ALTERNATIVE TO THE EQUIVALENT AIR ALTITUDE MODEL TO PREDICT ACUTE MOUNTAIN SICKNESS

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ABSTRACT

BACKGROUND: According to the Equivalent Air Altitude (EAA) model, combinations of ambient pressure (P_B) and inspired fraction of O_2 (F_IO_2) that result in the same inspired hypoxic partial pressure of O_2 (P_IO_2) produce the same physiological responses, such as the incidence of Acute Mountain Sickness (AMS). The EAA model is $P_IO_2 = (P_B - 47) \cdot F_IO_2$. However, recent research suggests that P_B has an independent effect on AMS. METHODS: We determined the probabilities of subjects having AMS [P(AMS)], using two models of hypoxic dose with literature data in which an independent P_B effect on AMS was evident. In the EAA model, hypoxic dose = $1 / P_IO_2$, and in our isohypoxic model, hypoxic dose = $1 / P_IO_2 \cdot [100 / (P_B - 47)^{0.5}] - 0.025$. Dose was transformed into P(AMS) through the Hill function with the two coefficients estimated using maximum likelihood. RESULTS: The isohypoxic model was superior to the EAA model (log likelihood of -252 vs. -278), and both were superior to the null model (-397). Using a one-sample $\chi 2$ test, the expected outcome from the isohypoxic model was similar to the AMS observations ($p = 0.30$), which was not the case for the EAA model ($p < 0.001$). CONCLUSION: Our manipulation of the P_B term increases hypoxic dose for the same P_IO_2, as P_B decreases. For example, the EAA model predicts 24% AMS at 522 mmHg altitude and at 281 mmHg altitude with F_IO_2 of 0.426 for the same P_IO_2 of 100 mmHg. In contrast, our isohypoxic model predicts 28% in the first case but 59% in the second.

INTRODUCTION

Paul Bert (1833 – 86) showed that it was the decrease in P_IO_2 that caused signs and symptoms of hypoxia.

The doctrine that low P_IO_2 alone is the cause of hypoxia is dogma – the basis of the equivalent air altitude (EAA) model: $P_IO_2 = (P_B - 47) \cdot F_IO_2$ and $F_IO_2 = P_IO_2 / (P_B - 47)$ (1).

10.3 ALTITUDE-PRESSURE TABLE

(1) Altitude m	(2) Altitude ft.	(3) P_B mm Hg	(4) (P_B-47) mm Hg	(5) $.209(P_B-47)$ mm Hg
0	0	760	713	149
610	2000	707	660	138
1220	4000	656	609	127
1830	6000	609	562	118
2440	8000	564	517	108
3050	10000	523	476	100
3660	12000	483	436	91
4270	14000	446	399	83
4880	16000	412	365	76
5490	18000	379	332	69
6100	20000	349	302	63
6710	22000	321	274	57
7320	24000	294	247	52
7930	26000	270	223	47
8540	28000	247	200	42
9150	30000	226	179	37
9760	32000	206	159	33
10370	34000	187	140	29
10980	36000	170	123	26
11590	38000	155	108	23
12200	40000	141	94	20
12810	42000	128	81	17
13420	44000	116	69	14
14030	46000	106	59	12
14640	48000	96	49	10
15250	50000	87	40	8
15215	63000	47	0	0

21% O_2 @ 10,000 ft
or
50% O_2 @ 28,000 ft
or
14% O_2 @ 0 ft (sea level) etc.

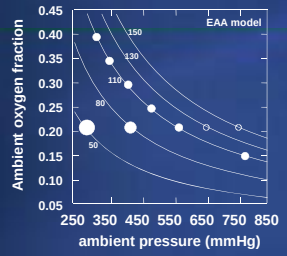


Fig. 1. As you move horizontal across P_IO_2 isopleths the incidence of AMS increases. And as you move along an isopleth the incidence of AMS is ***supposed*** to be constant.

EVIDENCE AGAINST THE EAA MODEL:

Rahn (6) disproved the simple notion of equivalent air altitude, and concluded, "It is evidently not enough to equate the inspired O_2 tensions …"

Since 1980s researchers have questioned the conventional wisdom that the symptoms of AMS are solely due to low O_2 partial pressure.

Accumulated anecdotal evidence shows descent is more effective for relief of AMS than enriched O_2 alone.

Savourey (8) speaks of the "specific response to hypobaric hypoxia".

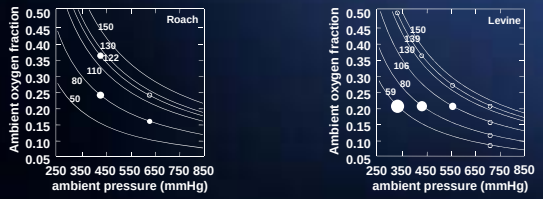


Fig. 2. Data from humans (2a) and animals (2b) show how movement along a hypoxic isopleth does not produce the same hypoxic outcome.

Hypothesis: low P_IO_2 AND P_B dictate hypoxic stress, not just low P_IO_2 (1).

We tested the hypothesis through analysis.

METHODS

Our probabilistic modeling approach required four items:

a) a data set (training data) that contained a dichotomous response variable (the presence or absence of AMS) and one or more explanatory variables;

b) an expression of hypoxic dose in terms of explanatory variables;

c) the Hill function, which structures the dose model so that the outcome is a calculated probability of AMS [P(AMS)] = hypoxic dose$^{\gamma}$ / (hypoxic dose$^{\alpha\gamma}$ + β^{α}) ; and

d) a parameter-estimation routine on a computer that uses maximum likelihood to optimize hypoxic dose to dichotomous AMS response.

Models for hypoxic dose were optimized to AMS response data from a matrix of tested P_B and F_IO_2 Conditions (see Table I).

Competing hypoxic dose models:

Eq. 1 EAA dose = $1 / P_IO_2$ (only P_IO_2 is important)

Eq. 2 Isohypoxic dose = $1 / P_IO_2 \cdot [100 / (P_B - 47)^{0.5}] - 0.025$ (P_IO_2 and P_B are important)

The optimization of dose to response data created a dose-response curve specific to the training data.

We used information from five published reports (2,4,5,7,9).
These data provide evidence for an independent effect of P_B on hypoxia and AMS: a person is more disadvantaged by a given low P_IO_2 when barometric pressure is low.

Data available over a narrow range of conditions.
Most human AMS experience is from 80 mmHg P_IO_2 isopleth.
Unfortunately, the best data are from subjects equilibrated to 1,524 m (5,000 ft) altitude.

No common response variable between reports.
Had to estimate AMS incidence from available information.

Primary goal was to quantify the P_B effect on AMS through a statistical probabilistic model.

TABLE I: DATA USED IN REGRESSIONS

P_B (mmHg)	F_IO_2	P_IO_2 (mmHg)	n	% AMS*	notes
760	0.21	150	1000	0	define dose curve at sea level
706	0.21	138	100	0	define dose curve near sea level
657	0.21	128	100	0	define dose curve near sea level
597	0.21	115	100	18.0	estimated from Honigman (2)
564	0.21	108	100	22.0	estimated from Honigman (2)
536	0.21	103	200	27.0	estimated from Honigman (2)
636	0.204	120	9	0	estimated from Roach (7) and Loeppky (4)
434	0.296	115	9	0	estimated from Roach (7) and Loeppky (4)
614	0.142	80	9	22.0	estimated from Roach (7) and Loeppky (4)
432	0.207	80	9	55.0	estimated from Roach (7) and Loeppky (4)
740	0.21	145	6	0	from Meehan (5)
740	0.125	86	6	0	from Meehan (5)
632	0.14	82	6	17.0	estimated from Tucker (9)
430	0.21	80	6	33.0	estimated from Tucker (9)
430	0.21	80	6	50.0	estimated from Tucker (9)
			1666		

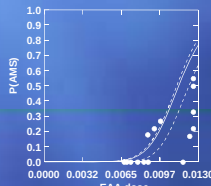
* Acute Mountain Sickness: Signs and symptoms include headache, nausea, dizziness, fatigue, vomiting and sleeplessness following a recent gain in altitude with at least several hours at the new altitude in a hypoxic environment; likened to a bad hangover.

RESULTS

TABLE II: COMPARISONS OF TWO AMS PREDICTIVE MODELS

Regression details	EAA model	Isohypoxic model		
null model LL n = 1,666	-397.2	-397.2		
model LL number, n = 1,666	-278.3	-252.6		
Hill equation coefficients α β	8.828 0.0113	1.994 0.0330		
correlation coefficient	-0.789	-0.861		
one-sample χ^2	p<0.001	p=0.30*		
hypoxia condition direct ascent	P_IO_2 (mmHg)	AMS %	EAA model P(AMS)	Isohypoxic model P(AMS)
2,134 m with $F_IO_2 = 0.21$	113	15%	10%	13%
4,572 m with $F_IO_2 = 0.21$	80	42% - 55%	70%	58%
1,524 m with $F_IO_2 = 0.142$	80	17% - 22%	70%	41%

* expected outcome from model is not significantly different from empirical observations.



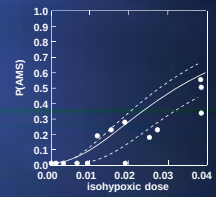


Fig. 3. The dose-response curve and 95% confidence interval for the regression of the EAA model (3a) and the isohypoxic model (3b). Same size circles do not reflect same sample sizes, which range from six to 1000.

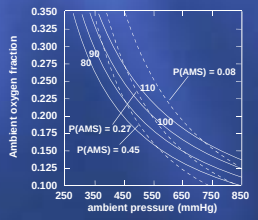


Fig. 4. Three isopleths (dashed) from the isohypoxic model show the combinations of P_B and F_IO_2 to achieve a computed incidence of AMS of 8%, 27%, and 45%. Each curve crosses several P_IO_2 isopleths (solid) from the EAA model, so isoP_IO_2 does not equate to isohypoxia.

CONCLUSIONS / DISCUSSION

Our proposed isohypoxic model is a refinement to the EAA model.

Clues for a potential model structure come from how alveolar ventilation is influenced by P_B:
Flow is $\propto$ to $1/\sqrt{}$ gas density
Work of breathing is $\propto$ to relative density $\cdot V_E^3$
Diffusivity of a gas is $\propto$ 1 / gas density

We will have greater confidence in a future model as more and better AMS data become available for analysis.

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