Limitations of Hyperbaric Oxygenation in Occlusive Arterial Disease

By James F. Gorman, M.D., G. B. Stansell, M.D., and Frederick M. Douglass, M.D.†

Occlusive arterial disease of the lower extremity is a common and disabling problem frequently encountered by the physician. Despite accurate methods of diagnosis and recent advances in restorative vascular surgery, amputation all too frequently becomes a necessity. This is particularly true in the diabetic and the nondiabetic patient with “small vessel” or end-artery disease. Unlike occlusive disease affecting major arterial trunks, these individuals have involvement of small arteries and arterioles supplying the skin and subcutaneous tissue where development of a collateral network is at a minimum. Consequently, when injury or infection increases the tissue requirement for oxygen that this arteriolar capillary system is unable to supply, tissue hypoxia and necrosis quickly supervene.1,2

Within the ischemic limb blood flow is critically deficient and tissue anoxia represents an ever-present danger. Once established, metabolites from dead and dying cells provoke an inflammatory reaction which in itself is detrimental to an already impaired capillary flow.3 Theoretically, by increasing the amount of oxygen dissolved in the plasma in sufficient amounts to interfere with the foregoing chain of events, high-pressure oxygenation (HPO) would appear beneficial. The following presentation describes our experiences utilizing HPO in the management of end-stage lower extremity ischemia.

Clinical Material

Beginning early in 1963, 42 patients have undergone hyperbaric oxygen therapy for all types of peripheral arterial vascular disease at the Maumee Valley Hospital. Of this number, 18 were selected for the present report on the basis of the following common criteria:

1. All demonstrated evidence of advanced ischemia with definite areas of potential or incipient gangrene.

2. Each patient had undergone a prior or concomitant sympathetic denervation of the extremity.

3. Angiographic evidence was found of either diffuse arterial disease or involvement of vessels too small for an effective angioplastic procedure.

4. Coexisting infection, if present, was easily controlled prior to the onset of therapy.

In an attempt to evaluate more closely the effectiveness of the treatment program, the patients were subdivided into four groups according to the site of trophic changes: Group I, one or more digits; Group II, forepart of foot; Group III, heel or ankle; Group IV, any combination of the above groups coupled with ischemic ulceration above the malleolus (fig. 1).

As would be expected, the majority of the patients were elderly men with an average age of 66. Of the entire group, four were female and seven had coexisting diabetes mellitus.

Method of Treatment and Results

As a group the patients were exposed to

Figure 1

Site of trophic involvement in 18 patients undergoing HPO therapy. Group I, limited to one or more toes; group II, forepart of foot; group III, heel; group IV, ischemic ulceration above malleolus.
oxygen at raised ambient pressures for a total of 176 hours or an average of 9.07 hours per patient. With the patient breathing 100 per cent oxygen, the chamber was pressurized with compressed air to three atmospheres absolute (3 ATA) and maintained at this level for 1 hour. Treatment schedule varied in many instances but usually consisted of several daily 1-hour exposures. Therapy was continued if improvement was evident but, as was more often the case, was discontinued when overt tissue necrosis became established. In no case was oxygen toxicity observed, and the sole complication was an instance of pneumothorax discovered 48 hours after exposure. Claustrophobia necessitated termination of therapy in two patients.

Shortly after exposure to 100 per cent oxygen at 3 ATA, the initial pallor of ischemia was replaced by a mottled effect followed by a pink flush which persisted for a short time following decompression. During, and for varying periods of time following exposure, many patients noted relief of rest pain and became aware of a sensation of warmth in a heretofore cool limb. Although one cannot deny the possible psychologic benefit of placing a patient in a hyperbaric chamber, the majority of patients required less analgesia following exposure than before treatment was instituted.

Table 1 summarizes the results of each patient group with respect to success or failure, and in the latter instance to the type of amputation employed. It is readily obvious that HPO had little influence in increasing limb salvage, as only two patients escaped some form of amputation. However, the final line of demarcation was lower than expected in several instances permitting amputation below the knee.

There appeared to be no appreciable delay in the development of frank gangrene between the patients reported and comparable cases not receiving HPO. In many instances the reverse was true, with the HPO-treated patients exhibiting an earlier line of demarcation than would be normally anticipated.

Pathologic examination of the amputated specimens proved to be of interest; the results are discussed in a separate publication.4 Briefly, the margin between viable and non-viable tissue was sharp, dry, and free from edema, the tissue proximal to the gangrenous margin possessing good color and tissue turgor. Histologically, the zone of edema, exudation, and cellular infiltration usually found adjacent to an area of ischemic necrosis was minimal or absent in the HPO-treated extremities. Instead, vascular proliferation and epidermal hyperplasia suggestive of tissue vitality were commonplace (figs. 2 and 3).

Discussion

The current resurgence of interest in hyperbaric oxygenation has resulted in numerous reports emphasizing the importance of this mode of therapy in a wide variety of anoxic conditions. Experimentally, the value of administering oxygen at high ambient pressures to ward off the deleterious effects of anoxia in the acute ischemic situation is generally accepted.5-7 In several aspects HPO would also appear to have merit in conditions of chronic ischemia where gangrene is imminent. If the tissue \( pO_2 \) is increased to meet local requirements, the viability of marginal areas would be maintained and resistance to infection increased. However, the results obtained in this report would clearly indicate that HPO has little, if any value, in the man-

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of patients</th>
<th>Improved</th>
<th>Digital Amputation</th>
<th>Below knee</th>
<th>Above knee</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>7</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>5</td>
<td>—</td>
<td>—</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>2</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>IV</td>
<td>4</td>
<td>1</td>
<td>—</td>
<td>—</td>
<td>3</td>
</tr>
</tbody>
</table>

Circulation, Volume XXXII, December 1965
cells of arterioles, resulting in vasodilatation and increase in cutaneous blood flow.\textsuperscript{10} Perhaps the relief of pain and warming observed during treatment is related to this direct effect of oxygen upon vasomotor tone at the capillary level. In any event this phenomenon was short-lived and did not materially alter the final outcome.

Microscopic review of amputated specimens revealed distinctly different patterns of response to ischemic injury between HPO-treated and nontreated individuals. The clarity of demarcation, absence of edema, and minimal cellular infiltration noted in the pa-

**Figure 2**

Photomicrographs (× 100) of demarcation zone in two nontreated patients. Distal gangrenous tissue on right. Upper. Wide marginal area of inflammation evident between viable and necrotic tissue with extension into deep dermis and subcutaneous tissue. Lower. Indefinite epidermal demarcation and edema in upper dermis and subcutaneous tissue.

agement of chronic occlusive arterial disease. The natural history of the disease and the resulting incidence of amputation were not influenced by hyperbaric therapy.

The temporary improvement noted during the actual exposure to HPO remains a matter of speculation. The diffusion of oxygen without organ perfusion despite a hyperbaric environment is extremely limited.\textsuperscript{8,9} Furthermore, there is no existing evidence to suggest gaseous oxygen diffusion from perfused tissue to adjacent areas of ischemia. At high concentrations, oxygen has been shown to stimulate the beta receptors within the smooth-muscle

**Figure 3**

Photomicrographs (× 100) of two HPO-treated cases. Upper. Note clarity of demarcation between gangrenous tissue at right and viable area with minimal cellular infiltration and edema. Lower. Prominent sharp margin of demarcation free from inflammatory response is observed.
tients who had undergone hyperbaric therapy are difficult to explain. For reasons mentioned earlier, it would be hazardous to assume that marginal tissue viability was solely maintained on the basis of a temporarily elevated $pO_2$.

At high partial pressures oxygen appears to inhibit several tissue enzyme and co-enzyme systems, some of which play vital roles in the process of inflammation.11,12 Thus, one might postulate that oxygen at raised ambient pressure inhibits or modifies the inflammatory response of marginal tissue to anoxic injury by means as yet not completely understood.

Further investigation into the complex biologic actions of HPO is warranted to insure rational and effective clinical utilization in the management of peripheral vascular ischemia.

Conclusion

Hyperbaric oxygen was utilized in the management of 18 patients with chronically advanced occlusive arterial disease. All exhibited areas of potential or incipient gangrene, had undergone a prior lumbar sympathectomy, and angiographically revealed either diffuse or small vessel atherosclerotic involvement.

The treatment program consisted of daily 1-hour exposures to 100 per cent oxygen at three atmospheres absolute as clinically indicated. The majority of patients experienced temporary relief of rest pain and warming of the extremity, which gradually disappeared following decompression. However, over-all limb salvage and progression of the ischemic process was not significantly altered by high-pressure oxygen therapy in this selected group of patients.

Microscopic review of marginal tissue adjacent to areas of ischemic necrosis disclosed a paucity of inflammatory findings regularly observed in nontreated extremities, suggesting an important relationship between hyperoxia and the cellular response to injury.

Acknowledgment

We wish to thank Mr. William Lawrence for his technical assistance.

References

Limitations of Hyperbaric Oxygenation in Occlusive Arterial Disease

JAMES F. GORMAN, G. B. STANSELL and FREDERICK M. DOUGLASS

Circulation. 1965;32:936-939
doi: 10.1161/01.CIR.32.6.936

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1965 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/32/6/936.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/