ARTERIAL OXYGENATION DURING TRANSITION FROM 100 PER CENT OXYGEN TO AIR BREATHING: POLAROGRAPHIC Pa_{O_2} STUDY

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It has been generally recognized that after the inhalation of 100 per cent oxygen the extra oxygen taken up by the body is dissipated rather rapidly when air breathing is resumed. Heretofore, percentage saturation of hemoglobin (or oxygen content) has provided us with some information concerning the rate of arterial oxygen saturation and desaturation. There are, however, limitations in this technique, which are best explained by an inspection of the S-shaped oxygen dissociation curve for human blood (fig. 1). Percentage saturation values which lie on the horizontal part of the curve may vary but little, yet the oxygen tension will show a great change. This is especially true as the saturation of hemoglobin approaches 100 per cent.

Hemoglobin is normally 97.5 per cent saturated with air breathing. The problems are enhanced when one attempts to calculate the arterial oxygen tension (Pa_{O_2}) from the dissociation curve, for an oxygen tension approach 400 mm. of mercury is required before the hemoglobin is completely saturated.[1] With high oxygen tensions, the values reported by saturation data give an incomplete picture regarding the actual state of oxygenation of the blood. This would include all studies where high O_2 concentrations are inhaled.

With the recent practical development of the polarograph, it is now possible to measure the arterial oxygen tension (Pa_{O_2}) directly and with a high degree of accuracy.[2, 3, 4] Determinations can be made for all concentrations of oxygen irrespective of the other gases in the inhaled mixture.[5]

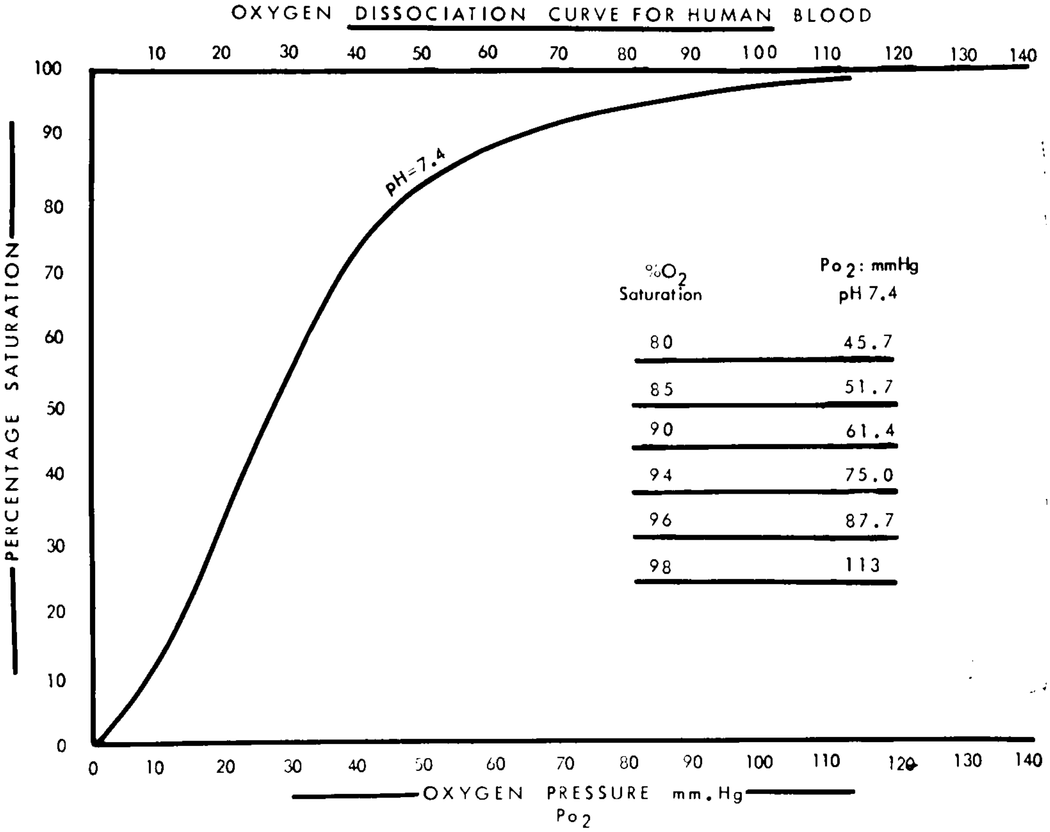
We have previously used the polarograph clinically to study arterial oxygenation during nitrous oxide–oxygen anesthesia,[5] during periods of apnea in man, and one of us (T.R.W. with F. Kreuzer) has determined oxygen tension values in normal students breathing air (unpublished data). This present study is concerned with the rate of uptake of arterial oxygen and the subsequent fall in P_{O_2} when the inspired mixture is changed from 100 per cent oxygen to atmospheric air. We have attempted to answer the question of how long does this extra oxygen remain in arterial blood.

Data of this nature is of value in various clinical situations where increased concentrations of inspired oxygen are desirable. The wisdom of intermittent oxygen therapy in patients with pulmonary and cardiac disease requires clarification. During anesthesia the patient may be allowed to breathe room air following a long period of high oxygen concentration in the inspired mixture. After prolonged anesthesia and surgery, especially of the thoracic and cardiac type, 100 per cent oxygen is usually administered by the anesthesiologist for several minutes with beneficial results, yet often the patient is transported to another area of the hospital and several minutes may elapse before the oxygen is restarted. In another field there has been recent controversy over the value of the use of 100 per cent oxygen by athletes at intervals during competitive sports. The rationale of giving athletes "whiffs of oxygen" is not clear.

Materials and Methods

The polarographic studies of arterial blood were done in the operating room on 7 surgical patients. All were considered clinically to have a normal pulmonary function. They were anesthetized in preparation for surgery with an intravenous barbiturate plus muscle relaxant, and the respirations were controlled by a constant volume nonrebreathing type of mechanical ventilation. In one patient the

Received from the Dartmouth Medical School, The Hitchcock Clinic, and the Cardio-Pulmonary Laboratory of The Hitchcock Foundation, and accepted for publication January 9, 1961. Dr. Heller is Assistant Professor of Pharmacology (Anesthesiology), and Dr. Watson is Instructor in Clinical Surgery, Dartmouth Medical School; Director, Cardio-Pulmonary Laboratory, Hanover, New Hampshire.



%O2 Saturation	Po2: mmHg pH 7.4
80	45.7
85	51.7
90	61.4
94	75.0
96	87.7
98	113

FIG. 1. Oxygen dissociation curve for human blood. (From Handbook of Respiratory Data in Aviation, Washington, D. C., National Research Council, 1944.)

respiration was spontaneous, using a semi-closed circle oxygen apparatus with some rebreathing. In the controlled cases the minute volume used was slightly greater than that calculated from Radford's breathing nomogram.[6] The time of oxygen ventilation varied from three to ten minutes, following which room air was administered. In 6 patients arterial samples were drawn at intervals during arterial deoxygenation when the change was made from oxygen to air. In 4 of these, P_{O_2} determinations were done during oxygen uptake, and in the single patient with spontaneous respiration mentioned above only oxygen uptake was studied. A no. 20 gauge intra-arterial needle was inserted previously into the brachial artery and 10 ml. heparinized arterial blood samples were drawn at intervals of 15 to 60 seconds.

The technique of polarography used in this study has been reported previously. Kreuzer and Watson have incorporated the oxygen electrode of Clark into a reliable arrangement for measuring the arterial blood oxygen tension *in vitro*.[2] The oxygen electrode contains in the same unit a silver anode and platinum cathode which are connected by an electrolyte bridge. A membrane of thin plastic material separates the electrode system from the blood to be analyzed for O_2 tension, and the current flows only within the electrode unit. The membrane is not permeable to water or electrolytes but the dissolved oxygen passes through the membrane and undergoes reduction at the cathode, which is maintained at 0.6 volts. The tiny current which flows as a result of this electrolysis is measured through a suitable circuit by a galvanometer.

The standard O_2 dissociation curve shows the relationship of the arterial O_2 content and the partial pressure of oxygen (Pa_{O_2}). Oxygen content is expressed as percentage hemoglobin saturation, whereas arterial oxygen tension is expressed as Pa_{O_2} in mm. of mercury (fig. 1).

The average normal P_{O_2} value in healthy students breathing air was found to be 97 mm. of mercury by Comroe and his co-workers.[7] A bubble equilibration technique was used by Lambertsen *et al.* to measure arterial oxygen tension in normal man.[8] In nonsmokers they found an average of 94 mm. of mercury. In our laboratory Watson and Kreuzer performed a similar study with the polarographic tech-

TABLE 1

OXYGEN UPTAKE—POLAROGRAPHIC PaO_2 VALUES EXPRESSED IN MM. OF MERCURY
100 PER CENT O_2 INHALATION

Study	Time in Minutes							
	Zero	¼ (15 secs.)	½ (30 secs.)	¾ (45 secs.)	1	2	3	4
E.T.	78	107	142	167	208	282	324	365
C.G.	68		167		252		364	
F.K.	65		143		252			
R.B.	104		283		417			
E.R.	98	165	278		463	473	492	

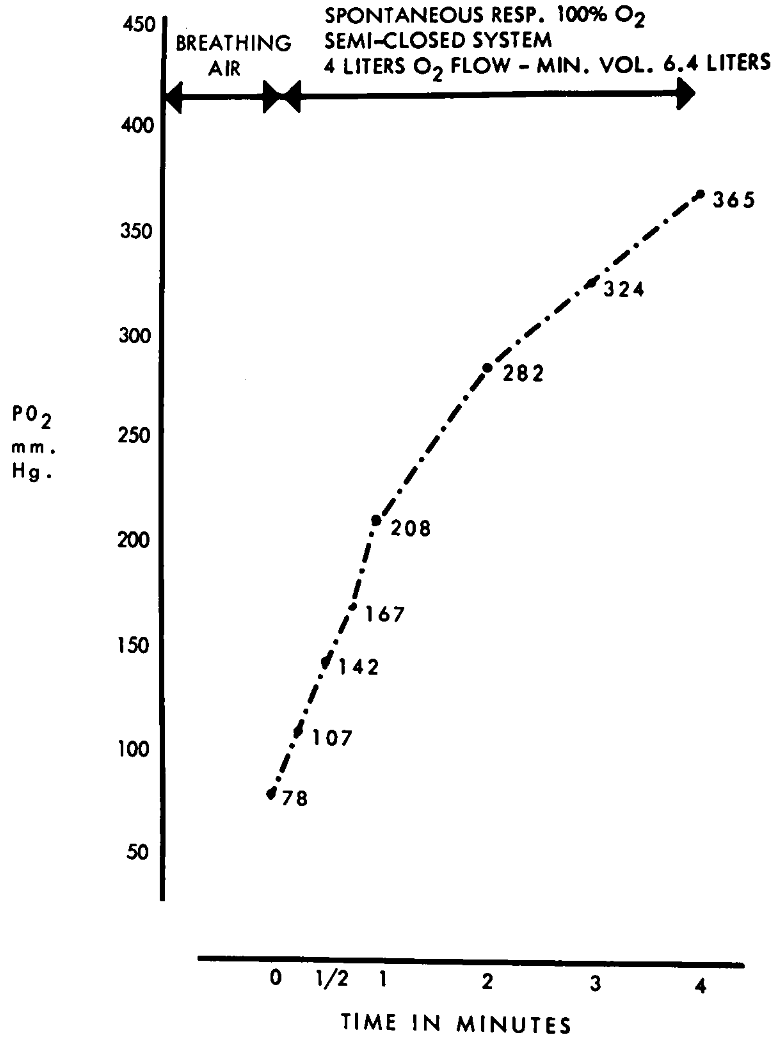


FIG. 2. Subject E. T. age 49. Arterial oxygen tension (Pa_{CO_2}) values during O_2 uptake, breathing 100 per cent O_2 from semiclosed system with O_2 flow 4 l./minute. Minute volume 6.4 liters, resulting in some rebreathing.

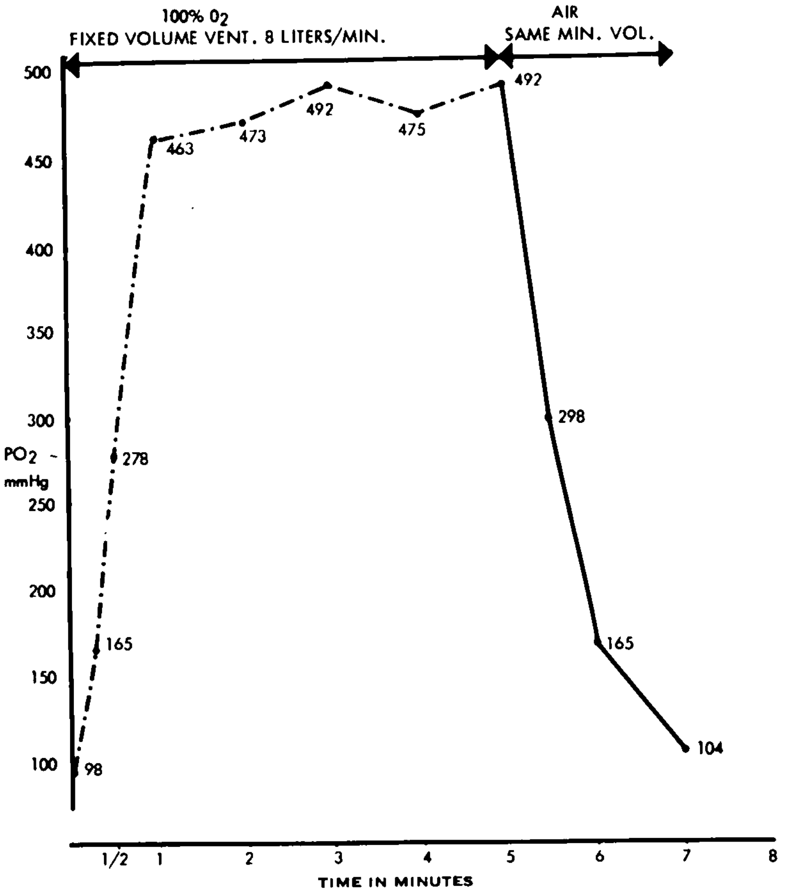


FIG. 3. Subject R. B. age 26. Ventilated with 100 per cent O_2 for 5 minutes, constant minute volume nonrebreathing ventilation 7.5 l./minute. P_{O_2} values recorded during air ventilation and during O_2 uptake when 100 per cent O_2 was readministered. Shows rapid shift in Pa_{O_2} with change in the inspired oxygen mixture.

nique. The average P_{O_2} value in a group of healthy medical students breathing air was 93 mm. of mercury. However the range of normal values can vary widely. We have noted that control readings in routine surgical bed patients were often in the 65 to 80 mm. of mercury range (unpublished data).

RESULTS

When the inspired mixture was changed from air to 100 per cent oxygen the arterial oxygen tension increased very rapidly (table 1 and figs. 2–4). The graph in figure 2 shows the increase in P_{O_2} in a subject inhaling oxygen from a semiclosed system with some rebreathing. This study was done to simulate, for example, oxygen breathing by an athlete where no attempt is made to eliminate rebreathing of some of the exhaled gases.

The studies shown in figures 3 and 4 were all carried out with a nonrebreathing mechanical ventilation, resulting in a more rapid oxygen uptake. This is shown in the P_{O_2} curves obtained in two healthy athletes (subjects R.B. and E.R.). Figure 3 shows a very rapid increase in arterial oxygen tension from 104 to 283 mm. of mercury within 30 seconds. After 100 per cent oxygen was administered for one minute the P_{O_2} reached a height of 417 mm. of mercury.

Figure 4 depicts a similar rate of oxygen uptake in an 18 year old male. In 15 seconds the P_{O_2} changed from 98 to 165 mm. of mercury; in 30 seconds it reached a level of 278 mm. of mercury; and in one minute the arterial

P_{O_2} was 463 mm. of mercury. During the next two minutes the oxygen tension showed a small increase, reaching a peak value of 492 mm. of mercury.

With 100 per cent oxygen breathing the arterial oxygen tensions varied greatly in different patients with a normal pulmonary system by clinical observation. One patient (C.G.) showed a P_{O_2} of 364 mm. of mercury after an oxygen ventilation period of three minutes. The peak value for patient F.K. was 312 mm. of mercury, and this was measured after ten minutes of pure oxygen. By contrast, two other patients (H.B. and M.P.) showed a peak P_{O_2} value of 491 and 475 mm. of mercury with a ventilation period of ten minutes and five minutes respectively.

When the inspired mixture was changed from oxygen to air the arterial oxygen tensions diminished rapidly. The rate of deoxygenation is shown in the P_{O_2} graphs (figs. 3 and 4 and table 2). In approximately two minutes the P_{O_2} fell from the original high values to the new stationary levels. In the 6 subjects studied, the average fall in P_{O_2} during the first one-half minute was 173 mm. of mercury; in one minute the average drop was 282 mm. of mercury, and in two minutes the average figure was 332 mm. of mercury. This did not change appreciably with further air breathing.

Discussion

The polarograph offers a practical and sensitive method of determining direct arterial

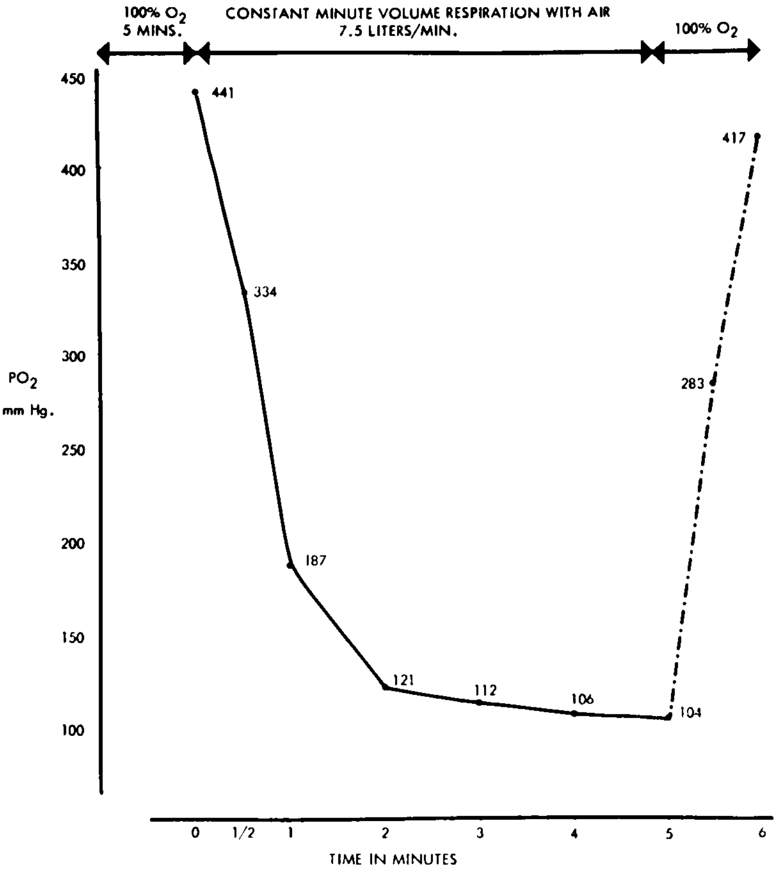


Fig. 4. Subject E. R. age 18. Polarographic arterial P_{O_2} values during O_2 uptake with constant minute volume ventilation–nonrebreathing 100 per cent O_2, 8 l./minute. Mixture changed to room air and P_{O_2} was again recorded during deoxygenation. Near peak values of P_{O_2} are reached in one minute of 100 per cent O_2 inhalation.

TABLE 2

ARTERIAL DEOXYGENATION AFTER CHANGING FROM 100 PER CENT OXYGEN TO AIR
POLAROGRAPHIC P_{O_2} VALUES EXPRESSED IN MM. OF MERCURY

Study (Subject)	Time of 100 Per Cent O_2 Inhalation (Minutes)	Time in Minutes of Air Inhalation												Fall in P_{O_2}		
		Zero	½	1	2	3	4	5	6	7	8	9	10	P_{O_2} Change In ½ Minute	P_{O_2} Change In 1 Minute	P_{O_2} Change In 2 Minutes
C.G.	3	364		85	75	68	64	61	61	61				-	279	289
F.K.	10	312	95	83	74	67	67	64		66			65	217	229	238
R.B.	5	441	334	187	112	112	106	101						107	254	320
E.R.	5	492	298	165	104									194	327	388
H.B.	10	491		204	100	89	89							-	287	382
M.P.	5	475	330	160	101	101	101	95	95					172	315	374
														Average 173	282	332

oxygen tension measurements (Pa_{O_2}) at all concentrations of inspired oxygen. This is particularly desirable in studies involving ventilation with 100 per cent oxygen.

The highest arterial tension values reached in some of the subjects in this study were in the vicinity of 500 mm. of mercury. P_{O_2} values in four other healthy patients breathing oxygen for 5 to 10 minutes recently studied by us were in the range of 400–500 mm. of mercury. However, readings of 300–400 mm. of mercury were also noted in apparently normal patients. Although simultaneous alveolar oxygen tensions were not measured by us, one would anticipate high arterial values in normal individuals after breathing 100 per cent oxygen in a nonrebreathing system, since alveolar nitrogen is said to be almost entirely eliminated within two minutes. However, in some individuals nitrogen washout may not be as efficient as this figure would indicate. At a standard pressure of 760 mm. of mercury, after accounting for the tension of water vapor 47 mm. of mercury, a P_{CO_2} of 40 mm. of mercury, and a small tension contributed by the residual arterial nitrogen, we should expect to find, perhaps, a P_{O_2} greater than 500 mm. of mercury in the perfect lung.* This value will be decreased by impairment of oxygen diffusion across the pulmonary membrane, although this factor has been shown to be usually of minimal importance. More often, the relatively lower peak P_{O_2} values can be explained by venous admixture of the pulmonary capillary bed. Another element in the lung contributing to a decreased arterial oxygen tension is contamination with blood from bronchial and pulmonary venous communications.[9]

It should be kept in mind that positive pressure controlled respiration may also influence the alveolar and arterial oxygen tension. Distribution of alveolar gases may be affected as well as pulmonary blood flow following this type of artificial ventilation. Obviously additional information is required and further studies should be carried out in subjects with spontaneous respiration.

In the healthy young adult the rate of oxygen uptake was rapid as determined by change in arterial P_{O_2}. Near peak values for P_{O_2} were approached within one to two minutes when 100 per cent O_2 was administered in a nonrebreathing system.

The rate of fall of the Pa_{O_2} was equally rapid when changing from oxygen to air breathing. The extra oxygen disappears almost completely in two minutes. The rapid fall is due to the fact that the body cannot store significant amounts of oxygen. A certain amount of oxygen can replace nitrogen in the functional residual capacity (FRC) of the lung and an additional small volume of oxygen is carried in the blood when 100 per cent O_2 is inhaled. The functional residual capacity consists of the expiratory reserve and pulmonary residual air. This volume varies in different people but is usually stated to be 2.5 liters in young adults. In the healthy individuals the alveolar nitrogen is washed out almost completely after 100 per cent O_2 has been breathed for two minutes. In the emphysema-

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* The present study was carried out at an altitude of 530 feet, barometric pressure = 745 – 750 mm. of mercury.

tous patient a longer period of time is required due to the poor ventilation of the lungs.

The saturation of the hemoglobin changes from 97.5 to 100 per cent when 100 per cent oxygen is inhaled. This adds about 0.5 volumes per cent of oxygen in combination with hemoglobin. The physically dissolved oxygen also increases slightly by 1.7 volumes per cent making a total of 2.2 volumes of additional oxygen carried by the blood.[10] This amounts to approximately 100 cc. oxygen.

Clinically, when 100 per cent is administered intermittently to a patient requiring high concentrations of this gas, the arterial oxygen tension changes rapidly in either direction when the concentration of the inspired mixture is altered.

Since there is such a rapid fall in oxygen tension when the inspired mixture is changed from 100 per cent oxygen to that containing a much lower percentage—20 per cent, for example—it would appear that there would be no advantage in administering pure oxygen for a few minutes prior to a nitrous oxide-oxygen induction. This technique has been advocated to achieve higher arterial oxygenation during nitrous oxide anesthesia. The present study would indicate that after 100 per cent oxygen, high oxygen levels are reached in a short period of time; however, with the change to an 80 per cent N_2O—20 per cent O_2 mixture the P_{O_2} will fall rapidly to the same level that would prevail without the previous denitrogenation with oxygen. Any oxygen advantage would definitely disappear after a 5 to 10 minute induction period. It is preferable to start with an 80–20 mixture of N_2O and O_2, rather than to subject the anxious wakeful patient to a preliminary period of oxygen breathing. Actually during the first few minutes of induction with nitrous oxide the arterial oxygen tension will show a significant increase even though the concentration of the oxygen in the anesthetic mixture is the same as that in atmospheric air. This is due to the greater solubility of N_2O in the pulmonary blood plasma as compared with nitrogen. Recent polarographic P_{O_2} studies made by us have corroborated this fact. The opposite occurs at the end of nitrous oxide anesthesia when a sudden change to air breathing is made. Here there is outward diffusion of large volumes of N_2O from pulmonary blood to alveoli, since a few milliliters of nitrogen displace 30 times their volume of soluble N_2O. The alveolar oxygen is diluted by the outpouring of N_2O and this has been described as diffusion anoxia by Fink and his group.[11]

The results of this study also cast doubt on the value of administering a few breaths of 100 per cent oxygen to the athlete prior to engaging in an athletic activity, or for short intervals during the contest. By the time the hockey player, for example, skates out onto the ice the extra oxygen in the lungs and arterial blood has disappeared. The more deeply he breathes, the faster the oxygen is washed out. It is theoretically possible that the athlete may receive a psychological lift by breathing oxygen, or that perhaps there is improved muscle metabolism, although neither has been proven. It appears certain, however, that the increased oxygen does not remain for long in the body.

Recently we studied with the polarograph the rate of fall of arterial oxygen during apnea following hyperventilation with 100 per cent oxygen. With apnea the decline in P_{O_2} is slower than with air breathing, requiring approximately four minutes before there is a return to control levels. This is explained by the fact that during apnea there is no oxygen washout through respiratory ventilation; the extra oxygen remains longer in the body. However, when the inhaled gas is changed from oxygen to air and the respirations continue, the arterial oxygen tension is reduced at a faster rate. It should be remembered that during apnea the carbon dioxide tension rises, whereas the accumulation of this gas is prevented by continuous pulmonary ventilation.

CONCLUSIONS AND SUMMARY

Direct polarographic arterial oxygen tension (Pa_{O_2}) determinations were made during the inhalation of 100 per cent oxygen and during subsequent air breathing.

The advantages of following the arterial P_{O_2} rather than percentage hemoglobin saturation in various clinical conditions are emphasized.

It was found that after the breathing of 100 per cent oxygen the arterial oxygen uptake is extremely rapid. When air breathing is re-

sumed the arterial oxygen tension likewise shows an equally rapid fall, with a return of the Pa_{O_2} to control levels in approximately two minutes.

The practical application of this P_{O_2} study is extensive and varied. From arterial P_{O_2} data it is evident that oxygen therapy should be continuous and not intermittent in those patients requiring increased oxygen concentrations. There is no advantage in preliminary denitrogenation with 100 per cent O_2 prior to a conventional 5 to 10 minute induction with 80 per cent N_2O–20 per cent O_2. The value of a "few whiffs of oxygen" to an athlete is negligible because of the transient storage of the extra oxygen.

The polarographic technique of studying blood oxygenation should be used more widely to investigate many important clinical respiratory problems.

This investigation was supported in part by a research grant from The New Hampshire Tuberculosis Association and The New Hampshire Heart Association.

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BRONCHOSCOPY General anesthesia with intravenous barbiturate and succinylcholine was used. In 8 cases pulmonary ventilation was maintained with diffusion respiration. This resulted in an arterial oxygen saturation of 92–95 per cent. Alveolar carbon dioxide tension increased an average of 9.1 mm. of mercury/minute, to reach 130–140 mm. after 10 minutes. In 6 cases intermittent positive pressure respiration, consisting of 10 breaths every three minutes, was employed. This resulted in alveolar P_{CO_2} values up to 98 mm. of mercury. Ten breaths every two minutes maintained alveolar P_{CO_2} levels of 50–60 mm. of mercury. With continued controlled respiration using a cuffed bronchoscope, normal and lowered alveolar P_{CO_2} levels were observed in 4 cases. (*Ey, W., Schwab, W., and Ulmer, W. T.: Ueber den Gasaustausch bei der Bronchoskopie in Narkose mit Relaxation, Der Anesthetist 9: 350 (Nov.) 1960.*)