EDITORIAL

The Possible Use of High Pressure Oxygen in the Treatment of Leprosy and Tuberculosis

In recent years, the incidence of drug-resistant cases of tuberculosis has been increasing steadily. In order to combat this disease, Doull and Schwartz have suggested the development of more effective drugs (bactericidal rather than bacteriostatic, and free of undesirable side effects) as well as drugs which will bring about the desired results more rapidly. It is our opinion that means of increasing the efficiency of drugs currently used should also be sought. On the basis of existing information, it appears that high-pressure oxygen, alone or in combination with various chemotherapeutic agents, may result in more efficacious treatment of mycobacterial diseases than is possible by present methods. What may be needed for the successful treatment of mycobacterial infections by oxygen is intermittent exposure of the infected persons to high partial pressures of oxygen for relatively short periods of time, perhaps followed by maintenance of increased oxygen partial pressures at a total pressure of 1 atmosphere.

Oxygen pressures greater than one atmosphere may be required to yield the high driving force needed for diffusing lethal concentrations of oxygen into the invading organisms. High-pressure oxygen alone may not be sufficient to be bactericidal; however, the use of high-pressure oxygen in conjunction with appropriate drugs may produce a synergistic effect which would result in killing the bacteria.

To support this area, the works of previous investigators are presented. Approximately 50 years ago, Moore and Williams showed that the avian, bovine, and human strains of the tubercle bacillus do not grow in a hyperoxic (80 to 90 per cent O₂) environment. They found that prolonged exposure of the tubercle bacillus to oxygen is bactericidal. Adams found that high oxygen tensions arrest the growth of the tubercle bacillus. He was unable to demonstrate the bactericidal effect of oxygen; however, the desiccator he used may have leaked, thus permitting the organism to reside in a gaseous environment in which the pO₂ continually decreased. This may have resulted in oxygen tensions sufficient only to inhibit growth, but not sufficient to kill the microorganisms. In a comprehensive study of the tubercle bacillus, Novy and Soule found that high oxygen pressures inhibit the growth of this organism, whereas growth still took place in the presence of 0.9 to 1.0 atmospheres of oxygen.

More recently, Knox et al. found that pure oxygen is bactericidal to M. tuberculosis. These investigators also found that the growth of BCG, “chromogenic” acid-fast bacilli, M. phlei, M. stercoris, and M. smegmatis, were inhibited by high oxygen pressures, the degree of inhibition being inversely related to the size of the inocula (this was also observed by Novy and Soule), and directly related to the partial pressure of oxygen. The inhibitory effects of oxygen were more apparent with the slower-growing strains, the order of susceptibility being BCG > M. tuberculosis > “chromogenic” acid-fast bacilli > saprophytic mycobacteria (M. phlei, M. stercoris, and M. smegmatis). These workers also reported that an isoniazid-resistant variant of M. tuberculosis var. hominis (H37RV) was less sensitive to oxygen than the parent isoniazid-sensitive strain. In contrast to the parent strain, the isoniazid-resistant variant of BCG was more sensitive to oxygen than the isoniazid-sensitive strain. Isoniazid-resistant and sensitive strains of M. smegmatis were equally sensitive to oxygen.

The early findings of Moore and Williams stimulated Adams and later Barach.
to study the effects of elevated oxygen tensions on animals infected with pulmonary tuberculosis. Neither investigator was able to demonstrate significant retardation of the disease process by the inhalation of 0.6 atmosphere of oxygen. These findings are not surprising, considering that these oxygen tensions have been shown to be insufficient to retard significantly the in vitro growth of the tubercle bacillus. Higher oxygen pressures used continually would have produced the added complication of pulmonary damage due to oxygen toxicity, and death from "oxygen pneumonia" would have ensued before any possible beneficial effects of oxygen therapy could have become evident.

There are clinical reports on the beneficial action of oxygen when introduced directly into local tuberculous lesions.11-18

The toxicity of oxygen is probably the main factor that has discouraged further study of the treatment of pulmonary tuberculosis and other mycobacterial infections. Oxygen toxicity is a time-pressure dependent phenomenon and may not be an important factor when man is exposed to high oxygen pressures for only short periods at a time. Techniques and knowledge are available for using high-pressure oxygen as an adjunct to therapy. Oxygen under pressure is being used for the treatment of anaerobic infections,19-24 carbon monoxide poisoning,25-28 and in conjunction with x-ray therapy for the treatment of cancer.29-33

It thus appears that research in this area may have a good chance to result in improved therapy for diseases caused by mycobacteria.

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REFERENCES
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HIGH PRESSURE OXYGEN IN LEPROSY AND TUBERCULOSIS


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CORRELATIVE RESPIRATORY AND HEMODYNAMIC STUDY OF BILHARZIAL COR PULMONAL

Bilharzial cor pulmonal cases with huge aneurysmal dilation of the pulmonary arteries show normal static pulmonary functions with increased minute ventilation and ventilatory equivalent, stated Dr. Aly Reda El-Henedly and co-authors, Alexandria, Egypt. Dyspnea was present on exercise. The oxygen debt was raised on mild exercise from 50-150 per cent of the resting level against normal of 20-30 per cent on the same load. Dyspnea is closely parallel to the pulmonary intravascular and tolerably well with the cardiac output and the central blood volume. Compliance curves at rest and on exercise show that the compliance is markedly diminished. Splenic arteriovenous shunting was demonstrated after splenectomy. The cardiac size is diminished, the pulmonary artery pressures reduced, and the ECG returned to normal while the O2 saturation dropped in the right auricle from 80 per cent to 64 per cent after splenectomy. Bronchial artery-pulmonary artery shunting is demonstrated by: (a) angiography

In the thoracic aorta visualizing the aorta and pulmonary artery simultaneously. Injecting a dye in the aorta and recovering it from the pulmonary artery in one and one-half seconds. Ten per cent of cases show hypoxia that is not relieved by 100 per cent O2 inhalation. These cases show significant gradient between arterial CO2 and alveolar CO2, the arterial being higher by 2-7 mmHg. Radioactive krypton injected in the duodenum showed important shunts between the portal vein and pulmonary veins. Krypton injected with a dye as a bolus in the subclavian vein and recovering both in one circulation from the radial artery revealed absence of shunts from the pulmonary artery to pulmonary veins.

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LETTERS TO THE EDITOR:

May 20, 1963

Dear Doctor Myers:

After scanning the contents of the April, 1963 issue of Diseases of the Chest, I quickly turned to the "Electrocardiogram of the Month," because of the rather startling title "Premature Systoles with Myocardial Injury Produced by Exercise Test." As you may know from the many publications by Dr. Arthur Master and myself, we believe that myocardial injury resulting from the exercise test is a rare occurrence indeed and we have not observed such dire sequela in almost 55,000 patients so tested.

I must say I was immensely relieved when I read the content of the report, which presented a very interesting response to exercise, and again demonstrated the great clinical usefulness of the Master Two Step Test. I am writing this note to you in order to express my regrets at the unfortunate title of the paper which conveys the erroneous impression that myocardial injury, rather than transient ischemia, was produced by the exercise test. A more accurate title of the event described might have been "Premature Systoles and Diagnostic Changes Revealed by the Exercise Test." With the large volume of reading material to be covered by the average physician, there is an unfortunate tendency to scan the literature by title.

Isadore Rosenfeld, M.D.
New York City

May 22, 1962

Dear Doctor Rosenfeld:

Thank you for sending me a copy of your letter to Dr. Myers. I must confess that you could not be more right in what you said. My only consolation is the fact that your justified criticism is directed against the "unfortunate title." I fully agree with you that "produced" was not the proper term. Indeed, if anyone only read the title it was outright misleading.

You recognized the fact that the purpose of publishing this case was to show the usefulness of the Master test and I regret that one bad word in the title dated the very purpose for which this graph was shown.

I wonder whether or not Dr. Elek or Dr. Myers would be willing to publish your letter. I would certainly feel better if they would!

My sincere appreciation for your excellent letter!

Siegfried Salomon, M.D.
Staten Island, New York