Has Oxygen Administration Delayed Appropriate Respiratory Care? Fallacies Regarding Oxygen Therapy

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Modern clinical use of supplemental oxygen supposes that: (1) exposure to $F_{IO_2} \leq 60\%$ is without adverse effects, (2) an individual at risk of developing arterial hypoxemia can be protected by administering high F_{IO_2}, and (3) routine administration of supplemental oxygen is useful, harmless, and clinically indicated. There is now substantial evidence that none of those 3 suppositions are correct, and, on the contrary, supplemental oxygen is actually detrimental to many of the patients who receive it. Supplemental oxygen is much overused and its use should be limited to the few conditions and situations in which it is truly effective, useful, and non-detrimental. *Key words: oxygen, inhalation therapy, atelectasis, hypoxia, adverse effects, right-to-left shunt.* [Respir Care 2003;48(6):611–620.

Introduction

A review of past Donald F Egan Scientific Lectures demonstrates a very distinguished group of presenters, and I am truly honored to be chosen as this year's honoree. Over the last 30 years I have been affiliated with no group more closely or consistently than I have respiratory therapists. A great deal of what I have achieved clearly is due to respiratory therapists with whom I have worked, beginning with David Desautels RRT, when I was a medical student at the University of Florida in the 1960s.

Oxygen and oxygen therapy have been discussed only twice previously at the Egan lecture, the first time in 1974 by John F Murray, the editor of the *American Review of Respiratory Disease* (which later became the *American Journal of Respiratory and Critical Care Medicine*). Subsequently, in 1987 David R Dantzker discussed whether or not we should be concerned with oxygen delivery. It is ironic that 29 years hence, I would raise the same question.

How could anyone possibly think that there is anything controversial about oxygen therapy? Is it possible to raise this question in a serious fashion? I believe that there are several fallacies regarding oxygen therapy. First is the belief that exposure to any fraction of inspired oxygen (F_{IO_2}) $\leq 60\%$ is without adverse effects. I don't believe that is true. Second is the notion that if an individual is at risk of developing arterial hypoxemia, you can protect the patient by administering a high F_{IO_2}. I *know* that is not true. Finally, there is a widely-held belief that routine oxygen supplementation is useful, harmless, and clinically indicated.

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Fallacy #1: Fraction of Inspired Oxygen ≤ 0.60 Is Safe

Let us examine the first hypothesis, that $F_{IO_2} \leq 60\%$ is safe. I participated in a study in which we randomly altered F_{IO_2} from 0.21 to up to 1.0 every 15 minutes with a group of patients who were sufficiently sick to warrant insertion of pulmonary and radial artery catheters. We drew paired blood samples and calculated the percentage of intrapulmonary shunting of blood at each F_{IO_2}. Technically, if the subject was not breathing 100% oxygen, the calculation included not only intrapulmonary shunt fraction but also the hypoxemia-producing effects of areas of lung that had low, but finite, ventilation/perfusion ratio and diffusion defect. Therefore, technically, we calculated venous admixture, not intrapulmonary shunting of blood. The combined results produced a U-shaped curve, with venous admixture decreasing as F_{IO_2} increased from 0.21 to 0.30, remaining unchanged with F_{IO_2} up to 0.60, and then with F_{IO_2} of 0.60 and 1.0 there was a linear increase

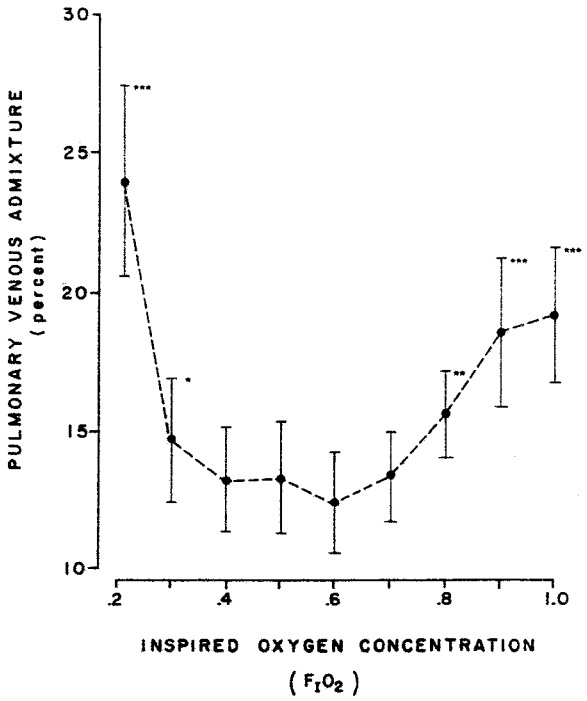

Fig. 1. The relationship between inspired oxygen concentration (F_{IO_2}) and pulmonary venous admixture (right-to-left intrapulmonary shunting of blood when $F_{IO_2} = 1.0$) in patients with acute respiratory distress syndrome. (From Reference 1, with permission.)

in intrapulmonary shunting of blood (Fig. 1). We hypothesized that the latter observation was secondary to absorption atelectasis: as oxygen left unstable alveolar spaces, they collapsed, and continued perfusion of those areas of lung caused increased intrapulmonary shunting of blood.[1]

The interesting part of the curve is between 21% and 30% oxygen. A number of prominent clinicians interpreted these data to mean that patients should be treated with 40% oxygen, because that seemed to minimize intrapulmonary shunting of blood; but of course it does *not*! Rather, it masks the arterial-hypoxemia-producing effect of areas of the lungs with low, but finite, ventilation/perfusion ratio. The classic clinical example is the patient with obstructive lung disease, who, when given just a small amount of supplemental oxygen, suddenly has an increase in arterial oxygen tension and a dramatic decrease in calculated venous admixture. This is a masking effect and does not represent therapeutic efficacy; it just keeps the clinician from appreciating the importance of the lung dysfunction and making an appropriate diagnosis.

In 1975 Michal Douglas and I began emphasizing the importance of decreasing F_{IO_2} as early as possible when treating patients with acute respiratory distress syndrome. We treated 54 patients whose tracheas were intubated for an average of only 4.6 days, and we had an 80% survival rate, which was the highest survival rate reported at that time and perhaps even today.[2] In 1983 I was invited to discuss how "Super PEEP" (positive end-expiratory pressure) could cause a higher survival rate than other ventilator modes. I proposed that the length of time a patient remains intubated and ventilator-dependent is the major determinant of mortality.[3] Data available at that time, and subsequently, support this contention. It seemed that the initial degree of pulmonary injury was not the major determinant of outcome. In fact, patients who had the highest P_{aO_2}/F_{IO_2} (nearly 200 mm Hg) had the highest mortality, and those with the lowest P_{aO_2}/F_{IO_2} (80 mm Hg) had the lowest mortality. There were 9 major differences in therapy applied in this study. Of those, one emphasized the importance of spontaneous breathing, which now is quite popular in Europe, if not yet in the United States.[4] However, the major emphasis was the early application of a low F_{IO_2} as soon as possible in therapy. This was facilitated by application of continuous positive airway pressure (CPAP) to allow the lowest F_{IO_2} possible, instead of titrating the supposedly nontoxic F_{IO_2} to the P_{aO_2}. Most patients breathed 30–40% oxygen within the first 6 hours of therapy, even if P_{aO_2} was as low as 50 mm Hg, oftentimes with very high levels of CPAP. This approach was, and to some extent still is, a radical departure from customary practice. We approached respiratory care from the standpoint of normalizing pulmonary function rather than achieving "acceptable" oxygenation.[5] In the last 5 years an increasing number of investigators have suggested applying CPAP to improve lung compliance *and* optimize gas exchange.[6] Experimental data suggest that $F_{IO_2} > 0.21$ may inhibit hypoxic pulmonary vasoconstriction. If we combine the postulate of absorption atelectasis with that of inhibition of hypoxic pulmonary vasoconstriction, we would hypothesize that, in an individual who has areas of lung that are poorly ventilated, even 30% inspired oxygen would probably lead to absorption atelectasis, decreased lung volume, and impaired lung function.[7]

Register et al studied patients undergoing open heart procedures, all of whom breathed room air preoperatively. Postoperatively the patients who received minimal oxygen supplementation (sufficient to maintain arterial oxygen saturation $> 60\%$) had nearly normal arterial oxygen tension when they breathed room air the day following surgery. Patients who postoperatively breathed 50% oxygen had substantial arterial hypoxemia when they breathed room air the day following surgery. These data suggested that postoperative arterial hypoxemia was induced by breathing supplemental oxygen in the immediate postoperative period.[8] Subsequently, we repeated this study, using only room air intraoperatively and postoperatively, and found that the vast majority of patients undergoing open heart surgery had no decrease in postoperative oxygen tension, compared to preoperative values.[9,10] It appears that postoperative arterial hypoxemia is an iatrogenic disease, in-

duced by breathing supplemental oxygen during and following surgery.

We also found that anesthetized animals that had chest restriction induced with a tight pneumatic band and given 50% oxygen had a much greater area of lung with low, but finite, ventilation/perfusion ratio than similarly chest-restricted animals that breathed room air.[11] In other words, it is likely that patients with restrictive ventilatory defects who are given oxygen supplementation up to 50% will develop areas of lung with low, but finite, ventilation/perfusion ratio that are greater than would occur in the absence of supplemental inspired oxygen. Of course, these results are particularly applicable to the postoperative patient.

I believe the most compelling bit of evidence that supplemental oxygen may be harmful was produced by Garner, who exposed a group of rats with peritonitis to variable F_{IO_2}. One group of rats breathed room air, another group breathed 40% oxygen, and a third group breathed 80% oxygen. Mortality was highest in the group that breathed 80% oxygen and least in the group that breathed room air.[12] I had an ongoing disagreement with an attending surgeon at Ohio State University, where the study was conducted, as to whether 40% inspired oxygen was harmful. This experiment seemed to prove that I was correct. At least that is what I believed, until the pathologist who performed postmortem examination of the animals informed me that he could not distinguish any difference between the groups, based on lung pathology. The observed difference was in the liver! Apparently, oxygen radical formation caused liver damage in most of the animals that breathed $F_{IO_2} > 0.21$. So oxygen supplementation contributed to the increased mortality, but its harmful effects were not restricted to the lung. It is unfortunate that this line of work was not continued.

Fallacy #2: High Fraction of Inspired Oxygen Is Protective

I was taught and I am guilty of having taught that high F_{IO_2} is protective and lends a margin of safety in many clinical settings. The validity of that statement appears to be so obvious that any challenge seems silly, but this is the next fallacy I would like to address.

It is true that if the lungs of an individual being prepared for tracheal intubation are filled with oxygen, thereby displacing nitrogen, there is more time for intubation before desaturation occurs. In other words, if you replace the nitrogen in the lung with oxygen before you paralyze a patient, the patient can tolerate a longer period of apnea. If you are not certain that you can intubate the trachea within 60 seconds or that you can ventilate the patient via mask, you must pre-oxygenate the patient.[13] However, I can think of no other advantage of "prophylactic" hyperoxygenation.

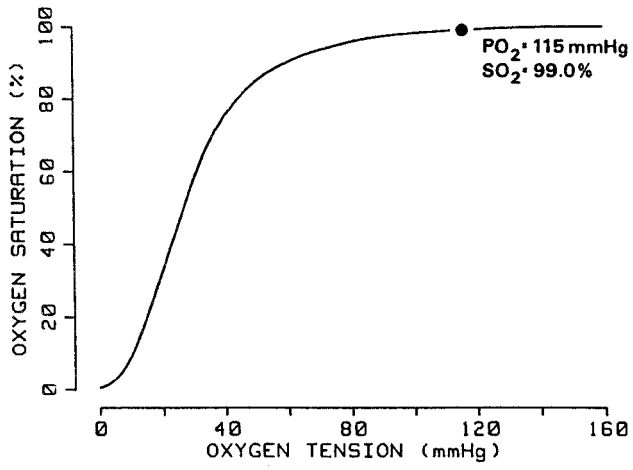

Fig. 2. The oxyhemoglobin dissociation curve produced by measuring oxyhemoglobin saturation that results when gas with a known P_{O_2} is used to tonometer blood.

The oxyhemoglobin dissociation curve originally was produced by astute physiologists who tonometered blood with a known oxygen tension and measured oxyhemoglobin saturation (Fig. 2). We all have been taught that you do not want a patient to get near the elbow of the resulting oxyhemoglobin dissociation curve, because if they do, they may "slide down the slippery slope" of rapid desaturation. That's the way we were taught and that's the way it's being taught today. But we should ask why such a counter-survival mechanism would have evolved; clearly it does not make sense. It is silly to suggest that evolving organisms would have to wait eons for clinicians to arrive with oxygen tanks to protect the individual with the potential for, or evolving, arterial hypoxemia.

There are numerous illustrations to demonstrate how pervasive this attitude is. It is widely believed that a leftward shift in the oxygen-hemoglobin dissociation curve results in less oxygen release to the tissue, because in that situation the hemoglobin holds on to the oxygen with increased affinity. A reference given to support this notion is to a study published in 1944.[14] The authors detailed the effect of carbon monoxide on the oxyhemoglobin dissociation curve, but they did not address release of oxygen for tissue metabolism. To my knowledge there is no such reference in the literature. It is assumed that if the oxygen is bound more tightly by the hemoglobin, it will not release it to the tissue. However, the oxygen tension at the mitochondrial level is only about 3 mm Hg. Therefore, as long as there is a diffusion gradient from the capillary to the tissue, oxygen delivery will occur. Even the Advanced Cardiac Life Support guidelines issued by the American Heart Association refer to a rightward and leftward shift of the oxyhemoglobin dissociation curve and how, as the P_{aO_2} remains constant, oxyhemoglobin saturation goes up and down. However, oxygen tension does not remain con-

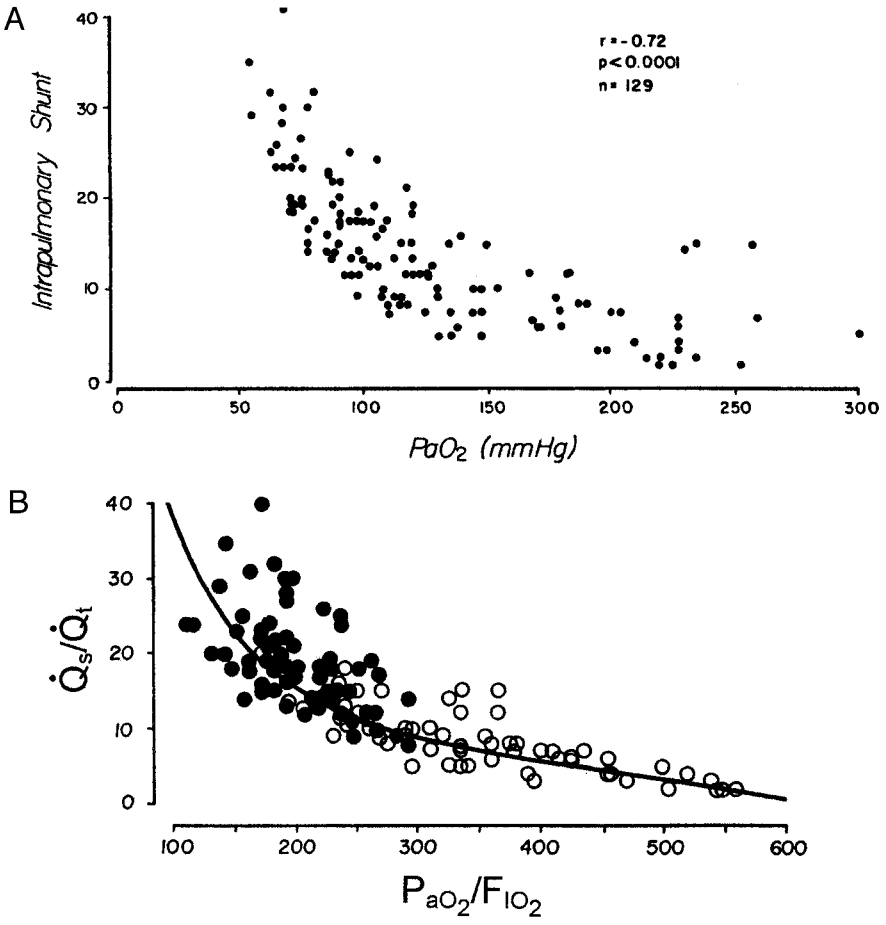

Fig. 3. A: P_{aO_2} resulting from right-to-left intrapulmonary shunting of blood in patients with respiratory insufficiency. B: Ratio of P_{aO_2} to fraction of inspired oxygen (P_{aO_2}/F_{IO_2}) varies with right-to-left intrapulmonary shunt fraction ($\dot{Q}s/\dot{Q}t$) in patients with various degrees of respiratory insufficiency.

stant in the body. Moreover, oxyhemoglobin saturation remains relatively constant and oxygen tension varies in response to the position of the oxyhemoglobin dissociation curve. That is, tissue oxygen consumption determines the amount of oxygen that remains on the hemoglobin molecule that has supplied oxygen to various tissues. Extraction of oxygen from the coronary circulation causes substantial desaturation of blood in the coronary sinus, relative to that observed in blood emanating from the kidneys, intestine, or skin. In each instance tissue oxygen consumption determines the amount of oxygen remaining in the blood, which, in turn, determines the saturation. The saturation then will determine the oxygen tension, rather than the converse. This confusion has led to an important misunderstanding of the utility and protective role of the hemoglobin molecule.

A plot of arterial oxygen tension observed in patients with various degrees of respiratory failure, as a function of their calculated intrapulmonary shunting of blood, reveals a significant but nonlinear relationship between the 2 variables (Fig. 3A). As shunt increases, arterial oxygen tension decreases. However, when intrapulmonary shunting of blood exceeds 15–20% of cardiac output, arterial oxygen tension tends to decrease to a much lesser extent. Some have suggested that dividing the arterial oxygen tension by the F_{IO_2} (the P_{aO_2}/F_{IO_2} ratio) will make the data tighter and allow greater accuracy in calculating right-to-left intrapulmonary shunting of blood from P_{aO_2}-based indices (see Fig. 3B). There is a linear relationship between the P_{aO_2}/F_{IO_2} ratio and shunting of blood, as long as intrapulmonary shunt is $< 10\%$ of cardiac output. In other words, in a healthy subject there is a good relationship between P_{aO_2}/F_{IO_2} and intrapulmonary shunting of blood, but who cares? If a patient is healthy, why would you calculate P_{aO_2}/F_{IO_2} in the first place? In contrast, as P_{aO_2}/F_{IO_2} declines to $<$ 200 mm Hg, there is a minimal relationship between shunt and P_{aO_2}/F_{IO_2}. The curve that results from plotting arterial oxygen as a function of intrapulmonary shunting of blood is unique and easily explained.

The oxyhemoglobin dissociation curve should look like the shunt/P_{aO_2} curve (Fig. 4). This is the way the physiol-

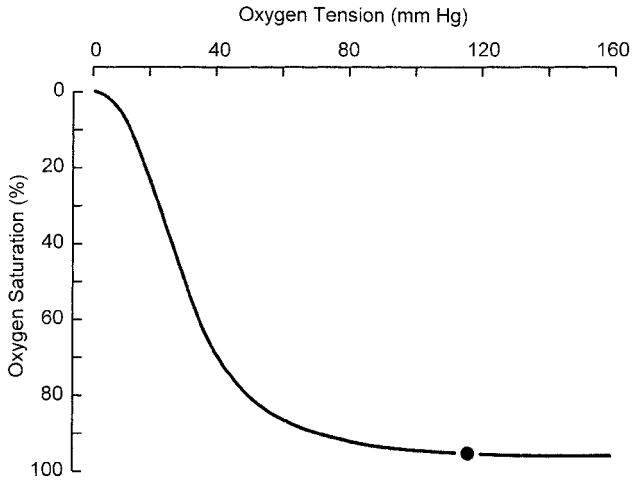

Fig. 4. The oxyhemoglobin dissociation curve oriented as it should be presented, to illustrate how the molecule functions in vivo, at the cellular level. Note that as oxyhemoglobin saturation decreases, as would occur with increasing right-to-left intrapulmonary shunting of blood, the decline in oxygen tension is substantially less. That is, P_{aO_2} remains relatively stable as oxyhemoglobin saturation declines from 90% to 10%.

ogists should have presented the curve to us in the first place. It does not make sense that the human organism would have evolved so that an insult that causes lung dysfunction would result in further damage to the organism by depriving it of oxygen. It does make sense that a defense mechanism would develop to protect a person from progressive arterial hypoxemia. That is, the hemoglobin molecule should protect the individual from progressive hypoxemia, not place him at increased risk. Indeed, I believe the hemoglobin molecule has evolved over millions of years so as to protect the organism from all sorts of risks and insults, including climbing mountains. But we have arrogantly assumed that our ability to supplement oxygen has greater protective ability than the hemoglobin molecule. In 1978 Rose and I determined how fast P_{aO_2} fell when PEEP was discontinued from animals with fresh water near-drowning injury.[15] In those days some practitioners disconnected the patient from the ventilator to measure central venous blood pressure. In essence, they removed useful therapy to gain less useful information. Our investigation showed that the maximum fall in oxygenation occurred within 1 minute of removing PEEP and then stabilized (Fig. 5A).

Twenty years later I realized, looking at the same data, that our conclusion was wrong! In looking back at the experiment and the data it is apparent that when we took the PEEP off, arterial oxygen tension fell from 400 mm Hg to 90 mm Hg, just as we had described, and then it *appeared* that arterial oxygen tension ceased to fall, but it didn't really. The initial decrease in oxygen tension was due to loss of dissolved oxygen from the pulmonary end-

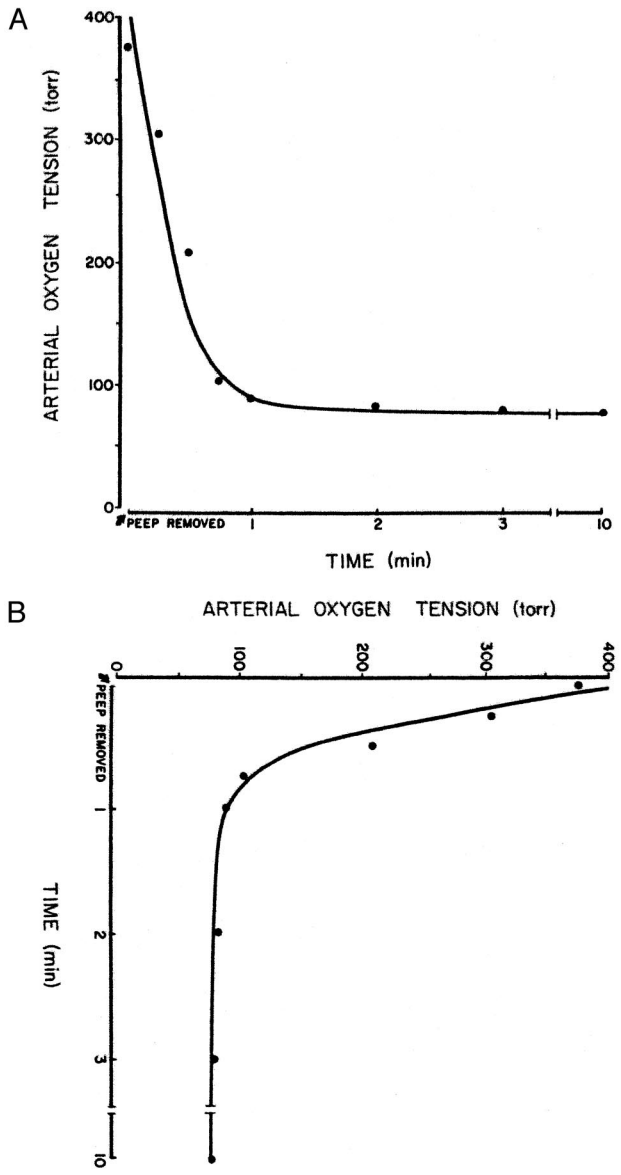

Fig. 5. A: Decline in arterial oxygen tension as a function of time, when PEEP was removed from the airway of a dog subjected to fresh water near-drowning injury. B: The true relationship between oxygen tension and time, created by the oxyhemoglobin dissociation curve.

capillary blood, mixing with shunted venous blood. Once the dissolved oxygen was no longer a factor, arterial blood hemoglobin continued to desaturate, but oxygen tension decreased at a far slower rate; this is because of the steep portion of the oxyhemoglobin dissociation curve. In other words, even though lung function continued to deteriorate, the hemoglobin molecule actually protected the animal by slowing the rate of decrease in oxygen tension (see Fig. 5B). Thus, the steep portion of the curve represents a protective trait of the molecule, which is the opposite of the interpretation drawn by laboratory analysis of the curve.

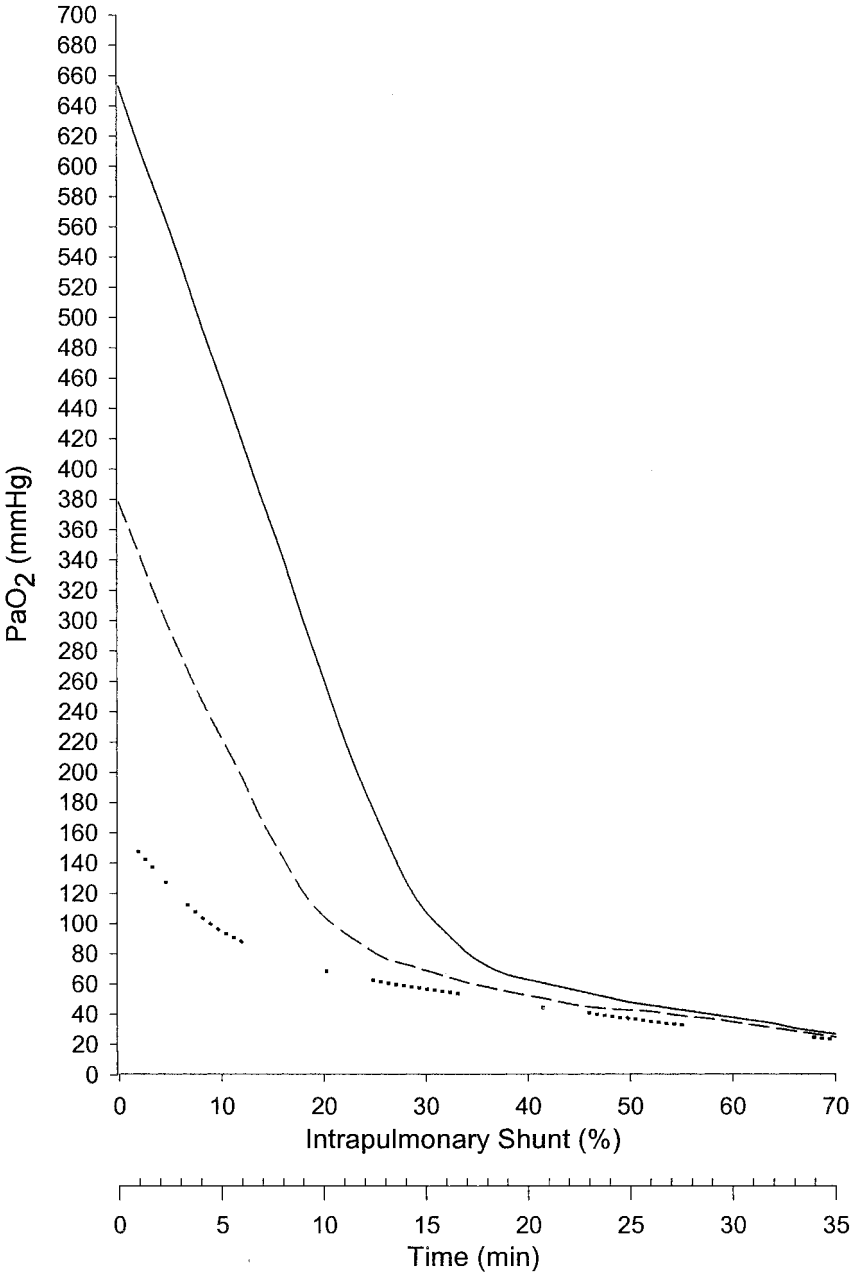

Fig. 6. P_{aO_2} as a function of time and right-to-left intrapulmonary shunting of blood, when shunt increases at a rate of 2% per minute, with 100% oxygen (solid line), 60% oxygen (dashed line), and 30% oxygen (dotted line). (From Reference 16, with permission.)

Recently, we constructed a computer program to plot arterial oxygen tension and oxyhemoglobin saturation as a function of time, as right-to-left intrapulmonary shunting of blood increased from 0 at a rate of 2% every minute. The program plotted data for F_{IO_2} of 0.3, 0.6, and 1.0.[16] This analysis allowed us to determine the efficacy of supplemental oxygen in detecting and treating ongoing lung dysfunction. As expected, it takes longer for a given degree of arterial hypoxemia and oxyhemoglobin desaturation to occur with increased F_{IO_2} (Figs. 6 and 7). However, the clinical application is not so obvious.

In a hypothetical situation in which a patient's lung function progressively deteriorates over time, an individual breathing 100% oxygen will suffer a substantial decrease in P_{aO_2}, from 650 mm Hg to 90 mm Hg, as shunt increases over 15–20 minutes. Yet a pulse oximeter would not allow an appreciation of deterioration in pulmonary function for more than 15 minutes, because the oximeter wouldn't decrease below 98% until at least 15 minutes passed. Then, over the next 5 minutes, the saturation would

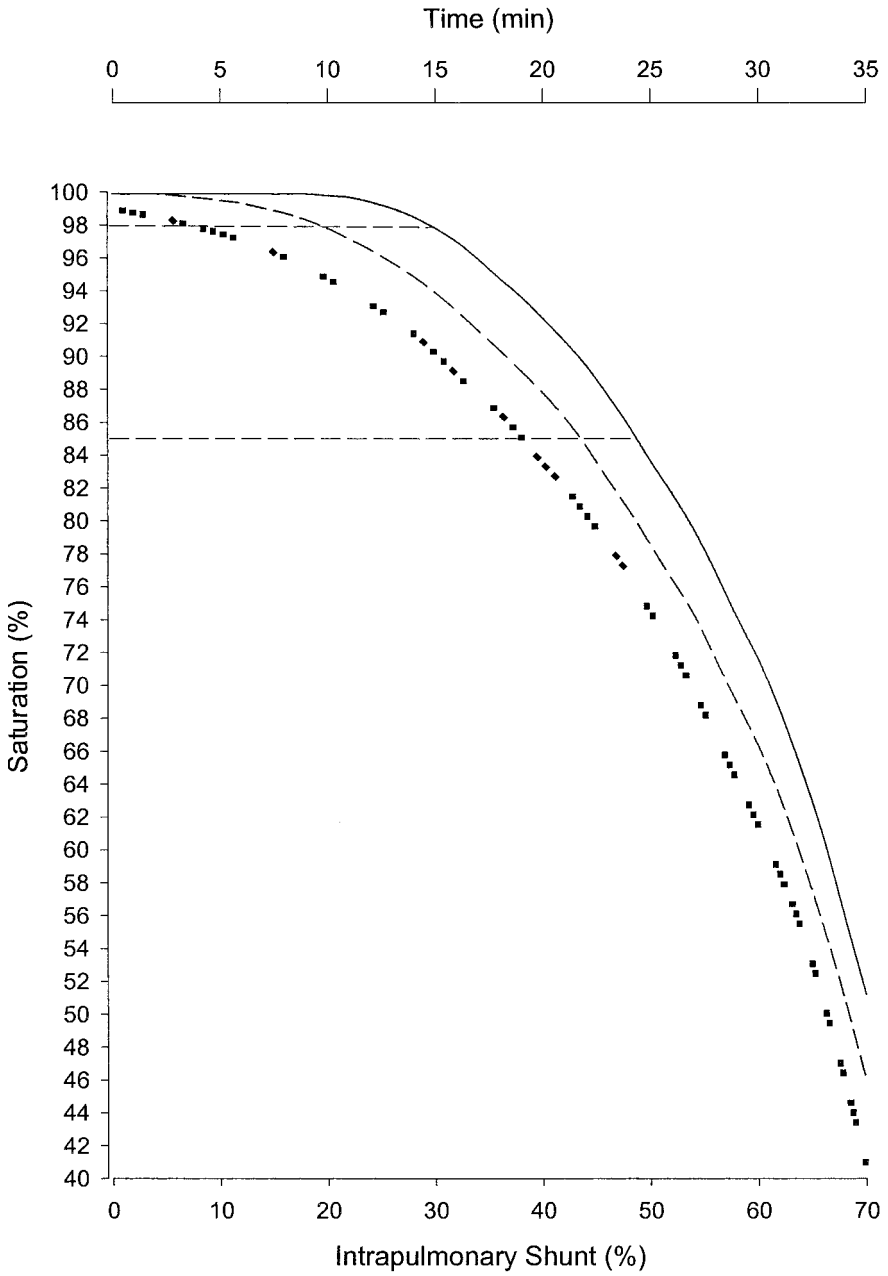

Fig. 7. Oxyhemoglobin saturation as a function of time and right-to-left intrapulmonary shunting of blood, as in Figure 6. (From Reference 16, with permission.)

fall to around 92%, alerting the clinician to a problem. In contrast, the individual breathing 30% oxygen would have a pulse oximeter reading decrease from 99% to 94% within 10 minutes of the onset of increasing shunt. Therefore, the clinician would be alerted to an impending problem sooner with lower F_{IO_2}. When F_{IO_2} is 1.0, the P_{aO_2} will decrease from 90 mm Hg to 60 mm Hg in less than 5 minutes and saturation will fall from 98% to 90% in a similar time frame. In contrast, in a patient breathing 30% oxygen it will take 8 minutes for the P_{aO_2} to get from 90 mm Hg to 60 mm Hg and saturation from 98% to 90%. The clinical implication is interesting. We apply the high F_{IO_2} thinking it is protective, but we observe a decrease in saturation from 98% to 90% over a 5-minute time span. Now what do we do? The F_{IO_2} cannot be increased further. We can buy no more time. We have only 5 minutes to determine the problem and initiate appropriate therapy. The scenario is much different if F_{IO_2} is 0.3. First, the decline in saturation takes several minutes longer to reach 90%. If the saturation reaches 90% before the appropriate intervention is

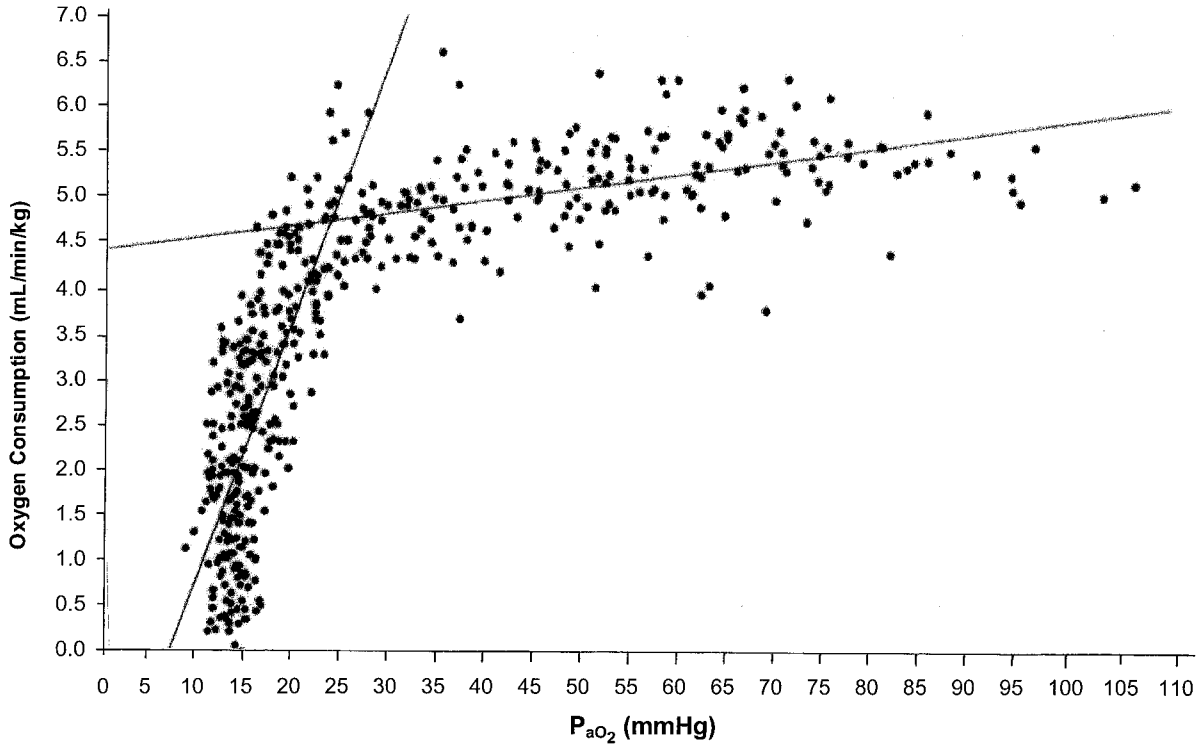

Fig. 8. Oxygen consumption as a function of P_{aO_2}. The slight and constant decline in oxygen consumption as P_{aO_2} decreases from 110 mm Hg to 23 mm Hg is a result of oxygen washout from tissue to blood as P_{aO_2} falls below oxygen tension in tissue. Oxygen consumption is constant from 110 mm Hg to 23 mm Hg, then oxygen consumption falls precipitously. Therefore oxygen consumption becomes delivery-dependent at approximately 23 mm Hg.

initiated, the F_{IO_2} can be increased and saturation transiently will increase while the etiology of the arterial hypoxemia is investigated. If saturation again decreases to 90%, F_{IO_2} may be increased to 1.0, buying further time. In fact, by increasing F_{IO_2} in a patient initially breathing 30% oxygen, P_{aO_2} and saturation can be maintained at "acceptable" levels for 14 minutes, as opposed to the 5 minutes provided when breathing 100% oxygen. Clearly, it is safer and more efficacious to provide the lowest F_{IO_2} possible when one wishes to maximize diagnostic sensitivity and time allowed for therapeutic intervention.

The concept of delivery-dependent oxygen consumption has been of interest to researchers and clinicians for decades. Generally, it is accepted that oxygen delivery as low 35% of normal will prevent a decrease in oxygen consumption. Whether the decrease in oxygen delivery is caused by a fall in cardiac output or by anemia does not seem to matter. Most investigations have ignored the role of oxygen saturation in the concept of delivery-dependent oxygen consumption. Oxygen delivery is the product of hemoglobin concentration, cardiac output, and oxyhemoglobin saturation. Most clinicians would easily tolerate (and may not even appreciate) a cardiac output decrease of 50% of normal in their patients. Most would tolerate a decline in hemoglobin concentration, even more than 50%, because of the risks of transfusion and the likelihood of the compensatory increase in cardiac output, which would serve to maintain oxygen delivery. Yet few clinicians would tolerate a similar decline in hemoglobin saturation. In fact, most investigators report oxygen saturation $<$ 90% as "unacceptable." To my knowledge, there is little if any prospective evidence to document harmful effects from an arterial oxygen saturation of 80%, 70%, or even 60% on organ function. Of course, the one exception to that statement is the well known increase in pulmonary artery pressure that occurs with moderate degrees of arterial hypoxemia. However, in terms of oxygen delivery I know of no evidence to support the efficacy of maintaining arterial oxygen saturation greater than 90%. In response to this thought, Kabemba et al sought to determine the oxygen tension and saturation levels associated with a decrease in systemic oxygen consumption.[17] In other words, we sought to determine when supply-dependent decreases in oxygen consumption would occur with progressive arterial hypoxemia. Results reported in October 2001 indicated that an arterial oxygen tension of 23 mm Hg and a concomitant hemoglobin saturation of

approximately 40% could produce a supply-dependent decrease in oxygen consumption (Fig. 8). Follow-up studies are in progress to determine if neurologic injury occurs in severe hypoxemia.[18] It appears that severe arterial hypoxemia may be better tolerated than was previously believed.

Fallacy #3: Supplemental Oxygen Is Useful

There are numerous clinical situations in which supplemental oxygen administration is considered efficacious. For example, numerous admissions to the emergency department result in immediate placement of devices to supplement inspired oxygen concentration. Similarly, in many, if not most, post-anesthesia care units throughout the United States supplementation of inspired oxygen is routine and precedes any other therapeutic or monitoring activity. Generally, supplemental oxygen is considered efficacious during any procedure requiring intravenous administration of sedative drugs. Yet there is little or no evidence to support the efficacy of such practice, except for demonstration of increased oxygen saturation in the blood. In other words, since it is assumed that an increased arterial oxygen saturation increases the margin of safety, it further is assumed that supplemental oxygen is beneficial. Recently, it was demonstrated that hyperoxic ventilation increased microcirculatory oxygen tension values but oxygen consumption remained unchanged.[19] In other words, there was no proven benefit in terms of cellular respiration.

One of the 6 primary causes of arterial hypoxemia is hypoventilation. However, with only a modest increase in inspired oxygen concentration substantial hypoventilation can occur without concomitant arterial hypoxemia. Of course, this well known phenomenon is the basis for recommending oxygen supplementation during procedures requiring intravenous sedation and for patients recovering from anesthesia, when hypoventilation can occur. However, these recommendations occurred prior to the advent of pulse oximeters in such environments. A profound degree of hypoventilation may be present before arterial hypoxemia occurs, when inspired oxygen concentration is supplemented, which renders pulse oximetry worthless as a monitor of ventilation. In contrast, patients breathing room air can have only a moderate decrease in ventilation before the pulse oximeter will warn the clinician of hypoventilation.[20] Therefore, oxygen supplementation during intravenous sedation and recovery from general anesthesia may prevent the early diagnosis of hypoventilation and thus prevent appropriate and timely intervention. With this in mind, the data strongly suggest that patients in post-anesthesia care units should not receive supplemental oxygen unless arterial oxygen saturation consistently falls below 90% and stimulation is ineffective in reversing the arterial hypoxemia.

Table 1. Primary Conditions That Result in Arterial Hypoxemia

Hypoventilation
Low, but finite, ventilation/perfusion ratio
Right-to-left intrapulmonary shunt
Diffusion defect
Low barometric pressure
Hypoxic inspired gas

Conclusions

One might ask why oxygen has become such a popular drug. It is my contention that the attitude "if some is good, more is better!" is pervasive. Further, oxygen is readily available and very inexpensive. Also, development of the Clark electrode in the 1950s made possible the quantification of arterial oxygen tension and, therefore, the diagnosis of arterial hypoxemia. I believe that the ability to quantify oxygen levels in arterial blood provided substantial impetus for the "treatment" of arterial hypoxemia.

There are 6 physiologic conditions that can lead to arterial hypoxemia: alveolar hypoventilation; decreased, but, finite ventilation/perfusion ratio; right-to-left intrapulmonary shunting of blood; diffusion defect; low barometric pressure; and subatmospheric F_{IO_2} (< 0.21) (Table 1). A decrease in cardiac output, increase in oxygen consumption, and anemia all can exacerbate the hypoxemia caused by these primary factors but may not produce arterial hypoxemia in their absence. It is interesting to speculate how arterial hypoxemia would be treated if supplemental oxygen was not an option (Table 2). Obviously, hypoventilation would be reversed, decreased ventilation/perfusion ratio would be improved with bronchodilators and/or CPAP, and increased shunting of blood due to lung collapse would be treated with elevated airway pressure. Appropriate treat-

Table 2. Specific Treatments for Arterial Hypoxemia

Cause	Treatment
Hypoventilation	Increase alveolar ventilation
Low ventilation/perfusion ratio	CPAP
Intrapulmonary shunt	CPAP
Diffusion defect	Steroids (?)
Low barometric pressure	Descent
Low inspired oxygen concentration ($< 21\%$)	Oxygen!

Although oxygen supplementation will increase oxygen tension in every instance, oxygen is the specific treatment for reversal of the pathologic condition causing arterial hypoxemia in only 1 instance: low inspired oxygen concentration ($< 21\%$).
CPAP = continuous positive airway pressure.

ment of a diffusion defect is still a subject of debate. Hypoxemia produced by low barometric pressure would be treated with return to sea level pressure. Arterial hypoxemia resulting from a subatmospheric F_{IO_2} (< 0.21) would be treated by restoration of normal inspired oxygen concentration, but it is unlikely that most clinicians will ever observe a patient with arterial hypoxemia secondary to subatmospheric F_{IO_2}. It is of great interest that supplemental oxygen is the specific "antidote" for only 1 of the major causes of arterial hypoxemia! Because increased F_{IO_2} will increase arterial oxygen tension in every single instance, appropriate therapy often is delayed until "oxygen therapy" is no longer effective. If supplemental oxygen were not readily available, the emphasis would shift to diagnosis and specific therapy. Therefore, it is my contention that supplemental oxygen has, for many years, delayed the appropriate diagnosis and specific therapy of numerous conditions that cause arterial hypoxemia. Only recently have clinicians begun to understand the importance of treating lung pathology with goals other than simply providing "adequate oxygenation." Recent trials of the "open-lung" strategy, improved lung compliance, and minimization of right-to-left intrapulmonary shunting of blood demonstrated better survival among patients with acute respiratory distress syndrome. Hopefully, similar research will occur on other conditions in which oxygen supplementation is commonly applied.

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