Journal of Hyperbaric Medicine, Vol. 1, No. 2, Spring 1986

Treating Acidemia in Carbon Monoxide Poisoning May Be Dangerous

E. Converse Peirce, II

Department of Surgery, Mount Sinai School of Medicine of the City University of New York and the North American Hyperbaric Center, City Island, NY

Peirce EC. Treating acidemia in carbon monoxide poisoning may be dangerous. *J Hyperbaric Med* 1986; 1(2)87–97.—In addition to reducing the available hemoglobin (Hb) by tightly combining with it, CO poisoning produces a substantial left shift in the oxyhemoglobin dissociation curve. This reduces the usual ready O_2 release in the tissue and is a major factor in the production of CNS hypoxia and damage. An acidemia, often present in severe CO poisoning, especially if there are also burns, moderates the left curve shift and may, therefore, facilitate tissue oxygenation. Usual emergency room regimens routinely employ alkali in the treatment of acidemia, and there is a tendency to give large amounts of sodium bicarbonate to a patient in coma with a substantial acidemia. This is potentially a very dangerous practice in CO victims as an alkalemia, or even a reduction in an acidemia, will further shift the O_2 dissociation curve and may aggravate any hypoxia, perhaps ensuring CNS damage. This paper gives the mathematical details of the curve shift produced by CO and pH change, and explains how to combine the two so that their total magnitude and the effect on available tissue O_2 can be known.

carbon monoxide poisoning, oxyhemoglobin dissociation curve, acid base, temperature, O_2 availability

Introduction

Patients severely poisoned with CO may develop very substantial metabolic acidosis and a considerable drop in their arterial pH. Such patients generally present in coma, respond poorly to therapy even when vigorously treated, and are considered to have a poor prognosis. O_2 is utilized as a specific therapy for the CO intoxication since it reduces hypoxia and hastens uncoupling of CO from hemoglobin and respiratory elimination of CO. Other treatments are given in emergency rooms, frequently following standard protocols, depending on the metabolic and cardiopulmonary status of the patient. If the pH is depressed (acidemia), sodium bicarbonate ($NaHCO_3$) is commonly given, sometimes in large amounts. Although it has become clear from experience in cardiopulmonary resuscitation that excessive alkali administration may jeopardize an otherwise successful effort, this is not widely known. The purpose of this paper is to review the effect of CO and pH on the oxyhemoglobin dissociation curve (O_2Hb curve) and on O_2 transport and to caution that raising the pHa may be dangerous.

The Normal Oxyhemoglobin Dissociation Curve (1)

Po_2 and So_2 values to construct most of a normal O_2Hb curve (Fig. 1) are shown in the left of Table 1. The P_{50} is 26.6 mmHg. On the average, in the normal subject at rest, the venous saturation and Po_2 do not fall below 70% and 37 mmHg, respectively. O_2 exchange and transport are accomplished by loading and unloading only about the top 25% of the hemoglobin. Since the cellular Po_2 is at most a few millimeters of mercury, the O_2 gradient from the capillary to the cell is substantial. This arrangement provides considerable O_2 reserve. O_2 transport and exchange are readily enhanced. A severalfold increase in cardiac output occurs on exercise even in sedentary people. In athletes this may be as much as six- or sevenfold. (In severe anemia an increase in cardiac output compensates for the decrease in Hb concentration). Venous Po_2 need only fall from about 40 to 27 mmHg to double the O_2 extraction. Greater alveolar ventilation increases the diffusion gradients for O_2 and carbon dioxide so that arterial saturation is little reduced with exercise.

The Haldane Effect (Table 1) (2)

The combination of CO with hemoglobin shifts the O_2Hb curve to the left of the normal one (Fig. 1). This change is substantial even at a fairly low

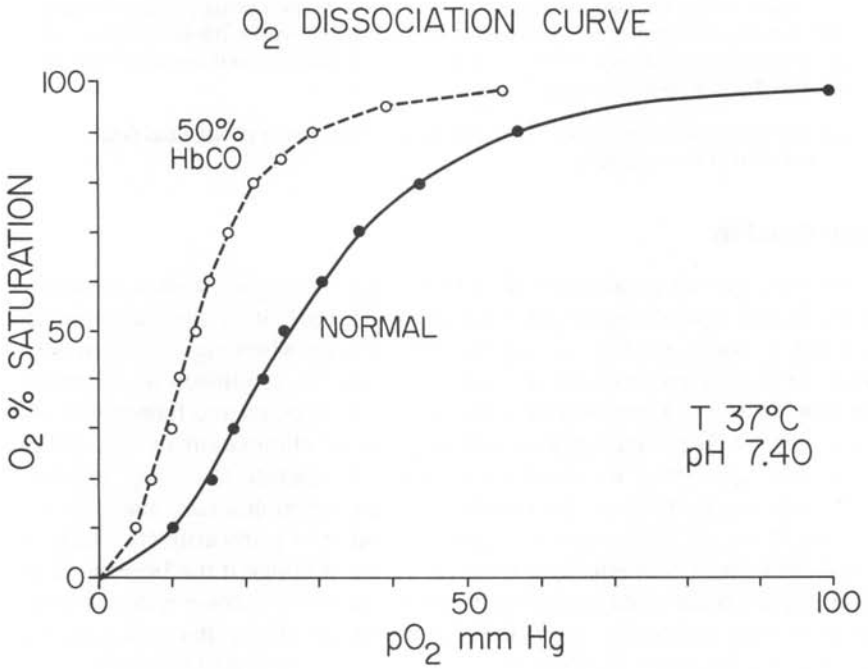

FIG. 1—The normal O_2 dissociation curve and the curve shift with 50% COHb (HbCO) are shown. *See* text for details. (Reprinted from *Surgery* (7) by permission.)

Table 1: The effect of carboxyhemoglobin COHb on the O_2Hb curve (2)

Normal Values		[COHb]	75	70	60	50	40	30	25	20
So_2	Po_2 mmHg	f[a]	3.6	3.04	2.38	2.00	1.67	1.45	1.40	1.27
95	75.0	20.8		24.7	31.5	37.5	44.9	51.7	53.6	59.1
90	58.0	16.1		19.1	24.4	29.0	34.7	40.0	41.4	45.7
80	44.7	12.4		14.7	18.8	22.4	26.8	30.8	31.9	35.2
70	37.0	10.3		12.2	15.5	18.5	22.2	25.5	26.4	29.1
60	31.3	8.7		10.3	13.2	15.7	18.7	21.6	22.4	24.6
50	26.6	7.4		8.8	11.2	13.3	15.9	18.3	19.0	20.9
40	22.8	6.3		7.5	9.6	11.4	13.7	15.7	16.3	18.0
30	19.3	5.4		6.3	8.1	9.7	11.6	13.3	13.8	15.2
20	15.4	4.3		5.1	6.5	7.7	9.2	10.6	11.0	12.1
15	13.1	3.6		4.3	5.5	6.6	7.8	9.0	9.4	10.3
10	10.4	2.9		3.4	4.4	5.2	6.2	7.2	7.4	8.2
$Sv\dot{O}_2$[b]		85.5		82.0	65.5	57.5	46.0	37.0	35.0	29.0
$_{Max}\dot{V}O_2$[c]		33.0		49.2	125.8	193.6	295.2	401.9	444.2	517.6

[a] f = Po_2 correction factor for COHb.

[b] $S\dot{v}O_2$ assumes a venous Po_2 = 15 mmHg.

[c] $_{Max}\dot{V}O_2$ assumes [Hb] = 15 g, cardiac output = 5 liter/min, 1.35 ml O_2/g O_2Hb, arterial Po_2 = 100 mmHg (full saturation), and venous Po_2 = 15 mmHg.

carboxyhemoglobin concentration ([COHb]). The effect is to increase the tightness with which the hemoglobin (Hb) in the blood binds O_2. For any given O_2 saturation, the P_{O_2} will be lower than usual. Tissue hypoxia may be produced by the increased affinity of the O_2 and the hemoglobin. This has been named "affinity hypoxia." The curve shift is most easily described by the change in the P_{50}.

Construction of the shifted curve does not require any assumptions regarding the mechanism of Hb and CO combination or the relative affinities of Hb for CO and O_2 (2).

$$\text{True } P_{O_2} = \text{Equivalent } P_{O_2}/(1 + [\text{COHb}]/[\text{O}_2\text{Hb}]) \qquad (1)$$

where true P_{O_2} is the value on the shifted curve that corresponds to the $[O_2Hb]$. For this only the Hb available for O_2 binding is used (this is [Hb]−[COHb]). Equivalent P_{O_2} is the value on the original O_2Hb curve (normal or shifted by pH or temperature, etc.) that corresponds to the sum of the [COHb] and the $[O_2HB]$. For this the total Hb is used. $[O_2Hb]$ is the percent concentration of O_2Hb; [COHb] is the percent concentration of COHb.

Example: In Fig. 1 the original curve is normal and the [COHb] is 50%. Only 50% of the original Hb is available for O_2 binding. At the P_{50} on the new (shifted) curve the P_{O_2} is calculated by Eq. *1*. The equivalent P_{O_2} corresponds to a saturation of 75% (the [COHb] = 50% and the $[O_2Hb]$ = 25% as only half of the remaining Hb carries O_2). Its value is 40 mmHg. The true P_{O_2} is, therefore, 40/3 or 13.3 mmHg.

Others have derived correction factors for the P_{50} when the O_2Hb curve has been shifted by the presence of COHb. A recent report gives the following equation (3):

$$\log P_{50x} = \log P_{50c} - fX \qquad (2)$$

where P_{50x} = the P_{50} at a [COHb] of X

P_{50c} = the P_{50} of the blood containing no COHb
f = the correction factor (here 0.00848)
X = the COHb.

The correction factor (f) has been variously reported to be 0.006 (2, 4) and 0.007 (5, 6). These and the corresponding P_{50} values for [COHb] = 50% are shown in Table 2.

The Bohr Effect (Table 3, Fig. 2) (1)

The tightness of O_2 binding to Hb is modified by the pH. When blood is more acid than 7.40, the O_2Hb curve is shifted to the right. A greater P_{O_2} is required to load the Hb in the lung but O_2 is released to the tissue at a higher P_{O_2}. This may be a useful mechanism in shock, etc., because it facilitates better tissue O_2 extraction. Conversely, a higher pH shifts the curve to the left and

Table 2: Correction factors and P_{50} values for blood containing COHb (3)

Source	f	P_{50} mmHg
(2,4)	0.006	13.3
(5,6)	0.007	11.9
(3)	0.00848	10.0

causes O_2 to be bound more tightly. Although this somewhat facilitates the uptake of O_2 in the lung, the effect is generally small as the O_2Hb curve is very flat at the top, and large changes in P_{O_2} produce only small changes in saturation. In the tissue, however, O_2 release is impeded. If the shift is large, hypoxia may result. Too zealous use of alkali in cardiopulmonary resuscitation may enhance brain damage by increasing cerebral hypoxia.

The Combined Haldane and Bohr Effects

The shifts of the O_2Hb curve produced by COHb (Haldane) and by pH (Bohr) are additive. To determine the combined effect it is only necessary to calculate sequentially. This is most easily appreciated by taking an example:

A 74-yr-old woman was removed in coma from a fire and rapidly transported to a large metropolitan hospital. In the emergency room she was found to be in deep coma and with severe burns including the airway. The arterial pH was 6.90 and the COHb 57%. She was intubated and vigorous resuscitative measures were taken including the administration of large amounts of $NaHCO_3$ IV (perhaps 10 ampoules). Although given hyperbaric therapy 90 min after reaching the hospital she did not respond and died soon afterwards. An estimate of the maximum COHb level (at the time of removal from the fire) is 70.2%.

The pH response to the alkali is not known, but for the purposes of this calculation is assumed not to have exceeded 7.40. Figure 2 and Table 4 show the following:

a. The normal O_2Hb curve.
b. The predicted curve at pH 6.90 with no COHb.
c. The curve at pH 6.90 and a [COHb] of 57%.
d. The curve for a [COHb] of 57% but with the pH returned to 7.40.

A vertical line is drawn for P_{O_2} = 15 mmHg. This represents a reasonable value for the lowest predicted venous P_{O_2}. From this are calculated the corresponding O_2 consumptions ($\dot{V}_{O_2}$'s) assuming a [Hb] of 13.5 g percent (13.5 g/dl) and a cardiac output of 5 liters/min.

To determine the net effect of both pH and COHb, the correction factor for the appropriate pH should be multiplied by the correction factor for COHb. For the case example just given Table 4 shows the P_{50} values, the saturation at a P_{O_2} of 15 mmHg, and the maximum available O_2 at that P_{O_2} for the curves

Table 3: The effect of pH on the oxyhemoglobin dissociation curve (1)

	pH	8.1	8.0	7.8	7.6	7.4	7.2	7.0	6.9
So_2%	f[a]	2.21	1.94	1.55	1.25	1.00	0.80	0.64	0.57
98		49.8	56.7	71.0	88.0	110.0	137.5	171.9	193.0
95		33.9	38.7	48.4	60.0	75.0	93.8	117.2	131.6
90		26.2	29.9	37.4	46.4	58.0	72.5	90.6	101.8
80		20.2	23.0	28.8	35.8	44.7	55.9	69.8	78.4
70		16.7	19.1	23.9	29.6	37.0	46.3	57.8	64.9
60		14.2	16.1	20.2	25.0	31.3	39.1	48.9	54.9
50		12.0	13.7	17.2	21.3	26.6	33.3	41.6	46.7
40		10.3	11.8	14.7	18.2	22.8	28.5	35.6	40.0
30		8.7	9.9	12.5	15.4	19.3	24.1	30.2	33.9
20		7.0	7.9	9.9	12.3	15.4	19.3	24.1	27.0
15		5.9	6.8	8.5	10.5	13.1	16.4	20.5	23.0
10		4.7	5.4	6.7	8.3	10.4	13.0	16.3	18.2
Svo_2[b]		63.0	56.0	41.0	29.0	18.0	13.0	9.0	8.0
Sao_2[c]		99.0	99.0	99.0	98.2	97.5	95.9	92.0	89.0
$_{Max}\dot{V}O_2$[d]		328	392	529	631	724	755	756	738

[a] f = Po_2 correction factor for pH.

[b] $S\dot{v}o_2$ values are at a venous Po_2 = 15 mmHg.

[c] Sao_2 values are at an arterial Po_2 = 100 mmHg.

[d] $_{Max}\dot{V}O_2$ assumes [Hb] = 13.5 g, cardiac output = 5 liter/min, 1.35 ml O_2/g O_2Hb, arterial Po_2 = 100 mmHg, and venous Po_2 = 15 mmHg.

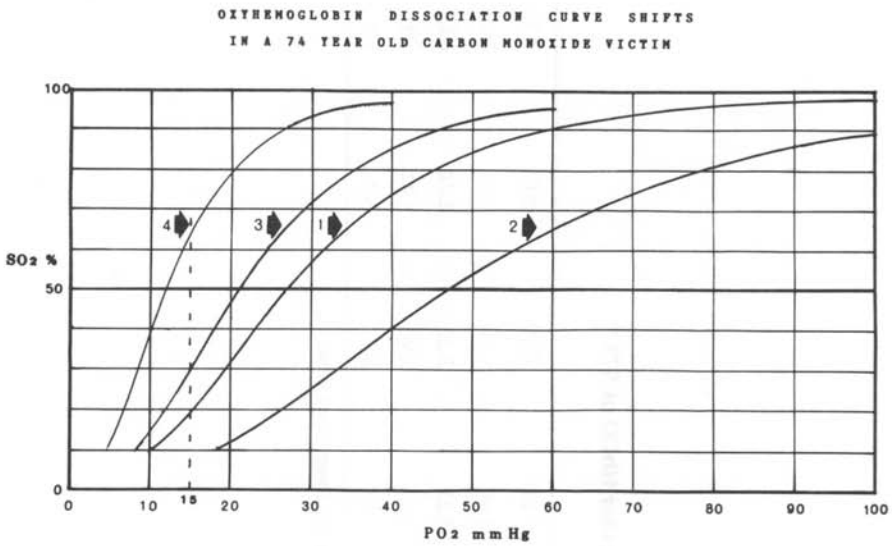

FIG. 2—Curves pertinent to the example showing the cumulative result of the Haldane (CO) and Bohr effects (pH). *(1)*, shows the "normal" O_2 dissociation curve. This means that the pH is 7.40, there is no COHb in the blood, the temperature is 37°C, and no other factors would cause a shift in the P_{50}. *(2)*, the curve from blood shown in *(1)* but after the pH has been decreased to 6.90 as might occur with a severe metabolic acidosis with no COHb in the blood. *(3)*, the curve from a 74-yr-old comatose woman with a [COHb] of 57% and an arterial pH of 6.9. *(4)*, the predicted curve for the same patient after administration of enough $NaHCO_3$ to bring the arterial pH to 7.40. *See* text and Table 4 for further details.

Table 4: Presentation of data from example: HbCO and pH corrections (*See* Fig. 2)

	Status				
Curve No.	pH	[HbCO] %	P_{50} mmHg	Sa_{O_2} at 15 mmHg[a]	$\dot{V}_{O_2}$ ml/min at 15 mmHg
1	7.4	0	26.6	19	820
2	6.9	0	46.7	8	932
3	6.9	57	21.0	29	337
4	7.4	57	12.0	64	141

[a]Venous P_{O_2}.

Table 5: Calculation of P_{50} at different pH values for HbCO of 57%[a]

pH	7.40	7.50	7.60	7.70	7.80	7.90	8.00	8.10
f(pH)	1.00	1.11	1.25	1.39	1.55	1.73	1.94	2.21
f(CO) (57%)	2.22	2.22	2.22	2.22	2.22	2.22	2.22	2.22
f(pH)xf(CO)	2.22	2.46	2.78	3.09	3.44	3.84	4.31	4.91
P_{50} mmHg	12.0	10.8	9.6	8.6	7.7	6.9	6.2	5.4

[a]The P_{50} for normal blood at 7.40 = 26.6 mmHg. Method: divide the normal P_{50} at pH 7.40 by the composite f value.

shown in Fig. 2. Table 5 shows the manner in which the pH and O_2Hb factors are used to determine the P_{50} at different pH values.

Temperature effect (1)

The O_2Hb curve is also shifted by temperature, the O_2Hb bond becoming tighter as the temperature is lowered from 37°C. If O_2 need is unchanged, an "affinity hypoxia" could develop. However, as temperature falls there is usually a drop in metabolic demand so that the curve shift is not very important (Table 6). This is true in accidental hypothermia during alcoholic or barbiturate intoxication and in medical hypothermia under general anesthesia. If the subject is fully responsive when exposed to cold, shivering may greatly increase the O_2 demand but this also delays or prevents the temperature change. To determine the net effect of the curve shift with temperature change, the metabolic status of the subject must be known.

To correct for any two of the pH, [COHb], T°C or for all 3, multiply the appropriate factors and divide the uncorrected P_{50} by the composite factor.

Discussion

Carbon monoxide poisoning, unlike exercise, is not, in clinical situations, reliably accompanied by much increase in cardiac output or ventilation (7). Although CO may produce profound hypoxia, the usual mechanisms operative in exercise, anemia, or stress are not strongly invoked. The more severe the CO poisoning, the less the stimulation. Furthermore, the common mechanism of increased O_2 extraction does not come into play; venous P_{O_2} and saturation rise because, when COHb is present, O_2Hb has a much increased affinity for O_2. Increased extraction is simply not possible. "... The percent of CO is not as important as the resultant P_{50} in determining the cardiovascular response to CO" (8).

A high pH, a low temperature, or COHb all shift the O_2Hb curve to the left and make it more difficult for O_2 to be extracted from the blood as it passes through the tissue. Of these factors the shift caused by COHb is the most serious since it is accompanied by a reduction in the available hemoglobin. Severe hypoxia may be expected when [COHb] reaches about 50% (Table 1). When the tissue P_{O_2} becomes very low, a point is reached where CO combines with cytochrome oxidase a_3 and disrupts the O_2 transport chain. If the pH is somewhat low (acidemia), the left shift caused by the [COHb] is reduced and the hypoxia may be moderated. Since the acidemia seems to be protective, alkali should rarely be administered in CO poisoning. If alkali is given, the pH should be carefully monitored to provide early warning of any elevation. Because CO has a direct cardiac effect and may lead to circulatory failure, a condition for which alkali is so commonly given, it requires special knowledge and commitment to avoid the pitfall of automatic infusion of IV $NaHCO_3$. The combination of severe CO poisoning and an alkalemia (or even a moderation

Table 6: The effect of temperature on P_{50} and available P_{O_2}

T °C	40	37	36	35	34	3	32	31	30	25	20
f (C)	0.85	1.00	1.06	1.12	1.18	1.25	1.32	1.40	1.47	1.95	2.29
P_{50}	31.3	26.6	25.2	23.8	22.5	21.3	20.2	19.1	18.1	13.6	11.6
$_{Max}\dot{V}O_2{}^a$	871	820	800	775	749	724	689	658	628	446	344

[a] $_{Max}\dot{V}O_2$ assumes [Hb] = 13.5 g, cardiac output = 5 liter/min, 1.35 ml O_2/g O_2Hb, arterial P_{O_2} = 100 mmHg (full saturation), and venous P_{O_2} = 15 mmHg.

of an acidemia) may be followed by irreversible brain damage or death from aggravated hypoxia. Physicians and others working in emergency rooms should become very familiar with the large, and potentially dangerous, O_2Hb curve shifts that occur with CO poisoning and with resuscitation.

Conclusion

Carbon monoxide reduces the Hb available to carry O_2, shifts the O_2Hb curve to the left producing "affinity hypoxia," and directly poisons the tissue. An increase in the pH further shifts the curve and increases the hypoxia. The pH effect may be very large and dangerous. For this reason, the administration of alkali should rarely be undertaken in CO poisoning. Other usual emergency measures should be carried out, but the only direct therapy is O_2 administration. In cases with CNS signs, 100% O_2 should be given continuously and followed, if available, by hyperbaric O_2 at 2 to 3 ATA for several CO half lives (7, 9).

References

1. Severinghaus JW. Oxyhemoglobin dissociation curve. In: Handbook of respiration and circulation. Bethesda, MD: Federation American Societies Experimental Biology; 1971:205.
2. Roughton FJW; Darling RC. The effect of carbon monoxide on the oxyhemoglobin dissociation curve. Am J Physiol 1944; 141:17–31.
3. Rovida E, Niggeler M, Carlone S, Samaja M. Carboxyhemoglobin and oxygen affinity of human blood. Clin Chem 1984; 30:1250–1251.
4. Goldsmith JR, Landaw SA. Carbon monoxide and human health. Science 1968; 162:1352–1359.
5. Okada Y, Tyuma I, Ueda Y, Sugimoto T. Effect of carbon monoxide on equilibrium between oxygen and hemoglobin. Am J Physiol 1976; 230:471–475.
6. Hlastala MP, McKenna HP, Franada RL, Detter JC. Influence of carbon monoxide on hemoglobin-oxygen binding. J Appl Physiol 1976; 41:893–899.
7. Peirce EC II. Carbon monoxide poisoning: Experimental hypothermic and hyperbaric studies. Surgery 1972; 72:229–237.
8. Koehler R, Traystman DJ, Rosenberg AA, Hudak ML, Jones MD Jr. Role of O_2-hemoglobin affinity on cerebrovascular response to CO hypoxia. Am J Physiol 1983; 245:H1019–1023.
9. Peirce EC II. Notes on carbon monoxide (CO) poisoning, especially the importance of vigorous early therapy. Emergency Medical System City of New York. Hyperbaric Oxygen Committee Rep. May 10, 1985.

Correspondence to: E. Converce Peirce, II, MD, Department of Surgery, Mt. Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029.