Carboxyhemoglobin Half-life in Carbon Monoxide-Poisoned Patients Treated With 100% Oxygen at Atmospheric Pressure*

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Study objectives: There are large reported differences for the carboxyhemoglobin (COHb) half-life (COHb t_{1/2}) in humans breathing 100% atmospheric O₂ following CO inhalation in tightly controlled experiments compared to the COHb t_{1/2} observed in clinical CO poisoning (range, 36 to 131 min, respectively). Other reports have suggested that the COHb t_{1/2} may be affected by gender differences, age, and lung function. We wished to test the hypothesis that the COHb t_{1/2} might also be influenced by CO poisoning vs experimental CO exposure, by a history of loss of consciousness (LOC), concurrent tobacco smoking, and by PaO₂. The purpose of the present study was to measure the COHb t_{1/2} in a cohort of CO-poisoned patients and to determine if those listed factors influenced the COHb t_{1/2}.

Design: Retrospective chart review from 1985 to 1995. We calculated the COHb t_{1/2} of CO-poisoned patients who were treated with high-flow supplemental atmospheric pressure O₂ delivered by nonrebreather face mask or endotracheal tube.

Setting: Hyperbaric medicine department of a tertiary-care teaching hospital.

Patients: Of 240 CO-poisoned patients, 93 had at least two COHb measurements > 2% (upper limit of normal) with recorded times of the measurements, permitting calculation of the COHb t_{1/2}.

Results: The COHb t_{1/2} was 74 ± 25 min (mean ± 1 SD) with a range from 26 to 148 min. By stepwise multiple linear regression analysis, the PaO₂ influenced the COHb t_{1/2} (R^2 = 0.19; p < 0.001), whereas the COHb t_{1/2} was not influenced by gender, age, smoke inhalation, history of LOC, concurrent tobacco smoking, degree of initial metabolic acidosis (base excess), or initial COHb level.

Conclusions: The COHb t_{1/2} of 93 CO-poisoned patients treated with 100% O₂ at atmospheric pressure was 74 ± 25 min, considerably shorter than the COHb t_{1/2} reported in prior clinical reports (approximately 130 ± 130 min) and was influenced only by the patient's PaO₂. (CHEST 2000; 117:801–808)

Key words: carbon monoxide elimination; carbon monoxide poisoning; carboxyhemoglobin elimination; carboxyhemoglobin half-life; carboxyhemoglobin kinetics

Abbreviations: COHb = carboxyhemoglobin; COHb t_{1/2} = carboxyhemoglobin half-life; ET = endotracheal tube; FIO₂ = fractional concentration of oxygen; k = decay constant; LOC = loss of consciousness

The carboxyhemoglobin (COHb) half-life (COHb t_{1/2}) in individuals with CO poisoning who are treated with 100% O₂ is frequently quoted as 80 min,¹,² which is taken from studies conducted by Peterson and Stewart,³ in which they averaged data from two healthy volunteers breathing O₂ by mask after experimental CO exposure. Peterson and Stewart did not measure the COHb t_{1/2} of patients who were accidentally or intentionally poisoned with CO. Data from other experimental CO-exposure studies...
have shown the COHb t\textsubscript{1/2} to be considerably shorter than that found by Peterson and Stewart (Table 1).\textsuperscript{3} Limitations of the previous studies include small sample sizes and incompletely reported statistics, so the conclusions drawn may not be supported by the data. Furthermore, extrapolating results from experimental studies of CO elimination to patients with CO poisoning might produce different results.

Comparing data from prior experimental and clinical studies suggests that the COHb t\textsubscript{1/2} of patients with CO poisoning is longer than the COHb t\textsubscript{1/2} of subjects with experimental CO exposures (Table 1). Several years ago, we began collecting COHb data and calculating the COHb t\textsubscript{1/2} of patients with CO poisoning. We observed that the COHb t\textsubscript{1/2} was generally shorter than that reported in other studies of clinical CO poisoning. Since many of the patients in our CO database had two or more COHb levels, we decided to perform a retrospective analysis to calculate the COHb t\textsubscript{1/2} of CO-poisoned patients treated with O\textsubscript{2} provided by nonrebreather face mask or endotracheal (ET) tube.

We hypothesize that the COHb t\textsubscript{1/2} of patients with CO poisoning will be longer than the COHb t\textsubscript{1/2} measured in human volunteers breathing CO while following a research protocol due to the following:

1. a greater CO burden in poisoned patients, with CO accumulation in tissues as well as onto hemoglobin, resulting in a longer time for COHb elimination;
2. reduced COHb elimination due to an increase in right-to-left intrapulmonary shunting caused by aspiration and/or smoke inhalation; and
3. a lower fractional inspired oxygen concentration (F\textsubscript{IO\textsubscript{2}}) in poisoned patients treated with supplemental O\textsubscript{2} than in volunteers breathing 100% O\textsubscript{2} as part of the research protocol (ie, a patient with CO poisoning is often treated with a nonrebreather face mask, which does not deliver 100% O\textsubscript{2}).

Based on other researchers’ prior studies, we also expected to find that the COHb t\textsubscript{1/2} should be influenced by the PaO\textsubscript{2} as well as by demographic and poisoning-related factors such as gender, age, or concomitant smoke inhalation. It is reasonable to postulate that concurrent tobacco smoking might influence CO elimination. We also hypothesized that the COHb t\textsubscript{1/2} might be linked to markers of the severity of CO poisoning, such as the initial degree of acidosis and/or a history of loss of consciousness (LOC). There is conflicting information regarding whether the COHb t\textsubscript{1/2} is affected by the initial COHb level.\textsuperscript{9,10} Therefore, in this study, we assessed whether the COHb t\textsubscript{1/2} was influenced by the patients’ PaO\textsubscript{2}, gender, age, smoke inhalation, concurrent tobacco smoking, degree of initial acidosis (ie, base excess), history of LOC, or initial COHb level.

### Materials and Methods

Medical records from 240 patients with acute CO poisoning evaluated at the Hyperbaric Medicine Department of the LDS Hospital (1985 to January 26, 1995) were reviewed. Because this study was retrospective, the Institutional Review Board on human research at the LDS Hospital exempted this study from the requirement of informed consent from the patients. Patients having at least two actual measurements of both COHb and the times of those measurements were selected (n = 93). For inclusion in the study, all COHb levels (including the final COHb levels) had to be > 2% (upper limit of normal).

All patients breathed O\textsubscript{2} by nonrebreather face mask (or received ventilation with 100% O\textsubscript{2} if intubated) at atmospheric pressure (647 mm Hg at 1,500 m above sea level). Seventy-nine patients were breathing O\textsubscript{2} by nonrebreather face mask or ET tube at the time of all COHb measurements. Fourteen patients were breathing air until the initial COHb level was measured, and when the COHb was found to be elevated, they were immediately given O\textsubscript{2} delivered by a nonrebreather face mask. For these 14 patients, we calculated what the COHb level would have been 15 min after the initial COHb level. Since the COHb t\textsubscript{1/2} of CO-poisoned patients is unknown, we used the 320 min COHb t\textsubscript{1/2} for breathing air derived from experimental human data. This calculated COHb level, and the corresponding time of the COHb measurement, minus 15 min, were used for the subsequent COHb t\textsubscript{1/2} calculations (we assumed that approximately 15 min of time elapsed between the time of the initial COHb and the institution of face-mask O\textsubscript{2}). Although the expected reduction in the initial COHb level with patients

### Table 1—Literature Summary of COHb t\textsubscript{1/2} in Humans Breathing O\textsubscript{2}*

<table>
<thead>
<tr>
<th>Reference</th>
<th>Condition</th>
<th>Year</th>
<th>n\textsuperscript{1}</th>
<th>Sex</th>
<th>Average Age, yr</th>
<th>COHb t\textsubscript{1/2}, min</th>
<th>Range, min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pace et al\textsuperscript{5}</td>
<td>Experimental</td>
<td>1950</td>
<td>10</td>
<td>M</td>
<td>27.1</td>
<td>47</td>
<td>?</td>
</tr>
<tr>
<td>Pace et al\textsuperscript{5}</td>
<td>Experimental</td>
<td>1950</td>
<td>5</td>
<td>F</td>
<td>26.6</td>
<td>36</td>
<td>?</td>
</tr>
<tr>
<td>Peterson and Stewart\textsuperscript{3}</td>
<td>Experimental</td>
<td>1970</td>
<td>2</td>
<td>M</td>
<td>?</td>
<td>80.3</td>
<td>?</td>
</tr>
<tr>
<td>Burney et al\textsuperscript{16}</td>
<td>Clinical</td>
<td>1982</td>
<td>33</td>
<td>Both</td>
<td>?</td>
<td>137</td>
<td>?</td>
</tr>
<tr>
<td>Myers et al\textsuperscript{14}</td>
<td>Clinical</td>
<td>1984</td>
<td>19</td>
<td>?</td>
<td>?</td>
<td>131 ± 133</td>
<td>27.1-462.1</td>
</tr>
<tr>
<td>Pierce and Bensky\textsuperscript{13}</td>
<td>Clinical</td>
<td>1987</td>
<td>12</td>
<td>?</td>
<td>?</td>
<td>126 ± 246</td>
<td>?</td>
</tr>
<tr>
<td>Jay et al\textsuperscript{15}</td>
<td>Experimental</td>
<td>1995</td>
<td>12</td>
<td>Both</td>
<td>33.9</td>
<td>90.1 ± 18.11</td>
<td>?</td>
</tr>
</tbody>
</table>

*M = male; F = female; ? = unknown.

1 Of total (n = 93), 29 were experimental and 64 were clinical.

1 Expressed as mean ± 1 SD.
breathing air for 15 min is negligible (COHb t1/2 = 320 min).\(^3\) for these 14 patients we attempted to calculate the COHb t1/2 with \(O_2\) inhalation as accurately as possible. In these 14 patients, nonrebreather face-mask (or ET tube) \(O_2\) was started 15 min after their initial COHb measurement and was continuous through all subsequent COHb measurements. All COHb measurements were obtained prior to hyperbaric \(O_2\) therapy.

COHb measurements were performed with a CO oximeter (IL-282; Instruments Laboratories; Lexington, MA) or with an OSM 3 Hemoximeter (Radiometer; Copenhagen, Denmark). All methemoglobin measurements were ≤ 1%. Each individual patient’s sample set in our institution was analyzed using the same instrument. We cannot determine how many samples were analyzed with the IL-282 or with the OSM 3, since this information was not recorded. The initial COHb was obtained from arterial blood in all patients. For patients with more than two COHb measurements, the COHb levels were from arterial blood. Some of the COHb levels from the patients with only two COHb measurements were obtained from venous blood. Differences in the COHb measurements between the two oximeters could account for errors in the calculation of the COHb t1/2. Individual patient samples were analyzed on the same instrument, but two instruments were used, so it is possible that COHb measurement discrepancies between instruments could contribute to COHb t1/2 errors. We inspected data from the Blood Oximetry Survey for 1998 regarding COHb measurement differences between the IL-282 and the OSM 3.\(^4\) For standards with COHb levels ranging from approximately 8 to 56%, the IL-282 reads approximately 8.6% greater than the OSM 3. If sample pairs were analyzed by the two different instruments, errors of as much as 18% could be introduced into the COHb t1/2 calculation. The percent error between the two instruments was relatively constant from COHb levels ranging from 8 to 56%. Since COHb sample pairs were analyzed by the same instrument, little error in the COHb t1/2 calculation would be expected.

The COHb t1/2 were calculated using the equation: \(C_t = C_0 \times e^{-kt} \), where \(C_t\) denotes the COHb concentration at any time, \(t\); \(C_0\) is the initial COHb concentration at time, 0; and \(k\) is the decay constant. The COHb t1/2 = \(\frac{(t_2 - t_1)}{\ln(2)}(\text{COHb } t_2/\text{COHb } t_1)\) where \(t_2 - t_1\) denotes the time between the two COHb measurements, and \(\ln = \text{natural logarithm}\).\(^5\) We performed a semilogarithmic regression using the natural logarithm of the two or more COHb measurements vs time. The slope of this regression is \(-k\), where \(k\) is the decay constant and the COHb t1/2 = \(\ln(2)/k\). When more than two COHb measurements were available, the \(k\) values were calculated identically using all COHb measurements. Values are expressed as mean values ± 1 standard deviation.

A stepwise multiple linear regression analysis was performed. The independent variables were as follows: \(\text{PaO}_2\), patient’s age, gender, LOC, \(O_2\) delivery method (mask vs ET tube), base excess (degree of metabolic acidosis), and initial COHb level. The dependent variable was the COHb t1/2. A \(p < 0.05\) was considered significant.

Independent \(t\) tests for COHb t1/2 were carried out comparing patients whose ages were < 40 to ≥ 40 years. The COHb t1/2 by smoke inhalation status (due to fire) was handled descriptively (reporting means and standard deviations), because of the small number of smoke inhalation patients (\(n = 4\)). Information regarding smoker status was incomplete; therefore, smoker status was not included in the regression analysis. However, an independent \(t\) test was performed with the available data in order to compare the COHb t1/2 in patients who were tobacco smokers vs nonsmokers. The COHb t1/2 determined from two COHb measurements was compared to the COHb t1/2 determined from more than two COHb measurements using independent \(t\) tests. In those patients who had more than two COHb measurements, we compared the COHb t1/2 derived from all COHb measurements to the COHb t1/2 determined from the first and second COHb measurements by paired \(t\) tests. Similarly, we compared the COHb t1/2 derived from all COHb measurements to the COHb t1/2 determined from the first and last COHb measurements in the same patients by paired \(t\) tests. Differences were considered significant if \(p < 0.05\).

**Table 2—Etiologies of CO Poisoning**

<table>
<thead>
<tr>
<th>Etiologies</th>
<th>(n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accidental</td>
<td>59</td>
</tr>
<tr>
<td>Furnace</td>
<td>21</td>
</tr>
<tr>
<td>Auto</td>
<td>18</td>
</tr>
<tr>
<td>Industrial</td>
<td>9</td>
</tr>
<tr>
<td>Propane buffer</td>
<td>3</td>
</tr>
<tr>
<td>Propane heater</td>
<td>3</td>
</tr>
<tr>
<td>Gas saw</td>
<td>2</td>
</tr>
<tr>
<td>Propane forklift</td>
<td>1</td>
</tr>
<tr>
<td>Charcoal grills</td>
<td>6</td>
</tr>
<tr>
<td>Fires</td>
<td>4</td>
</tr>
<tr>
<td>Water heater</td>
<td>1</td>
</tr>
<tr>
<td>Suicide</td>
<td>34</td>
</tr>
<tr>
<td>Auto</td>
<td>33</td>
</tr>
<tr>
<td>Charcoal grill</td>
<td>1</td>
</tr>
</tbody>
</table>

Results

There were 93 CO-poisoned patients (Table 2) who had two or more COHb measurements > 2% with recorded times between the measurements. The COHb t1/2 for all 93 patients was 74 ± 25 min, with a range from 26 to 148 min (Table 3). By stepwise multiple linear regression, the only independent variable influencing the COHb t1/2 was the \(\text{PaO}_2\) (COHb t1/2 = 106.6 - 0.1 [\(\text{PaO}_2\]; \(R^2 = 0.19; p < 0.001; \text{Fig 1}\). There was no difference in the COHb t1/2 between patients with smoke inhalation (\(n = 4\)) compared to patients without smoke inhalation (\(n = 89\); \(p = 0.59\)), or between tobacco smokers (\(n = 15\)) compared to nonsmokers (\(n = 46\); \(p = 0.382\)). One additional finding was smaller standard deviations for the COHb t1/2 (less variability about the mean COHb t1/2) in our study compared to previous clinical reports (Tables 1, 3).

The COHb t1/2 was shorter in a subgroup of patients whose COHb t1/2 was calculated using more than two COHb measurements compared to the subgroup of patients whose COHb t1/2 was calculated from only two COHb measurements. There were 76 patients with only two COHb measurements (COHb t1/2 = 77 ± 25 min) compared to 17 patients with more than two COHb measurements (COHb t1/2 = 63 ± 23 min; \(p = 0.031\)). In the subgroup of patients with more than two COHb measurements, 10 patients had three COHb measurements, 2 had four COHb measurements, 2 had five COHb measurements, we compared the COHb t1/2 derived from all COHb measurements to the COHb t1/2 determined from the first and second COHb measurements by paired \(t\) tests. Similarly, we compared the COHb t1/2 derived from all COHb measurements to the COHb t1/2 determined from the first and last COHb measurements in the same patients by paired \(t\) tests. Differences were considered significant if \(p < 0.05\).
measurements, and 3 had six COHb measurements. In the subgroup with more than two COHb measurements, we found no significant differences between the calculated COHb t1/2 using the first and second COHb measurements or the first and last COHb measurements and the COHb t1/2 calculated from all of their COHb measurements.

There was no significant difference in the PaO2 between patients breathing supplemental O2 by nonrebreather face mask or by ET tube (p = 0.648; Table 4). There were no differences in the PaO2 between patients with smoke inhalation and those without (p = 0.751), and between patients who had LOC and those who did not have LOC (p = 0.105; Table 3).

### DISCUSSION

The COHb t1/2 in our patients was longer than the COHb t1/2 in one experimental study, but shorter than that in the other two experimental studies (Tables 1, 3). Prior clinical reports of the COHb t1/2 in patients with acute CO poisoning have demonstrated COHb t1/2 that were considerably longer, with a wider distribution about the mean COHb t1/2 than we observed in our study (Tables 1, 3). One explanation for this difference might be that the other studies had smaller sample sizes, where a greater variability might occur. Another explanation may be the etiology of the poisoning, poisoning severity, underlying health of the patients, and the amounts of O2 that the patients breathed in previous studies might have been different than in our patients. It is also possible that the times between COHb measurement used to calculate the COHb t1/2 were longer in the other clinical reports than in our study, and the final COHb values in those studies might have been normal. Once a normal (COHb ≤ 2%) or baseline COHb value is reached, it will be maintained indefinitely. The final COHb values used to calculate the COHb t1/2 in the other clinical reports are not stated; therefore, it is not possible to test this explanation. In our study, all final COHb levels were higher than normal, so a prolonged COHb t1/2 due to a spuriously lengthened time between the COHb measurements is not supported by our data.

Eighty minutes is frequently quoted as the COHb t1/2 in humans breathing 100% O2 at atmospheric pressure,1,2 and our findings demonstrate a mean COHb t1/2 that is similar (74 ± 25 min; Table 3). One concern is that the COHb t1/2 of 80 min3 was reported by our data.

**Table 3—** COHb t1/2 in Patients With Acute CO Poisoning Treated With 100% O2 at Atmospheric Pressure

<table>
<thead>
<tr>
<th>Variables</th>
<th>n</th>
<th>Age, yr</th>
<th>COHb, %</th>
<th>COHb t1/2, min</th>
<th>PaO2, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>93</td>
<td>35 ± 15</td>
<td>32 ± 9</td>
<td>6–57</td>
<td>74 ± 25</td>
</tr>
<tr>
<td>Males</td>
<td>71</td>
<td>35 ± 15</td>
<td>32 ± 9</td>
<td>6–53</td>
<td>77 ± 25</td>
</tr>
<tr>
<td>Females</td>
<td>22</td>
<td>35 ± 15</td>
<td>33 ± 9</td>
<td>21–57</td>
<td>67 ± 23</td>
</tr>
<tr>
<td>Age ≥ 40 yr</td>
<td>31</td>
<td>53 ± 11</td>
<td>30 ± 12</td>
<td>6–57</td>
<td>77 ± 28</td>
</tr>
<tr>
<td>Age &lt; 40 yr</td>
<td>62</td>
<td>25 ± 7</td>
<td>34 ± 8</td>
<td>18–53</td>
<td>73 ± 23</td>
</tr>
<tr>
<td>Smoke inhalation</td>
<td>4</td>
<td>20 ± 16</td>
<td>35 ± 16</td>
<td>20–53</td>
<td>68 ± 32</td>
</tr>
<tr>
<td>Non-smoke inhalation</td>
<td>89</td>
<td>36 ± 15</td>
<td>32 ± 9</td>
<td>6–57</td>
<td>75 ± 23</td>
</tr>
<tr>
<td>+ LOC</td>
<td>62</td>
<td>36 ± 16</td>
<td>33 ± 10</td>
<td>6–57</td>
<td>71 ± 26</td>
</tr>
<tr>
<td>− LOC</td>
<td>28</td>
<td>33 ± 14</td>
<td>31 ± 8</td>
<td>16–44</td>
<td>82 ± 24</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD; + LOC = positive LOC; − LOC = negative LOC.

†Significant statistical difference between these groups for this parameter.

‡Significant statistical difference between these groups for this parameter.
ing CO in a poisoning circumstance,\textsuperscript{13,14,16} where the concentration of CO exposure, duration of exposure, type of exposure, and underlying health of the individuals is uncontrolled.

The COHb \( t_{1/2} \) was shorter in patients with more than two COHb measurements than in those patients with only two COHb measurements. The patients with more than two COHb measurements all had arterial catheters that were placed for clinical reasons. Many of these patients were critically ill, with some requiring vasoactive drugs for maintenance of an adequate BP. The shorter COHb \( t_{1/2} \) in these “sicker” patients is probably due to several factors. The COHb \( t_{1/2} \) would be expected to decrease if the cardiac output were reduced, and the COHb \( t_{1/2} \) would increase if the cardiac output were elevated.\textsuperscript{17} By virtue of some of these patients requiring vasoactive drugs, we might assume that their cardiac outputs were reduced; therefore, the COHb \( t_{1/2} \) would be expected to be decreased. Another factor that influences the COHb \( t_{1/2} \) is the patient’s alveolar ventilation. If the alveolar ventilation is high, the COHb \( t_{1/2} \) would be reduced, and the COHb \( t_{1/2} \) would be lengthened if the alveolar ventilation were reduced.\textsuperscript{18,19} Many of these patients required mechanical ventilation, so their alveolar ventilation may have been greater than in patients who were not as ill or who were not intubated. Ventilation/perfusion inequality (from aspiration or smoke inhalation) and the nonhemoglobin uptake of CO would be expected to lengthen the COHb \( t_{1/2} \), compared to those who were not as critically ill. Conversely, it is possible that these 17 patients breathed a high ambient concentration of CO for a relatively brief period of time, resulting in high initial COHb levels. Because of the short duration of exposure to CO, the tissue burden of CO might therefore have been lower in these patients, with a resultant lower COHb \( t_{1/2} \) than in patients who were exposed to lower ambient levels of CO for a longer period of time, which might permit a higher tissue burden of CO and, therefore, a longer COHb \( t_{1/2} \).

Unfortunately, cardiac output data, minute ventilation data, the duration of exposure to CO, and the concentration of inhaled CO is unknown in most of these patients, so we cannot make definitive inferences regarding the influence of these factors on the COHb \( t_{1/2} \). It is possible that these 17 patients are not representative of the other patients who we studied, and the statistically different COHb \( t_{1/2} \) is a random event. Lastly, multiple COHb measurements may lessen, or dampen, inaccuracies of recorded times and COHb measurements, which could influence the COHb \( t_{1/2} \) calculation.

Our data indicate that COHb elimination follows exponential decay. In the 17 patients who had more than two COHb measurements, the best fit of their COHb data using all COHb values to calculate the COHb \( t_{1/2} \) was an exponential decay. We found no statistical differences in the COHb \( t_{1/2} \) if calculated using all COHb measurements compared to the COHb \( t_{1/2} \) calculated by using either the first and second or the first and last COHb measurements in these same patients. Pace et al\textsuperscript{20} demonstrated that COHb elimination follows exponential decay. In their study, the \( k \) values were calculated using five COHb values, measured in triplicate every 15 min.

Concomitant smoke inhalation does not appear to influence the COHb \( t_{1/2} \) in CO poisoning. The COHb \( t_{1/2} \) reported by Myers et al\textsuperscript{14} (Table 1) includes patients with smoke inhalation, although the sample size is not reported. The data by Burney et al\textsuperscript{16} represent CO poisoning due to a forced heating system without concomitant smoke inhalation. The COHb \( t_{1/2} \) in these two reports is similar (approximately 130 min), although considerably
longer than found in our patients. Wu$^6$ found longer COHb $t_{1/2}$ in healthy dogs that breathed air following CO exposure compared to CO-exposed dogs with acute lung injury due to inhaled hydrochloric acid. He did not find a correlation between the intrapulmonary shunt fraction and the COHb $t_{1/2}$ in dogs breathing air or O$_2$. Our data suggest that the COHb $t_{1/2}$ of patients with smoke inhalation is not different than in patients without smoke inhalation. Elimination of a gas with high solubility in blood (ie, CO), is influenced little by alveolar/perfusion mismatch. Patients with lung disease might have a lower PaO$_2$ and hence have a lower rate of CO elimination. However, a large right-to-left shunting of blood containing increased amounts of COHb would be expected to exhibit a longer COHb $t_{1/2}$. Our findings may be influenced by the low number of patients with smoke inhalation in our study; therefore, we most likely have inadequate power to detect a difference.

Stepwise linear multiple regression analysis demonstrated that the COHb $t_{1/2}$ was not significantly related to age, gender, initial COHb level, degree of initial acidosis (base excess), history of LOC, or if the patients were breathing O$_2$ by mask or through an ET tube. Other studies have found age and gender differences in COHb elimination. One study of experimental CO exposure found a correlation between COHb $t_{1/2}$ and age, with the elimination of CO reduced approximately 1%/yr for ages $>42$ years.$^7$ We found no relationship between COHb $t_{1/2}$ and age. Pace et al$^7$ also demonstrated gender differences in the COHb $t_{1/2}$ but offered no explanation. Deller et al$^6$ demonstrated gender differences in the COHb $t_{1/2}$ in smokers breathing air. They postulated that the lower muscle mass in women, with correspondingly less myoglobin, could account for female subjects having lower COHb $t_{1/2}$ than male subjects. Although it has been suggested that the COHb $t_{1/2}$ varies as a function of the initial COHb level,$^10$ our findings agree with those of Myers and Britten,$^9$ who found no relationship between the COHb $t_{1/2}$ and the initial COHb measurements.

Our data support the observation that the COHb $t_{1/2}$ is moderately related to the PaO$_2$ (Fig 1). Despite caregivers attempting to keep $O_2$ delivery face masks on CO-poisoned patients, undoubtedly some of the time the patients may not have been inhaling 100% $O_2$, which is the most likely explanation for the lower-than-expected correlation found between the COHb $t_{1/2}$ and the PaO$_2$. Observations from experimental human CO-exposure studies indicate that the COHb $t_{1/2}$ is reduced with increased alveolar partial pressures of $O_2$ and a related increase in the PaO$_2$. One might expect that the PaO$_2$ would influence kinetics of COHb elimination more than the alveolar partial pressures of $O_2$ because the PaO$_2$ measurement takes into consideration abnormal pulmonary function. Furthermore, it is the PaO$_2$ to which erythrocytes, and hence hemoglobin, are exposed and which governs the physical chemistry of CO-to-hemoglobin binding.

Strengths of our clinical CO elimination study include a larger sample size than in any prior studies, and all patients had clinical CO poisoning as compared to experimental CO exposures in normal humans. In addition, our study provides information regarding the influence of demographic and CO-poisoning-related factors on CO elimination.

Weaknesses of our study include the possible errors in recorded values, because this study was retrospective and possible differences in COHb values between arterial and venous blood. There may be some minor inaccuracies in the recorded times that would influence the COHb $t_{1/2}$ calculation. We would expect these small time recording errors to be randomly distributed; hence, we postulate that inaccuracies in the times of the COHb measurements contribute minimally to our results. Alveolar ventilation influences the rate of COHb elimination,$^{18,19}$ with a shorter COHb $t_{1/2}$ with high minute ventilations. The minute ventilations in our study population is unknown, but may be variable, which might account for the relatively large standard deviations that we report. It is also possible that the patients treated with nonrebreather face mask $O_2$ had varying FIO$_2$ levels between the times when the COHb samples were obtained. All intubated patients were intubated for clinical reasons, not as a method to provide an FIO$_2$ of 1.00. We and other care providers clearly made every attempt to keep the masks on these patients for clinical reasons but, admittedly, it is possible that some patients failed to breath high FIO$_2$ levels between the COHb measurements. Furthermore, there is no guarantee that the FIO$_2$ delivered by nonrebreather face-mask $O_2$ will be 1.00.$^4$ Therefore, if the patients assigned to face-mask $O_2$ failed to breath the provided FIO$_2$ they would be expected to exhibit a longer COHb $t_{1/2}$ than patients who were intubated where a FIO$_2$ of 1.00 is guaranteed. Interestingly, in our study, there was no difference in the COHb $t_{1/2}$ or in the PaO$_2$ of patients who were intubated compared to patients treated with nonrebreather face mask $O_2$, so we infer that the patients who were provided face mask $O_2$ received high FIO$_2$ measures for the majority of the time between the initial and final COHb measurements. It is possible that the PaO$_2$ of the intubated patients was reduced due to aspiration and/or lung injury from smoke inhalation, and the PaO$_2$ of the nonintubated patients was lower than if they were breathing 100% $O_2$ as
O₂ was delivered via nonrebreather face mask. It may be a coincidence that the PaO₂ of the intubated patients was not statistically different from that of the nonintubated patients. However, it is clear from data presented in Table 3, that the PaO₂ of our patients was lower than would be expected at our altitude if the patients were receiving a FiO₂ of 1.00. In addition to a FiO₂ that is < 1.00, the PaO₂ can be reduced because of concomitant alterations in alveolar/perfusion matching (eg, due to aspiration, smoke inhalation, etc.). The other clinical reports (Table 1) also have limitations in their data because the FiO₂ delivered to the reported patients were not 1.00. Nevertheless, our study provides information regarding the COHb t₁/₂ derived from CO-poisoned patients, so we assume that our data are reasonably extrapolatable to the “real world,” where the FiO₂ and minute ventilation in treated cases of CO poisoning is generally not tightly controlled.

An error in the COHb t₁/₂ calculation may occur if the COHb levels in arterial blood and venous blood samples are different, and the samples pairs used to calculate the COHb t₁/₂ were not both arterial or both venous. We assumed that the COHb levels were equivalent in both arterial and venous blood. Benignus et al have demonstrated that there is a difference between COHb levels in simultaneously analyzed arterial and venous blood samples for up to 10 min following cessation of the CO exposure. The magnitude of the differences in arterial and venous COHb sample pairs was 4 to 12%. However, by 5 to 15 min after CO exposure, the COHb levels between paired arterial and venous specimens were identical. The patients in our study had COHb levels that were measured > 15 min after removal from the CO-poisoning environment. Therefore, we have assumed that the COHb in both arterial and venous blood are equivalent.

COHb measurement errors could be introduced by different CO oximeters, but, as explained in the Methods section, we believe that these errors would not influence our findings significantly.

The final COHb had to be > 2% for the patient's data to be included in our analysis. One could argue that if the COHb reached its final normal value some time prior to the measurement of the COHb, the COHb t₁/₂ would be falsely prolonged. We discount that if the COHb reached its final normal value some time prior to the measurement of the COHb, because in a subgroup comparison of those patients with final COHb levels < 6% (n = 23; final mean COHb = 4.04 ± 0.84; COHb t₁/₂ = 68.2 ± 24), the COHb t₁/₂ was no different than in the group with final COHb levels ≥ 6%.

We calculated the COHb t₁/₂ and correlated the COHb t₁/₂ to the initial COHb levels, PaO₂ levels, and base excess of CO-poisoned patients treated with nonrebreather face mask (or ET tube) O₂ delivered at atmospheric pressure. Ideally, blood lactate measurements would have been helpful to perform correlations with the COHb t₁/₂, but blood lactate levels were not available on most of the patients. Since the base excess (calculated from the arterial blood gas) is a reflection of the degree of metabolic acidosis, we used base excess as a surrogate for blood lactate.

We were unable to link the COHb t₁/₂ data to patient outcome, since long-term outcome was unknown to us for most of these patients. A prospective study is ongoing, in which it may be possible to perform correlations between the COHb t₁/₂ and the patients’ neuropsychological outcomes.

In summary, the COHb t₁/₂ in 93 patients with acute CO poisoning treated with 100% O₂ at atmospheric pressure was 74 ± 26 min, with a range from 26 to 148 min. Our hypothesis that the COHb t₁/₂ of CO-poisoned patients should be longer than the COHb t₁/₂ derived from human experimental exposure studies was not completely fulfilled. The COHb t₁/₂ observed in one prior experimental report was shorter than in our study; however, the COHb t₁/₂ in two other experimental studies were greater than in our study. The COHb t₁/₂ in our study is considerably shorter than in previous clinical reports due to reasons that are unclear. As expected, we found an inverse relationship between the COHb t₁/₂ and the PaO₂. The COHb t₁/₂ was not influenced in our study by the patients’ ages, genders, smoke inhalation, history of LOC, concurrent tobacco smoking, whether intubated or breathing O₂ by face mask, or the initial COHb measurements.

This study provides new information about the COHb t₁/₂ of CO-poisoned patients that might be helpful in determining the duration of supplemental O₂ therapy for a CO-poisoned patient. High-concentration supplemental O₂ therapy has been recommended until the COHb level is < 5%. Our data may help guide the treating clinician regarding when to inspect for a COHb level < 5%. The COHb t₁/₂ may be used to estimate the COHb level at a given time prior to the measurement of the initial COHb level (eg, for medicolegal and/or epidemiologic purposes). However, given the variability in COHb t₁/₂ that we found in our patients, considerable uncertainty might apply to “back-calculating” the COHb level to some time prior to the initial COHb measurement. Our observations regarding demographic and clinical factors in CO poisoning, which may influence the COHb t₁/₂, may further our understanding of CO poisoning and stimulate additional thought and research in CO toxicology.
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REFERENCES

8 Wu WX. Factors influencing carboxyhemoglobin kinetics in inhalation lung injury. Chung Hua Nei Ko Tsa Chih 1992; 31:689–691
17 Eger EI II. Anesthetic uptake and action. Baltimore, MD: Williams & Wilkins, 1974; 77–96