# PREVENTION OF OVEROXYGENATION DURING TREATMENT WITH A HEART-LUNG MACHINE IN CARDIAC OPERATIONS

*Use of Clark Polarograph for Regulating Oxygen Tension*

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MANY improvements have been made on oxygenators of heart-lung machines to assure sufficient oxygenation of blood, but little attention has been given to the problem of avoiding *over*oxygenation of blood. The possible dangers of overoxygenation, and its prevention by means of a polarograph are discussed in this paper.

Overoxygenation of blood is likely to occur under the following conditions: (1) during recirculation of blood through an oxygenator prior to connection of a patient to the machine; (2) during partial cardiac bypass with a small flow rate, which is a routine procedure at the beginning and at the end of many perfusions; and (3) during perfusion of a small patient with an oxygenator of large capacity.

Our use of the polarograph in the control of oxygenation was based on our impression that some sudden and unexpected fatalities that occurred 10 to 12 hours after perfusion might be due to overoxygenation of the patients' blood during treatment with heart-lung machines. Kirklin[1] has reported a similar impression.

## Effect of Oxygen Excess

The data on toxicity of oxygen are scarce. Ninety to 95 per cent of oxygen at atmospheric pressure can be breathed by man for short periods without ill effects; however, Pichotka and Kühn[2,3] found that in guinea pigs and rabbits degenerative changes of the liver occur after exposure to 90 per cent of oxygen for eight hours every day for 90 days, and that death eventuates after continuous exposure of from 65 to 75 hours. Necropsy of these animals showed severe damage of the lungs, consisting of thickening of alveolar wall with desquamation of epithelium, pulmonary edema, and pleural exudation; dilatation of the heart; necrosis of the myocardium; and congestion of the liver and the kidney.**

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***Retrolental fibroplasia in premature children maintained in an oxygen tent also is attributed to high oxygen tension. (Arnall Patz in Report of 16th M. and R. Pediatric Research Conference on Retrolental Fibroplasia, Role of Oxygen, 1955.)*

Exposure of animals to oxygen at 3 or 3.5 atmospheres of pressure is more harmful than exposure at atmospheric pressure. Under such high oxygen pressure all hemoglobin in venous blood exists as oxyhemoglobin and thus the hemoglobin, the most important mechanism for carrying $CO_2$, is eliminated.[4] This results in the retention of $CO_2$ in peripheral tissues. Under such circumstances animals usually die within a few hours from tissue acidosis. Suppression of pyruvate oxidase and impairment of oxidative metabolism of carbohydrate in the central nervous system also is attributed to the acute oxygen intoxication.[5] According to the results of experiments on isolated slices of brain,[6] high oxygen pressure causes poisoning of many of the enzymes concerned with oxidative processes, thus paradoxically inducing cerebral anoxia. Dickens[7] recently collected available data and arguments to show the toxicity of high oxygen tension on nervous tissue.

If a human being is exposed to a high pressure of oxygen, manifestations of oxygen intoxication rapidly appear. A common early symptom is twitching of the lips or in the arms; other symptoms are dizziness, nausea, vomiting, irregular respiration, confusion, and in some instances convulsions and unconsciousness.[8]

Though oxygenation of blood by most heart-lung machines takes place under atmospheric pressure, the partial pressure of oxygen in the oxygenators can approach 700 mm. Hg if the blood is oxygenated with oxygen plus 1.5 per cent of $CO_2$ at a barometric pressure of 760 mm. Hg and at a temperature of 37 degrees Centigrade (the water vapor pressure is 47 mm. Hg and 1.5 per cent of $CO_2$ would account for 11 mm. Hg.). Recently Penido, Swan, and Kirklin[9] warned of the possibility of overoxygenation of blood with a bubble oxygenator, particularly when there is a temperature gradient between the oxygenator and the patient's body. Clark's oxygen dispersion oxygenator circumvents this problem.[10] The solubility of oxygen in blood decreases with a rise in temperature.[11] If, for example, the temperature of the blood of 30 degrees Centigrade in the oxygenator increases to 37 degrees in the patient's body, the $pO_2$ would increase from 700 to about 800 mm. Hg.[12] It is conceivable that such increased oxygen tension harms the patient, especially when the blood flow is large in relation to the physiologic demands of the patient, or when cavitation occurs in areas of high velocity flow.

## Prevention of Overoxygenation of Blood in Oxygenators

Clark, Wolf, Granger, and Taylor[13] have pointed out that there is a proportional relationship between polarographic reading and oxygen tension. On the other hand, oxygen content increases only slightly after the hemoglobin has been fully oxygenated. As seen in Figure 1 the oxygen tension rises from 140 to 690 mm. Hg while the oxygen content increases only 1.4 volumes per cent, most of which represents physically dissolved oxygen. At an oxygen tension of more than 400 mm. Hg, no further increase in oxygen saturation of hemoglobin occurs.[14] Thus, measurement of oxygen tension by a polarograph provides

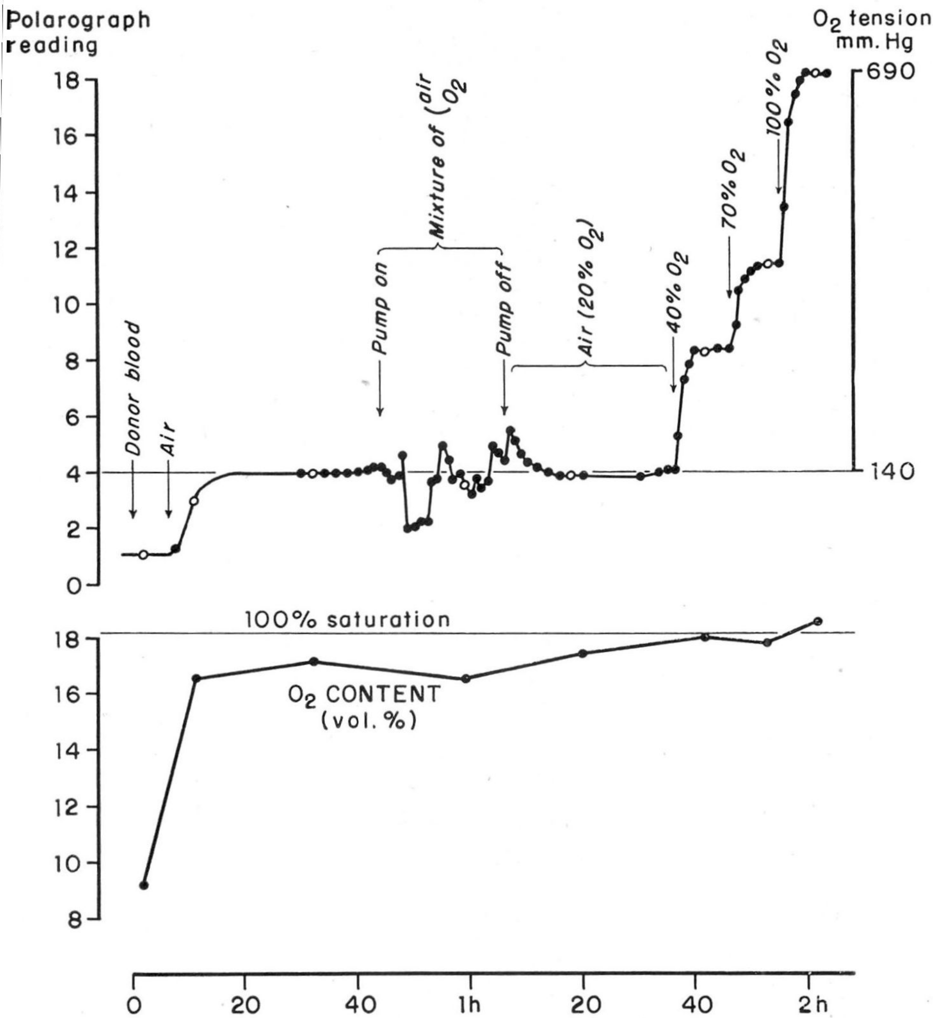


**Fig. 1.** Record of polarographic reading actually is a reading of the galvanometer scale in one case. Before the perfusion the polarographic reading gradually increases as the donor blood is oxygenated by 98.5 per cent of air and 1.5 per cent of $CO_2$ and reaches a stabilized level that is used as a base line. During the bypass period (from "pump on" to "pump off"), the polarographic reading is maintained near the base line by sending suitable gas mixtures to the oxygenator. The blood in the oxygenator was overoxygenated purposely after the perfusion had been completed. The polarographic reading and oxygen content obtained from overoxygenated blood are presented. As the oxygen tension of blood rises, the polarographic reading increases proportionally while the oxygen content increases only slightly. All gas mixtures sent to the oxygenator contained 1.5 per cent of $CO_2$ to maintain a constant pH.

a better estimate of high oxygen values than does measurement of oxygen content or oxygen saturation, and polarography is most suitable for the study and prevention of overoxygenation.

The polarograph* we use is that described by Clark and associates.[15] Briefly, the polarographic determination of oxygen depends upon the reduction of oxygen by hydrogen ions at a cathode maintained near 0.6 volt, according to the equation: $O_2 + 4H^+ + 4e = 2H_2O$. The tiny current that flows as a result of this electrolysis is measured through a suitable circuit by a galvanometer. The amount of current flowing is directly proportional to the oxygen tension in the electrolyte solution, if other variables are controlled or corrected. The electrode of the Clark polarograph consists of a silver chloride anode and a platinum cathode bathed in saturated potassium chloride solution and covered by a polyethylene membrane. The polyethylene membrane readily permits the passage of oxygen but prevents the exchange of electrolytes between blood and potassium chloride solution. As the polarograph utilizes oxygen the blood must be vigorously stirred. Changes in the temperature of blood influence the readings.

## Technic

For this study the Björk rotating disc oxygenator modified by Kay and associates**[16] was used. The electrode of the Clark polarograph (Fig. 2) was inserted in the oxygenator on the arterial or outflow end. Two gas tanks were prepared, one containing 98.5 per cent of air and 1.5 per cent of $CO_2$, and the other containing 98.5 per cent of oxygen and 1.5 per cent of $CO_2$. This amount of $CO_2$ maintained the pH of the blood within approximately normal limits.[17] Prior to connecting the machine to the patient the donor blood was oxygenated in the oxygenator by the air-$CO_2$ mixture until the reading of the galvanometer connected with the polarograph became stabilized at a certain level. The oxygen tension of the blood was then considered to be about 140 mm. Hg [(760-47) x 98.5% x 20%], which is higher than that of normal arterial blood (90 to 100 mm. Hg), and oxygenation of the hemoglobin must be close to 100 per cent.

The polarographic reading obtained from this air-oxygenated blood was then used as a base line. During cardiac bypass adequate amounts of oxygen (with $CO_2$) from the second tank were mixed with the air going into the oxygenator so that the polarographic reading was roughly maintained at this base line. The speed of the rotating discs also was adjusted. By these procedures both overoxygenation and underoxygenation of the blood were avoided.

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**Made by Yellow Springs Instrument Company, Inc., Yellow Springs, Ohio.*

***Kay and Cross oxygenator made by Pemco, Incorporated, 5663 Brecksville Road, Cleveland, Ohio.*


**Fig. 2.** Photograph of the Clark electrode with its polarograph and galvanometer. The electrode is covered with polyethylene membrane and is fixed in the oxygenator near the outflow end.

## Results

The Clark polarograph connected to a heart-lung machine has been used and the data in 20 consecutive patients have been analyzed.* The patients' ages ranged from 20 months to 53 years, and the weights varied from 9.5 to 77.3 kg. The rates of perfusion ranged from 40 to 120 ml. per kilogram per minute, and the duration of the perfusion from 17 to 67 minutes. Cardiac arrest by potassium citrate, lasting from 5 to 29 minutes, was used in all cases. Nineteen of these 20 patients recovered; the one death was unrelated to problems of oxygenation as here discussed.

The polarographic readings during bypass show some fluctuation but generally they remain near the base line as seen in Figure 3. In two cases,

*L. K. Groves, M.D., and W. V. Martinez, M.D., of the Department of Thoracic Surgery, co-operated in this work.

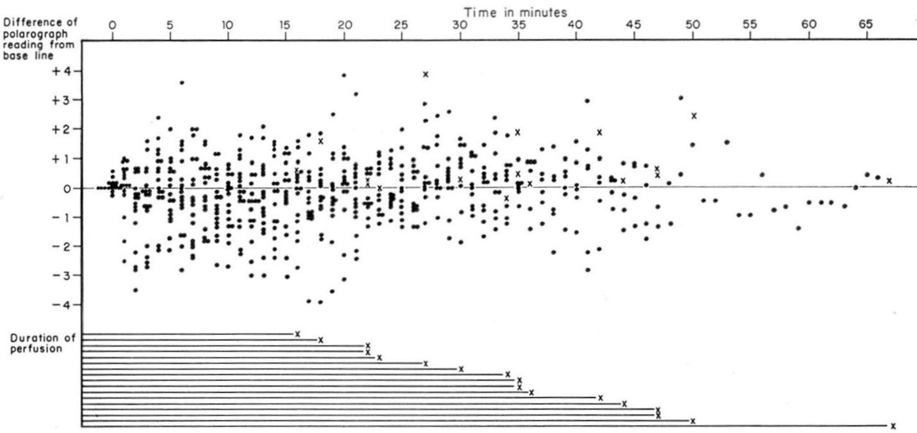


**Fig. 3.** The differences between the polarographic readings during perfusion and the base-line readings are plotted for 17 patients. (Polarographic readings in three patients are not included. Two will be presented separately and in the third the data were not complete. The base line indicated by **O** corresponds to about 140 mm. Hg of oxygen tension. **X** represents the end of perfusion. In most cases oxygen tension of the blood in the oxygenator was maintained near the base line throughout the perfusion. The actual reading of the galvanometer for the base line in our setup ranged from 4.0 to 6.1.

Patients 105 and 111, abnormal polarographic readings were recorded. Patient 105 (Fig. 4) weighed 75 kg. and was perfused with a flow rate of from 50 to 60 ml. per kilogram per minute. The patient's body weight proved to be above the upper limit of the oxygenating capacity of a 20-inch Kay and Cross oxygenator. The readings indicated that the blood was not sufficiently oxygenated. However, as the base line of 6.0 corresponds to an oxygen tension of 140 mm. Hg, a polarographic reading of 3.0 indicates an oxygen tension of about 70 mm. Hg. According to the oxygen-dissociation curve of blood,[18] this corresponds to 90 per cent of oxygen saturation of hemoglobin. In Patient 111 (Fig. 5) an example occurred of an increased base line. Usually our base line lies between 4 and 6 but in this case the reading of the base line was 9.2. This may be due to a change in permeability or thickness of the polyethylene membrane or other variables. At the end of perfusion, oxygenation with air (+1.5 per cent $CO_2$) returned the readings to the same base line. Although in this case the condition was not ideal, the polarograph still gave a fair estimate of oxygenation. In both Patients 105 and 111 the postoperative course was uneventful.

## Summary

Overoxygenation of blood in heart-lung machines may in the past have led to sudden death in the postoperative phase.

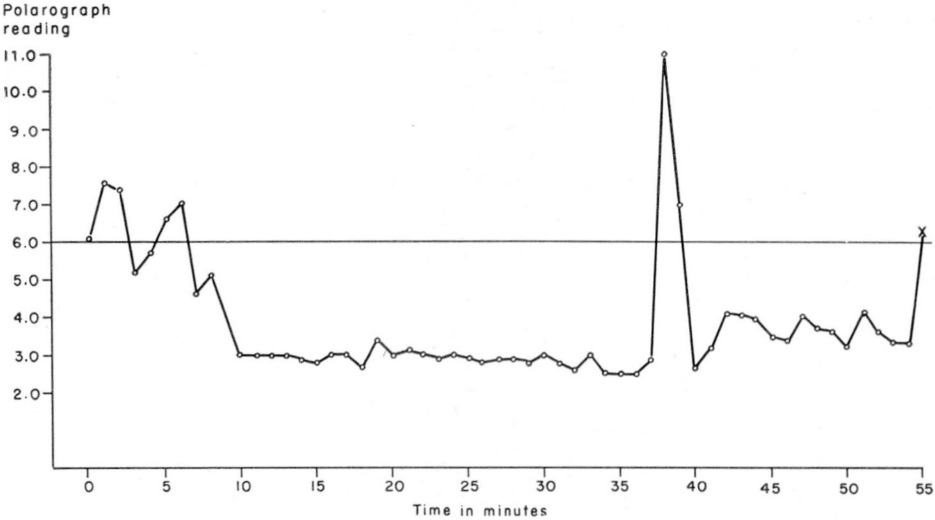


**Fig. 4.** (Case 105.) The low polarographic readings show insufficient oxygenation which probably resulted from the great body weight of the patient in relation to the capacity of the oxygenator. However, the reading of 3.0 indicates about 70 mm. Hg of oxygen tension, which still corresponds to 90 per cent of oxygen saturation of hemoglobin. The high peak of the polarographic readings was caused by a temporarily reduced flow through the oxygenator.

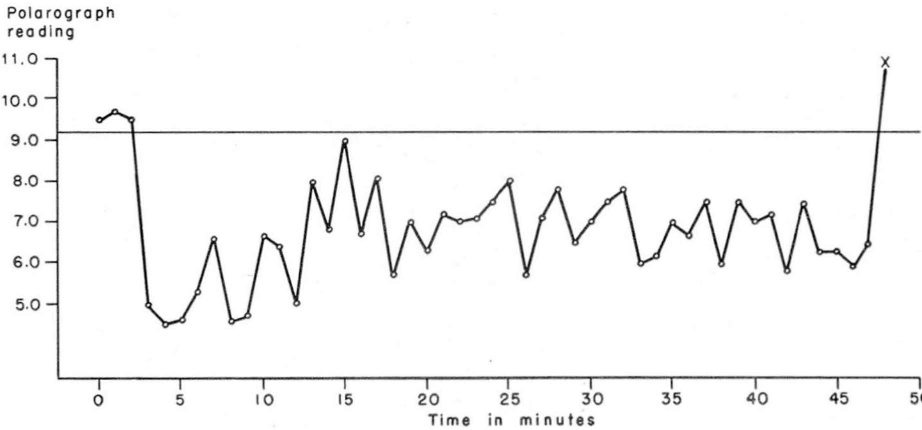


**Fig. 5.** (Case 111.) An unusually high base-line reading was obtained: the reading of 5.0 is considered to correspond to more than 70 mm. Hg of oxygen tension.

Overoxygenation can occur under the following conditions: (1) during recirculation of blood through an oxygenator prior to connection of a patient to the machine; (2) during partial cardiac bypass with a small flow rate, which is a routine procedure at the beginning and at the end of many perfusions; and

(3) during perfusion of a small patient with an oxygenator of large capacity. A Clark polarograph was connected to a heart-lung machine to avoid overoxygenation of blood. The polarograph measures oxygen tension, which provides a better estimate of high oxygen values than does measurement of oxygen content or of oxygen saturation.

Results are reported in a series of 20 consecutive patients in whom oxygen tension of blood had been regulated according to polarographic readings during treatment with a heart-lung machine. There has been one postoperative death in these 20 consecutive cases and this was not related to the problem here discussed.

## Acknowledgment

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