COMMITTEE REPORT

Recommendations for Continuous Oxygen Therapy in Chronic Obstructive Lung Disease
Report of the Committee on Emphysema
American College of Chest Physicians

PHYSIOLOGY OF HYPOXIA

Although expiratory air flow obstruction is the physiologic sine qua non of chronic obstructive lung disease, tissue hypoxia ultimately accounts for the bulk of systemic physiologic changes. Tissue hypoxia results not only from an inadequate pulmonary gas exchange resulting in decreased oxygenation of arterial blood leaving the lungs (hypoxemia), but also from reductions in hemoglobin concentration and thus oxygen-carrying capacity of the blood. Hypoxia is also caused by inadequate tissue perfusion due to low cardiac output, structurally altered or poorly regulated regional circulation and from an inability of cellular enzymes to utilize the oxygen presented. In addition to these factors which result in tissue hypoxia, oxygen transport is influenced by the hemoglobin-oxygen affinity described by the oxyhemoglobin-dissociation curve and by the body's oxygen consumption influenced by such factors as temperature, pH and muscular activity. Oxygen therapy changes only the level of oxygen in the arterial blood. But to the extent that there is less hypoxemia, total oxygen transport increases and improved tissue oxygenation occurs.

Because multiple factors influence the degree of tissue hypoxia, it is not possible to delineate precisely a value of arterial oxygen saturation or oxygen tension (PaO₂), which will result in adequate oxygenation for all organs. Disregarding the precise level at which alterations occur the major immediate effects of hypoxia include altered physiology in the pulmonary vasculature, systemic circulation, central nervous system and kidneys. The predominant pulmonary response to hypoxemia is an increase in pulmonary vascular resistance while systemically there is increased cardiac output and decreased vascular resistance, sometimes associated with tachycardia and sometimes with small increases in mean arterial pressure. Acute hypoxemia may produce a variety of cardiac arrhythmias and persistent pulmonary hypertension results in right ventricular hypertrophy. The effects of hypoxia on cerebral function encompass a wide spectrum of deficits from the most subtle personality changes to headache, somnolence, convulsions and syncope. Altered renal physiology attributable to hypoxemia ranges from an increase in renal blood flow with mild degrees of hypoxemia to decreased blood flow and decreased excretion of salt and water with more severe hypoxemia.

Systemic oxygen transport is the product of arterial blood oxygen content and the cardiac output. Some altered cardiovascular responses, particularly those related to increases in blood flow, may be considered compensatory mechanisms since oxygen transport is thereby improved. Through stimulation of erythropoietin, erythrocytosis follows hypoxemia. The magnitude of the bone marrow response is roughly proportional to the degree of hypoxemia and the increase in oxygen carried is proportional to the amount of circulating hemoglobin. Each gram of normal adult hemoglobin is capable of transporting 1.39 ml of oxygen when completely saturated. The amount of oxygen transported by hemoglobin in 100 ml of blood is equal to the hemoglobin concentration times 1.39 times the percent saturation per 100 (Hgb x 1.39 x sat O₂). Thus, the presence of anemia may have an overriding influence upon the amount of oxygen delivered to tissues even when hypoxemia is corrected.

The amount of oxygen carried by a molecule of hemoglobin is further dependent upon the physico-chemical characteristics of the hemoglobin protein and the factors which affect the affinity of oxygen for hemoglobin. Red cell age, blood hydrogen ion concentration [H+] and Pco₂, temperature, genetic type of hemoglobin and the quantity of 2,3 diphosphoglycerate (DPG) are known to influence oxygen-hemoglobin affinity. Less affinity of hemoglobin for oxygen is seen with acidosis, hypercapnia, elevated
temperature, and increased red cell concentrations of DPG (rightward shift of the oxyhemoglobin-dissociation curve). Abnormal hemoglobins may be associated with increased or decreased affinity for oxygen.

When cellular hypoxia exists, metabolism shifts from the usual oxidative phosphorylation system producing water and carbon dioxide to an energy producing system which functions anaerobically. This anaerobic system, the glycolytic pathway, yields pyruvate and lactate and delivers to the blood increased quantities of lactate and lactic acid. The result is metabolic acidosis. In the lung, acidosis potentiates the hypoxemia-induced increased pulmonary vascular resistance.

It is evident from the above discussion that arterial oxygenation represents only the initial phase in the transport of oxygen from the lungs to the body. Arterial hypoxemia may be present without tissue hypoxia because the ratio of O₂ supply to O₂ demand and tissue PO₂ may be normal even though arterial PO₂ is low. Because of the sigma shape of the oxyhemoglobin-dissociation curve, relatively slight increases in PO₂ in the steep portion of the curve, result in relatively great increases in O₂ content. The aim of oxygen therapy in ambulatory patients with chronic obstructive lung disease is to overcome tissue hypoxia; it is usually necessary only to improve hypoxemia rather than to correct it completely. Thus, some portion of hypoxemic ventilatory drive may be retained minimizing the worsening of hypercapnia which could occur from oxygen therapy.

In patients with acute respiratory insufficiency, therapy is directed at correction of arterial hypoxemia while treating the underlying disease and precipitating event. Once a chronic stable state of severe hypoxemia is reached in the patient with obstructive lung disease, consideration for continuous oxygen therapy must be made.

**Criterion for Patient Selection**

Patients should be considered for longterm oxygen therapy only when severe hypoxemia continues despite an active in-hospital program utilizing all other modalities of proper respiratory care. In general, patients selected for therapy demonstrate both marked hypoxemia and a significant number of symptoms which may be directly related to that hypoxemia. These symptoms may include: 1) severe exercise dyspnea and fatigue out of proportion to mechanical lung dysfunction and correlating with lowered arterial oxygen tensions; 2) recurring congestive failure not readily responsive to usual measures of therapy; 3) severe, recurring secondary erythrocytosis; 4) impairment of cognitive processes which improve with oxygen therapy; 5) restlessness and/or insomnia correctable with use of oxygen.

Some generalizations may be drawn in relationship to the level of hypoxemia per se and oxygen need. Nearly all patients with resting arterial oxygen tensions below 40 mm Hg and most patients with resting tensions below 45 mm Hg will require continuous oxygen therapy. In those patients with severe oxygen-related symptomatology and in patients with hypoxemia and accompanying arteriosclerotic vascular disease, continuous oxygen therapy should be considered when the PO₂ is in the range of 50 mm Hg at rest. In patients with moderate hypoxemia at rest but with severe exercise hypoxemia and exercise limitation secondary to hypoxemia, the use of oxygen at exercise should be considered. Lastly, since arterial hypoxemia is greatest during sleep in patients with chronic airway obstruction, oxygen may be beneficial during resting hours in those patients whose arterial oxygen tensions are in the range of 45 to 55 mm Hg while awake. This is especially true in the patient who demonstrates sleeplessness or restlessness.

**Oxygen Dosage**

Oxygen dosage should be individualized at that level adequate to maintain an arterial oxygen tension over 55 mm Hg at rest and over 50 mm Hg at exercise. In patients with chronic airway obstruction, usually an oxygen flow of 1-3 L/min at rest and 1-4 L/min at exercise is required. Once a dose is established, the arterial PO₂ should be periodically monitored at approximately monthly intervals. Patients beginning on continuous oxygen therapy should remain in the hospital until they fully understand the use of oxygen, have demonstrated that they tolerate oxygen therapy, and if at all possible, until they have begun an active program of ambulation. It is all-important that the patient look at oxygen as something that will increase his ambulatory capacity rather than limit it.

Generally, continuous oxygen therapy patients utilize oxygen as near to 24 hours a day as possible. A recent paper suggests, however, that pulmonary arterial resistance may be effectively lowered with oxygen usage only 15 to 18 hours a day.

**Oxygen Delivery Systems**

The most convenient method of delivery of ambulatory oxygen is through use of nasal prongs. Oxygen may be supplied either using conventional cylinders or with a liquid oxygen system. In those patients who are predominantly housebound or minimally ambulatory, the use of cylinder oxygen is most convenient and most practical. A large cylinder is kept at the bedside and a small portable cylinder with a
dolly is utilized for ambulation in and around the house. The dolly should be constructed to give maximum support for the weak or debilitated patient, but be capable of being raised up and down short steps or curbs and being carried in a car. The portable liquid oxygen system is indicated for patients who are fully ambulatory outside the house, especially for those who are potentially employable.

**Cost of Oxygen**

The cost of continuous therapy using cylinder oxygen varies from $120 to $200 per month. The average cost is approximately $160 per month. The cost of liquid oxygen systems is generally greater than cylinder oxygen systems.

**Anticipated Results and Complications**

Hypoxemia is not the cause of chronic obstructive lung disease. Therefore, the use of oxygen in therapy must be considered supportive. Clearly, correction of hypoxemia cannot be expected to improve altered ventilatory function. On the other hand, continuous oxygen therapy has been shown to: 1) reverse hypoxia-induced increases in pulmonary vascular resistance and pulmonary hypertension; 2) increase exercise tolerance and the potential for physical rehabilitation; 3) decrease secondary erythrocytosis; 4) improve clinical status. In studies from Denver, mortality associated with cor pulmonale was decreased by 30 percent, although cor pulmonale still occurred late in the course of the disease. Well-controlled prospective studies of continuous ambulatory oxygen therapy at sea level are not available, but clinical experience suggests the drug is equally as valuable in near sea level locations as at higher altitudes when used to treat specific levels of arterial hypoxemia. As might be anticipated, the greatest benefits from oxygen therapy are noted in those patients who have severe hypoxemia out of proportion to their mechanical lung dysfunction.

Respiratory depression manifested by an abrupt rise in carbon dioxide tension (PCO2) and accompanied by a drop in pH is well described in some patients following correction of hypoxemia during episodes of acute ventilatory failure. However, when low-flow controlled oxygen is administered, this is an unusual phenomenon. When long-term continuous ambulatory oxygen is given, hypercapnia does not appear to progress more rapidly than would be expected from the natural history of chronic obstructive lung disease. Furthermore, when adequate oxygenation is accomplished, very high levels of PCO2 (greater than 90 mm Hg) are tolerated in the chronic steady state for long periods.

Acute oxygen toxicity, described in patients utilizing high oxygen concentrations for periods over 24 hours, would not be expected and has not been reported as being a problem in the patients on low-flow oxygen. In a recent postmortem study, 6 of 12 patients dying after 7 to 61 months of continuous oxygen therapy showed nonspecific exudative or proliferative lung changes. The cause or mechanism for the changes was unclear, but the findings are compatible with an oxygen toxic effect. In the opinion of the authors, the pathologic lung findings did not appear to have any clinical significance, and should not preclude the use of low-flow controlled oxygen in properly selected patients.

In conclusion, oxygen is an important drug for patients with chronic airway obstruction. It must be administered for specific indications and at well-controlled dosages selected after repeated accurate analysis of arterial blood.

**References**