Idiopathic Scoliosis

GAS EXCHANGE AND THE AGE DEPENDENCE
OF ARTERIAL BLOOD GASES

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A B S T R A C T The aims were to examine the gas exchange and arterial blood gas abnormalities among patients with scoliosis, and the correlation of these abnormalities with age and severity of deformity.

Means among 51 patients were as follows: age 25.4 ± 17.5 yr, angle of scoliosis 80.2 ± 29.9 (SD), vital capacity 1.94 ± 0.91 (SD) (i.e. $60.6 \pm 19.2\%$ of predicted), Pa_{O_2} 85.8 ± 12.0 (SD), Pa_{CO_2} 42.4 ± 8.0, physiological dead space to tidal volume ratio 0.438 ± 0.074 (SD), and alveolar-arterial oxygen difference breathing air 14.9 ± 8.9 (SD).

Statistically significant correlations were as follows: the Pa_{CO_2} and physiological dead space to tidal volume ratio increased with age, and the Pa_{O_2} and alveolar ventilation decreased with age. The Pa_{O_2}, alveolar ventilation, and tidal volume were inversely related to the angle of scoliosis and directly related to the vital capacity, percent predicted vital capacity, and the compliance of the respiratory system. The physiological dead space to tidal volume ratio and the alveolar-arterial oxygen difference were inversely related to the vital capacity, percent predicted vital capacity, and the compliance of the respiratory system. Pa_{CO_2} was directly related to the elastance of the respiratory system.

We conclude that ventilation-blood flow maldistribution as a result of deformity of the rib cage was the primary abnormality in gas exchange, and that with age there was progressive deterioration in gas exchange. The age-dependent increase in Pa_{CO_2} and decrease in alveolar ventilation were due to the increasing physiological dead space to tidal volume ratio and failure of a compensatory increase in ventilation.

INTRODUCTION

Respiratory function abnormalities are common in idiopathic scoliosis and may lead to respiratory failure (1–5). Blood gas abnormalities in scoliosis have been attributed to alveolar hypoventilation as a result of a ventilatory pattern of small tidal volumes (V_T)[1] and a high respiratory frequency (3–5). However, the most common blood gas abnormality is a reduced arterial oxygen tension (Pa_{O_2}) with a normal arterial carbon dioxide tension (Pa_{CO_2}) (1–10). The reduced Pa_{O_2} and elevated alveolar-arterial oxygen differences $(Aa_{D_{O_2}})$, and dead space (V_D)-tidal volume ratios (V_D/V_T) are indicative of ventilation/blood flow maldistribution (1–3, 6–10). Interpretation of previous data on gas exchange and arterial blood gases in scoliosis is difficult because some of the studies have included patients with scoliosis due to different etiologies or coexistent chronic pulmonary disease, some have too few patients for statistical analyses, and in some the severity of scoliosis has not been documented.

The objectives of the present investigation were to measure the steady-state gas exchange and arterial blood gases in large number of patients with idiopathic scoliosis, ranging widely in age and severity of scoliosis, and free of coexistent pulmonary disease; to utilize statistical techniques in the examination of the factors associated with blood gas and gas exchange abnormalities; and to examine the relative contribution of ventilation-blood

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[1] *Abbreviation used in this paper:* $Aa_{D_{O_2}}$, alveolar-arterial oxygen differences; Crs, compliance of the respiratory system; Pa_{CO_2}, arterial carbon dioxide tension; Pa_{O_2}, arterial oxygen tension; $\dot{V}_A/\dot{Q}$, ventilation/perfusion ratio; VC, vital capacity; V_D, dead space; $V_{D_{anat}}$, anatomical dead space; V_T, tidal volume.

flow maldistribution and hypoventilation in the genesis and progression of blood gas abnormalities. This study was combined with an examination of lung volumes, mechanical properties of the respiratory system, ventilatory response to CO_2 (which demonstrated associations between angle of scoliosis and lung volumes), and the elastic properties of the respiratory system, and between these variables and the slope and pattern of the ventilatory response to CO_2. There was also evidence of an age-dependent decrease in the slope of the ventilatory response to CO_2 (11).

To circumvent the inadequacy of the angle of scoliosis as an esimate of the deformity of the rib cage, for which there is no quantitative estimate, the data on the lung volumes and the elastic properties of the respiratory system were used as indices of the severity of the deformity. In the analyses of the data, attention was directed to the association of gas exchange and blood gas abnormalities with age, angle of scoliosis, lung volumes, and the elastic properties of the respiratory system.

METHODS

Patients. Studies were performed on 51 patients with idiopathic scoliosis (14 male, 37 female) (Table I). The methods and results of measurement of lung volumes, mechanical properties of the respiratory system, and the ventilatory response to CO_2 have been reported in an earlier paper (11), as has the method of measurement of the angle of scoliosis. The patients were in their usual state of health, and they were asymptomatic except for dyspnea in some patients. Patients with coexistent obstructive pulmonary disease were excluded from the series. No patient had received any corrective procedure for scoliosis, and they were life-long residents of Sydney or rural New South Wales. All were nonsmokers. The electrocardiograms were normal in all except two patients and the abnormalities were, respectively, right ventricular hypertrophy (patient 50) and poor progression of the R wave in the precordial leads (patient 51).

Steady-state gas exchange studies. Studies were performed with the patients sitting. The patient breathed air from a Tissot gasometer via a one-way respiratory valve; expired gas was collected for two periods of 2–3 min, and arterial blood was withdrawn during each collection. The apparatus dead space of the valve and mouthpiece was 30 ml. The patient then breathed 100% oxygen from the gasometer for 12 min, and during the last 2 min the expired gas and arterial blood were collected. The data from the second of the two periods breathing air and from the oxygen-breathing period are reported. The expired gas was analyzed for carbon dioxide and oxygen concentration with a respiratory mass spectrometer (MS4 Associated Electrical Industries Ltd., London, U. K.); or CO_2 was measured by an infrared CO_2 analyzer (Godart Capnograph, De Bilt, Holland), and oxygen concentration was measured by a paramagnetic oxygen analyzer (Servomex oxygen analyzer DCL 101 Mark II, Crowborough, U. K.).

The carbon dioxide tension in the arterial blood was measured with a carbon dioxide electrode (Instrumentation Laboratory, Inc., Lexington, Mass.) and oxygen tension with a polarographic electrode. Both electrodes were cali-

brated with three standard gas mixtures saturated with water vapor at 37°C, and Pao$_2$ was corrected for the difference between gas and tonometered blood (blood gas factor). The coefficients of variation of measurement of Paco$_2$ and Pao$_2$ were 1.4% and 1.0%, respectively. The pH was measured with an Electronics Instrumentation Laboratory microcapillary electrode (London, U. K.) and an EIL Vibron pH meter. Conventional methods were used for the calculation of Vd/Vt, and AaDo$_2$ during air-breathing, and oxygen-breathing.

Analyses of data. To evaluate the effects of scoliosis independently of development during childhood and adolescence, the data for patients 18 yr or older were examined, and to examine the effects of severe scoliosis, the data on patients with an angle of 80° or more were also examined.

RESULTS

Physical characteristics. The age, angle of scoliosis, and body weight are in Table I. The mean vital capacity (VC), was 1.94 liters±0.91 (SD), the mean percent predicted vital capacity was 60.6±19.2 (SD), and the mean compliance of the respiratory system (C$_{rs}$) was 48 ml/cm H_2O±25 (SD). Significant correlations were found between the angle and the VC ($r = -0.485$, $P < 0.001$), percent predicted VC ($r = -0.523$, $P < 0.001$), and C$_{rs}$ ($r = -0.625$, $P < 0.001$).

Gas exchange and arterial blood gases. The mean values for gas exchange and arterial blood gases for the total and for the subgroups are similar. In the total group (Fig. 1a) and both subgroups of patients, the Pao$_2$ was inversely related to the age. In that subgroup where the angle was 80° or more, the correlation coefficient was -0.507 ($P = 0.001 - 0.01$) and in that subgroup where the age was 18 yr or older, the correlation coefficient was -0.715 ($P < 0.001$). All three intercepts were below 100 mm Hg, and the rate of decline was 3.1–4.5 mm Hg/decade. In the total group, the Pao$_2$ was also inversely related to the angle (Fig. 1b), and directly related to the VC ($r = 0.562$, $P < 0.001$), the percent predicted VC ($r = 0.539$, $P < 0.001$), and the C$_{rs}$ ($r = 0.450$, $P = 0.001$). The correlation coefficients for both subgroups were similar to those for the total group.

The Paco$_2$ was directly related to the age; for the total group the increase per decade was 3.23 mm Hg (Fig. 2a). There were also statistically significant correlation coefficients between the Paco$_2$ and the elastance of the respiratory system for the total group (Fig. 2b) and for both subgroups, i.e. for those with an angle of 80° or more, $r = 0.497$ ($P = 0.001–0.01$), and for those 18 yr or older, $r = 0.562$ ($P = 0.01$). The Paco$_2$ was also inversely related to the VC ($r = -0.467$, $P = 0.01–0.05$), percent predicted VC ($r = -0.507$, $P = 0.001–0.01$) and to the Crs ($r = -0.426$, $P = 0.01–0.05$) for the patients 18 yr or older.

The incidence of elevated Vd/Vt ratios and AaDo$_2$ were high, and to estimate the incidence and severity of

TABLE I

Gas Exchange, Arterial Blood Gases, V_D/V_T Ratios, and Alveolar-Arterial Oxygen Difference while Breathing Air, and Alveolar-Arterial Oxygen Difference while Breathing 100% Oxygen

Patient number	Age	Angle of scoliosis	Weight	V̇E	VT	V̇O₂	RQ	PaO₂	PaCO₂	VD/VT ratio	AaDO₂	V̇A	AaDO₂ 100% oxygen
	yr	°	kg	liter/min BTPS	ml BTPS	ml/min STPD		mm Hg	mm Hg		mm Hg	liter/min BTPS	
1	9	120	18	4.40	281	141	0.91	94	37	0.317	15	3.01	70
2	10	110	35	4.33	352	129	0.89	66	40	0.421	19	2.51	23
3	11	85	47	6.41	352	182	0.87	75	40	0.464	30	3.43	30
4	11	38	53	6.81	426	230	0.87	92	40	0.362	14	4.34	13
5	12	54	47	5.26	437	187	0.83	95	43	0.403	4	3.14	85
6	13	35	66	6.92	350	227	0.87	85	46	0.462	14	3.73	33
7	13	82	49	7.88	360	207	0.94	93	39	0.449	16	4.34	
8	13	35	45	6.47	315	198	0.87	103	37	0.373	7	4.06	8
9	13	45	49	6.61	382	190	0.98	86	40	0.377	25	4.12	47
10	14	45	45	7.00	369	265	0.77	98	42	0.384	2	4.35	12
11	14	60	32	5.15	207	146	0.93	98	39	0.410	11	3.04	9
12	14	93	37	7.67	387	221	0.97	102	39	0.378	8	4.77	34
13	14	50	51	6.29	411	206	0.80	100	35	0.352	8	4.08	
14	14	65	55	7.29	552	231	0.85	105	38	0.301	0	4.51	22
15	14	110	38	6.21	280	187	0.79	79	37	0.411	28	3.65	132
16	14	88	32				—	84	39				48
17	15	80	48	6.05	414	211	0.89	97	43	0.377	6	3.77	9
18	15	52	36	5.38	261	157	0.86	90	39	0.438	16	3.02	59
19	15	48	50	7.57	352	184	0.91	102	38	0.486	7	3.89	22
20	15	55	51	5.31	322	104	0.93	91	30	0.477	25	2.78	55
21	15	130	29	5.81	292	192	0.78	88	35	0.394	19	3.52	92
22	16	70	52	6.86	333	280	0.82	63	41	0.450	13	3.77	32
23	16	35	57	6.23	485	209	0.88	95	44	0.412	7	3.66	1
24	16	100	37	6.74	222	144	0.93	76	41	0.576	33	2.86	149
25	17	45	48	5.10	433	145	0.95	98	33	0.274	6	3.41	
26	17	95	39	6.58	325	165	0.95	78	37	0.442	33	3.67	169
27	18	56	52	5.95	345	147	0.94	91	39	0.444	17	3.31	19
28	19	90	38	5.40	325	148	0.92	89	43	0.491	17	2.75	19
29	19	90	61	8.56	399	279	0.86	97	45	0.537	0	3.96	129
30	20	70	61	6.15	442	209	0.81	95	41	0.416	6	3.59	0
31	20	130	42	5.49	268	193	0.84	73	46	0.441	24	3.07	89
32	22	98	46	6.42	526	215	0.86	89	39	0.368	15	4.06	48
33	23	98	44	8.46	601	225	0.88	87	34	0.404	23	5.04	60
34	23	100	49	6.21	320	228	0.75	75	45	0.470	20	3.29	92
35	23	90	61	7.67	355	225	0.81	91	40	0.435	12	4.00	
36	25	90	45	6.26	344	176	0.80	83	38	0.482	20	3.24	79
37	25	95	25	5.57	230	140	0.76	89	33	0.496	19	2.81	90
38	26	68	57	5.98	871	238	0.79	94	39	0.289	6	4.25	79
39	28	80	57	7.22	363	197	0.85	91	40	0.492	12	3.67	16
40	29	85	41	6.55	339	169	0.87	91	40	0.517	14	3.16	69
41	36	125	53	6.33	358	211	0.75	88	45	0.514	5	3.08	42
42	42	150	39	3.81	246	173	0.76	79	56	0.467	1	2.03	21
43	44	45	38	5.97	412	214	0.93	74	44	0.459	28	3.23	156
44	52	92	36	4.00	219	157	0.72	73	53	0.538	9	1.85	47
45	56	110	50	4.94	286	168	0.82	66	50	0.518	26	2.38	160
46	57	75	58	7.70	295	221	0.93	53	78	0.431	15	4.38	289
47	58	120	64	7.11	281	243	0.84	61	53	0.548	29	3.22	212
48	61	110	43				—	72	62				
49	65	40	55	6.63	289	195	0.85	78	52	0.593	13	2.78	78
50	70	120	46	6.33	198	190	0.70		48	0.365		2.44	125
51	72	40	54	10.61	455	278	0.91	77	49	0.576	19	4.50	59
Mean	25.4	80.2	46.3	6.36	360	196	0.857	85.8	42.4	0.434	14.9	3.50	68.1
SD	17.5	29.9	10.2	1.22	114	40	0.068	12.0	8.0	0.074	8.9	0.71	60.7

the ventilation-blood flow maldistribution, these data were compared with normal data. With the data of Hart et al. (12), the anatomical dead space (V_{Danat}) for each patient was predicted from the body weight, and V_{Danat}/V_T ratio estimated from the tidal volumes at which the V_D/V_T ratios were measured (Fig. 3). The figure illustrates a high incidence of V_D/V_T ratios substantially greater than the predicted V_{Danat}/V_T. The mean measured V_D/V_T was 0.438 ± 0.074 (SD) and the mean predicted V_{Danat}/V_T was 0.332 ± 0.079 (SD) (statistical significance of difference ($P < 0.001$). The AaDO₂'s are compared with the data of Raine and Bishop (13) (Fig.
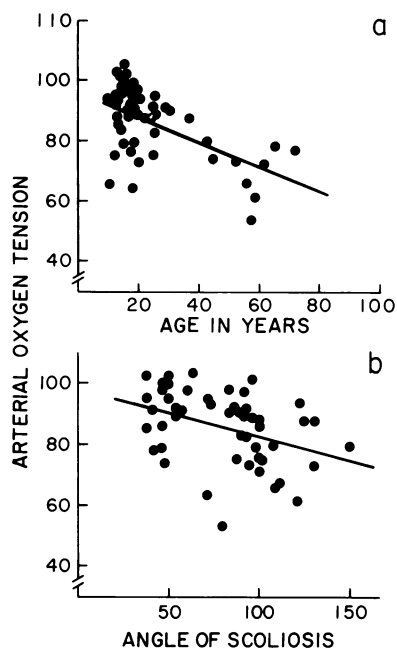
FIGURE 1 a. The relationship between age and the Pa_{O_2} while breathing air: the regression equation was $Pa_{O_2} = 95.8 - 0.394$ yr, SE slope±0.094, and $r = -0.574$ ($P < 0.001$). b. The relationship between the angle and the Pa_{O_2} while breathing air: the regression equation was $Pa_{O_2} = 98.0 - 0.152$ angle, SE slope 0.062, and $r = -0.377$ ($P = 0.01 - 0.05$).

4): the data in the patients with scoliosis reveal a high level of AaD_{O_2}, greater than that predicted by Raine and Bishop for the patient's age but in the patients with scoliosis there was no significant increase in this gradient with age. The AaD_{O_2} was also inversely related to the VC (Fig. 5), percent predicted VC ($r = -0.339$, $P = 0.01 - 0.05$), and to the Crs ($r = -0.463$, $P < 0.01$).

The V_D/V_T was directly related to the age, and the correlation coefficient for the total group was 0.473 ($P < 0.01$) (Fig. 6a). Although the correlation coefficients between angle and V_D/V_T were not significant, the correlation coefficients between V_D/V_T and the VC (Fig. 6b), and the Crs were significant ($r = -0.318$, $P = 0.01 - 0.05$).

The alveolar ventilation was inversely related to the age, and the angle of scoliosis (Fig. 7a and b), and directly related to the VC ($r = 0.544$, $P < 0.001$), percent predicted VC ($r = 0.475$, $P < 0.01$) and Crs ($r = 0.453$, $P < 0.01$). These relationships were significant for the total group, as shown above, and both subgroups.

Oxygen consumption was directly related to the body weight ($r = 0.581$), and height ($r = 0.593$), and was also directly related to the VC, percent predicted VC, and Crs. The correlation coefficients between oxygen consumption and age and angle were not significant.

For each patient the oxygen consumption was normal for body size.

Relationships between age, angle, mechanical properties of the respiratory system, and the pattern of ventilation. These analyses were undertaken to test the hypothesis that the mechanical properties or age in scoliosis contribute to the pattern of ventilation, and by this mechanism contribute to the gas exchange abnormalities.

The minute ventilation was directly related to body weight, height, lung volumes, and the Crs. For the patients 18 yr or older, and for the patients with an angle of scoliosis 80° or more, the minute ventilation was inversely related to the angle of scoliosis ($r = -0.423$ and -0.480, respectively). The correlation coefficients between age and minute ventilation were not significant. The relationships between tidal volume and body size, lung volumes, and the elastic properties of the respiratory system were similar to those of minute ventilation. For the total group, and for the patients with angle of scoliosis 80° or more the tidal volume was inversely proportional to the angle ($r = -0.312$ and $r = -0.389$, respectively). Therefore, in severe scoliosis there is a consistent inverse relationship between the angle and
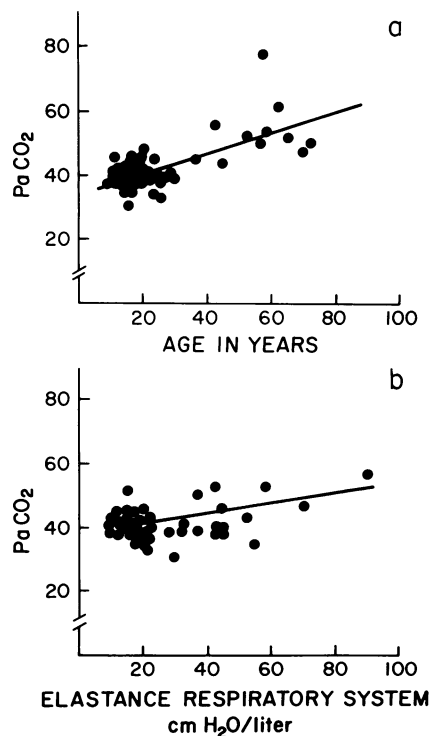

FIGURE 2 a. The relationship between age and the Pa_{CO_2} while breathing air: the regression equation was $Pa_{CO_2} = 34.2 + 0.323$ yr, SE slope±0.052 and $r = 0.710$ ($P < 0.001$). b. The relationship between elastance of the respiratory system and the $Pa_{CO_2} = 37.7 + 0.166$ elastance, SE slope 0.068, and $r = 0.379$ ($P = 0.001 - 0.01$).
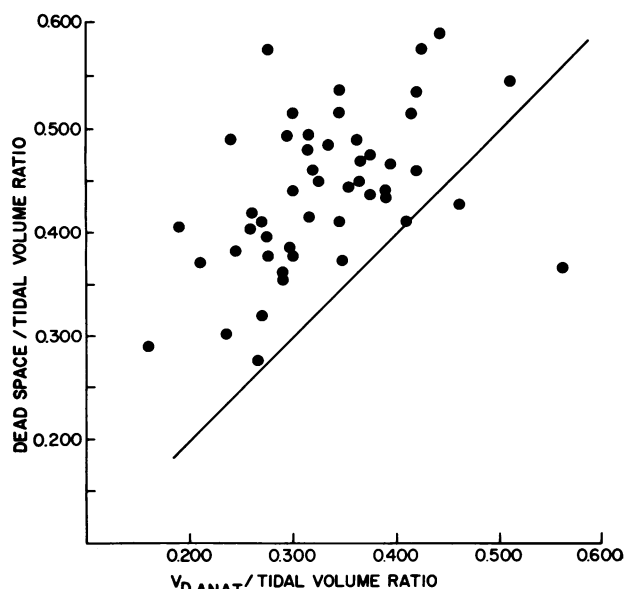
FIGURE 3 The relationship between the measured V_D/V_T (V_D physiological/V_T) and the predicted V_{Danat}/V_T. The V_{Danat} was predicted from the body weight of each patient from the regression equation $V_{Danat} = 1.835$ weight (in kilograms) $+ 26.6$; $r = 0.829$ (12). The V_T was the tidal volume under the conditions of measurement of V_D/V_T. Continuous line is the line of identity.

both the minute ventilation and the tidal volume. The correlation coefficient between age and tidal volume was also statistically significant for patients with angle of scoliosis 80° or more ($r = -0.374$). The correlation coefficients between respiratory frequency and age, angle, and mechanical properties of the respiratory system were also significant. For the total group, and both subgroups, there was a direct relationship between age and the respiratory frequency: total group, $r = 0.411$; angle 80° or more, $r = 0.419$, and patients 18 yr or over $r = 0.580$. For all patients the respiratory frequency was also inversely proportional to the VC ($r = -0.393$), percent predicted VC ($r = -0.449$), and the Crs ($r = -0.463$); however, these relationships were not consistently significant for the two subgroups.

Relationships between the pattern of ventilation and the arterial blood gases and gas exchange variables. Statistically significant relationships were also demonstrable between the pattern of ventilation and the arterial blood gases and indices of ventilation/blood flow. The correlation coefficients between tidal volume and the following variables for the total group were: Pao_2, $r = 0.343$ ($P = 0.001-0.01$); $Paco_2$, $r = -0.232$ ($P > 0.05$); V_D/V_T, $r = -0.458$ ($P < 0.001$); $AaDo_2$, $r = -0.303$ ($P = 0.01-0.05$), and alveolar ventilation, $r = 0.606$ ($P < 0.01$). In general the relationships between tidal volume and the gas exchange variables were similar for each of the subgroups. The correlation coefficients between
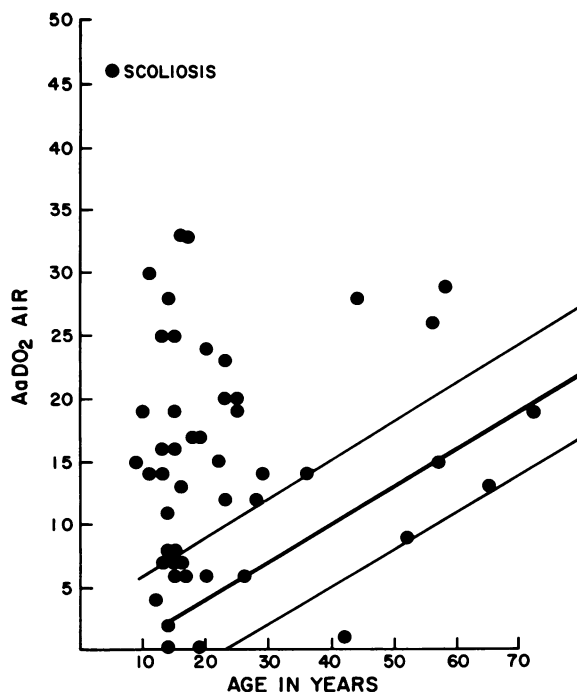

FIGURE 4 The relationship between the measured $AaDo_2$ (air) and the $AaDo_2$ (air) predicted from age on the basis of the regression equation of Raine and Bishop (13): $AaDo_2$ (air) $= 0.36$ yr $- 4.3$, SD of estimate±5.6 mm Hg.

respiratory frequency, and the following variables for the total group were : Pao_2, $r = -0.365$ ($P = 0.001-0.01$); $Paco_2$, $r = 0.326$ ($P = 0.01-0.05$); V_D/V_T, $r = 0.519$ ($P < 0.001$); $AaDo_2$, $r - 0.381$ ($P = 0.001-0.01$), and alveolar ventilation, $r = -0.175$ ($P < 0.05$). Although these relationships were similar for the patients
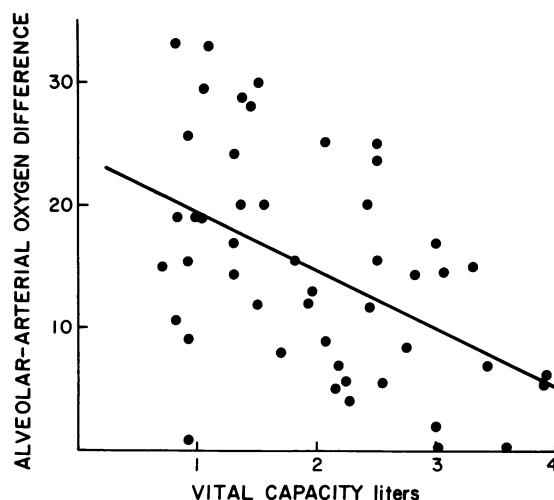

FIGURE 5 The relationship between the VC and the $AaDo_2$ breathing air: the regression equation was $AaDo_2 = 24.2 - 4.78$ vital capacity, SE slope 1.429, and $r = -0.487$ ($P < 0.001$).
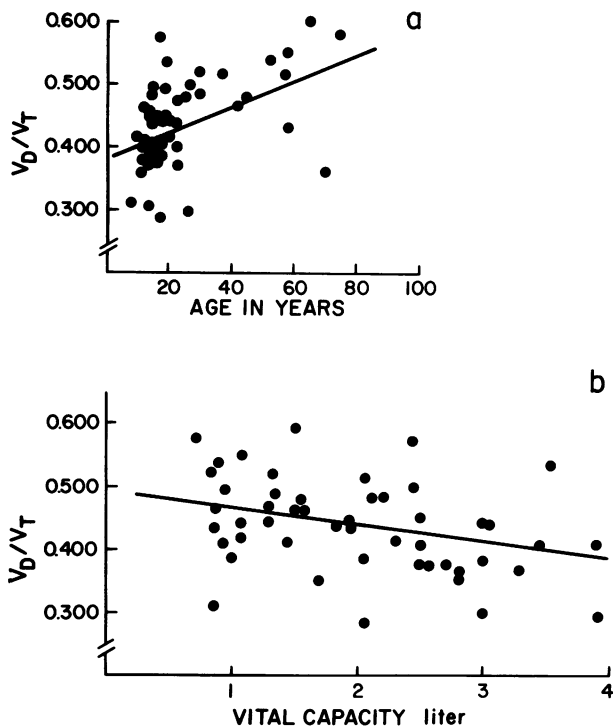
show a greater rate of decrease in Pao₂ with age, this was not evidenced by comparisons between or within these series. In contrast to normal man, in whom there is no variation in Paco₂ with age (13, 14, 16–18), in scoliosis the Paco₂ increased with age. Therefore, throughout the evolution of the respiratory function abnormalities in scoliosis, there is a progressive decrease in Pao₂, and an increase in Paco₂. Since the AaDo₂ breathing air does not increase with age, the decrement in Pao₂ with age seems best explained by the progressive fall in alveolar ventilation and consequent hypercapnia.

Ventilation-blood flow maldistribution and impaired ventilatory compensation. Three major mechanisms contribute to blood gas abnormalities while breathing air: hypoventilation, ventilation-blood flow maldistribution, and impairment to diffusion (19). In examining the mechanism of blood gas abnormalities in scoliosis, a distinction must be made between alveolar hypoventilation due to reduction in ventilation and that due to ventilation-blood flow maldistribution. Ventilation-blood flow maldistribution not only impairs the exchange of oxygen but also of carbon dioxide, and hypercapnia occurs in the absence of a compensatory increase in ventilation (20, 21). It also follows that normocapnia in the
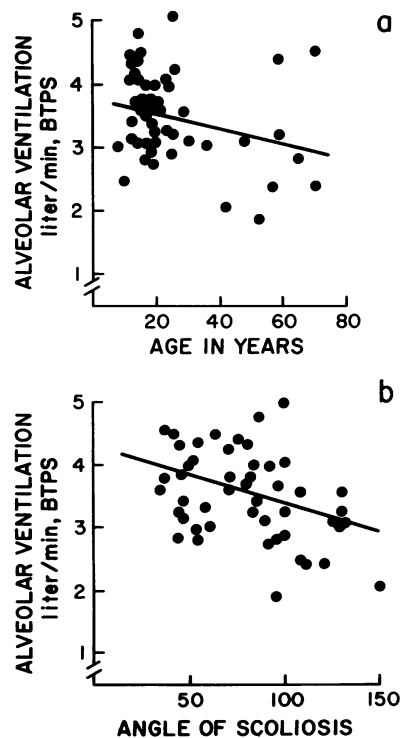
Figure 6 *a.* The relationship between the age and the V_D/V_T while breathing air: the regression equation was $V_D/V_T = 0.387 + 0.002$ yr, SE slope±0.0006 and $r = 0.473$ ($P < 0.001$). *b.* The relationship between the vital capacity and the V_D/V_T: regression $= 0.495 - 0.029$ VC, SE slope 0.013, and $r = -0.361$ ($P < 0.001$).

18 yr or over, only the correlation coefficient between respiratory frequency and AaDo₂ was significant for patients with angle 80° or more.

PaO₂ and AaDO₂ breathing 100% oxygen. The mean Pao₂ breathing 100% oxygen was 607±70 (SD) mm Hg, and the mean AaDo₂ was 64±61 (SD) mm Hg. The AaDo₂ (oxygen) was directly related to age, $r = -0.480$ ($P < 0.01$), and the regression equation was AaDo₂ (oxygen)$= 25.6 + 1.676$ yr.

DISCUSSION

Age-dependent changes in arterial blood gases. In normal man throughout life there is an age-dependent decrease in the Pao₂; and although the populations and the criteria for normality varied between studies, the relationships between the age and the Pao₂ were consistent (13–17). However, in the patients with scoliosis both the intercept on the ordinate was lower, and the rate of decrease of Pao₂ with age (ΔPao₂/Δ yr) was greater than in the normal subjects, except for the rate of decrement with age the study of Sorbini et al. (17). The reason for the differences between Sorbini and associates' study and the others is unknown. Although it might be reasoned that an industrial urban population (13), smokers, and supine subjects (13, 14, 17) would

Figure 7 *a.* The relationship between the age and alveolar ventilation: regression equation was $V_A = 3.797 - 0.012$ yr, SE slope 0.0065, and $r = -0.289$ ($P = 0.01 - 0.05$). *b.* The relationship between the angle and the alveolar ventilation: regression equation was $V_A = 4.248 - 0.009$ angle, SE slope 0.004, and $r = -0.391$ ($P = 0.001 - 0.01$).

presence of ventilation-blood flow maldistribution is evidence of a compensatory increase in ventilation.

In scoliosis, as evidenced by the elevated V_D/V_T ratios and AaD_{O_2}, ventilation-blood flow maldistribution is a mechanism of the blood gas abnormalities. Furthermore, the association of normocapnia and ventilation-blood flow maldistribution in the early decades of evolution of the functional changes confirms the presence of a compensatory increase in ventilation. Hence it is argued that the primary mechanism of blood gas abnormalities in scoliosis is ventilation-blood flow maldistribution. However, with increasing age several processes occur. First, as in normal man, the V_D/V_T increases, but in contrast to the normal data, in scoliosis both the intercept and the rate of increase per year are greater (13, 16). The rate of increase in V_D/V_T ratio per year in the sitting position in Raine and Bishop's study was 0.001, and this slope is not significantly different from zero (SD of estimate 0.062) (13). The rate of increase per year in Mellemgaard's study (16) did approach that of the patients with scoliosis and was 0.0017/yr. Second, the alveolar ventilation decreases and the Pa_{CO_2} increases with age. The simplest explanation of these events is a progressive deterioration of ventilation-blood flow maldistribution, as evidenced by the increasing V_D/V_T, and failure of a compensatory increase in ventilation to maintain normocapnia.

The data presented in an earlier paper on the mechanical properties of the respiratory system and the ventilatory response to CO_2 show that several factors may contribute to an impaired chemical regulation of ventilation and hence, by inference, impair compensation for ventilation-blood flow maldistribution (11). The slope of both the tidal volume and the minute ventilation response to CO_2 were directly proportional to the VC, and the C_{rs}. It may be argued, therefore, that severe deformity prevents the compensatory increase in ventilation by mechanically impeding ventilation. Several age-related changes may also contribute to the failure of a compensatory increase in ventilation. First, as has been shown in normals, there is an age-dependent decrease in the slope of the ventilatory response to CO_2 (11, 22). Second, the compensatory increase in ventilation may have been overwhelmed by the magnitude of increase in V_D/V_T.

In several of the older patients, the AaD_{O_2} breathing oxygen was greater than 200 mm Hg, and in these patients pulmonary arteriovenous shunt may have contributed to the AaD_{O_2} while breathing air. However this interpretation is questionable on the basis of the studies by Wagner and associates (23, 24) who, using multiple inert gas elimination techniques to measure continuous $\dot{V}_A/\dot{Q}$ distribution, demonstrated the development of shunt in awake subjects spontaneously breathing 100% oxy-gen. These changes were most frequent in the older subjects. In a theoretical paper (24), they provided evidence that the shunt on 100% O_2 would develop in lung units with critically low ventilation-perfusion ratios. The possibilities are, therefore: with increasing age, the contribution of pulmonary arteriovenous shunt to the AaD_{O_2} breathing air increases; and/or areas with critically low $\dot{V}_A/\dot{Q}$ ratios increase with age and are evidenced as large AaD_{O_2} while breathing oxygen.

Mechanism of elevated V_D/V_T and ventilation-blood flow maldistribution. The conventional concept of the mechanism of elevated V_D/V_T ratios and the ensuing alveolar hypoventilation in scoliosis was that these were due to the abnormal ventilatory pattern of small tidal volumes with a high respiratory frequency (3–5). The respiratory frequency was directly related and the tidal volume inversely related to the V_D/V_T, which would support the conventional concept; however, these associations do not necessarily provide evidence of cause-and-effect relationships. Physiological dead space consistently exceeded the predicted anatomical dead space; suggesting a significant component of mismatching between blood flow and ventilation in patients with scoliosis. Therefore it may be argued that the physiological dead space/tidal volume ratio is elevated as a result of ventilation/blood flow maldistribution due to the deformity of the rib cage, and that the pattern of ventilation (abnormally high respiratory frequency and small tidal volumes) may further contribute to the elevated V_D/V_T ratios.

It may be postulated that the ventilation-blood flow maldistribution is the result of several mechanisms. First, histologic studies of the lungs in scoliosis have shown a nonuniform distribution of alveolar volume with areas of compression, and a nonuniform distribution of vessels with areas of decreased vascularity (25–26). Second, in scoliosis the relative contribution of the diaphragm to the tidal volume is greater than normal (27), and this decreased contribution of the rib cage to inflation may contribute to an abnormal distribution of ventilation. Regional studies on the distribution of ventilation and blood flow have shown an abnormal distribution of ventilation and blood flow in scoliosis; however, there are no data on quantitative relationships between these abnormalities and indices of ventilation-blood flow maldistribution of blood gases (28–31). Although our study has demonstrated statistically significant quantitative relationships between the indices of ventilation-blood flow maldistribution and the lung volumes and the mechanical properties of the respiratory system, other techniques are required to demonstrate the mechanism of ventilation-blood flow maldistribution in scoliosis.

Pattern of ventilation. The data have shown that the respiratory frequency is inversely related to the C_{rs} and

the VC, and the tidal volume is directly related to the C_{rs} and the VC. These associations are consistent with the hypotheses of optimal respiratory frequency to minimize inspiratory work or force (32, 33); however, the absence of data on the total resistance of the respiratory system and the limitations of the sine wave model of breathing precluded a rigorous examination of these hypotheses.

In conclusion, this study has demonstrated that in scoliosis two primary variables, age and the degree of chest wall deformity, contribute to the abnormalities in gas exchange and arterial blood gases. Ventilation-blood flow maldistribution, directly related to the deformity of the rib cage, is the major source of impaired gas exchange in young patients with scoliosis; aging causes further deterioration in ventilation-blood flow maldistribution, and finally failure of the expected response to a rising physiological dead space ultimately leads to hypercapnia. Age-dependent changes in the pattern of the ventilation (i.e. a rising frequency and falling tidal volume) and the age-dependent decreases in the slope of the ventilatory response to CO_2 both may contribute to the ultimate CO_2 retention. This is the first demonstration in scoliosis of statistically significant relationships between the deformity, as expressed by the angle or as lung volumes, the elastic properties of the respiratory system, age, and the arterial blood gases and gas exchange variables.

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