Arterial Blood Gas Reference Values for Sea Level and an Altitude of 1,400 Meters

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Blood gas measurements were collected on healthy lifetime nonsmokers at sea level (n = 96) and at an altitude of 1,400 meters (n = 243) to establish reference equations. At each study site, arterial blood samples were analyzed in duplicate on two separate blood gas analyzers and CO-oximeters. Arterial blood gas variables included Pa_{O_2}, Pa_{CO_2}, pH, and calculated alveolar-arterial P_{O_2} difference (AaP_{O_2}). CO-oximeter variables were Hb, COHb, MetHb, and Sa_{O_2}. Subjects were 18 to 81 yr of age with 166 male and 173 female. Outlier data were excluded from multiple regression analysis, and reference equations were fitted to the data in two ways: (*1*) best fit using linear, squared, and cross-product terms; (*2*) simple equations, including only the variables that explained at least 3% of the variance. Two sets of equations were created: (*1*) using only the sea level data and (*2*) using the combined data with barometric pressure as an independent variable. Comparisons with earlier studies revealed small but significant differences; the decline in Pa_{O_2} with age at each altitude was consistent with most previous studies. At sea level, the equation that included barometric pressure predicted Pa_{O_2} slightly better than the sea level specific equation. The inclusion of barometric pressure in the equations allows better prediction of blood gas reference values at sea level and at altitudes as high as 1,400 meters. Crapo RO, Jensen RL, Hegewald M, Tashkin DP. Arterial blood gas reference values for sea level and an altitude of 1,400 meters. AM J RESPIR CRIT CARE MED 1999;160:1525–1531.

Arterial blood gas analysis has played an important role in managing patients with cardiopulmonary diseases for approximately 30 yr. Most reference equations used to predict "normal" arterial blood gas values are now more than 20 yr old (1–12). The most recent study of blood gases in healthy subjects studied subjects between 40 and 90 yr of age (13). Blood gases are now routinely analyzed on automated machines that use computer algorithms to adjust for system nonlinearities and inaccuracies; as a result, they may produce results significantly different from those of the manual instruments used in earlier studies. Earlier studies typically used only one analyzer model at a single study site, which ignores the small but statistically significant interinstrument and interlaboratory differences in blood gas measurements (14, 15). Finally, CO-oximetry, now an integral part of blood gas analysis, was not available at the time of the earlier studies, and altitude effects on blood gas reference values were not studied.

We sought to define reference equations based on healthy lifetime nonsmokers for arterial blood gas and CO-oximeter analytes at two different altitudes. We anticipated small but statistically significant changes from previous reference equations because of differences in study design and blood gas analyzer technology.

METHODS

The study population consisted of a convenience sample of healthy nonsmoking volunteers. Many of our subjects were hospital employees, their family members, or acquaintances at the study sites. There were three study sites (Table 1): one site at an altitude of 1,400 meters (Salt Lake City, UT) and two near sea level (Los Angeles, CA and Hartford, CT). All three study sites were reference laboratories for the American Thoracic Society blood gas proficiency testing program at the time of the study. Exclusion criteria were (*1*) greater than one-half pack-year smoking history or any regular smoking in the previous 6 mo, (*2*) history of cardiopulmonary disease or persistent cardiopulmonary symptoms (cough, sputum production, dyspnea, or wheezing), (*3*) weight greater than 120% of average based on actuarial tables (16), (*4*) presence of thoracic cage deformities, (*5*) history of a bleeding disorder, (*6*) current use of aspirin or anticoagulants, (*7*) history of vascular or nerve problems with hands or arms, (*8*) history of wrist or hand surgery or injury. Recruitment was designed to provide an even distribution of subjects by decade of age.

The study protocol was approved by the institutional review board at each study institution. The risks of radial artery puncture were explained to each subject, and each gave written consent. Barometric pressure (PB) and room temperature were recorded at each subject's test session. Subjects' sex, age, standing height, weight, and oral temperature were recorded. Height and weight were measured with subjects wearing indoor clothing without shoes. Prior to arterial puncture, the subjects sat quietly for 10 min; a modified Allen's test was performed to check for adequate collateral circulation (17). Local anesthesia was not applied to the skin or tissues surrounding the radial artery prior to radial artery puncture. An experienced technician collected an arterial sample of at least 4 ml, puncturing a radial artery using a 1-inch 22-gauge thin-wall needle attached to a five-ml glass syringe with 0.2 ml of liquid sodium heparin (1,000 U/ml) in the syringe dead space. Average syringe dead space volume was estimated as 0.2 ml

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TABLE 1

INSTRUMENTS USED IN THE STUDY AND MEAN BAROMETRIC PRESSURE BY SITE

Site	Mean Barometric Pressure ± SD (*mm Hg*)	Blood Gas Analyzer Models	CO-oximeter Models
Salt Lake City, UT	645 ± 3.7	Radiometer ABL3* Corning 178	IL482† Radiometer OSM3
Los Angeles, CA	752 ± 1.8	Corning 178‡ Corning 278	IL282 IL482
Hartford, CT	756 ± 4.9	IL1312 IL1312	IL482 IL482

* Radiometer Instruments (Radiometer, Cleveland, OH) ABL3 and OSM3.
† Instrumentation Laboratory (Lexington, MA) IL1312, IL282, and IL482.
‡ Corning Instruments (Medfield, MA) Model 178 and Model 278.

by precision weighing five syringes with and without liquid heparin and was similar to previously reported syringe dead space volumes (17). Our goal was to analyze all specimens within 30 min of the arterial puncture. Samples were stored in an ice-water slurry if they could not be analyzed immediately. Specimens were analyzed on machines in clinical use at each participating laboratory (Table 1), using an electrode temperature of 37° C. Each sample was analyzed in duplicate on each of two automated blood gas analyzers and on each of two CO-oximeters (a total of four measurements of each analyte). Measured values were not temperature adjusted to body temperature for this analysis.

Standard quality control measures were followed in each laboratory. Blood gas analyzers were required to measure three known perfluorocarbon containing proficiency-testing standard solutions within each laboratory's established control limits. On each testing day, accuracy was also confirmed with tonometry using fresh whole blood. The blood gas analyzers were required to measure P_{O_2} and P_{CO_2} within ± 2 mm Hg in blood tonometered to 75 mm Hg P_{O_2} and 40 mm Hg P_{CO_2}.

Statistical Methods

Data were analyzed using Statistica software (Statsoft Inc., Tulsa, OK). Outlier measurements for individual subjects were first identified and excluded. Outlier values were identified when they met any of three outlier criteria. The first, from Dixon and Massey (18), was a statistical test where outliers were identified using a ratio where the numerator was the distance from one end of the distribution to its neighbor and the denominator was the entire range of values. A critical ratio defined in table A3 in Dixon and Massey (18) was used to define outliers. Second, outlier criteria were determined by visual examination of histograms of the intramachine and intermachine differences for each analyte. For each subject's data, the criteria were: Pa_{O_2} greater than 3 mm Hg from the next closest value, Pa_{CO_2} greater than 2 mm Hg from the next closest value, pH greater than 0.03 units from the next closest value, Sa_{O_2} greater than 2.0% from the next closest value, Hb greater than 1.0 g/dl from the next closest value, and metHb and COHb values greater than 0.5% from the next closest value. Finally, all negative metHb and COHb values were classified as outliers.

TABLE 2

DEMOGRAPHIC INFORMATION

	Sea Level		1,400 Meters	
	Men (*n = 44*)	Women (*n = 52*)	Men (*n = 122*)	Women (*n = 121*)
Mean age, yr (range)	40.6 (18–79)	46.5 (19–79)	47.7 (25–81)	48.6 (25–75)
Mean height, cm (range)	176.8 (162–195)	162.2 (146–178)	179.5 (161–198)	165.0 (150–182)
Mean weight, kg (range)	76.0 (56–104)	62.6 (48–100)	81.4 (58–110)	65.9 (45–108)

TABLE 3

CORRELATION MATRIX FOR BLOOD GAS ANALYTES AND AGE, SEX, HEIGHT, WEIGHT, AND BAROMETRIC PRESSURE

	Age	Sex	Height	Weight	P_B
Pa_{O_2}	$r^2 = 0.173$ $p < 0.001$	$r^2 = 0.006$ $p = 0.16$	$r^2 = 0.007$ $p = 0.13$	$r^2 = 0.081$ $p < 0.001$	$r^2 = 0.652$ $p < 0.001$
Pa_{CO_2}	$r^2 = 0.0002$ $p = 0.80$	$r^2 = 0.021$ $p = 0.007$	$r^2 = 0.0004$ $p = 0.72$	$r^2 = 0.002$ $p = 0.40$	$r^2 = 0.325$ $p < 0.001$
pH	$r^2 = 0.019$ $p = 0.01$	$r^2 = 0.019$ $p = 0.011$	$r^2 = 0.004$ $p = 0.26$	$r^2 = 0.002$ $p = 0.48$	$r^2 = 0.092$ $p < 0.001$
Sa_{O_2}	$r^2 = 0.270$ $p < 0.001$	$r^2 = 0.002$ $p = 0.45$	$r^2 = 0.0004$ $p = 0.70$	$r^2 = 0.083$ $p < 0.001$	$r^2 = 0.312$ $p < 0.001$
AaP_{O_2}	$r^2 = 0.344$ $p < 0.001$	$r^2 = 0.004$ $p = 0.24$	$r^2 = 0.017$ $p = 0.01$	$r^2 = 0.056$ $p < 0.001$	$r^2 = 0.041$ $p < 0.001$
Hb	$r^2 = 0.002$ $p = 0.46$	$r^2 = 0.467$ $p < 0.001$	$r^2 = 0.266$ $p < 0.001$	$r^2 = 0.210$ $p < 0.001$	$r^2 = 0.0396$ $p < 0.001$
COHb	$r^2 = 0.008$ $p = 0.11$	$r^2 = 0.003$ $p = 0.36$	$r^2 = 0.0011$ $p = 0.55$	$r^2 = 0.0054$ $p = 0.18$	$r^2 = 0.348$ $p < 0.001$
metHb	$r^2 = 0.005$ $p = 0.18$	$r^2 = 0.076$ $p < 0.001$	$r^2 = 0.054$ $p < 0.001$	$r^2 = 0.012$ $p = 0.04$	$r^2 = 0.177$ $p < 0.001$

Simple means of the nonexcluded Pa_{O_2}, Pa_{CO_2}, pH, Sa_{O_2}, Hb, COHb, and metHb values were calculated for each subject. The individual mean values were then used to calculate a population mean, standard deviation (SD), 95% confidence interval (95% CI) (calculated as 1.96 times standard error of the mean) and range for each of the blood gas analytes. Intrainstrument and interinstrument differences were calculated for all analytes for each subject and averaged. For each subject with a complete set of four measurements, the differences were calculated as: mean value from instrument no. 1 minus mean value from instrument no. 2. For each analyte, the larger of the two intrainstrument differences was reported for each laboratory.

The alveolar–arterial oxygen difference for P_{O_2} (AaP_{O_2}) was calculated using the following equation:

$$AaP_{O_2} = 0.2093 \times (P_B - 47) - Pa_{CO_2} \times [0.2093 + (1.0 - 0.2093/R)] - Pa_{O_2}$$

where P_B was measured atmospheric pressure in mm Hg, Pa_{O_2} and Pa_{CO_2} were the mean values obtained for each subject, and R was assumed to be 0.8.

A correlation matrix was created comparing blood gas analytes and calculated AaP_{O_2} to the independent variables age, sex, height, weight and barometric pressure. In addition, the squares and cubes of height and age and their cross-products and the square of barometric pressure were analyzed. Independent variables with significant corre-

TABLE 4

Pa_{O_2}, Sa_{O_2}, AND AaP_{O_2} BY ALTITUDE AND AGE GROUP

	Sea Level				1,400 Meters			
Age (*yr*)	n	Pa_{O_2} (*mm Hg*)	Sa_{O_2} (*%*)	AaP_{O_2} (*mm Hg*)	n	Pa_{O_2} (*mm Hg*)	Sa_{O_2} (*%*)	AaP_{O_2} (*mm Hg*)
18–24	17	99.9 (5.3)	96.9 (0.4)	2.0 (5.7)				
25–34	19	99.8 (4.9)	96.7 (0.7)	3.3 (4.3)	57	79.2 (4.1)	95.4 (0.6)	6.1 (4.2)
35–44	22	98.3 (7.6)	96.7 (0.6)	4.7 (7.5)	48	77.5 (4.4)	95.3 (0.7)	7.9 (5.1)
45–54	8	97.0 (8.0)	96.5 (1.0)	6.5 (6.4)	48	75.0 (5.1)	94.8 (0.8)	10.5 (5.0)
55–64	8	90.2 (4.5)	95.9 (0.7)	12.1 (3.7)	42	71.0 (5.7)	94.0 (1.2)	13.4 (5.7)
> 64	22	88.7 (10.7)	95.5 (1.4)	14.8 (8.8)	48	70.8 (4.9)	94.0 (1.0)	14.1 (4.9)

* Values are means with SD shown in parentheses.

TABLE 5*

Pa_{CO_2}, pH, Hb, MetHb, COHb BY ALTITUDE AND SEX

	Sea Level						1,400 Meters Altitude					
Sex	n	Pa_{CO_2} (*mm Hg*)	pH	Hb (*g/dl*)	metHb (*%*)	COHb (*%*)	n	Pa_{CO_2} (*mm Hg*)	pH	Hb (*g/dl*)	metHb (*%*)	COHb (*%*)
Male	44	38.1	7.42	14.0	0.50	1.69	122	33.9	7.43	14.7	0.34	0.95
		(3.3)	(0.023)	(1.0)	(0.18)	(0.46)		(2.2)	(0.020)	(1.0)	(0.13)	(0.43)
Female	52	36.8	7.43	12.3	0.60	1.58	121	32.8	7.44	12.7	0.43	0.86
		(2.9)	(0.019)	(0.9)	(0.24)	(0.60)		(3.0)	(0.020)	(1.0)	(0.12)	(0.36)

* Values are means with SD shown in parentheses.

lation coefficients ($p < 0.05$) were considered for further analysis. Backward stepwise linear regression was then performed to determine which combination of these independent variables significantly correlated ($p < 0.05$) with each blood gas analyte. A second linear regression analysis was performed to create "simple" equations by adding only the independent variables, identified from the original backwards stepwise regression, that increased r^2 by at least 0.03.

The two regression equations generated for each parameter were: (*1*) the most accurate, which consisted of all statistically significant independent variables, and (*2*) the simplest, which contained only independent variables that increased r^2 by at least 0.03.

Our sea level results for Pa_{O_2} were compared with the studies of Marshall and Millar (5) and Sorbini and coworkers (7). The study of Sorbini and coworkers was selected because it is a large study commonly used to predict reference values; the study of Marshall and Millar (5) was selected as a representative study of a group of studies reporting an age coefficient of about −0.25 mm Hg/yr (2, 4–6) because it had a relatively even age distribution of subjects. The sea level AaP_{O_2} results were compared with the study of Harris and coworkers (11) and the 1,400-meter altitude results were compared with the study of Begin and Renzetti (12). Predicted values using these studies were created for each of our subjects and averaged by decade of age. Mean values per decade of age that fell outside our measured 95% confidence interval were considered significantly different.

We also performed an analysis of residuals for three different sea level sites. We used the data from our two sea level sites (Los Angeles, CA, and Hartford, CT) and an independent set of data from the study of Cardús and colleagues (19) in Barcelona, Spain. Residuals were calculated as measured Pa_{O_2} minus predicted Pa_{O_2} using four different equations: (*1*) The present study equation, which included barometric pressure as an independent variable; (*2*) The present study equation using only sea level data; (*3*) the equation of Sorbini and coworkers (7); (*4*) the equation of Marshall and Millar (5).

RESULTS

Demographic information is summarized in Table 2. The study population consisted of 339 subjects (166 male, 173 female) divided fairly evenly by decade from ages 18 to 81. In one site (Los Angeles) four African Americans and one Asian were included. These subjects' data could not be distinguished from the rest of the data, and a literature search revealed no information concerning ethnic differences for blood gas measures. The data were included since there is no reason to expect ethnic differences in blood gas values and because the non-Caucasian values could not be distinguished from the Caucasian values. No other deviations from the protocol were noted. Two hundred forty-three subjects were residents of the Salt Lake City, UT area (altitude, 1,400 meters) and 96 resided near sea level (Los Angeles, CA or Hartford, CT). The number of subjects at sea level was less than desired and the distribution of subjects by age was uneven because of difficulties recruiting subjects who met entry criteria at both sites. The overall average oral temperature was 36.4 ± 0.5° C (range, 34.0 to 37.8° C).

The mean ± SD time between drawing a sample and analysis was 10.4 ± 9.4 min (range, 1 to 59 min; median, 8 min); 96% of the samples were analyzed in less than 30 min). Outlier criteria resulted in exclusions of less than 0.4% of all Pa_{O_2} ($n = 5$), pH ($n = 1$), Hb ($n = 4$), metHb ($n = 5$), and COHb ($n = 3$) values; 0.9% of all Pa_{CO_2} values ($n = 12$) and 1.8% of all Sa_{O_2} values ($n = 24$) from the data set.

Intercorrelations between independent and dependent variables are shown in Table 3. All blood gas analytes corre-

TABLE 6

INTRAINSTRUMENT AND INTERINSTRUMENT DIFFERENCES*

Site	Pa_{O_2} (*mm Hg*)	Pa_{CO_2} (*mm Hg*)	pH	Hemoglobin (*g/dl*)	O_2 Saturation (%)	COHb (%)	MetHb (%)
Intrainstrument differences							
Salt Lake City	0.03	0.13	0.003	0.07	0.09	0.11	0.02
	(1.11)	(1.08)	(0.005)	(0.35)	(0.26)	(0.29)	(0.12)
Los Angeles	0.44	0.16	0.003	0.11	0.18	0.28	0.05
	(2.14)	(1.0)	(0.009)	(0.29)	(0.42)	(0.24)	(0.31)
Hartford	1.85	0.12	0.001	0.08	0.06	0.03	0.02
	(2.43)	(0.86)	(0.005)	(0.44)	(0.62)	(0.42)	(0.35)
Interinstrument differences							
Salt Lake City	0.48	0.67	0.0089	0.55	0.20	1.42	0.04
	(1.18)	(1.31)	(0.0065)	(0.34)	(0.44)	(0.32)	(0.24)
Los Angeles	0.50	0.61	0.0047	0.04	0.53	0.58	0.11
	(3.05)	(2.13)	(0.0134)	(0.27)	(0.92)	(0.66)	(0.26)
Hartford	0.50	0.24	0.0021	0.05	0.17	0.19	0.01
	(1.44)	(1.13)	(0.0064)	(0.23)	(0.46)	(0.19)	(0.18)

* Larger of the two intradevice differences for each site. Values are means with SD shown in parentheses.

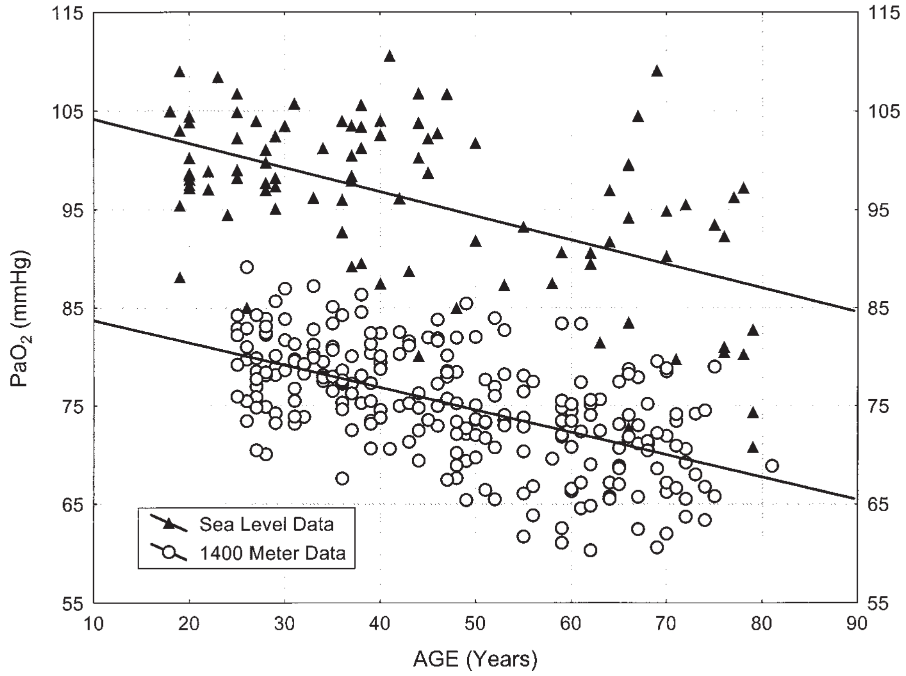

Figure 1. Pa_{O_2} as a function of age at sea level and at 1,400 meters altitude in Salt Lake City, UT. The slope for sea level data is −0.23 mm Hg/yr; at 1,400 meters it is −0.25 mm Hg/yr. The slopes are not statistically different ($p = 0.30$).

lated significantly with PB ($p < 0.001$). The analytes Pa_{O_2}, Sa_{O_2}, and AaPO_2 also correlated ($p < 0.01$) with age. For these variables, means and SDs are summarized in Table 4 by decade of age. Pa_{CO_2}, pH, Hb, and metHb correlated significantly ($p < 0.012$) with sex (Table 3). Their means and SDs by sex and altitude are listed in Table 5. COHb correlated significantly only with PB ($p < 0.001$), reflecting a small increase in COHb in the Los Angeles subjects. The overall mean sea level COHb was 1.63 ± 0.54% (95% CI, 1.51 to 1.75%). When the sea level sites were considered separately, mean COHb in Los Angeles was 1.87 ± 0.42% and mean COHb in Hartford was 1.00 ± 0.20% ($p < 0.01$, independent *t* test). At Salt Lake City, mean COHb was 0.91 ± 0.40% (95% CI, 0.86 to 0.96%). There was no difference in COHb levels between Hartford and Salt Lake City ($p = 0.24$, independent *t* test). Intrainstrument (within-instrument) and interinstrument (between-instrument) differences were small and are summarized in Table 6.

No cross products or squared or cubed terms explained more than 3% of the variance of Pa_{O_2}, leaving only linear terms in the reference equations. Pa_{O_2} correlated significantly only with age and PB. The declines in Pa_{O_2} with age were not different when separate equations were fitted for each altitude (Figure 1). The equations differed significantly only in their constant terms. Reference equations for each analyte, using combined data from both altitudes, are listed in Table 7. Because most of the world's population lives at or near sea level, some laboratories may prefer equations based only on sea-level data. Those equations are provided in Table 8.

Average measured Pa_{O_2} values were compared with values predicted by Marshall and Millar (5) and Sorbini and cowork-

TABLE 7

REGRESSION EQUATIONS FOR ARTERIAL BLOOD GAS MEASUREMENTS*

	r^2†	SEE‡	Constant	Age (*yr*)	Sex§	Height (*cm*)	Weight (*kg*)	PB (*mm Hg*)
Pa_{O_2}	0.77	5.539	−31.453	−0.2452				0.1834
Pa_{CO_2}	0.34	2.728	7.916		1.1620			0.0385
pH	0.12	0.019	7.522		−0.0063			−0.000127
AaPO_2								
Simple	0.37	5.364	11.799	0.2344				−0.0200
Best	0.44	5.058	33.365	0.1996		−0.2008	0.1906	−0.0190
Sa_{O_2}								
Simple	0.53	0.874	87.830	−0.0369				0.0135
Best	0.56	0.851	89.421	−0.0362			−0.0159	0.0128
Hb	0.49	0.989	15.68		1.8685			−0.0045
COHb	0.35	0.439	−3.37					0.0066
MetHb	0.24	0.158	−0.53		−0.0909			0.0015

* Values under age, sex, height, weight, and PB are regression coefficients.

† r^2 = coefficient of determination.

‡ Standard error of estimate. The lower limit of the reference range is calculated as: predicted value = 1.96 SEE.

§ Male = 1; female = 0. Therefore, the sex coefficient is zero for females.

TABLE 8

REGRESSION EQUATIONS FOR ARTERIAL BLOOD GAS MEASUREMENTS USING ONLY SEA LEVEL DATA*

	$r^{2\dagger}$	SEE‡	Constant	Age (*yr*)	Sex
Pa_{O_2}	0.30	7.301	106.603	−0.2447	
Pa_{CO_2}	0.41	3.059	36.837		1.256
AaP_{O_2}	0.38	6.478	−4.404	0.2610	
Sa_{O_2}	0.32	0.847	97.659	−0.0296	
Hb	0.45	0.952	12.32		1.717
MetHb	0.04	0.218	0.596		−0.0928

* No significant regressions were found for pH and COHb. Reference values are calculated using the mean and standard deviation of the measured values. Mean ± SD for pH = 7.423 ± 0.021. Mean ± SD for COHb = 1.627 ± 0.540, (n = 96: 54 women and 44 men).

† r^2 = coefficient of determination.

‡ SEE = standard error of estimate. The lower limit of the range is calculated as: predicted value = 1.96 SEE.

§ Male = 1, female = 0 (the sex coefficient is zero for females).

ers (7) at sea level and by Begin and Renzetti (12) at an altitude of 1,400 meters (Table 9). Statistically significant differences were found for several age groups for both the Sorbini and coworkers (7) and Begin and Renzetti (12) predicted values, but not for the Marshall and Millar predicted values. The equation of Sorbini and coworkers (7) underestimated measured Pa_{O_2} for sea level subjects older than 34 yr of age. At an altitude of 1,400 meters, the equations of Begin and Renzetti predicted a higher Pa_{O_2} for subjects 25 to 64 yr of age.

The AaP_{O_2} difference increased with age; the slopes of the increases with age for the two altitudes were not different. Sea level AaP_{O_2} predicted by Harris and colleagues (11) was significantly larger than our measured or predicted values (Table 10). At 1,400 meters, Begin and Renzetti (12) predicted higher AaP_{O_2} values only for subjects older than 64 yr of age.

Marshall and Millar (5) reported an average sea level Pa_{CO_2} of 37.2 mm Hg, similar to our mean value of 37.4 mm Hg (95% CI, 36.8 to 38.0). Sorbini and coworkers reported a significantly larger average Pa_{CO_2} of 39.1 mm Hg. At an altitude of 1,400 meters, the predicted average Pa_{CO_2} of Begin and Renzetti was 30.6 for both men and women, which was significantly lower than our data: average = 33.9 mm Hg (95% CI, 33.5 to 34.3) for men; 32.8 mm Hg (95% CI, 32.3 to 33.3) for women.

The analysis of residuals for Pa_{O_2} in the three sea level sites is presented in Table 11. In each instance, the distribution of residuals was reasonably homoscedastic. As expected for the Hartford and Los Angeles sites, both equations from our study resulted in smaller average residuals than the two outside equations. The equation that included barometric pressure resulted in slightly lower average residuals than the equation that did not contain barometric pressure. The standard deviations of the residuals were not different. In comparison with the outside equations, both of the present study equations resulted in smaller average residuals in the independent study from Barcelona, and the equation containing barometric pressure again outperformed the age only equation.

DISCUSSION

This is a cross-sectional blood gas reference value study using fully automated analyzers. The data from two different altitudes allows the generation of reference equations that include barometric pressure, thus allowing the prediction of blood gas values at intermediate altitudes. Our finding of a linear relationship between P_B and Pa_{O_2} reflects the fact that only two altitudes were studied. In addition, the pressure differences were only about 110 mm Hg. It is not likely that the relationship between Pa_{O_2} and P_B is linear over the full range of barometric pressures where humans live. The finding of a linear relationship between Pa_{O_2} and P_B for these altitudes is supported by an analysis showing a linear relationship when results from 15 studies were combined using an altitude-based weighting scheme to ensure that the final equations closely matched the data from each study (20).

In each of our sea level sites and an independent site, the equation containing P_B out performed the equation using only age as an independent variable. This is an expected finding when one adds an additional correlated variable to a prediction equation. In this case, the addition of P_B to the equation likely accounts for some of the variability in Pa_{O_2} resulting from small variations in P_B at a sea level altitude. We believe these Pa_{O_2} reference equations will likely be applicable at altitudes between sea level and 1,400 meters, but presently have no validation of their performance at the intermediate altitudes. Extrapolation of the regression equations to altitudes much greater than 1,400 meters (e.g., 1,600 meters) is not recommended unless further evidence confirms their accuracy at higher altitudes.

The decline in Pa_{O_2} with age in our study (−0.245 mm Hg/yr) is consistent with the studies of Raine and Bishop (2) (−0.24 mm Hg/yr), Conway and colleagues (4) (−0.22 mm Hg/yr), Marshall and Millar (5) (−0.25 mm Hg/yr), and Mellemgaard

TABLE 9

COMPARISON OF THIS STUDY'S MEASURED AND PREDICTED Pa_{O_2} VALUES WITH OTHER REFERENCE EQUATIONS

	Sea Level				1,400 Meters Altitude		
Age (*yr*)	Measured Pa_{O_2}	Predicted Pa_{O_2} (*1*)	Predicted Pa_{O_2} (*2*)	Predicted Pa_{O_2} (*3*)	Measured Pa_{O_2}	Predicted Pa_{O_2} (*1*)	Predicted Pa_{O_2} (*4*)
18–24	99.9	101.3	100.3	98.9			
25–34	99.8	99.7	96.9*	97.0*	79.2	79.3	85.0*
35–44	98.3	97.1	92.1*	94.1*	77.5	77.0	81.7*
45–54	97.0	94.7	88.4*	92.0	75.0	74.8	78.2*
55–64	90.2	91.7	82.8*	88.8	71.0	72.5	74.7*
> 64	88.7	89.1	78.0*	86.0	70.8	70.1	71.3

* Outside 95% confidence interval from the current data.

(*1*) Predicted Pa_{O_2} using our reference equation ($Pa_{O_2} = 0.1834\ P_B - 0.2452$ age $- 31.453$)

(*2*) Predicted Pa_{O_2} at sea level using Sorbini's (7) reference equation corrected to barometric pressure = 760 mm Hg ($Pa_{O_2} = 109 - 0.43$ age)

(*3*) Predicted Pa_{O_2} at sea level using Marshall's (5) reference equation ($Pa_{O_2} = 104.0 - 0.25$ age)

(*4*) Predicted Pa_{O_2} at 1,400 meters altitude using Begin's (12) reference equation ($Pa_{O_2} = 94.9 - 0.34$ age)

TABLE 10

COMPARISON OF THIS STUDY'S MEASURED AND PREDICTED AaP_{O_2} VALUES WITH COMMONLY USED REFERENCE EQUATIONS

	Sea Level			1,400 Meters		
Age (*yr*)	Measured AaP_{O_2}	Predicted AaP_{O_2} (*1*)	Predicted AaP_{O_2} (*2*)	Measured AaP_{O_2}	Predicted AaP_{O_2} (*1*)	Predicted AaP_{O_2} (*3*)
18–24	2.0	1.3	4.9*	—	—	—
25–34	3.3	3.6	7.0*	6.1	5.4	5.1
35–44	4.7	6.0	10.0*	7.9	8.2	7.8
45–54	6.5	8.5	12.2*	10.5	10.7	10.7
55–64	12.1	11.4	15.6*	13.4	13.1	13.6
> 64	14.8	13.2	18.6*	14.1	14.8	16.4*

* Outside 95% confidence interval from the current data.

(*1*) Predicted AaP_{O_2} using our reference equation ($AaP_{O_2} = 33.3652 + 0.1996$ age $-$ 0.2008 height $+ 0.1906$ weight $- 0.0190$ P_B).

(*2*) Predicted AaP_{O_2} using Harris' (11) reference equation ($AaP_{O_2} = 0.264$ age $- 0.43$).

(*3*) Predicted AaP_{O_2} using Begin's (12) linear reference equation ($AaP_{O_2} = 0.28$ age $- 3.06$).

(6) (−0.27 mm Hg/yr). In contrast, Sorbini and coworkers (7) found a decline with age of 0.43 mm Hg/yr. Our data compared closely to that of Marshall and Millar (5), the difference being a small bias in Pa_{O_2} that might be explained by interinstrument differences (14, 15). The comparison with the equation of Sorbini and coworkers (7) showed more striking differences explained primarily by the different age coefficients. We did not identify any specific study design or technical elements that would explain the age coefficient differences.

The subjects in the present study were paid volunteers. Ideally, reference value studies should identify study subjects from a random sample of a population. As in this study, volunteers are often used because of financial constraints. In pulmonary function studies, the method of patient selection has not influenced the results as long as hospitalized subjects are excluded (21).

Temperature correction of pH, Pa_{CO_2}, and Sa_{O_2} are not generally recommended (20), and correcting Pa_{O_2} for temperature is controversial (22). We chose not to temperature-correct our measured Pa_{O_2} values. Correcting our data to oral temperature could introduce both bias and noise. Oral temperature is known to underestimate core temperature by 0.2 to 0.5° C and is associated with increased variability because of local changes from eating and drinking (23). The average oral temperature of our subjects was 35.5° C, suggesting core temperature was indeed underestimated. Another important issue is reference value comparability. Valid reference comparisons can be made only when the reference value and the observed value are comparable in terms of biologic and analytical sources of variability (24). If temperature-corrected reference values are used, temperature should be measured in every patient at the time of a blood gas draw by methods comparable to the reference value study. Temperature is not routinely measured in settings where reference comparisons to healthy subjects are likely to be used. Even in hospital settings where temperatures are easily available, temperature correction of blood gases varies among hospitals and is not recommended by some investigators (22). In seriously ill patients, reference comparisons based on healthy subjects are of little utility. Blood gases are most often used in these instances to estimate potential for injury and determine when Pa_{O_2} has changed.

Approximately 0.2 ml of liquid sodium heparin (1,000 U/ml) anticoagulant occupied the syringe dead space volume. Because at least 4 ml of blood were obtained from each subject, this amount of heparin would not significantly affect our results (25).

Our subjects were studied in the sitting position, a commonly used position in clinical practice. Most studies that have addressed changes in Pa_{O_2} with posture have found no overall significant change between the supine and sitting positions, although individual subjects may have significant changes (26–28).

We assumed a respiratory exchange ratio (R) of 0.8 in calculating AaP_{O_2} because of cost constraints. Harris and colleagues (11) measured R and Begin and Renzetti (12) used an assumed R of 0.8 for their healthy subjects. In subjects with stable COPD, Begin and Renzetti found that assuming R to be 0.8 was acceptable for clinical purposes (mean AaP_{O_2} was 16.9 mm Hg with a measured R and 17.2 mm Hg with an assumed R). In a study of 70 consecutive outpatients, Cinel and colleagues (29) found the mean error in AaP_{O_2} (AaP_{O_2} with measured R minus AaP_{O_2} with assumed R of 0.8) was 0.93 mm Hg. Both studies suggest that the assumed R technique is, on average, clinically acceptable. Because an R of 0.8 is assumed in the calculation of AaP_{O_2} for most clinical blood gas analyses, reference values based on an assumed R are the proper reference choice.

The predicted AaP_{O_2} values of Harris and colleagues (11) were consistently higher than our measured sea level values (Table 10). This could, in part, relate to the fact that they included smokers without cough and used a measured R in the calculation. The Pa_{O_2} values of Begin and Renzetti (12) were significantly higher than ours, whereas their AaP_{O_2} values were

TABLE 11

COMPARISONS OF RESIDUALS FOR Pa_{O_2}*

	Study Site		
	Los Angeles, CA (*n = 70*)	Hartford, CT (*n = 26*)	Barcelona, Spain (*n = 64*)
Our combined equation containing barometric pressure	−0.74 ± 7.45	2.06 ± 6.09	1.1 ± 8.04
Our equation based only on sea level data	−0.97 ± 7.47	2.62 ± 6.08	2.89 ± 8.28
Sorbini equation (7)	4.51 ± 8.15	8.97 ± 7.17	7.41 ± 9.3
Marshall equation (8)	1.86 ± 7.47	5.47 ± 6.09	5.70 ± 8.30

* Values are mean residuals ± SD. Residuals = measured Pa_{O_2} − predicted Pa_{O_2}. Data in mm Hg.

Our combined equation: $Pa_{O_2} = 0.1834\ P_B - 0.2452$ age $- 31.453$.

Our sea level only equation: $Pa_{O_2} = 106.603 - 0.2447$ age.

Sorbini equation: $Pa_{O_2} = 109.0 - 0.43$ age.

Marshall equation: $Pa_{O_2} = 104.0 - 0.25$ age.

essentially the same. The higher Pa_{O_2} values may be partially explained by their lower average Pa_{CO_2} (30.6 versus 33.4 mm Hg), which would be associated with a higher alveolar P_{O_2}.

This study has some potential advantages over previous arterial blood gas reference values studies. (*1*) The healthy subjects were strictly defined. (*2*) Multiple automated analyzers were used. (*3*) CO-oximetry values were reported. (*4*) Sample collection was similar to that used in clinical practice. (*5*) Cross-altitude reference equations were generated, which appear to provide a small advantage, even at sea level. They also allow computation of reference values at intermediate altitudes. As always, the selection of reference values is a matter best determined by individual laboratories selecting reference values that best match the clientele they serve.

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