

Rules on Oxygen Therapy:

- Physiology:
1. PO_2 , SaO_2 , CaO_2 are all related but different.
 2. PaO_2 is a sensitive and non-specific indicator of the lungs' ability to exchange gases with the atmosphere.
 3. FIO_2 is the same at all altitudes
 4. Normal PaO_2 decreases with age
 5. The body does not store oxygen

Therapy & Diagnosis:

1. Supplemental O_2 is an $FIO_2 > 21\%$ and is a drug.
2. A reduced PaO_2 is a non-specific finding.
3. A normal PaO_2 and alveolar-arterial PO_2 difference (A-a gradient) do NOT rule out pulmonary embolism.
4. High FIO_2 doesn't affect COPD hypoxic drive
5. A given liter flow rate of nasal O_2 does not equal any specific FIO_2 .
6. Face masks cannot deliver 100% oxygen unless there is a tight seal.
7. No need to humidify if flow of 4 LPM or less

Indications for Oxygen Therapy:

1. Hypoxemia
2. Increased work of breathing
3. Increased myocardial work
4. Pulmonary hypertension

Delivery Devices:

1. Nasal Cannula
 - a. 1 – 6 LPM
 - b. FIO_2 0.24 – 0.44 (approx 4% per liter flow)
 - c. FIO_2 decreases as V_e increases
2. Simple Mask
 - a. 5 – 8 LPM
 - b. FIO_2 0.35 – 0.55 (approx 4% per liter flow)
 - c. Minimum flow 5 LPM to flush CO_2 from mask
3. Venturi Mask
 - a. Variable LPM
 - b. FIO_2 0.24 – 0.50
 - c. Flow and corresponding FIO_2 varies by manufacturer
4. Partial Rebreather
 - a. 6 – 10 LPM
 - b. FIO_2 0.50 – 0.70
 - c. Flow must be sufficient to keep reservoir bag from deflating upon inspiration
5. Nonrebreather
 - a. 6 – 10 LPM
 - b. FIO_2 0.70 – 1.0
 - c. Flow must be sufficient to keep reservoir bag from deflating upon inspiration
6. With the exception of the Venti mask, the above are all low flow oxygen delivery systems and therefore the exact F_iO_2 will be based on the patient's anatomic reservoir and minute ventilation.

1. PO_2 , SaO_2 , CaO_2 are all related but different.

PaO_2 , the partial pressure of oxygen in the arterial blood, is determined solely by the pressure of inhaled oxygen (the PIO_2), the $PaCO_2$, and the architecture of the lungs. The most common physiologic disturbance of lung architecture is ventilation-perfusion (V-Q) abnormality; less commonly, there can be diffusion block or anatomic right to left shunts. If the lungs are normal, then PaO_2 is affected only by the alveolar PO_2 (PAO_2), which is determined by the fraction of inspired oxygen, the barometric pressure and the $PaCO_2$ (i.e., the alveolar gas equation).

PaO_2 is a major determinant of SaO_2 , and the relationship is the familiar sigmoid-shaped oxygen dissociation curve. SaO_2 is the percentage of available binding sites on hemoglobin that are bound with oxygen in arterial blood. The O_2 dissociation curve (and hence the SaO_2 for a given PaO_2) is affected by $PaCO_2$, body temperature, pH and other factors. However, SaO_2 is unaffected by the content of hemoglobin, so anemia does not affect SaO_2 .

CaO_2 is arterial oxygen content. Unlike either PaO_2 or SaO_2 , the value of CaO_2 directly reflects the total number of oxygen molecules in arterial blood, both bound and unbound to hemoglobin. CaO_2 depends on the hemoglobin content, SaO_2 , and the amount of dissolved oxygen. Units for CaO_2 are ml oxygen/100 ml blood (see below).

2. PaO_2 is a sensitive and non-specific indicator of the lungs' ability to exchange gases with the atmosphere.

In patients breathing ambient or "room" air ($FIO_2 = .21$), a decreased PaO_2 indicates impairment in the gas exchange properties of the lungs, usually signifying V-Q imbalance. PaO_2 is a very sensitive indicator of gas exchange impairment; it can be reduced from virtually any parenchymal lung problem, including asthma, chronic obstructive pulmonary disease, and atelectasis that doesn't show up on a chest x-ray.

3. FIO_2 is the same at all altitudes.

The percentage of individual gases in air (oxygen, nitrogen, etc.) doesn't change with altitude, but the atmospheric (or barometric) pressure does. FIO_2 , the fraction of inspired oxygen in the air, is thus 21% (or .21) throughout the breathable atmosphere. PaO_2 declines with altitude because the inspired oxygen pressure declines with altitude (inspired oxygen pressure is fraction of oxygen times the atmospheric pressure). Average barometric pressure at sea level is 760 mm Hg; it has been measured at 253 mm Hg on the top of Mt. Everest.

4. Normal PaO_2 decreases with age.

A patient over age 70 may have a normal PaO_2 around 70-80 mm Hg, at sea level. A useful rule of thumb is normal PaO_2 at sea level (in mm Hg) = 100 minus the number of years over age 40.

5. The body does not store oxygen.

If a patient needs supplemental oxygen it should be for a specific physiologic need, e.g., hypoxemia during sleep or exercise, or even continuously (24 hours a day) as in some patients with severe, chronic lung disease.

6. Supplemental O_2 is an $FIO_2 > 21\%$.

Supplemental oxygen means an FIO_2 greater than the 21% oxygen in room (ambient) air. When you give supplemental oxygen you are raising the patient's inhaled FIO_2 to something over 21%; the highest FIO_2 possible is 100%. To give more oxygen requires a hyperbaric chamber.

7. A reduced PaO_2 is a non-specific finding.

It can occur from any parenchymal lung problem, and only signifies a disturbance of gas exchange

(usually due to V/Q imbalance). A low PaO₂ should not be used to make any particular diagnosis, including pulmonary embolism.

8. A normal PaO₂ and Alveolar-arterial PO₂ difference (A-a gradient) do not rule out pulmonary embolism.

About 5% of confirmed cases of PE manifest a normal A-a gradient.

9. High FIO₂ doesn't affect COPD hypoxic drive.

The reason a high FIO₂ may raise PaCO₂ in a patient with COPD is not because the extra oxygen cuts off the hypoxic drive. Modest rise in PaCO₂ occurs mainly because the extra oxygen alters V/Q relationships within the lungs, creating more physiologic dead space.

10. A given liter flow rate of nasal O₂ does not = any specific FIO₂.

The oft-quoted rule that 2 l/min = an FIO₂ of 24%, 3 l/min = 28%, etc., is an illusion, based on nothing experimental or scientific. The actual FIO₂ with nasal oxygen depends on the patient's breathing rate and tidal volume, i.e., the amount of room air inhaled through the mouth and nose that mixes with the supplemental oxygen.

11. Face masks cannot deliver 100% oxygen unless there is a tight seal.

So-called non-rebreather face masks can deliver an FIO₂ up to around 80%. It is a mistake to label a patient with any loose-fitting face mask as receiving an "FIO₂ of 100%." (Again, 100% oxygen can only be delivered with a ventilator or tight-fitting face mask.)

SIGNS OF OBVIOUS BREATHING

If a patient's breathing is obvious on initial contact (for example, when you first see the patient on walking into the room) *it is abnormal*. Normal breathing at rest is simply not obvious; one has to look very closely for chest movement to appreciate breathing. Six signs that may make someone's breathing obvious to the observer - all abnormal - are:

- flaring of nostrils with breathing
- tachypnea (generally, to be obvious, respiratory rate is > 24 breaths/min)
- noisy breathing (wheezing, stridor, moaning, etc.)
- use of accessory breathing muscles (neck muscles, intercostal muscles, etc.)
- pursed lip breathing (often seen in severe COPD)
- Cheyne-Stokes breathing (alternating periods of apnea with tachypnea; apnea periods may last up to 30 seconds)

FOUR IMPORTANT EQUATIONS IN CLINICAL PRACTICE

Equation Title	Complete Equation	Abbreviation Sufficient for Most Clinical Applications
1. PCO₂ equation	$\text{PaCO}_2 = \text{VCO}_2 \times 0.863 / \text{VA}$ where $\text{VA} = \text{VE} - \text{VD}$	$\text{PaCO}_2 \sim \text{VCO}_2 / \text{VA}$
2. Henderson-Hasselbalch equation	$\text{pH} = \text{pK} + \log \text{HCO}_3^- / 0.03(\text{PaCO}_2)$	$\text{pH} \sim \text{HCO}_3^- / \text{PaCO}_2$
3. Alveolar gas equation	$\text{PAO}_2 = \text{FIO}_2(\text{P}_B - \text{P}_{\text{H}_2\text{O}}) - \text{PaCO}_2[\text{FIO}_2 + (1 - \text{FIO}_2) / \text{R}]$	$\text{PAO}_2 = \text{FIO}_2(\text{P}_B - 47) - 1.2(\text{PaCO}_2)$
4. Oxygen content equation	$\text{CaO}_2 = (\text{SaO}_2 \times \text{Hb} \times 1.34) + .003(\text{PaO}_2)$ where: 1.34=ml O ₂ /gram Hb .003=ml O ₂ /mm Hg PaO ₂ /dl Hb=content in grams/dl	$\text{CaO}_2 = \text{SaO}_2 \times 1.34 \times \text{Hb}$

1. The PCO₂ Equation

The PCO₂ equation puts into physiologic perspective one of the most common of all clinical observations: a patient's respiratory rate and breathing effort. The equation states that alveolar PCO₂ (PACO₂) is directly proportional to the amount of CO₂ produced by metabolism and delivered to the lungs (VCO₂) and inversely proportional to the alveolar ventilation (VA). While the derivation of the equation is for alveolar PCO₂, its great clinical utility stems from the fact that alveolar and arterial PCO₂ can be assumed to be equal. Thus:

$$\text{PaCO}_2 = \frac{\dot{\text{VCO}}_2 \times 0.863}{\dot{\text{V}}_A}$$

The constant 0.863 is necessary to equate dissimilar units for VCO₂ (ml/min) and VA (L/min) to PACO₂ pressure units (mm Hg). Alveolar ventilation is the total amount of air breathed per minute (VE; minute ventilation) minus that air which goes to dead space per minute (VD). Dead space includes all airways larger than alveoli *plus* air entering alveoli in excess of that which can take part in gas exchange.

Even when alveolar and arterial PCO₂ are not equal (as in states of severe ventilation-perfusion imbalance), the relationship expressed by the equation remains valid:

$$\text{PaCO}_2 = \frac{\dot{\text{VCO}}_2}{\dot{\text{V}}_A}$$

In the clinical setting we don't need to know the actual amount of CO₂ production or alveolar ventilation. We just need to know *if* VA is adequate for VCO₂; if it is, then PaCO₂ will be in the normal range (35-45 mm Hg). Conversely, a normal PaCO₂ means only that alveolar ventilation is adequate for the patient's level of CO₂ production at the moment PaCO₂ was measured.

From the PCO_2 equation it is evident that a level of alveolar ventilation inadequate for CO_2 production will result in an elevated PaCO_2 (> 45 mm Hg; hypercapnia). Thus patients with *hypercapnia* are *hypoventilating*. Conversely, alveolar ventilation in excess of that needed for CO_2 production will result in a low PaCO_2 (< 35 mm Hg; hypocapnia) and the patient will be *hyperventilating*. For reasons that will be discussed below, the terms hypo- and hyper- ventilation refer *only* to high or low PaCO_2 , respectively, and should not be used to characterize any patient's respiratory rate, depth, or breathing effort.

From the PCO_2 equation it follows that the only physiologic reason for elevated PaCO_2 is a level of alveolar ventilation inadequate for the amount of CO_2 produced and delivered to the lungs.

2. The Henderson-Hasselbalch Equation

The bicarbonate buffer system, quantitatively the largest in the extracellular fluid, instantaneously reflects any blood acid-base disturbance in one or both of its buffer components (HCO_3^- and PaCO_2). The ratio of HCO_3^- to PaCO_2 determines pH and therefore the acidity of the blood:

$$\text{pH} = \text{pK} + \log \frac{\text{HCO}_3^-}{0.03(\text{PaCO}_2)}$$

pH is the negative logarithm of the hydrogen ion concentration, $[\text{H}^+]$, in nM/L (nM = nanomole = 1×10^{-9} moles; $\text{pH} 7.40 = 40$ nM/L $[\text{H}^+]$). Because of the negative logarithm, small numerical changes of pH in one direction represent large changes of $[\text{H}^+]$ in the other direction. An 0.1 unit fall in pH from 7.4 to 7.3 represents a 25% increase in $[\text{H}^+]$; a similar percentage change in serum sodium would increase its value from a normal 140 mEq/L to 175 mEq/L!

Unfortunately, the logarithmic nature of pH and the fact that acid-base disorders involve simultaneous changes in three biochemical variables and in the function of two organ systems (renal and respiratory), have all combined to made acid-base a difficult subject for many clinicians. In the 1970s nomograms incorporating the H-H variables and compensation bands for the four primary acid-base disorders were introduced as aids to determining a patient's acid-base status. While nomograms can be helpful if readily available and properly used, there is much to be gained by simply knowing the relationship among the three H-H variables and the type of changes expected with each disorder. In this regard the following items of clinical importance bear emphasis.

a) If any of the three H-H variables is truly abnormal the patient has an acid-base disturbance *without exception*. Thus any patient with an abnormal HCO_3^- or PaCO_2 , not just abnormal pH, has an acid-base disorder. Most hospitalized patients have at least one bicarbonate measurement as part of routine serum electrolytes; this is usually called the 'CO₂' or 'total CO₂' when measured in venous blood. (Total CO₂ includes bicarbonate and the CO₂ contributed by dissolved carbon dioxide, the latter 1.2 mEq/L when PaCO_2 is 40 mm Hg. For this reason, and because bicarbonate concentration is slightly higher in venous than in arterial blood, total CO₂ runs a few mEq/L higher than the bicarbonate value calculated using the H-H equation.) If total CO₂ is truly abnormal the patient has an acid-base disorder.

b) The simplified version of the H-H equation eliminates the log and the pK, and expresses the relationships among the three key values.

$$\text{pH} \sim \frac{\text{HCO}_3^-}{\text{PaCO}_2}$$

This version is sufficient for describing the four primary acid-base disturbances and their compensatory changes listed in Table III. If the numerator is first to change the problem is either metabolic acidosis (reduced HCO_3^-) or metabolic alkalosis (elevated HCO_3^-); if the denominator is first to change the problem is either respiratory alkalosis (reduced PaCO_2) or respiratory acidosis (elevated PaCO_2).

TABLE III. The four primary acid-base disorders and their compensatory changes. The primary event leads to a large change in pH (larger arrows). Compensation (changes in HCO_3^- and PaCO_2 represented by smaller arrows) attempts to normalize the ratio of $\text{HCO}_3^-/\text{PaCO}_2$ and bring the pH back toward normal (smaller arrows next to pH). Each primary disorder may be caused by a variety of specific clinical conditions.

Table III Four Primary Acid-Base Disorders and their Compensatory Changes

Primary Event	Compensatory Event
Metabolic Acidosis	
$\downarrow \text{pH} \equiv \frac{\downarrow \text{HCO}_3^-}{\text{PaCO}_2}$	$\downarrow \text{pH} \equiv \frac{\downarrow \text{HCO}_3^-}{\downarrow \text{PaCO}_2}$
Metabolic Alkalosis	
$\uparrow \text{pH} \equiv \frac{\uparrow \text{HCO}_3^-}{\text{PaCO}_2}$	$\uparrow \text{pH} \equiv \frac{\uparrow \text{HCO}_3^-}{\uparrow \text{PaCO}_2}$
Respiratory Acidosis	
$\downarrow \text{pH} \equiv \frac{\text{HCO}_3^-}{\uparrow \text{PaCO}_2}$	$\downarrow \text{pH} \equiv \frac{\uparrow \text{HCO}_3^-}{\uparrow \text{PaCO}_2}$
Respiratory Alkalosis	
$\uparrow \text{pH} \equiv \frac{\text{HCO}_3^-}{\downarrow \text{PaCO}_2}$	$\uparrow \text{pH} \equiv \frac{\downarrow \text{HCO}_3^-}{\downarrow \text{PaCO}_2}$

c) By convention 'acidosis' and 'alkalosis' refer to in-vivo physiologic derangements and not to any change in pH. Each primary acid-base disorder arises from one or more specific clinical conditions, e.g., metabolic acidosis from diabetic ketoacidosis or hypoperfusion lactic acidosis; metabolic alkalosis from diuretics or nasogastric suctioning; etc. Thus the diagnosis of any primary acid-base disorder is analogous to diagnoses like "anemia" or "fever"; a specific cause must be sought in order to provide proper treatment. Because of the presence of more than one acid-base disorder ('mixed disorders') a patient with any acidosis or alkalosis may end up with a high, low or normal pH. For example, a patient with obvious metabolic acidosis from uremia could present with a high pH due to a concomitant metabolic alkalosis (which may not be as clinically obvious). Acidemia (low pH) and alkalemia (high pH) are terms reserved for derangements in blood pH only.

d) Compensation for a primary disorder takes place when the other component in the H-H ratio changes *as a result* of the primary event; these compensatory changes are not classified by the terms used for the four primary acid-base disturbances. For example, a patient who hyperventilates (lowers PaCO_2) solely as compensation for metabolic acidosis does *not* have a primary respiratory alkalosis but simply compensatory hyperventilation. This terminology helps separate diagnosable and treatable clinical disorders from derangements in acid-base that exist only because of the primary disorder.

e) Compensatory changes for acute respiratory acidosis and alkalosis and metabolic acidosis and alkalosis occur in a predictable fashion, making it relatively easy to spot the presence of a mixed disorder in many situations. For example, single acid-base disorders do not lead to normal pH. Two or more disorders can be manifested by normal pH when they are opposing, e.g., respiratory alkalosis and metabolic acidosis in a septic patient. Although pH can end up in the normal range (7.35-7.45) in single disorders of a mild degree when fully compensated, a truly normal pH with abnormal HCO_3^- and PaCO_2 should make one think of two or more primary acid-base disorders. Similarly, a high pH in a case of acidosis or a low pH in a case of alkalosis signifies two or more primary disorders.

f) Maximal respiratory compensation for a metabolic disorder takes about 12-24 hours and maximal renal compensation for a respiratory disorder takes up to several days. As a rule of thumb, in maximally compensated metabolic acidosis the last two digits of the pH approximate the PaCO_2 . For example, a patient with a disease causing uncomplicated metabolic acidosis over 24 hours' duration, whose pH is 7.25, should have a PaCO_2 equal or close to 25 mm Hg. In metabolic alkalosis respiratory compensation is more variable and there is no simple relationship by which to predict the final PaCO_2 .

g) Acute, uncompensated respiratory alkalosis (acute hyperventilation) and acidosis (acute hypoventilation) cause predictable changes in pH and bicarbonate (Table IV). Bicarbonate increases slightly from the biochemical reaction of acutely retained CO_2 and decreases when CO_2 is acutely excreted; these changes are *instantaneous and independent of any renal compensation*. Extreme acute hyperventilation can lower the bicarbonate to about 15 mEq/L and extreme acute hypoventilation can raise it to about 29 mEq/L (Table IV); a bicarbonate value outside this range must indicate either a renal compensatory mechanism or a primary metabolic acid-base disorder. The biochemical changes in bicarbonate from acute shifts in PaCO_2 point to another particularly useful clue to the presence of a mixed disorder: a higher- or lower-than- expected bicarbonate value with any change in PaCO_2 . Thus a slightly low HCO_3^- concentration in the presence of hypercapnia suggests a concomitant metabolic acidosis (e.g., PCO_2 50 mm Hg, pH 7.27, HCO_3^- 22 mEq/L); a slightly elevated HCO_3^- in the presence of hypocapnia suggests a concomitant metabolic alkalosis (e.g. PCO_2 30 mm Hg, pH 7.56, HCO_3^- 26 mEq/L).

TABLE IV. Changes in arterial pH and bicarbonate with acute changes in PaCO_2 . The ranges represent the 95% confidence limits for pH and bicarbonate when PaCO_2 changes acutely (before any renal compensation takes place). Note that bicarbonate decreases with acute hyperventilation and increases with acute hypoventilation.

TABLE IV		
PaCO_2 (mm Hg)	pH	HCO_3^-
15	7.61-7.74	15.3-20.5
20	7.55-7.66	17.7-22.8
30	7.45-7.53	21.0-25.6
40	7.38-7.45	22.8-26.8
50	7.31-7.36	24.1-27.5
60	7.24-7.29	25.1-27.9
70	7.19-7.23	25.7-28.5
80	7.14-7.18	26.2-28.9
90	7.13-7.09	26.5-29.2

h) The bicarbonate (or total CO₂) should also be examined in relation to the other measured electrolytes, specifically to calculate the anion gap (AG). AG is the Na⁺ concentration minus (total CO₂ + Cl⁻). The normal AG, 12 +/- 4 mEq/L, is an artifact of measurement since these three electrolytes are only the ones most commonly measured. (Since the value of K⁺ is small and relatively constant it is not usually used to calculate the AG; if K⁺ is used then the normal AG is about 16 +/- 4 mEq/L). If all the serum anions and cations were measured anions would equal cations and there would be no anion gap. The importance of the anion gap is that it can help both to diagnose the presence of a metabolic acidosis and characterize its cause. Thus, regardless of pH an elevated AG suggests a metabolic acidosis from unmeasured organic anions, e.g., lactic acidosis or ketoacidosis; the higher the AG the more likely it reflects an organic acidosis. On the other hand a normal AG in a patient with metabolic acidosis indicates a hyperchloremic acidosis, most commonly from renal or gastrointestinal bicarbonate loss, e.g., renal tubular acidosis or diarrhea.

3. Alveolar Gas Equation

The alveolar gas equation for calculating PAO₂ is essential to understanding any PaO₂ value and in assessing if the lungs are properly transferring oxygen into the blood. Is a PaO₂ of 28 mm Hg abnormal? How about 55 mm Hg? 95 mm Hg? To clinically interpret PaO₂ one has to also know the patient's PaCO₂, FIO₂ (fraction of inspired oxygen) and the P_B (barometric pressure), all components of the equation for PAO₂:

$$PAO_2 = FIO_2(P_B - P_{H_2O}) - PaCO_2 \left[FIO_2 + \frac{1 - FIO_2}{R} \right]$$

The abbreviated equation below is useful for clinical purposes; in this version alveolar PO₂ equals inspired PO₂ (PIO₂) minus arterial PCO₂ x 1.2, assuming the R value is 0.8 (and assuming identical values for arterial and alveolar PCO₂. Water vapor pressure in the airways is dependent only on body temperature and is 47 mm Hg at normal body temperature (37 degrees C).

$$PAO_2 = FIO_2(P_B - 47) - 1.2(PaCO_2)$$

Ambient FIO₂ is the same at all altitudes, 0.21. It is usually not necessary to measure P_B if you know its approximate average value where the blood was drawn (e.g. sea level 760 mm Hg; Cleveland 747 mm Hg; Denver 640 mm Hg). In the abbreviated equation PaCO₂ is multiplied by 1.2, a factor based on assumed respiratory quotient (CO₂ excretion over O₂ uptake in the lungs) of 0.8; this factor becomes 1.0 when the FIO₂ is 1.0. The following comments are meant to show how the alveolar gas equation can be clinically helpful without the need for anything more than mental calculation.

a) If PIO₂ is held constant and PaCO₂ increases, PAO₂ and PaO₂ will always decrease. Since PAO₂ is a calculation based on known (or assumed) factors, its change is predictable. PaO₂, by contrast, is a measurement whose theoretical maximum value is defined by PAO₂ but whose lower limit is determined by ventilation-perfusion (V-Q) imbalance, pulmonary diffusing capacity and oxygen content of blood entering the pulmonary artery (mixed venous blood). In particular, the greater the imbalance of ventilation-perfusion ratios the more PaO₂ tends to differ from the calculated PAO₂. (The difference between PAO₂ and PaO₂ is commonly referred to as the 'A-a gradient.' However, 'gradient' is a misnomer since the difference is not due to any diffusion gradient, but instead to V-Q imbalance and/or right to left shunting of blood past ventilating alveoli. Hence 'A- a O₂ difference' is the more appropriate term.)

b) The alveolar-arterial PO₂ difference, notated P(A-a)O₂, varies normally with age and FIO₂. Up to middle age, breathing ambient air, normal P(A-a)O₂ ranges between 5 and 20 mm Hg. Breathing an

FIO₂ of 1.0 the normal P(A-a)O₂ ranges up to about 110 mm Hg. If P(A-a)O₂ is increased above normal there is a defect of gas transfer within the lungs; this defect is almost always due to V-Q imbalance.

c) Because of several assumptions in clinical use of the alveolar gas equation, precision in calculating PAO₂ is not achievable. Fortunately an estimate of P(A-a) O₂ is usually sufficient for clinical purposes

d) Since oxygen enters the pulmonary capillary blood by passive diffusion, it follows that in a steady state the alveolar PO₂ must always be higher than the arterial PO₂. This fact is useful to spot 'garbage' blood gas data, a not infrequent problem. For example, a PaO₂ of 150 mm Hg in a patient breathing 'room air' at sea level (FIO₂ = .21) must represent some kind of error, since at all conceivable PaCO₂ values the P(A-a)O₂ would have a negative value; even with extreme hyperventilation (PaCO₂ 10 mm Hg) the *alveolar* PO₂ would be no higher than 140 mm Hg. A moment's reflection will reveal several possible explanations for the apparently negative alveolar-arterial PO₂ difference: the patient was in fact breathing supplemental oxygen during or just prior to the sample drawing; an air bubble in the arterial sample syringe; a quality control or reporting error from the lab; a transcription error - someone wrote down the wrong number; etc.

What about the oxygen values mentioned at the beginning of this section? A PaO₂ of 28 mm Hg would be normal on the summit of Mt. Everest for a climber breathing ambient air. At the summit barometric pressure is 253 mm Hg, which provides a PIO₂ of only 43 mm Hg²⁴ (Table V).

LOCATION	ALT.	P _B	FIO ₂	PIO ₂	PaCO ₂	PAO ₂	PaO ₂
Sea Level	0	760	.21	150	40	102	95
Cleveland	500	747	.21	147	40	99	92
Denver	5280	640	.21	125	34	84	77
*Pikes's Peak	14114	450	.21	85	30	62	55
*Mt. Everest	29028	253	.21	43	7.5	35	28

*All pressures in mm Hg; Pike's Peak and Mt. Everest data from summits

ALT. = altitude in feet

P_B = barometric pressure

FIO₂ = fraction of inspired oxygen

PIO₂ = pressure of inspired oxygen in the trachea

PaCO₂ = arterial PCO₂, assumed to = alveolar PCO₂

PAO₂ = alveolar PO₂, PAO₂ is calculated using an assumed R value of 0.8 except for the summit of Mt. Everest, where 0.85 is used

PaO₂ = arterial PO₂, assuming a P(A-a)O₂ of 7 mm Hg at each altitude; each PaO₂ value is normal for its respective altitude

4. Oxygen Content Equation

All physicians know that hemoglobin carries oxygen and that anemia can lead to severe hypoxemia. Making the necessary connection between PaO₂ and O₂ content requires knowledge of the oxygen content equation.

$$CaO_2 = (SaO_2 \times Hb \times 1.34) + .003(PaO_2)$$

How much glucose is in the blood if the glucose level is 80 mm Hg? This question makes no sense, of course, because glucose is not a gas and therefore exerts no pressure in solution; any question regarding 'how much' is answered by determining its content, which in the case of glucose is usually reported as mg/dl blood. Oxygen is a gas and its molecules do exert a pressure but, like glucose, oxygen

also has a finite content in the blood, in units of ml O₂/dl blood. To remain viable tissues require a certain amount of oxygen per minute, a need met by a requisite oxygen content, not oxygen pressure. (Patients can and do live with very low PaO₂ values, as long as their oxygen content and cardiac output are adequate -- note that oxygen delivery to tissue is dependent upon oxygen content in the blood, as described in the above equation, and delivery of that blood to the tissue, a function of cardiac output and patent vessels).

The oxygen carrying capacity of one gram of hemoglobin is 1.34 ml. With a hemoglobin content of 15 grams/dl blood and a normal hemoglobin oxygen saturation (SaO₂) of 98%, arterial blood has a hemoglobin-bound oxygen content of $15 \times .98 \times 1.34 = 19.7$ ml O₂/dl blood. An additional small quantity of O₂ is carried dissolved in plasma: .003 ml O₂/dl plasma/mm Hg PaO₂, or .3 ml O₂/dl plasma when PaO₂ is 100 mm Hg. Since normal CaO₂ is 16-22 ml O₂/dl blood, the amount contributed by dissolved (unbound) oxygen is very small, only about 1.4% to 1.9% of the total.

Given normal pulmonary gas exchange (i.e., a normal respiratory system), factors that lower oxygen content - such as anemia, carbon monoxide poisoning, methemoglobinemia, shifts of the oxygen dissociation curve - do not affect PaO₂. PaO₂ is a measurement of pressure exerted by uncombined oxygen molecules dissolved in plasma; once oxygen molecules chemically bind to hemoglobin they no longer exert any pressure.

PaO₂ affects oxygen content by determining, along with other factors such as pH and temperature, the oxygen saturation of hemoglobin (SaO₂). The familiar O₂-dissociation curve can be plotted as SaO₂ vs. PaO₂ and as PaO₂ vs. oxygen content. For the latter plot the hemoglobin concentration must be stipulated.

When hemoglobin content is adequate, patients can have a reduced PaO₂ (defect in gas transfer) and still have sufficient oxygen content for the tissues (e.g., hemoglobin 15 grams%, PaO₂ 55 mm Hg, SaO₂ 88%, CaO₂ 17.8 ml O₂/dl blood). Conversely, patients can have a normal PaO₂ and be *profoundly hypoxemic* by virtue of a reduced CaO₂. This paradox - normal PaO₂ and hypoxemia - generally occurs one of two ways: 1) anemia, or 2) altered affinity of hemoglobin for binding oxygen.

A common misconception is that anemia affects PaO₂ and/or SaO₂; if the respiratory system is normal, anemia affects neither value. (In the presence of a right to left intrapulmonary shunt anemia can lower PaO₂ by lowering the mixed venous oxygen content; when mixed venous blood shunted past the lungs mixes with oxygenated blood leaving the pulmonary capillaries, lowering the resulting PaO₂. With a normal respiratory system mixed venous blood is fully oxygenated - as much as allowed by the alveolar PO₂ - as it passes through the pulmonary capillaries.)

Obviously, however, the lower the hemoglobin content the lower the oxygen content. It is not unusual to see priority placed on improving a chronically hypoxemic patient's low PaO₂ when a blood transfusion would be far more beneficial.

Anemia can also confound the clinical suspicion of hypoxemia since anemic patients do not generally manifest cyanosis even when PaO₂ is very low. Cyanosis requires a minimum quantity of deoxygenated hemoglobin to be manifest - approximately 5 grams% in the capillaries. A patient whose hemoglobin content is 15 grams% would not generate this much reduced hemoglobin in the capillaries until the SaO₂ reached 78% (PaO₂ 44 mm Hg); when hemoglobin is 9 grams% the threshold SaO₂ for cyanosis is lowered to 65% (PaO₂ 34 mm Hg).

Altered hemoglobin affinity may occur from shifts of the oxygen dissociation curve (e.g., acidosis, hyperthermia), from alteration of the oxidation state of iron in the hemoglobin (methemoglobinemia), or from carbon monoxide poisoning. Carbon monoxide by itself does not affect PaO₂ but only SaO₂ and O₂ content.

To know the oxygen content one needs to know the hemoglobin content and the SaO₂; both should be measured as part of each arterial blood gas test. A calculated SaO₂ may be way off the mark and can be clinically misleading. This is true even without excess CO in the blood.

Finally, it should be noted that pulse oximeters are not reliable in the presence of dyshemoglobins - hemoglobins that cannot bind oxygen. The two major dyshemoglobins encountered in clinical practice are carboxyhemoglobin (COHb) and methemoglobin (Methb). Oximeters do not differentiate hemoglobin bound to carbon monoxide from hemoglobin bound to oxygen; the machines report the sum of both values as oxyhemoglobin. In contrast to blood co-oximeters, which utilize four wavelengths of light to separate out oxyhemoglobin from reduced hemoglobin, methemoglobin and carboxyhemoglobin, pulse oximeters utilize only two wavelengths of light. As a result, pulse oximeters measure COHb and part of any MethHb along with oxyhemoglobin, and combine the three into a single reading, the SpO₂. (MethHb absorbs both wavelengths of light emitted by pulse oximeters, so that SpO₂ is not affected as much by MethHb as for a comparable level of COHb). Thus a patient with 80% oxyhemoglobin and 15% carboxyhemoglobin would show a pulse oximetry oxygen saturation (SpO₂) of 95%, a value too high by 15%. For this reason pulse oximeters should be used cautiously (if at all) when there may be an elevated carbon monoxide level, for example in patients assessed in an emergency department. Note that excess carboxyhemoglobin is present in all cigarette and cigar smokers. A resting SpO₂ should be interpreted cautiously in any outpatient who has smoked within 24 hours. The half-life of CO breathing ambient air is about 6 hours, so 24 hours after smoking cessation the CO level should be normal, i.e., less than 2.5%. If there is concern about the true SaO₂, it should be measured on an arterial blood sample; alternatively, the percent COHb can be measured on a venous sample, and the value subtracted from the SpO₂. The spectrophotometric technique used by pulse oximeters also makes their oxygen saturation reading less reliable in the presence of excess methemoglobin (metHb). MethHb reduces the SpO₂ linearly until a level of about 85%, at which point further increases in metHb do not cause further lowering of SpO₂. A finding of unexpectedly low SpO₂ (e.g., 91% in a patient with normal cardiorespiratory system who is receiving nasal oxygen) should make one think of excess methb; in such cases an arterial blood sample should be obtained for direct measurement of SaO₂ and PaO₂.

REFERENCES: Lawrence Martin, <http://www.mtsinai.org/pulmonary/> and references therein.