TOTAL ACID-BASE EQUILIBRIUM OF PLASMA IN HEALTH AND DISEASE: *IX. High Serum Bicarbonate in Heart Failure. Asphyctic Anoxemia*

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TOTAL ACID-BASE EQUILIBRIUM OF PLASMA IN HEALTH AND DISEASE

IX. High Serum Bicarbonate in Heart Failure. Asphyctic Anoxemia

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In the preceding paper of this series (1) it was pointed out that the concentrations of bicarbonate and of chloride in the serum of patients with heart failure are far more variable than those of normals. From this it was inferred that the factors that provoke disturbances of these elements in heart disease are not uniform. Attention was called especially to two contrasted types of extreme abnormalities, one characterized by high bicarbonate, the other by high chloride.

The present paper will be devoted to a discussion of the production and significance of high serum bicarbonate in patients with heart failure. The technical procedures employed have been described at length in earlier articles of this series (1, 2).

Scott (3), in 1917, first called attention to the fact that the bicarbonate content and capacity of the blood and the alveolar CO_2-tension of patients with chronic emphysema were abnormally high. These observations have since then been verified by a number of investigators and similar disturbances have been found in other chronic pulmonary diseases. Essen, Kauders and Porges (4) have shown that the higher CO_2 of these conditions is associated with a reduction of Cl.

The first three cases in table 1, although they are not cases of essential emphysema, have comparable pathologic pulmonary lesions and all present high serum carbon dioxide. The elevation of bicarbonate is in no instance so extreme as to necessitate a recession of Cl, although the latter is, in every case below the average normal. The

TABLE 1

Electrolyte equilibrium of serum of patients with pulmonary diseases

Patient	Oxygen capacity	Cell volume	Proteins (1)		HCO_3 (2)	Cl (3)	PO_4 (4)	Total acid 1 + 2 + 3 + 4 (5)	Base (6)	Organic acid 6 − 5 (7)	HCO_3 + Cl 2 + 3	Treatment of blood	Remarks
	vols. per cent	*vols. per cent*	*per cent*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*		
33008					31.4	100.5	1.9		161.1		131.9	V. cont.	Chronic bronchitis and emphysema
45918	21.3	50.5	6.15	10.7	25.7	101.8		138.2§	165.0	26.8§	127.5	V. cap.	Chronic bronchitis with bronchiectases
53439	23.9	57.8	7.08	12.3	25.9	99.0		136.9§	159.0	22.1§	124.9	V. cap.	
	24.0	58.9	8.02	13.9	26.0	99.3		139.2§	150.4	11.2§	125.3	V. cap.	
35966	16.8	40.2	5.63	10.1	26.0	80.0	1.9	118.0§	126.4	8.4	106.0	V. cont.	Generalized tuberculous bronchopneumonia. Pleurisy with effusion. Serum pH 7.44*
33372	4.9	18.6	3.68	6.6	25.3	99.5	2.3	133.7	148.7	15.0	124.8	V. cont.	Diffuse pulmonary tuberculosis with massive pleuritic effusion and generalized edema. Serum pH 7.43†

* By new gasometric technique.

† By Cullen colorimetric technique.

§ PO_4 was not determined in these cases; therefore *total acid* appears somewhat low and *organic acid* proportionately too high. The error probably does not exceed 2 mM.

sum, HCO_3 + Cl is entirely normal. All of these patients, although free from all symptoms and signs of diseases of the heart or circulatory system exhibited marked cyanosis, evidence presumably, of arterial or "anoxic" anoxemia. The latter is, in turn, an indication that the lungs are not efficiently performing their function of oxygenating the blood in the pulmonary circulation.

Because of the more rapid diffusion and greater solubility of CO_2, Van Slyke (5) and others (10) have concluded that before pulmonary impairment can result in clinically serious carbon dioxide retention the most extreme anoxemia must develop. Although these pulmonary cases cannot be said to have CO_2 acidosis, they do show a high plasma CO_2 and bicarbonate content, which are most easily explained as a response to a retention of carbon dioxide. This retention is attended by no reduction of pH because the retained CO_2 is neutralized by base. In order that the total electrolyte concentration of the blood need not increase Cl is diminished, presumably excreted in the urine. The effect of the changes is quite apparent. Increase of bicarbonate permits the carbon dioxide tension of the blood and the pulmonary air to rise without disturbing the pH of the blood. Because of the higher carbon dioxide tension of the pulmonary air the individual is enabled to excrete more CO_2 per unit volume of respiratory air.

It might almost be proper to speak of this group of reactions as the picture of anoxic anoxemia due to impairment of the pulmonary mechanism, a condition to which the term *asphyctic* anoxemia might well be applied. This is not meant to imply that the high CO_2 is a direct response to anoxemia or one that facilitates oxygenation of the blood. Conditions which seriously interfere with the ventilation of the blood in the lungs, however, are likely to be attended by high CO_2 inasmuch as they interfere with the discharge of carbon dioxide from the blood. Because the rate of diffusion of oxygen is less than that of CO_2, it is hardly conceivable that retention of CO_2 can appear before a definite anoxemia has developed.

The conception that high CO_2 is to be expected in asphyctic anoxemia has certain useful implications. First of all it disposes definitely of the idea that anoxemia *per se* leads to reduction of bicarbonate and alkalosis. The only type of anoxemia that has been shown to cause such changes is the anoxic anoxemia due to reduction of oxygen ten-

sion in the inspired air. There is no evidence that stagnant or anemic anoxemia have similar effects. Experimental studies have forced the conclusion that the alkalosis that results from breathing oxygen-poor air is not directly referable to the anoxemia but is due to the overventilation which this anoxemia causes. Koehler et al. (6) have shown that the alkalosis can be modified to any extent by adding carbon dioxide to the inspiratory air.

Secondly, if high blood CO_2 is the usual reaction to asphyctic anoxemia, its absence in patients with pathologic processes that produce such a condition would indicate the presence of other factors that have a contrary effect. This is the reasoning that led the authors to propose in an earlier publication (7) that CO_2 retention occurred in lobar pneumonia, but was masked by the effects of temperature and changes in the other electrolytes.

That such factors may modify the electrolyte picture of asphyctic anoxemia is evidenced by the studies on the last two patients in table 1 (nos. 35966 and 33372). The former, no. 35966, was in the last stages of tuberculosis, with generalized bronchopneumonia, purulent bronchitis and a small pleuritic effusion. Besides this he was extremely cachectic and dehydrated and would take only enough fluid and carbohydrate to prevent starvation acidosis. He was deeply cyanotic and presented an extraordinary degree of dyspnea. The breath sounds were everywhere obscured by profuse, sticky râles. In spite of the unmistakable signs of asphyctic anoxemia serum CO_2 was not elevated. On the other hand, in keeping with the dehydration, serum base was extremely low, only 126 mm. This compelled an equivalent reduction of acid. Such a reduction of acid was observed, but was entirely at the expense of Cl, which is only 80 mM., bicarbonate remaining unaffected in spite of dyspnea.

The last case, no. 33372, also in the terminal stages of tuberculosis, presents a more complicated picture. Besides the pulmonary lesions she presented a profound anemia and generalized edema. The latter was probably largely cachectic in origin, although the urine showed morphological changes indicative of a renal lesion. With low plasma proteins and edema, when salt has not been restricted, serum chloride is, in our experience, more frequently high than low. In this case the concentration of electrolytes, as evidenced by base, and Cl were

at the lower normal limits, while CO_2 was at about the usual level. With forces tending to produce an accumulation of both bicarbonate and chloride a compromise has been effected and a comparatively normal total electrolyte picture results. Such conclusions are so largely built on inference that they can be advanced only as hypotheses. Evidences of such conflicts and compromises will, however, appear with such frequency in the cardiac cases to be presented subsequently that it seems worth while to present the suggestive data from these cases for future reference and comparison.

Deficient oxygenation of the arterial blood has been observed in a certain proportion of patients with cardiac disease, especially with heart failure and evidences of pulmonary disorders such as congestion or edema of the lungs; or concomitant diseases of the lungs, such as emphysema, bronchitis or broncho pneumonia. The first 5 cases in table 2 (nos. 32567, 33568, 3807, 25835 and 9426) exhibit quite clearly the high CO_2 of asphyctic anoxemia with low Cl. CO_2 + Cl is, in every case normal and total electrolytes are also normal in the four instances in which they were determined. All of these patients presented definite evidences of pathologic lesions of the lungs other than those due to heart failure.

The next four patients (nos. 21460, 15325, 18112 and 18668) presented the typical electrolyte disturbance with pulmonary conditions which were entirely referable to cardiac decompensation. Both arterial and venous blood samples from the last three of these cases were examined for oxygen as well as carbon dioxide. In every instance definite arterial anoxemia was found.

Case no. 18292 presents an interesting series of changes. At the time of the first observation he had distinct evidences of bronchitis and possibly bronchopneumonia as well as considerable edema. At the time of the third observation his condition was quite similar. In spite of a well marked asphyctic anoxemia CO_2 was at the low normal level and Cl above the average. When the second examination was made the pulmonary signs and symptoms were unrelieved, but the edema had disappeared. At this time CO_2 had risen above normal, and Cl had fallen, although the arterial anoxemia had diminished. If the high CO_2 of the second study was due to asphyctic anoxemia, something must have modified the electrolyte picture on the two other occasions, possibly edema which determined a retention

TABLE 2

Electrolyte equilibrium of blood serum of cardiac patients with high serum CO_2

Patient	Oxygen capacity	Cell volume	Protein (1)		HCO_3 (2)	Cl (3)	PO_4 (4)	Total acid 1+2+3+4 (5)	Base (6)	Organic acid 6−5 (7)	HCO_3+Cl 2+3	Treatment of blood	Remarks
	vols. per cent	*vols. per cent*	*per cent*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*		
32567	18.3	41.6	5.89s	10.4	30.2	103.7	1.4	145.7	154.3	8.6	133.9	V. cont.	Chronic bronchitis and emphysema; hypertension; heart failure. Edema of legs. Serum pH 7.39*
33568			5.39s	9.7	28.2	99.4	2.0	139.3	146.4	7.1	127.6	A. cont.	Chronic bronchitis and emphysema; hypertension; heart failure. Slight edema of legs. Serum pH 7.44†
3807	23.6	53.5	6.26		28.7	98.8					127.5	V. cap.	Chronic bronchitis and emphysema
	21.7	46.9	7.05		30.5	98.8					129.3	V. cap.	Later, while recovering from edema due to heart failure
25835	16.4	40.5	6.63s	11.8	32.0	92.2	2.0	138.0	160.1	22.1	124.2	V. cont.	Syphilitic aortitis with aneurysmal dilation of aortic arch. Heart failure Expiratory dyspnea and stridor; intense cyanosis; edema of legs. Serum pH 7.43†
	16.6	41.7	6.81s	11.8	31.8	99.3	2.4	145.3	159.3	14.0	131.1	V. cont.	Edema has disappeared, but cyanosis and dyspnea continue. Serum pH 7.35†
9426	18.9	43.2	6.67		27.2	96.6					123.8	V. cap.	Advanced bilateral pulmonary tuberculosis; pericarditis with effusion. Heart failure; edema of legs

21460	17.5	38.0	5.67s	10.1	29.9	105.6	2.0	147.6	161.1	13.5	135.5	V. cont.	Arteriosclerosis; hypertension; heart failure. Slight hypernea and cyanosis. Rhonchi and râles over whole chest. No edema. Serum pH 7.41†
15325	19.3	41.5	6.79		24.9	108.0					132.9	V. cap.	Arteriosclerotic heart disease; heart failure. Rhonchi and râles over whole chest; right hydrothorax. Extreme dyspnea orthopnea and cyanosis. Edema of lower extremities and trunk
	22.6	48.0	6.49		26.8	111.2					138.0	V. cap.	Edema has disappeared. Dyspnea and cyanosis continue
18112	18.1	38.2			29.3	107.1					136.4	A. cont.	Arteriosclerosis with hypertension and heart disea e. Heart failure. Hepatic cirrhosis. Orthopnea and hyperpnea with wheezing respiration and well marked cyanosis. Edema of extremities and trunk. Ascites. Arterial O_2 saturation 75.4 per cent
	17.7	36.5			29.3	110.0					139.3	V. cont.	
	16.5	36.7			28.3	101.5					129.8	A. cont.	Considerable subjective improvement; less dyspnea. Edema confined to legs and lower trunk. Ascites persists. Arterial O_2 saturation 88.2 per cent
	17.2	37.7	7.13		30.1	101.6					131.7	V. cont.	
	16.2	35.0			27.2	100.9					128.1	A. cont.	Condition little changed. Arterial O_2 satura'ion 77.8 per cent
	16.2	35.0			24.7	102.8					127.5	V. cont.	
18668	13.8	31.2			32.0							A. cont.	Hypertension; heart failure. Orthopnea and cyanosis. Râles scattered throughout chest. Arterial O_2 saturation 87.4 per cent
	14.6	32.5			32.7							V. cont.	
	10.1	22.9			31.7	90.4					122.1	A. cont.	Two weeks later. Condition unchanged. Arterial O_2 saturation 77.1 per cent
	10.5	23.6			33.0	89.7					122.7	V. cont.	
18292	15.4	33.7			21.4	108.2					129.6	A. cont.	Arteriosclerotic heart disease; heart failure. Right hydrothorax; pulmonary congestion and bronchitis. Increasing subcutaneous edema. Temperature 101°F. Arterial O_2 saturation 80.1 per cent
	14.8	32.5	6.87		24.5	106.2					130.7	V. cont.	

TABLE 2—*Concluded*

Patient	Oxygen capacity	Cell volume	Protein (1)		HCO_3 (2)	Cl (3)	PO_4 (4)	Total acid 1+2+3+4 (5)	Base (6)	Organic acid 6−5 (7)	HCO_3+Cl 2+3	Treatment of blood	Remarks
	vols. per cent	*vols. per cent*	*per cent*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*	*mM.*		
18292	19.1	39.4			28.2	101.5					129.7	A. cont.	Nine days later. Edema and hydrothorax gone; temperature 97°F.; pulmonary signs persist. Arterial O_2 saturation 85.1 per cent
cont.	19.3	39.8	7.47		30.9	101.1					132.0	V. cont.	
	15.3	32.9			21.8	102.4					124.2	A. cont.	Twenty-one days later. Decompensation has recurred, again attended by respiratory infection, edema and hydrothorax. Arterial O_2 saturation 77.2 per cent
	15.4	33.8			22.7	106.5					129.2	V. cont.	
18267	18.3	38.6			29.0	100.1					129.1	A. cont.	Rheumatic heart disease with mitral and aortic lesions. Possibly congenital heart disease. No dyspnea nor edema, but striking cyanosis and enlarged liver. Vital capacity 2900 cc. Arterial O_2 saturation 85.2 per cent
	19.2	39.2	6.30		29.7	100.0					129.7	V. cont.	

* By new gasometric technique.

† By Cullen colorimetric method.

s For protein determination marked s serum and not plasma was employed.

of Cl. This retention of Cl appears to have been attended in both instances by a dilution of the blood, as if the latter had shared in the edema. At least this offers the simplest explanation for the alterations of oxygen-capacity, cell-volume and plasma proteins.

The last case, no. 18267, raises some points of peculiar interest. The patient apparently had severe healed rheumatic valvular lesions. In spite of the absence of symptoms of decompensation and the facts that his lungs were entirely clear and his vital capacity comparatively large, he presented such striking cyanosis that a congenital heart lesion was suspected. The cyanosis was associated with an arterial oxygen saturation of only 85 per cent. The association of arterial anoxemia with normal lungs is itself presumptive evidence that, in spite of the history and physical signs the patient did have a congenital heart lesion which permitted part of the blood to pass from the right heart to the general circulation without traversing the lungs. Pearce (9), Lundsgaard and Van Slyke (9) and others have pointed out that it is impossible under these circumstances for an individual to effect complete oxygenation of the blood by increasing the pulmonary ventilation. On the other hand by hyperpnea more than the usual amount of CO_2 can be removed from the blood that passes through the lungs to make up for the excess CO_2 contributed by the unaërated blood. The carbon dioxide tension of the arterial blood of the greater circulation would, in this case, be normal, while the oxygen tension would be somewhat reduced. The possibility that compensation might be aided, as it is when the lungs are affected, by an increase of bicarbonate, is not precluded by this theory. This would, of course, afford an explanation of the high CO_2 in this case if the patient actually had congenital heart disease.

SUMMARY AND CONCLUSIONS

Cardiac patients with high bicarbonate regularly present evidences of pathologic changes in the lungs which interfere with the proper ventilation of the blood, and deficient oxygenation of the arterial blood. The high bicarbonate is probably invoked in these cases as it is in pulmonary emphysema and other diseases by accumulation of carbon dioxide in the blood. It permits the tension of CO_2 to be maintained at a higher level than usual without reduction of pH and thus facilitates discharge of the CO_2 by the lungs.

If the bicarbonate rises excessively chloride is forced to recede.

It is suggested that high bicarbonate and low chloride is the typical result of conditions that produce anoxic anoxemia and, at the same time, interfere with the discharge of CO_2 from the pulmonary circulation. To this condition the term "asphyctic" anoxemia has been applied to distinguish it from the anoxemia produced by reduction of oxygen tension in the inspired air which leads to overventilation, bicarbonate deficiency and hyperchloremia.

If the typical picture of high CO_2 and low Cl is not found in diseases with pulmonary lesions that lead to asphyctic anoxemia, it may be inferred that other disturbances due to unrelated factors have modified the electrolyte equilibrium. Illustrations are given of such compromises due to chloride increases or total electrolyte deficiency.

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