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.

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

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(Introduced by C. A. Maaske.)
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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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TABLE I. Hypoxic Thresholds in Various Situations.

Situation	Tracheal P_{O_2} at hypoxic threshold (mm)	Range	No. of subjects
Mt. Evans	179	174 -182.5	6
Acidosis at Denver	164	153 -185	5
Normal at Denver	127	121 -131	5
Alkalosis at Denver	107	103.5-110	3
Normal at sea level	93	(Rahn and Otis)	

daily for 5 days, were tested as described above, and showed elevation in hypoxic threshold to 164 mm. Following this finding it was natural to test the effect of bicarbonate. This was done by 3 subjects who ingested 15-30 g $NaHCO_3$ per day for five days and exhibited an average hypoxic threshold drop to 107 mm which is close to that exhibited by normal subjects acclimatized to sea level.

Results. A definite threshold for Denver residents was found at about 127 mm $P_{I_{O_2}}$. This suggests that most Denverites have slight hypoxic drives since average Denver tracheal air P_{O_2} is about 122 mm. Mt. Evans residents also exhibited thresholds but these averaged 179 mm $P_{I_{O_2}}$. Since sea level subjects are believed by many to reach the hypoxic threshold only when inspired oxygen falls to 12 to 14%, there appears to be an orderly progression of hypoxic threshold with altitude.

Table I shows the mean hypoxic thresholds in each of 4 experimental situations together with the ranges and number of subjects. In addition a sea level figure from Rahn and Otis is included.

Discussion. One might argue, since the hypoxic threshold varies directly with altitude, that it varies inversely with the P_{O_2} at which one is acclimatized. However, since NH_4Cl ingestion at Denver results in hyperventilation and slightly elevated $P_{A_{O_2}}$ and at the same time increases the hypoxic threshold, this thesis would not appear to be tenable. It might be further argued that pH determines the threshold. However, since altitude acclimatization probably results in slightly elevated pH while NH_4Cl administration lowers pH somewhat and since they both elevate the hypoxic threshold, this thesis seems untenable. It seems more likely that the hypoxic threshold varies with the resting P_{CO_2} level or some function thereof. P_{CO_2} is low in individuals acclimatized to altitude and in those in chronic NH_4Cl acidosis. Both of these groups exhibit high thresholds. P_{CO_2} is higher in individuals acclimatized to sea level than in Denverites and it is also high in Denverites receiving bicarbonate. Both of these groups show low hypoxic thresholds.

Still further possibilities remain. Acclimatization of the chemoreceptors to the bicarbonate level of the arterial blood may govern the threshold. The chemoreceptors may be involved only indirectly and the level of their response to anoxia may be set by the P_{CO_2} or long term bicarbonate level of the respiratory center. In some way the volume of ventilation, apart from CO_2 level, might set the threshold. On the other hand, if it is CO_2 or bicarbonate level to which one is acclimatized which determines the threshold for hypoxic response, this test might be a more sensitive measure of the extent of CO_2 acclimatization than those we now have.

Fig. 1 shows a plot of these points on a Fenn CO_2-O_2 diagram. Inspired tensions have been converted to probable alveolar values and alveolar hypoxic threshold CO_2 tensions have been calculated assuming a steady state and assuming that high oxygen depresses breathing in subjects acclimatized to altitude (3). A hypoxic threshold line has been drawn connecting the threshold values. This line confirms the suggestion that a resident of about four thousand feet would be living at his hypoxic threshold. However an alkalotic individual would be above and an acidotic individual would be below the threshold and the latter would be under some hypoxic ven-

† Although it would be conventional where the threshold occurs at a higher O_2 tension to refer to it as a reduced hypoxic threshold (lower intensity of a liminal stimulus), we feel such usage would be more confusing than to refer to the threshold in terms of the oxygen tension at which it occurs. The above situation, therefore, would be called an increase in hypoxic threshold.

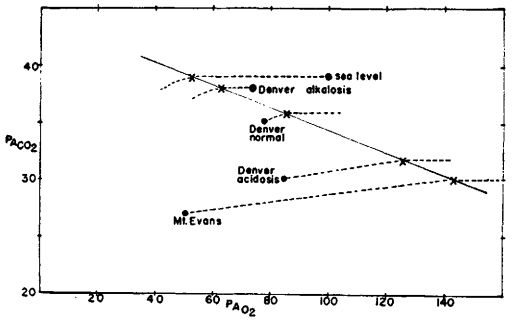

FIG. 1. Hypoxic threshold line is the solid line drawn between probable hypoxic thresholds of residents at sea level, Denver, Mt. Evans, and of Denver residents who are acidotic and alkalotic. Dashed lines indicate probable alveolar gas changes resulting from gradual decreases in alveolar oxygen tensions. When the threshold line is crossed, breathing increases and $^{P_A}CO_2$ decreases.

tilatory drive.

Summary. 1. Inspired oxygen tensions which produce the first discernible increases in ventilation (hypoxic thresholds) were measured in subjects acclimatized to Mt. Evans, Colo. (14,150 feet) and to Denver, Colo. (5300 feet). In addition thresholds were measured in subjects living in Denver who were in chronic metabolic acidosis (NH_4Cl) and in chronic metabolic alkalosis ($NaHCO_3$). 2. Mt. Evans subjects showed an average threshold of 179 mm tracheal $^{P}O_2$ and those at Denver 127 mm. Reports in the literature pinpoint the threshold for sea level dwellers at about 93 mm. Furthermore the threshold for Denverites ingesting NH_4Cl was 163 mm and for those ingesting $NaHCO_3$ was 107 mm. 3. Since NH_4Cl changed $^{P_A}O_2$ and pH in the opposite direction from altitude but changed the hypoxic threshold in the same direction, these agents were ruled out as threshold governors. It was suggested that probably the hypoxic threshold is a function of either the resting $^{P}CO_2$ or the bicarbonate level to which the individual had acclimatized.

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Prevention and Treatment of Motion Sickness by Intranasal Medication. (22131)

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Rapid absorption of hyoscine hydrobromide (scopolamine) after intranasal instillation has recently been reported(1,2). This route of administration combines simplicity of self-medication with rapid drug absorption. It has the further advantage of circumventing the oral route when nausea, psychic factors, or lack of cooperation make swallowing difficult. This technic should be especially valuable in prevention and treatment of motion sickness. Its effectiveness against swing- and airsickness is the subject of this report.

Experimental. Scopolamine Spray and Swing Sickness. Healthy, male adults ranging in age from 17 to 24 years (average 19 years) were used as subjects. The experimental group were given varying amounts of scopolamine in each nostril by a plastic spray bottle† and the remainder were given saline in a similar manner. Exact amount of fluid instilled was determined by loss in weight of spray bottle. Thirty minutes after spraying, the subject was placed in the carriage of a motor-driven swing and swung through an arc of 120° for 20 min-

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