjects, residents of Denver, Colo. (5300 feet) and on 5 others, 4 of whom had spent 2 months and one who had spent 1 month living on Mt. Evans, Colorado (14,150 feet). Subjects rested on a cot throughout experiment. After a 10 minute period to bring them to a resting state they breathed a gas mixture containing 50% oxygen in nitrogen so the ventilation changes incident to breathing oxygen mixtures described by Chapin(3) would not be introduced into the critical phase of experiment. Following this phase subjects immediately switched to rebreathing from calibrated Collins 13.5 L recording spirometer equipped with soda lime CO_2 absorber and initial gas mixture of 50% O_2 in N_2 at Mt. Evans and 35% O_2 in N_2 at Denver. By this method inspired $^{P}O_2$ was gradually reduced. Terminal gas (Scholander) analyses showed no CO_2 in spirometer at end of experiment. Spirometer O_2 was analysed each minute by pulling small samples through a Beckman infrared oxygen analyzer. The point at which ventilation began to increase was taken as hypoxic threshold.† Since, in some respects, chronic NH_4Cl ingestion simulates altitude acclimatization, we thought that testing the effect of NH_4Cl on hypoxic threshold would be interesting. Five of the Denver subjects ingested 6 g of NH_4Cl

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