ARTERIAL BLOOD GASES AND ACID-BASE BALANCE IN CYANOTIC CONGENITAL HEART DISEASE [1]

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The purpose of this report is to present data concerning the arterial blood gases and the acid-base balance in patients with cyanosis due to congenital heart disease. Since the study is related to cyanosis and abnormalities of the blood consequent to this, no distinction is made between the various anatomical defects producing cyanosis.

Compensatory or adaptive mechanisms in the presence of cyanosis related to congenital heart disease have been the subject of a number of studies (1–6). The present study was undertaken to obtain further information concerning the arterial blood gases in this disease, especially in relation to age and in respect to the influence of arterial unsaturation on the acid-base balance.

Sixty cyanotic patients were studied, varying in age from 1 to 36 years. The methods used have been described in a preceding report (7).

RESULTS

Because age has been found to affect the concentrations of the blood gases (7), especially the HbO_2 capacity, the CO_2 content and the alkaline reserve, it was necessary to evaluate the results for an individual of a given age in terms of deviations from the mean values for that age. Normal values for children of different ages are given in the preceding report (7). Table I gives the results of single tests on each of 60 patients with cyanotic congenital heart disease, in terms both of absolute values and of deviations from the normal. In Figures 1 and 2 deviations from the normal are plotted for each age group against a background which represents the range of variation found in normal, healthy individuals of the same age group. Table II gives the results of repeated tests on seven individuals. It includes cases of pulmonary stenosis in which pulmonary blood flow was increased by aortic-pulmonary artery anastomosis or pulmonary valvulotomy.

Certain differences in distribution with respect to age are evident in the data of Table I and Figures 1 and 2. Arterial oxygen saturation below 50 per cent was found only in children of 7 years and younger. The fact that all but one of the adults had arterial saturations above 79 per cent is misleading and an artifact of sampling. Of the adult group only one was believed to have pulmonary stenosis. It should be noted that in the reports of Talbott et al. (1), Bing, Vandam, and Gray (8), and Suarez, Chiodi, Fasciolo, and Taquini (3), of 33 patients with cyanotic congenital heart disease who were over 18 years of age, 15 were found to have arterial saturations below 75 per cent. However, only one of these patients had a saturation below 60 per cent. The great majority of patients of our study who had HbO_2 capacities within the normal range were younger children. On the other hand, the majority of very high HbO_2 capacities, over 32 vol. per cent, were found in older children and adults. One child of 6 years was found to have a HbO_2 capacity of 32.5 vol. per cent. In regard to the alkaline reserve of the plasma there seems to be no special trend with age. The lowest values were found in children of 7 and 8 years. It may be significant that in spite of the fairly high arterial oxygen saturations found in the adults of this study, all values for alkaline reserve were below the normal range of variation. In the case of the arterial pCO_2, about a third of the children of 12 years and younger had values above the normal mean, whereas in children above that age and in adults all values but one lay below the normal mean. The great majority of the lower than normal pH_s values were found in children between 6 and 10 years.

Since the data of Table I are arranged in the order of increasing arterial saturation, it can be

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TABLE I

Oxygen saturation, HbO_2 capacity, plasma CO_2 T_{40}, pCO_2 and pH_a of arterial blood of patients with cyanotic congenital heart disease*

No.	Subject	Age	Sex	Arterial saturation	HbO_2 capacity		Plasma CO_2 T_{40}*		Arterial pCO_2		Arterial pH_a	
					Value found	Dev. from normal	Value found	Dev. from normal	Value found	Dev. from normal	Value found	Dev. from normal
		yr.		*per cent*	*vol. %*	*vol. %*	*vol. %*	*vol. %*	*mm.*	*mm.*		
1	S. D.	2	F	21.0	14.5	− 2.0	37.3	−11.1	41.7	+ 4.4	7.227	−.122
2	R. E.	2	M	21.4	28.6	+12.1	37.4	−11.0	40.2	+ 2.9	7.266	−.083
3	P. S.	1	F	21.6	18.0	+ 1.5	39.6	− 8.8	42.1	+ 4.8	7.257	−.092
4	R. B.	6	M	40.5	28.6	+10.2	35.7	−18.9	37.8	− 0.2	7.244	−.155
5	J. M.	7	M	40.6	31.1	+12.7	34.6	−20.0	35.9	− 2.1	7.244	−.155
6	J. A.	2	M	41.7	25.6	+ 9.1	37.3	−11.1	35.0	− 2.3	7.279	−.070
7	H. R.	2	M	46.9	14.0	− 2.5	42.6	− 5.8	25.5	−11.8	7.423	+.074
8	J. G.	4	F	49.8	30.9	+13.2	41.5	−12.0	39.3	+ 2.0	7.297	−.093
9	M. P.	14	M	52.0	33.8	+15.4	43.3	−12.2	40.8	− 0.5	7.308	−.073
10	J. W.	9	M	58.7	32.8	+14.4	33.6	−21.0	38.3	+ 0.3	7.203	−.201
11	S. X.	15	M	59.1	35.1	+16.7	41.6	−13.9	31.6	− 9.7	7.348	−.033
12	V. S.	7	F	61.8	26.6	+ 8.2	45.3	− 9.3	37.9	− 0.1	7.334	−.065
13	W. B.	6	M	63.2	28.4	+10.0	40.8	−12.7	32.9	− 4.4	7.322	−.077
14	M. M.	36	F	63.4	35.1	+14.6	45.6	−12.6	30.2	−10.9	7.399	−.003
15	L. C.	14	F	65.4	32.4	+14.0	41.2	−14.3	32.8	− 8.5	7.328	−.053
16	C. F.	6	M	65.6	32.5	+14.1	42.4	−11.1	41.6	+ 4.3	7.283	−.107
17	J. R.	10	F	65.7	25.0	+ 6.6	50.6	− 4.0	39.5	+ 1.5	7.369	−.034
18	V. J.	3	F	68.3	19.7	+ 2.0	43.6	− 4.8	40.7	− 3.4	7.289	−.060
19	N. H.	4	M	68.6	29.9	+11.5	46.4	− 7.1	29.4	− 7.9	7.407	+.017
20	A. F.	5	M	70.4	27.8	+ 9.4	49.4	− 4.1	34.5	− 2.8	7.392	+.002
21	B. G.	7	M	70.6	27.8	+ 9.4	45.9	− 8.7	37.8	− 0.2	7.333	−.066
22	L. S.	17	M	71.2	26.4	+ 6.7	49.5	− 6.3	29.7	−11.6	7.434	+.053
23	J. S.	10	M	72.1	27.3	+ 8.9	49.0	− 5.6	33.4	− 4.6	7.398	−.006
24	B. M.	13	M	72.2	22.7	+ 4.3	54.2	− 1.3	27.5	−13.8	7.502	+.121
25	C. L.	2	M	73.0	16.6	− 0.1	49.1	+ 0.7	32.4	− 4.9	7.407	+.058
26	P. M.	5	F	73.3	21.0	+ 2.6	45.9	− 7.6	29.4	− 7.9	7.401	+.011
27	S. D.	10	M	74.2	31.2	+12.8	46.2	− 8.4	38.4	+ 0.4	7.333	−.071
28	R. B.	8	M	74.3	28.1	+ 9.7	48.9	− 5.7	39.4	+ 1.4	7.351	−.053
29	R. J.	2	M	74.9	19.1	+ 2.6	43.6	− 4.8	34.7	− 2.6	7.330	−.019
30	P. K.	5	F	75.4	22.7	+ 4.3	45.5	− 8.0	37.7	+ 0.4	7.328	−.062
31	R. F.	4	M	76.8	24.6	+ 6.9	42.5	−11.0	35.2	− 2.1	7.313	−.077
32	R. D.	10	M	77.0	36.5	+18.1	43.8	−10.8	27.7	−10.3	7.391	+.013
33	R. M.	6	M	77.4	17.4	− 1.0	49.6	− 3.9	44.7	+ 7.4	7.311	−.092
34	L. Z.	24	F	79.0	22.7	+ 2.2	55.5	− 2.9	28.5	−12.6	7.496	+.094
35	E. V.	11	M	79.3	25.3	+ 6.9	46.1	− 9.4	34.4	− 3.6	7.355	−.049
36	G. H.	35	F	79.4	29.1	+ 8.6	48.0	−10.2	46.8	+ 5.7	7.296	−.106
37	R. G.	25	M	79.7	25.7	+ 5.2	52.2	− 6.0	34.3	− 6.8	7.408	+.006
38	G. N.	31	M	79.9	22.6†	+ 2.1	50.9	− 7.3	38.8	− 2.3	7.367	−.035
39	C. L.	4	M	80.0	18.2	+ 0.5	41.1	−12.4	23.5	−13.8	7.412	+.022
40	D. R.	8	M	80.7	24.6	+ 6.2	48.6	− 6.9	34.5	− 6.8	7.379	−.002
41	S. L.	7	F	80.8	23.9	+ 5.5	43.7	−10.9	33.1	− 4.9	7.340	−.001
42	M. C.	16	F	81.0	26.2	+ 7.0	45.6	− 9.9	34.4	− 6.7	7.351	−.030
43	D. B.	19	M	82.4	35.7	+15.2	47.6	−10.6	37.2	− 3.9	7.352	−.029
44	D. M.	8	M	82.8	22.5	+ 4.1	49.3	− 5.3	29.5	− 8.5	7.429	+.025
45	J. T.	5	F	83.6	23.8	+ 5.4	49.2	− 4.3	34.7	− 2.6	7.377	−.022
46	I. B.	23	F	83.8	25.2	+ 4.7	51.5	− 6.7	33.7	− 7.4	7.407	+.005
47	A. G.	12	M	84.9	22.5	+ 4.1	47.6	− 7.0	30.0	− 8.0	7.407	+.003
48	C. K.	9	M	85.9	21.6	+ 3.2	50.9	− 3.7	35.9	− 2.1	7.387	−.017
49	M. M.	10	F	87.1	20.0	+ 1.6	46.6	− 8.1	42.2	+ 4.2	7.298	−.105
50	J. M.	12	M	88.0	21.6	+ 3.2	55.6	+ 1.0	26.5	−11.5	7.519	+.116
51	B. Z.	31	M	89.0	28.5	+ 8.0	51.6	− 6.6	37.1	− 4.0	7.380	−.022
52	M. D.	12	F	89.8	17.2	− 1.2	52.7	− 2.8	34.0	− 4.0	7.421	+.022
53	P. T.	25	M	89.9	24.4	+ 3.9	54.3	− 3.9	37.9	− 3.2	7.399	−.003
54	B. N.	16	M	90.1	27.9	+ 8.2	50.0	− 5.5	33.5	− 7.8	7.394	+.013
55	P. B.	9	F	90.5	18.4	0.0	48.7	− 5.9	40.2	+ 2.2	7.330	−.074
56	W. G.	9	M	90.8	18.4	0.0	52.3	− 2.4	45.7	+ 7.7	7.323	−.080
57	B. V.	10	M	91.7	21.1	+ 2.7	53.0	− 1.6	32.8	− 5.2	7.428	+.025
58	P. C.	4	F	91.7	17.2	− 0.5	53.0	− 0.5	43.7	+ 6.4	7.340	−.050
59	R. W.	4	M	91.9	18.6	+ 0.2	47.1	− 6.4	39.7	+ 2.4	7.317	−.073
60	T. A.	9	M	92.7	26.1	+ 7.7	48.6	+ 0.2	28.7	− 8.6	7.420	+.016

* Plasma CO_2 T_{40}, or alkaline reserve, is defined as the CO_2 content of plasma from fully oxygenated blood which has been equilibrated with CO_2 at a tension of 40 mm. Hg.

† The moderately low HbO_2 capacity in this case is due to repeated phlebotomy.

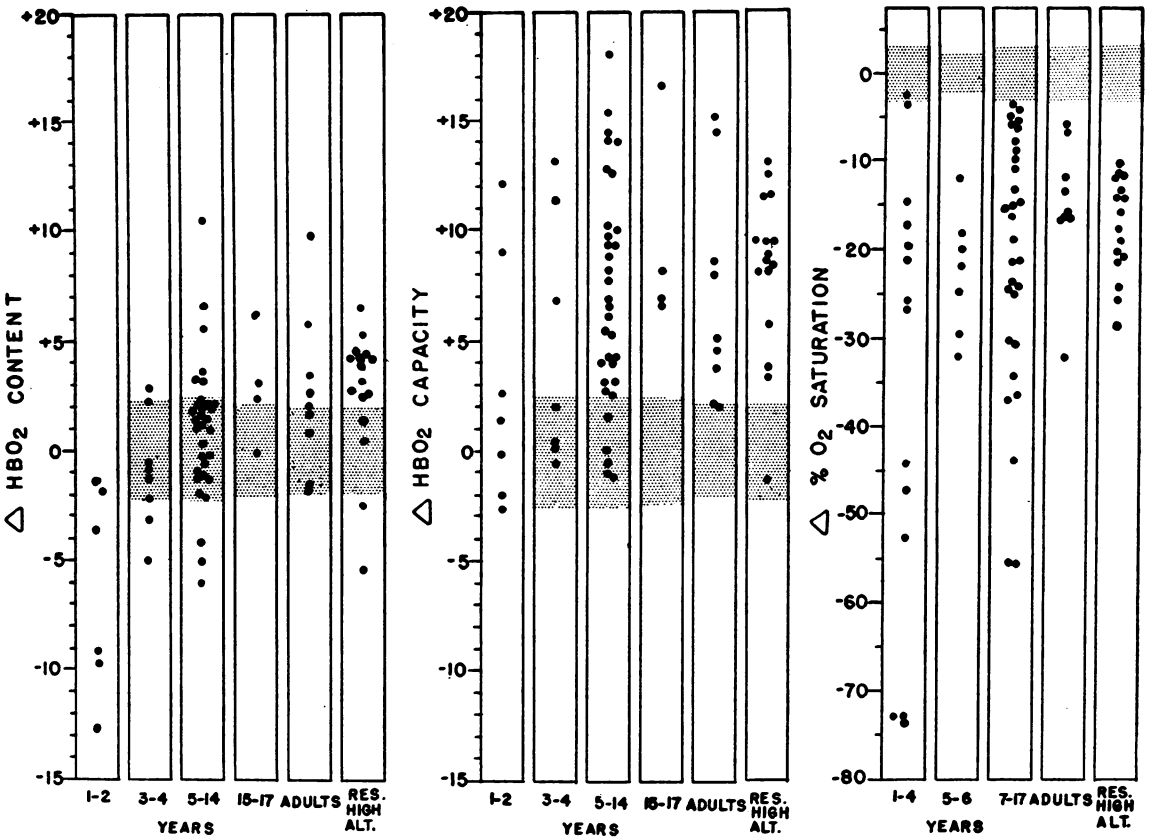

FIG. 1. ARTERIAL HbO_2 CONTENT, HbO_2 CAPACITY, AND PERCENTAGE OXYGEN SATURATION OF THE BLOOD OF PATIENTS WITH CYANOTIC CONGENITAL HEART DISEASE, SHOWN AS DISTRIBUTIONS OF THE DEVIATIONS FROM THE NORMAL MEAN FOR THE VARIOUS AGE GROUPS

seen that rough relationships exist between the degree of arterial unsaturation and the extent of the deviations of the HbO_2 capacity, alkaline reserve and arterial pH_s from the normal mean. These relationships are more clearly apparent in Table III which gives mean values for the three groups into which the material was divided on the basis of arterial unsaturation. The more marked deviations from the normal tend to occur in patients with arterial saturations below 70 per cent. In each group there are marked exceptions.

The acid-base balance of the arterial blood of patients with cyanotic congenital heart disease is shown in Figure 3, in which the individual data for $(HCO_3)_s$, pCO_2 and pH_s are plotted on triaxial charts according to the method of Hastings and Steinhaus (9) and of Shock and Hastings (10). The shaded area in each chart represents the range of variation which we have found for normal healthy children of corresponding age groups and for adults (7). It is evident that in the great majority of cases the acid-base balance may be described as that due to fixed acid excess or to a combination of fixed acid excess and CO_2 deficit.

Data concerning serum chloride, protein and lactic acid were obtained for 15 of the patients with cyanotic congenital heart disease in the hopes of observing changes in the electrolyte balance of the serum which might compensate for the reduced bicarbonate concentration. The data include two independent determinations on three of the patients, in one case separated in time by three years. The results in Table IV show that in half of the cases the sum of the three ions which constitute the great part of the anion moiety of the serum electrolytes, bicarbonate, chloride, and proteinate, falls within the normal range of variation, while in the other half the sum of the three major anions is below normal. The table shows

clearly that the difference in the sum of the three anions is due almost entirely to a difference in the mean chloride level. Thus, in approximately half of the cases a reduction in the bicarbonate level is almost balanced by a rise in the serum chloride level, but in the other half there is no apparent rise in chloride concentration. Those in the group without chloride compensation tend to have lower saturations and higher HbO_2 capacities, although the values of the two groups overlap. The mean pH_s of the group without chloride compensation is 7.332 as compared with a mean value of 7.382 for the other group, but the low mean pH_s of the former group is due to lower than normal values in only half of the group. The blood lactate concentration of the group without chloride compensation is not significantly higher than in the other group.

In Figures 1 and 2 the last column of each group contains corresponding data for residents at high altitude, taken from the reports of Dill et al. (11–13) and of Hurtado and Aste-Salazar (14). The triangles and squares of Figure 3 also show these data. They are given for the purpose of comparison since both residents at high altitude and patients with cyanotic congenital heart disease represent hypoxic states to which the individual has become acclimatized over a long period of time. Both groups show approximately the same degree of arterial unsaturation, although the spread of values in cyanotic congenital heart disease is greater and much lower values are sometimes found. Figure 2 shows that the alkaline reserve of the plasma tends to be lower in residents at high altitude than in patients with cyanotic congenital heart disease. Table III includes data for residents at high altitude in terms of mean deviations from the normal. Of the three groups of patients with cyanotic congenital heart disease which are shown in this table, the second group,

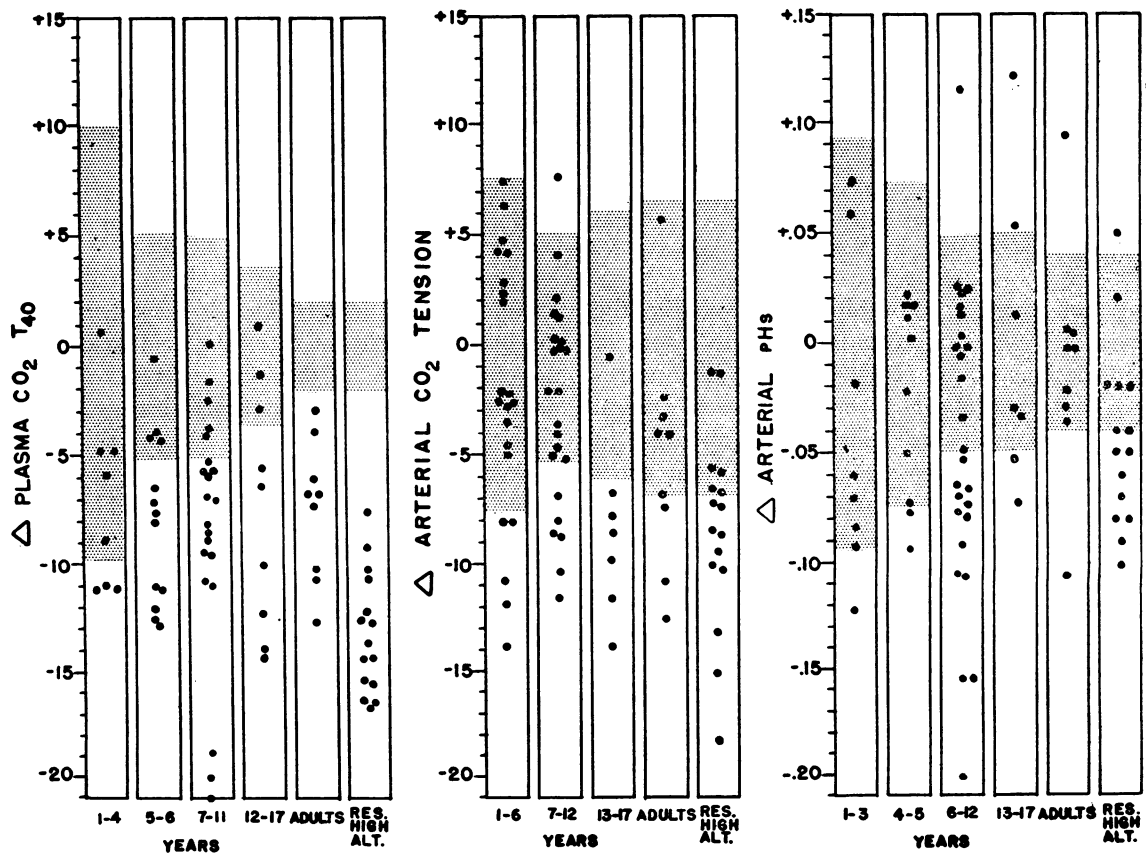

FIG. 2. PLASMA CO_2 T_{40}, ARTERIAL pCO_2, AND ARTERIAL pH_s OF PATIENTS WITH CYANOTIC CONGENITAL HEART DISEASE, SHOWN AS DISTRIBUTIONS OF THE DEVIATIONS FROM THE NORMAL MEAN FOR THE VARIOUS AGE GROUPS

TABLE II

Results of repeated tests on the same individual

No.	Date	Subject	Age		Notes	Arterial saturation	HbO_2 capacity	Plasma* CO_2 T_{40}	Arterial pCO_2	Arterial pH_a
			Yr.	*Mo.*		*per cent*	*vol. %*	*vol. %*	*mm. Hg*	
5	2–25–42	J. Mu.	2	7		54.9	27.1	41.7	43.4	7.266
	9– 8–43		4	2		54.2	31.4	40.0	47.7	7.232
	12– 3–46		7	4		40.6	31.1	34.6	35.9	7.244
	4–22–47		7	9		53.1	27.9	33.5	40.8	7.186
	Post-op., 5–14–47		7	10	Aortic-pulmonary artery anastomosis, 4–24–47	72.2	23.9	47.0	44.9	7.295
	3–10–49		9	8		75.2	25.7	53.0	34.7	7.422
17	10–14–47	J. R.	9	8	Blalock anastomosis, 3–29–47	71.8	18.7	54.6	47.3	7.340
	Post-op., 11–18–47		9	9	Obliteration of anastomosis, 10–17–47	65.7	25.0	50.6	39.5	7.369
22	4–11–52	L. S.	16	10		71.2	26.4	49.5	29.7	7.434
	Post-op., 10–15–52		17	4	Pulmonary valvulotomy, 4–14–52	96.6	19.7	57.0	48.6	7.387
27	6–12–44	S. D.	8	0		68.8	31.5	47.1	34.7	7.373
	10–11–46		10	4		70.8	31.1	42.7	36.3	7.314
	10–17–46		10	4		74.2	31.1	46.2	38.4	7.333
	10–28–46		10	5	Phlebotomy, 10–24–46	62.6	27.4	49.3	39.0	7.365
	12–12–46		10	6	Iron medication begun 10–30–46	66.1	29.4	42.8	35.2	7.325
	9– 9–47		11	3		77.1	27.9	47.0	33.9	7.372
	Post-op., 10– 8–47		11	4	Aortic-pulmonary artery anastomosis, 9–14–47	84.3	24.0	52.4	33.5	7.422
	12– 8–47		11	6		83.8	25.4	51.4	31.4	7.431
	3– 8–49		12	9		83.2	26.0	53.4	32.4	7.438
28	5– 5–47	R. B.	8	0		74.3	28.1	48.9	39.4	7.351
	Post-op., 5–23–47		8	1	Aortic-pulmonary artery anastomosis, 5–6–47	77.6	21.9	52.3	33.3	7.426
	8–20–52		13	2		74.1	24.2	47.6	30.2	7.401
29	1–10–49	R. J.	2	0		74.9	19.1	43.6	34.7	7.330
	Post-op., 2– 4–49		2	1	Aortic-pulmonary artery anastomosis, 1–11–49	76.8	16.4	47.5	31.1	7.403
50	12–11–47	J. Mr.	10	10		84.0	22.0	51.7	30.1	7.447
	1–18–49		11	11		88.0	21.6	55.6	26.5	7.519
	4– 2–51		14	1		81.0	23.1	54.9	37.1	7.415
	Post-op., 6–29–51		14	4	Pulmonary valvulotomy, 6–13–51	95.1	20.9	53.6	39.7	7.375

* Plasma CO_2 T_{40}, or alkaline reserve, is defined as the CO_2 content of plasma from oxygenated blood which has been equilibrated with CO_2 at a tension of 40 mm. Hg.

with arterial saturations of 70 to 88 per cent, compares well in arterial saturation with residents at high altitude. It is evident that for comparable degrees of arterial unsaturation the blood of residents at high altitudes has a slightly higher HbO_2 capacity, a much lower alkaline reserve and arterial pCO_2, and a slightly lower pH_a. The acid-base picture in Figure 3 is quite similar in both groups, *i.e.*, a combination of fixed acid excess and CO_2 deficit.

The post-operative results in Table II give information as to the effects of increased pulmonary blood flow on the arterial blood gases and the acid-base balance. In four cases of Tetralogy of Fallot, two, J. Mu. and S. D., showed marked improvement in arterial saturation, but little change was observed in R. B. and R. J. Not shown in the table is the fact that R. J. showed marked clinical improvement and little evidence of cyanosis when seen four years later. L. S. and J. Mr., who had diagnoses of pulmonary stenosis and atrial septal defect, showed arterial saturations of 96.6 and 95.0 per cent respectively following valvulotomy. A reduction of HbO_2 capacity occurred in all cases. Those patients who had a marked rise in arterial saturation also showed a marked rise in the alkaline reserve of the plasma. In the cases of J. Mu. and S. D. the alkaline re-

TABLE III

*Relation of the degree of arterial unsaturation to the deviations from the normal of the HbO_2 capacity and the acid base balance of the blood of patients with cyanotic congenital heart disease—a comparison of these deviations from the normal with comparable values in native residents at high altitude**

No. of cases	Arterial saturation *per cent*	Mean deviations from the normal mean			
		HbO_2 capacity *vol. %*	Plasma CO_2 T_{40}† *vol. %*	Arterial pCO_2 *mm.*	Arterial pH_s
		Patients with cyanotic congenital heart disease			
10	93–88	+ 2.9 ± 1.21‡	− 3.5 ± 0.79	−1.4 ± 1.81	−0.023 ± 0.0136
31	88–70	+ 5.8 ± 1.31	− 5.4 ± 1.18	−4.6 ± 1.29	−0.010 ± 0.0104
12	70–40	+12.9 ± 0.72	−13.8 ± 1.72	−3.1 ± 1.44	−0.083 ± 0.0185
		Residents at high altitudes			
15	85–68	+ 8.5 ± 0.95	−13.2 ± 0.73	−8.4 ± 1.19	−0.043 ± 0.0106

* Data for residents at high altitude are taken from the reports of Dill et al. (11–13) and of Hurtada and Aste-Salazar (14).

† Plasma CO_2 T_{40}, or alkaline reserve, is defined as the CO_2 content of plasma from fully oxygenated blood which has been equilibrated with CO_2 at a tension of 40 mm. Hg.

‡ The figures following the ± signs represent the standard error of the mean.

serve of the plasma rose to levels within the normal range in spite of the fact that their arterial blood still contained a considerable degree of venous admixture. Their pH_s levels, which previously had been consistently low, rose to normal levels after an aortic-pulmonary artery anastomosis had been made. In the case of J. R. the preoperative values are comparable to the postoperative values in the other patients. A Blalock anastomosis had been performed some time before but cardiac decompensation followed. Subsequent surgical obliteration of the anastomosis reduced the arterial saturation, raised the HbO_2 capacity, and decreased the alkaline reserve of the plasma. It also reduced the arterial pCO_2 which presumably had been high because of pulmonary congestion.

DISCUSSION

The fact that the great majority of patients with cyanotic congenital heart disease have a normal or higher than normal arterial oxygen content is due to the fact that the great majority have a high HbO_2 capacity. The high arterial oxygen content loses much of its value in the presence of reduced arterial saturation since the arterial oxygen tension rather than its concentration determines the level of the mean capillary oxygen pressure and the resultant pressure gradient or diffusion pressure head between capillaries and tissues. Studies of cyanotic congenital heart disease by Bing et al. (2) and Ernsting and Shephard (6) have emphasized the great part played by the sigmoid shape of the oxygen dissociation curve in reducing the arterial-mean capillary oxygen tension gradient, in contrast to the small effect of the greatly increased HbO_2 capacity. The latter exerts its effect on the mean capillary oxygen pressure by raising the venous level of saturation since, of two bloods equally saturated, the one with high HbO_2 capacity will remain more highly saturated after equal quantities of oxygen per unit of blood have been transferred to the tissues.

It is of interest to find that 12 patients with cyanotic congenital heart disease, or 20 per cent of the number studied, did not have an elevated HbO_2 capacity. Half of these had mild cyanosis and arterial saturations between 87 and 92 per cent. The majority of the remainder were infants not over 2 years of age. The fact that blood counts in these infants showed elevated values, with red cell counts of 6.2 to 8.5 million per cu. mm., suggests that the low HbO_2 capacity is due to a nutritional deficiency. Administration of ferrous sulfate to one infant raised his HbO_2 capacity. Talbott and associates' (1) summary of the literature shows several cases of congenital heart disease in which the blood HbO_2 capacity was not elevated. Burchell, Taylor, Knutson, and Wood (4) have also noted a case with 68 per cent saturation and with an HbO_2 capacity of only 15.2 vol. per cent.

The arterial saturation found in patients with cyanotic congenital heart disease covers a wide

range. Eight cases showed arterial saturations below 50 per cent. It is probably significant that saturations below 25 per cent were found only in infants and that no saturation below 50 per cent was observed in children over 7 years of age. A very low arterial saturation suggests a poor prognosis unless remedial operative procedures can be used. Operation was attempted in the case of two infants with arterial saturations below 25 per cent but death followed. The third infant with this low saturation survived only a few months after she was studied. Autopsy revealed transposition of the great vessels. There is suggestive evidence that correction of the iron deficiency present in cyanotic infants with low HbO_2 capacity improves their status.

We believe that many of the saturation values found in arterial samples in children may represent the lower limit of a variable quantity which is determined by factors which regulate both the amount of right to left shunt and the venous oxygen level. Saturation levels determined by the ear oximeter are usually higher because they are measured under conditions that are less disturbing to the patient than are arterial punctures.

The finding of a low alkaline reserve of the plasma in patients with cyanotic congenital heart disease has been reported previously by Talbott et al. (1) and by Suarez, Chiodi, Fasciolo, and Taquini (3). It has also been suggested by the low CO_2 contents of arterial blood found in Talbott's summary of the literature (1), and in the serum of arterial blood as reported by Bing et al. (2).

Talbott et al. (1) first described the analogy between the tissue anoxia of patients with cyanotic congenital heart disease and that of persons living under the low oxygen pressure of high altitudes. He attributed the low alkaline reserve of the blood in these patients to the effects of chronic hyperven-

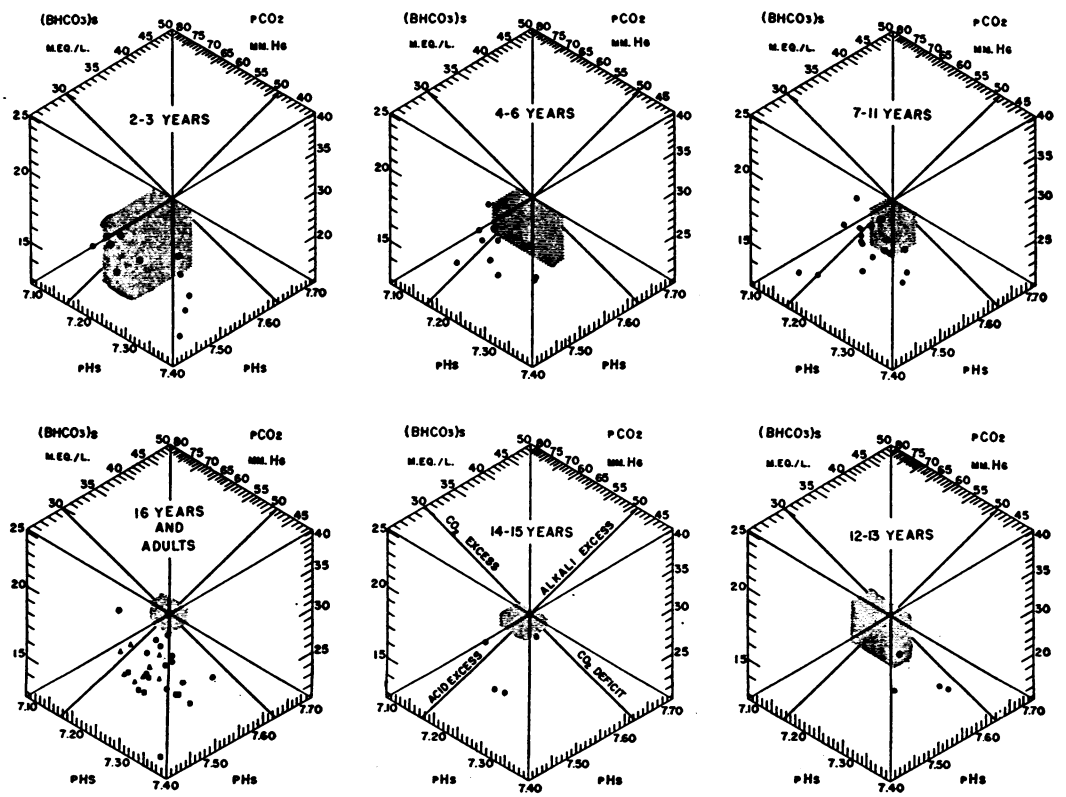

FIG. 3. ARTERIAL $(HCO_3)_s$, pCO_2 AND pH_s OF THE BLOOD OF PATIENTS WITH CYANOTIC CONGENITAL HEART DISEASE, PLOTTED ON TRIAXIAL COORDINATES

The shaded areas represent the range of normal variation for the various age groups as determined by ± 2 standard deviations from the mean value of each group.

tilation, but he also recognized that some other factors caused the acidosis which was observed in the patient he had studied so extensively and in several other cases reported in the literature. Bing et al. (2) found that the minute volume of respiration was increased above the normal in 29 out of 30 cases of cyanotic congenital heart disease, but the arterial pCO_2 and the alkaline reserve were reduced proportionately and the arterial pH_s remained within normal limits. Suarez, Chiodi, Fasciolo, and Taquini (3) found hyperventilation to be characteristic of the six patients with this disease which they studied and arterial pH_s in the normal range or slightly low.

Bing et al. (2) emphasized the difference in conditions under which tissue anoxia is produced in patients with congenital heart disease and in residents at high altitudes. In the latter a low alveolar oxygen pressure produces the low arterial pO_2 and saturation. Hyperventilation is beneficial in that it raises the alveolar pO_2. In patients with cyanotic congenital heart disease on the other hand low arterial pO_2 and saturation levels are caused by venous admixture through abnormal channels. Beneficial effects of hyperventilation are questionable in such patients since the blood that passes through the lungs is exposed to a high oxygen tension and is well oxygenated, while the blood shunted from the right to the left side of the heart does not pass through the lungs.

Presumably hyperventilation rises in response to an anoxic stimulus both in patients with cyanotic congenital heart disease and in residents at high altitude. Dill, Talbott and Consolazio (13) showed that an essential process in acclimatization to high altitude consists first of hyperventilation to increase alveolar oxygen pressure, followed later by a reduction of the alkaline reserve of the plasma by kidney action to the point where the normal ratio between the pCO_2 and the serum bicarbonate is reached. Both Dill, Talbott and Consolazio (13) and Hurtado and Aste-Salazar (14) found that the arterial blood serum of permanent residents at high altitude is characterized by a lowering of the pCO_2 proportional to that of the alkaline reserve, with a normal or slightly low pH_s, in contrast to the elevated pH_s of the arterial blood of temporary residents at high altitude. Patients with cyanotic congenital heart disease resemble residents at high altitude in that they are acclimatized to their state of anoxia. Our results show that for a given degree of arterial unsaturation the blood of patients with cyanotic congenital heart disease shows less of a depression of alkaline reserve than that of residents at high altitude. Since for equal degrees of alveolar hyperventilation the arterial pCO_2 must remain higher in the blood of patients with cyanotic congenital heart disease because of the venous admixture it contains, there is need for less decrease in the alkaline reserve of the blood in these patients in order to maintain a normal arterial pH_s.

The case of cyanotic congenital heart disease studied by Talbott et al. (1) was unusual because of the low arterial pH_s which was observed. The present report shows 32 per cent of pH_s values below the lower limit of normal. The great majority of pH_s values below 7.30 were found in samples showing less than 60 per cent saturation and are therefore associated with large venous-arterial shunts. In such cases of severe hypoxia a low pH_s offers compensation by raising arterial oxygen tension, hence mean capillary oxygen pressure, through the Bohr effect on the oxygen dissociation curve.

The low pH_s of the arterial blood and the lack of balance in the common electrolytes of the serum in cases of severe hypoxia led Talbott to suggest the presence of increased concentrations of organic acids in the blood. Since tissue metabolism apparently proceeds at relatively low levels of oxygen tension, it is conceivable that enzyme reactions involved in muscle metabolism operate at a more anaerobic level, with production of lactic acid in larger quantities than normal. Our results agree with those of Hallock (15), Bing et al. (2), and Havel and Watkins (5) in showing that in the resting state the lactic acid concentration in the blood of cyanotic patients with congenital heart disease is not significantly higher than in the normal person, and that the slightly elevated lactic acid levels that are occasionally found are not great enough to explain the deficiencies in the electrolyte balance.

It is important to note also that although Bing et al. (2) found that the basal oxygen consump-

TABLE IV

Serum electrolyte concentrations in the arterial blood of patients with cyanotic congenital heart disease

Age *yr.*	Subject	Oxygen saturation *per cent*	HbO_2 capacity *vol. %*	$(HCO_3)_a$ *mEq./L.*	$(Cl)_a$ *mEq./L.*	$(Proteinate)_a$ *mEq./L.*	$(HCO_3)_a + (Cl)_a + (Proteinate)_a$ *mEq./L.*	$(Lactate)_a$ *mEq./L.*	$(Sodium)_a$ *mEq./L.*	pH_a
				Group I. Normal values for $(HCO_3)_a + (Cl)_a + (Proteinate)_a$						
3	W. B.	63.4	23.2	18.8	110.0	16.6	145.4	1.9		7.414
6	J. T.	83.6	23.8	20.0	106.3	18.1	144.4	2.9		7.377
7	V. S.	61.8	26.6	19.8	105.6	19.6	145.0	1.2		7.234
10	J. S.	72.1	27.3	20.3	105.1	20.4	145.8	1.0		7.398
16	B. N.	90.1	27.9	20.2	106.3	18.0	144.5	1.8		7.394
16	M. C.	81.0	26.2	18.7	106.6	17.5	142.8	1.0		7.351
Adult	R. G.	79.7	25.7	21.2	108.2	15.6	145.0	0.6		7.408
Mean		76.0	25.8	19.9	106.9	18.0	144.7	1.5		7.382
				Group II. Low values for $(HCO_3)_a + (Cl)_a + (Proteinate)_a$						
3	N. H.	84.1	26.0	17.6	99.8	17.8	135.2	1.5		7.432
4	J. M.	54.3	31.4	19.7	100.6	15.0	135.3	1.2	133.6	7.232
5	A. F.	70.4	27.8	20.7	103.2	14.0	137.9	1.6		7.392
6	R. B.	40.5	28.6	16.1	104.2	18.0	138.3	2.9		7.244
6	R. B.	39.2	26.5	16.9	103.2	17.8	137.9	2.6		7.300
7	J. M.	40.6	31.1	15.3	104.2	16.6	136.1	1.7	146.3	7.244
7	W. G.	70.6	27.8	19.8	101.7	18.5	140.0	1.6		7.333
8	D. M.	82.8	22.5	19.2	104.1	17.3	140.6	1.8		7.429
10	S. D.	66.1	29.4	18.1	98.3	19.5	135.9	2.1	139.8	7.325
11	S. D.	77.1	35.7	19.3	101.5	16.4	137.2	1.7		7.372
Adult	D. B.	82.4	35.7	20.2	103.3	16.3	139.8	1.1		7.352
Mean		64.4	29.3	18.4	102.2	17.0	137.7	1.8		7.332

tion was usually below the normal mean in these patients, that finding has not been corroborated in our laboratory or by other investigators such as Burchell, Taylor, Knutson, and Wood (4), Suarez, Chiodi, Fasciolo, and Taquini (3) and Ernsting and Shephard (6). We must conclude that metabolic requirements for the resting state are met by adequate oxygen consumption in patients with marked arterial unsaturation. At present it is not known whether this is made possible by modifications in the complex of enzymatic processes involved in tissue metabolism and whether the production of organic acids other than lactic acid are increased under these conditions. The problem requires further study. The possibility of alterations in renal excretion also must be studied in this connection.

SUMMARY

The blood gases and acid-base balance of the blood were determined in arterial samples from 60 patients with cyanotic congenital heart disease who varied in age from 1 to 36 years. The results may be summarized as follows:

Arterial saturation varied from 21 to 93 per cent. Saturations below 50 per cent were found only in children under 8 years of age.

In 80 per cent of the cases HbO_2 capacities were more than 2 vol. per cent higher than the normal mean for the appropriate age. Of those with normal or below normal HbO_2 capacities, half were cases with arterial saturation between 87 and 92 per cent, and the majority of the remainder were infants in whom a nutritional iron deficiency was suspected. Very high HbO_2 capacities, over 32 vol. per cent, were usually found only in older children and in adults.

By means of high HbO_2 capacities the oxygen content of the arterial blood was maintained within the normal range in all but 15 per cent of the cases.

The alkaline reserve of the plasma tended to be reduced, for approximately two-thirds of the observed values were below the lower limit of normal. Arterial pCO_2 was below the normal range in only one-third of the cases. As a result, values for arterial pH_a were below the lower limit of normal in approximately one-third of the cases.

A rough relationship was found to exist be-

tween the degree of arterial unsaturation and the extent of the deviations of the HbO_2 capacity, alkaline reserve and arterial pH_s from the normal mean.

Deviations of the acid-base characteristics of the serum from the normal were found to be due in most cases either to fixed acid excess or to a combination of fixed acid excess and CO_2 deficit.

Calculation of a partial electrolyte balance showed that in some cases the reduced bicarbonate concentration of the serum was balanced by a rise in serum chloride concentration. In other cases there was no evidence of replacement of serum bicarbonate by chloride, nor by increased lactate concentration. The question of a corresponding reduction of total fixed base or an increase in other organic acids has not been investigated sufficiently.

The determination of arterial blood gases in samples drawn post-operatively, after pulmonary blood flow had been increased by aortic-pulmonary artery anastomosis or pulmonary valvulotomy, showed a marked rise in the alkaline reserve and the arterial pH_s of the blood, in addition to the well-known increase in arterial saturation and reduction of HbO_2 capacity.

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