Effect of Carbon Monoxide Exposure on Intermittent Claudication

By Wilbert S. Aronow, M.D., Edward A. Stemmer, M.D.,
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SUMMARY
The effect of breathing 50 ppm of carbon monoxide for two hours versus compressed, purified air for two hours on intermittent claudication was evaluated in ten men in a double-blind study. The mean venous carboxyhemoglobin level insignificantly decreased from 1.12% to 0.90% after breathing compressed, purified air but significantly increased from 1.08% to 2.77% after breathing carbon monoxide ($P < 0.001$). The mean exercise time until the onset of intermittent claudication insignificantly increased from 169 sec to 173 sec after breathing compressed, purified air but significantly decreased from 174 sec to 144 sec after breathing carbon monoxide ($P < 0.001$). Breathing 50 ppm of carbon monoxide for 2 hr significantly aggravated intermittent claudication of the calf or thigh due to angiographically documented occlusive arterial disease.

Additional Indexing Words: Arterial disease Atherosclerosis Exercise

Patients with angina pectoris due to coronary artery disease have a decrease in exercise performance until the onset of angina pectoris following less myocardial work after carbon monoxide exposure from smoking nicotine cigarettes\(^1\) or heavy freeway traffic.\(^2\) Double-blind studies have also demonstrated that anginal patients who breathe 50 ppm of carbon monoxide for four hours\(^8\) or for two hours\(^4\) significantly decrease their exercise performance until angina pectoris develops compared to breathing compressed, purified air.

These data led us to wonder what effect carbon monoxide exposure would have on intermittent claudication due to occlusive arterial disease. Therefore, we performed a double-blind study evaluating the effect of breathing 50 ppm of carbon monoxide for two hours versus compressed, purified air for two hours on intermittent claudication in ten men with intermittent claudication of the calf or thigh due to angiographically documented occlusive arterial disease.

Materials and Methods
Ten men, mean age 51 ± 7 years (range 33 to 58 years), with classic intermittent claudication of the calf or thigh due to angiographically documented occlusive ilio-femoral arterial disease with patent distal vessels were subjects. These men did not have coronary heart disease or hypertension. They were disabled by their intermittent claudication. Informed consent was obtained from the 10 men who participated in this study.

The patients were brought to the laboratory and familiarized with the equipment and the procedures before the study was done. They practiced exercising upright on a Collins constant-load bicycle ergometer\(^*\) many times prior to the study. All subjects were hospitalized on the nights before the four successive study mornings. Two of the 10 patients were smokers at the time of this study. Two of these patients did not smoke for at least 12 hr prior to the study each morning or during the study.

On four successive study mornings, at 7:45 a.m., with the subject in the fasting state, venous blood was drawn and analyzed for carboxyhemoglobin and hemoglobin levels with a 182 Co-Oximeter.\(^+\) All determinations were made in duplicate. Each subject then exercised upright on the constant-load bicycle ergometer with a work load of 25 watts until the onset of intermittent claudication; the duration of exercise was recorded with a stopwatch.

In a double-blind randomized fashion, each patient then breathed 50 ppm of carbon monoxide for 2 hr on two mornings and compressed, purified air for 2 hr on two mornings. The carbon monoxide and compressed,

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\(^{1}\) Breathing compressed, purified air.
\(^{2}\) Carboxyhemoglobin.
\(^{3}\) Exercise in the laboratory.
\(^{4}\) Exercising on a Collins constant-load bicycle ergometer.
\(^{5}\) All determinations were made in duplicate.

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†Instrumentation Laboratory, Inc., Lexington, Mass.
purified air were breathed from a tank through a mask, using a Bird Mark 7 Respirator* with pressure settings and flow rates reduced and a built-in expiratory leak, so that significant positive pressure was not applied. Five of the 10 patients breathed carbon monoxide on days 1 and 4 and compressed, purified air on days 2 and 3. The other five patients breathed carbon monoxide on days 2 and 3 and compressed, purified air on days 1 and 4.

After breathing carbon monoxide or compressed, purified air for 2 hr, venous blood was again drawn and analyzed for carboxyhemoglobin and hemoglobin levels. All determinations were made in duplicate. The subject then exercised upright on the constant-load bicycle ergometer with a work load of 25 watts until the onset of intermittent claudication, and the duration of exercise was recorded with a stopwatch. The t-test for correlated means was used to analyze the data.

**Results**

All of the hemoglobin values were within normal limits and showed no significant change.

Table 1 shows the venous carboxyhemoglobin levels for each patient in the control periods and after breathing carbon monoxide or compressed, purified air for two hours. The mean venous carboxyhemoglobin level decreased from 1.12 ± 0.29% to 0.90 ± 0.22% after breathing compressed, purified air for two hours (P > 0.05). The mean venous carboxyhemoglobin level increased from 1.08 ± 0.24% to 2.77 ± 0.19% after breathing 50 ppm of carbon monoxide for two hours (t = 8.090; P < 0.001).

Table 2 illustrates the exercise performance until the onset of intermittent claudication for each patient in the control periods and after breathing carbon monoxide and compressed, purified air. No significant difference in the mean exercise performance until the development of intermittent claudication occurred between the control period and after breathing compressed, purified air for two hours. The mean exercise time until the onset of intermittent claudication significantly decreased from 174.3 sec in the control period to 144.0 sec after breathing carbon monoxide for two hours (t = 15.442; P < 0.001).

**Discussion**

Carboxyhemoglobin decreases oxygen extraction and causes a greater reduction in mixed venous oxygen tension relative to the increase in venous

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*Bird Corporation, Palm Springs, Calif.

**Table 1**  
Venous Carboxyhemoglobin Levels (%) Before and After Breathing Carbon Monoxide and Compressed, Purified Air

<table>
<thead>
<tr>
<th>Patient</th>
<th>Control</th>
<th>After carbon monoxide</th>
<th>Control</th>
<th>After purified air</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.7</td>
<td>2.7</td>
<td>0.9</td>
<td>0.7</td>
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<tr>
<td>2</td>
<td>1.4</td>
<td>3.1</td>
<td>1.5</td>
<td>1.2</td>
</tr>
<tr>
<td>3</td>
<td>0.8</td>
<td>2.4</td>
<td>1.1</td>
<td>0.9</td>
</tr>
<tr>
<td>4</td>
<td>1.4</td>
<td>3.0</td>
<td>1.0</td>
<td>0.8</td>
</tr>
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<td>5</td>
<td>0.9</td>
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<td>1.2</td>
<td>1.0</td>
</tr>
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<td>1.3</td>
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<td>1.4</td>
<td>1.1</td>
</tr>
<tr>
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<td>1.1</td>
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<td>0.7</td>
<td>0.6</td>
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<td>0.9</td>
<td>2.8</td>
<td>1.4</td>
<td>1.0</td>
</tr>
<tr>
<td>9</td>
<td>1.2</td>
<td>2.8</td>
<td>1.1</td>
<td>0.8</td>
</tr>
<tr>
<td>10</td>
<td>1.4</td>
<td>2.9</td>
<td>1.0</td>
<td>0.8</td>
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<tr>
<td>Mean</td>
<td>1.08</td>
<td>2.77</td>
<td>1.12</td>
<td>0.90</td>
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<td>One sd</td>
<td>0.24</td>
<td>0.19</td>
<td>0.29</td>
<td>0.22</td>
</tr>
</tbody>
</table>

**Table 2**  
Exercise Performance Until Intermittent Claudication (sec) Before and After Breathing Carbon Monoxide and Compressed, Purified Air

<table>
<thead>
<tr>
<th>Patient</th>
<th>Control</th>
<th>After carbon monoxide</th>
<th>Control</th>
<th>After purified air</th>
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<tr>
<td>Mean</td>
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<td>171</td>
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<td>185</td>
</tr>
<tr>
<td>One sd</td>
<td>188</td>
<td>156</td>
<td>182</td>
<td>194</td>
</tr>
</tbody>
</table>

*ARONOW, STEMMER, ISBELL*
CARBON MONOXIDE AND CLAUDICATION

carboxyhemoglobin level by causing a leftward shift of the oxyhemoglobin dissociation curve, with tighter binding of oxygen to hemoglobin. The data from this double-blind study show that the mean venous carboxyhemoglobin level significantly increased from 1.08% to 2.77% (P < 0.001) after our patients breathed 50 ppm of carbon monoxide for two hours. These data also demonstrate that this increase in carboxyhemoglobin level was of sufficient magnitude to cause intermittent claudication to develop significantly sooner (P<0.001) in our patients with angiographically documented occlusive arterial disease.

Since our patients with documented ilio-femoral occlusive arterial disease could not adequately increase the blood flow to their thigh and calf muscles while exercising, and since the elevated carboxyhemoglobin levels caused by carbon monoxide inhalation made less oxygen deliverable to the thigh and calf muscles, the oxygen demand exceeded the oxygen supply to these muscles, inducing intermittent claudication sooner after equivalent exercise. That the intermittent claudication-inducing effect was related to carbon monoxide acquisition is supported by the absence of this effect when compressed, purified air was breathed by our subjects during their double-blind study.

Double-blind studies have shown that exposure to 50 ppm of carbon monoxide for two or four hours aggravates angina pectoris due to documented coronary artery disease. This study shows that exposure to 50 ppm of carbon monoxide for two hours also aggravates intermittent claudication of the calf or thigh due to documented ilio-femoral occlusive arterial disease.

**Acknowledgment**

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**References**

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