TECHNICAL NOTE

The Oxygen Window and Decompression Bubbles: Estimates and Significance

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The "oxygen window" causes a partial pressure difference of inert gas between the inside and outside of decompression bubbles. Estimates of Po_2 and Pco_2 in tissue are necessary for O_2 window calculations and any calculations about growth or decay of decompression sickness bubbles, but the estimates involve many uncertainties. Using simplifying assumptions, we estimated the O_2 window over a broad range of environments for tissues having a wide range of O_2 extractions. The results were as follows: a) the window increases with ambient pressure, but levels off at very high pressure; b) the window is only 1 or 2 kPa for air breathing at extreme altitudes, and 200 kPa or more in hyperbaric environments; c) when O_2 is breathed instead of air, the window is as much as 50 times larger at altitude but only about 10 times larger in hyperbaric environments; d) changes in bubble size due to the window decrease as barometric pressure increases; and e) there are seven additional factors which may supplement or oppose the action of the oxygen window.

WHEN LIVING ANIMALS are in a steady state, the sum of the partial pressures of dissolved gases in the tissues is usually less than atmospheric pressure, a phenomenon known as the "oxygen window", "partial pressure vacancy" or "inherent unsaturation" (3,8,18,21). This is because metabolism lowers partial pressure of O_2 in tissue below the value in arterial blood and the binding of O_2 by hemoglobin causes a relatively large Po_2 difference between tissues and arterial blood. Production of CO_2 is usually about the same as consumption of O_2 on a mole-for-mole basis, but there is little rise of Pco_2 because of its high effective solubility. Levels of O_2 and CO_2 in tissue can influence blood flow and thereby influence washout of dissolved inert gas, but the magnitude of the oxygen window has no direct effect on inert-gas washout. The oxygen window provides a tendency for absorption of gas quantities in the body such as pneumothoraces or decompression sickness (DCS) bubbles (18). With DCS bubbles, the window is a major factor in the rate of bubble shrinkage when the subject is in a steady state, modifies bubble dynamics when inert gas is being taken up or given off by the tissues, and may sometimes prevent the transformation of bubble nuclei into stable bubbles (17).

There have been a few measurements that are pertinent to the oxygen window (1,9,12,18), but it is helpful to resort to calculations to understand how the window varies from situation to situation. The calculations depend on values for partial pressures of O_2 and CO_2 in tissues, which are elusive; tissue Po_2 and Pco_2 are not easily measured and are variable from location to location in the body and from time to time at a location (11).

One of the purposes of this communication is to describe, in detail, the method for estimation of tissue Po_2 and Pco_2 that has been used previously to evaluate the oxygen window (8,18,21,22). The calculations are for persons breathing either air or pure oxygen, but the procedure can be applied to calculation of the O_2 window for other gaseous environments, or to other cases, such as the O_2 window that can occur in arterial blood (22). A second purpose is to use the best simplifying assumptions available for the existing complex anatomical and physiological situation to provide calculations, over a wide range of exposures, of the oxygen window. The broad range covered yields a perspective on the pressure dependence of the O_2 window and its importance to the dynamics of DCS bubbles. Finally, we review the assumptions involved, enumerate some of the phenomena which may operate together with, or compete with, the O_2 window, and point out that for discussion of changes of bubble size, the calculated window must be normalized to account for gas diffusion's effect on bubble sizes at various total pressures.

METHODS

The oxygen window can be defined in terms of inherent unsaturation: the difference between the barometric

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pressure and the sum of partial pressures of all gases in the tissue. For air-breathing persons, this equation is:

$$P_W = P_B - (P_{tis}N_2 + P_{tis}O_2 + P_{tis}CO_2 + P_{tis}U + P_{H_2O}) \quad \text{Eq. 1}$$

Definitions of symbols appear in Table I. Assumptions which are involved in what follows are enumerated at the end of the Results and Discussion section and handled mathematically in Appendix A. To proceed with a simplified version of a complex situation, assume that P_{N_2} in the tissues is equal to P_{N_2} in alveolar gas:

$$P_{tis}N_2 = P_{AN_2} = P_B - P_{AO_2} - P_{ACO_2} - P_{H_2O} \quad \text{Eq. 2}$$

The left-hand equality in Eq. 2 is valid only when the body is in a steady state with no washin or washout of inert gas occurring. Assume that $P_{tis}U$ in Eq. 1 is zero, that the partial pressures of O_2 and CO_2 in the bubble equal their counterparts in tissue, and that total pressure in the bubble equals P_B. Then substitution of Eq. 2 into Eq. 1 yields equations which are useful for application to a DCS bubble; they characterize the oxygen window in terms of the metabolic gases and show that the window is equal to a partial pressure difference for driving N_2 diffusion:

$$P_W = P_{AO_2} + P_{ACO_2} - P_{tis}O_2 - P_{tis}CO_2 = P_{bub}N_2 - P_{AN_2} \quad \text{Eq. 3}$$

The rationale behind Eq. 3 is that oxygen, CO_2 and H_2O equilibrate easily between the inside and outside of the bubble, so they determine the P_{N_2} inside (see Fig. 1); the P_{N_2} equals total pressure inside minus partial pressures of O_2, CO_2 and H_2O. Further, P_{N_2} in blood and tissue is set by blood/gas exchange of N_2 in the lung where the P_{N_2} is lower than in bubbles because O_2 in alveolar gas is higher than in tissue. Size of the arrows penetrating the wall of the bubble in Fig. 1 indicate the magnitude of the permeation coefficients; reported values are 1.14×10^{-5} and 2.22×10^{-5} $cm^2 \cdot min^{-1} \cdot atm^{-1}$ for N_2 and O_2, respectively, in urinary bladders of cats (5,19), and the coefficient for CO_2 is about 20 times larger than for O_2 (16). The permeation coefficient for water vapor can be considered infinite, since water will vaporize or condense whenever conditions dictate. Exit of N_2 caused by the O_2 window tends to increase P_{O_2}, P_{CO_2}, and P_{H_2O}, but these gases permeate so readily that they do not build up in the bubble. The rapid permeation of O_2 and CO_2 causes a volume readjustment immediately after a pressure change (18).

TABLE I. DEFINITIONS OF SYMBOLS.

Blood contents, *vol% [= milliliter of gas (STPD) per deciliter]*
C_{a_i} = content of a gas in arterial blood.
CaO_2' = total content of O_2 in arterial blood, physically dissolved and combined with hemoglobin.
$Co_2physoln$ = content of O_2 dissolved in any blood.
C_{v_i} = content of a gas in venous blood from a particular tissue.
Hydrostatic pressures, *kPa*
P_B = barometric pressure.
P_{el} = inside a bubble, pressure due to elastic forces.
P_{hy} = inside a bubble, pressure due to hydrostatic pressures of body fluids and of liquids outside the body if the body is immersed.
P_{other} = inside a bubble, pressure attributable to unknown or unnamed forces.
P_γ = inside a bubble, pressure due to action of surface tension.
P_{tot} = total pressure inside a bubble.
Partial pressures, *kPa*
P_{A_i} = partial pressure of a gas in alveolar gas.
P_{a_i} = partial pressure of a gas in arterial blood.
P_{bub_i} = partial pressure of a gas inside a gas bubble.
P_{H_2O} = partial pressure of water vapor at body temperature.
P_{IO_2} = partial pressure of O_2 in inspired gas.
P_{tis_i} = partial pressure of a gas in a particular tissue.
P_{v_i} = partial pressure of a gas in venous blood from a particular tissue.
P_W = the "oxygen window" in tissue; the difference in the sum of the N_2 partial pressures inside and outside of a bubble, defined by Eq. 1.
$P_{W_{norm}}$ = the normalized oxygen window in tissue, defined by Eq. 9.
ΔP_i = partial pressure difference of a gas between the inside of a bubble and its immediate surroundings (except for N_2, see ΔP_{N_2}).
ΔP_{N_2} = P_{N_2} difference between the alveolar gas and tissue surrounding a bubble.
Other variables
dr/dt = change of bubble radius with respect to time.
F_{IO_2} = fraction of O_2 in inhaled gas, either 0.2094 or 1.0 for calculations of this paper, dimensionless.
K = proportionality constant, defined by Eq. 8.
R = respiratory exchange ratio of the whole body or of a tissue, CO_2 produced divided by O_2 consumed, dimensionless.
αO_2 = solubility of O_2 in blood plasma, vol%/kPa.

Note: Subscript i represents O_2, CO_2, N_2, or the sum of other, unnamed gases (U).

Procedure for the Estimations

The top four lines of Table II show the starting information for the estimation process. Pairs of alveolar gas values, P_{AO_2} and P_{ACO_2} (lines 3 and 4), are obtained for various, arbitrarily chosen barometric pressures (line 1). For hypobaric conditions, we accounted for the lowering of P_{ACO_2} caused by ventilatory response to low O_2 by using data from Rahn and Otis (15) on alveolar gases during acute exposure to altitude, recognizing that the measured values vary depending on the prevailing conditions and experimental techniques. In particular, acclimatization to altitude causes a considerably lower P_{ACO_2} for any particular P_{AO_2}.

In all cases we calculated alveolar P_{O_2} for various choices of respiratory exchange ratio, R, from the alveolar gas equation (14):

$$P_{AO_2} = P_{IO_2} + P_{ACO_2} \cdot F_{IO_2} \cdot \frac{(1 - R)}{R} - \frac{P_{ACO_2}}{R} \quad \text{Eq. 4}$$

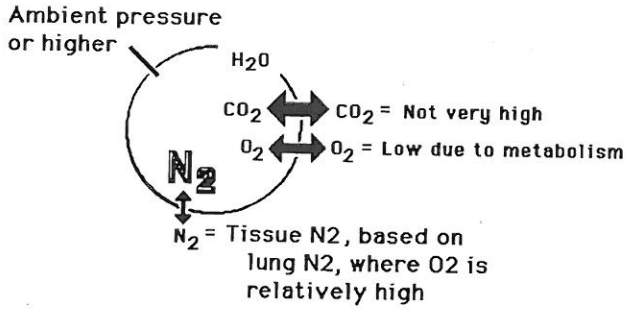

Fig. 1. Diagram to illustrate the application of the O_2 window phenomenon to decompression sickness bubbles. Partial pressure of N_2 inside the bubble is high because P_{O_2} and P_{CO_2} are low. Size of the arrows signifies the relative magnitude of the permeation coefficients for the gases.

TABLE II. ESTIMATES OF P_{O_2} AND P_{CO_2} IN TISSUE AND THE OXYGEN WINDOW.*

	Altitude, Air Breathing				Normal Air	Hyperbaric, Air Breathing					
1) P_B	40	50	60	80	100	200	300	400	600	1000	2000
2) P_{IO_2}	7	9	11	15	20	41	62	82	124	208	418
3) P_{AO_2}	4.2	4.8	5.9	9.5	13.6	34.6	55.5	76.5	118	202	411
4) P_{ACO_2}	2.5	3.8	4.7	5.3	5.3	5.3	5.3	5.3	5.3	5.3	5.3
5) O_2physoln	0.10	0.11	0.14	0.22	0.31	0.80	1.28	1.76	2.72	4.65	9.46
6) CaO_2on Hb	14.3	14.7	16.4	19	19.8	20	20	20	20	20	20
7) CaO_2'	14.4	14.8	16.5	19.2	20.1	20.8	21.3	21.8	22.7	24.6	29.5
8) $CaCO_2$	37	44	47.5	48.5	48.2	48.2	48.2	48.2	48.2	48.2	48.2
9) CvO_2	9.4	9.8	11.5	14.2	15.1	15.8	16.3	16.8	17.7	19.6	24.5
10) $CvCO_2$	41.3	48.3	51.8	52.8	52.5	52.5	52.5	52.5	52.5	52.5	52.5
11) PvO_2	2.8	3.0	3.8	5.1	5.7	6.2	6.4	7.0	7.9	13.2	207.3
12) $PvCO_2$	2.9	4.5	5.5	6.1	6.1	6.1	6.1	6.2	6.3	6.4	6.4
13) $PtisN_2$	27.1	35.2	43.2	59.1	74.9	154	233	312	470	786	1577
14) $PbubN_2$	28.2	36.3	44.5	62.7	82.1	181	281	380	579	974	1780
15) P_W	1.1	1.1	1.3	3.6	7.2	27.5	48.2	68.6	109	188	203
16) $P_{W_{norm}}$	0.038	0.032	0.030	0.058	0.088	0.152	0.172	0.180	0.189	0.193	0.114

Note: Air breathing, R = 0.85; O_2 solubility = 0.023 vol%/kPa; arteriovenous O_2 difference = 5 vol%.
Units for lines 1–4 and 11–15 are kPa; units for lines 5–10 are vol%; and line 16 is dimensionless.
* Many of the calculations were done automatically with the aid of a spreadsheet (Excel, MacIntosh IIcx microcomputer), but the steps involving translation between P_{CO_2},P_{O_2} and C_{O_2},C_{CO_2} pairs must be entered by hand.

In the hypobaric region, we made trial and error choices of P_{ACO_2} and recalculation of P_{AO_2} by Eq. 4 to locate a P_{ACO_2},P_{AO_2} pair that would fall on the Rahn-Otis data curve. In the normal and hyperbaric regions we assumed P_{ACO_2} was 5.26 kPa (100 kPa = 1 bar = 0.987 atm) and calculated P_{AO_2} from Eq. 4.

Blood-gas data: Interactions between O_2 and CO_2 in blood are complex. Translation between P_{O_2},P_{CO_2} pairs and C_{O_2},C_{CO_2} pairs can be accomplished by using blood/gas graphs, nomograms or computer programs (10,13). We used the nomogram of Dill for man at sea level (6,14). Steps for deriving estimates follow:

a) With a blood-gas nomogram or computer program, find the C_aO_2,C_aCO_2 pair that corresponds to a given P_{AO_2},P_{ACO_2} pair from lines 3 and 4, Table II (assumed to be equal to a P_aO_2,P_aCO_2 pair). Enter result on lines 6 and 8 of the table.

b) Calculate the physically dissolved O_2:

$$C_{O_2}\text{physoln} = \alpha_{O_2} \cdot P_{AO_2} \qquad \text{Eq. 5}$$

Add the physically dissolved O_2 to the C_aO_2 to obtain the corrected C_aO_2 (line 7).

c) Obtain a C_vO_2,C_vCO_2 pair from decisions for the arteriovenous O_2 difference and R. From the C_aO_2' subtract the chosen O_2 content difference, and to C_aCO_2 add the appropriate content to satisfy the chosen R. Enter on lines 9 and 10.

d) Using the nomogram or program, read the P_vO_2,P_vCO_2 pair for the C_vO_2,C_vCO_2 pair and enter on lines 11 and 12. These are the estimates of $P_{tis}O_2$,$P_{tis}CO_2$ and $P_{bub}O_2$,$P_{bub}CO_2$ pairs. When P_{O_2} is so high that the C_vO_2 is above the range of the nomogram, calculate the P_vO_2 from:

$$P_vO_2 = 13.15 + (C_vO_2 - 20)/\alpha_{O_2} \qquad \text{Eq. 6}$$

e) Calculate $P_{tis}N_2$ by Eq. 2 and enter on line 13. Calculate $P_{bub}N_2$ by Eq. 7 and enter on line 14.

$$P_{bub}N_2 = P_B - P_{tis}O_2 - P_{tis}CO_2 - P_{H_2O} \qquad \text{Eq. 7}$$

f) Compute the O_2 window from Eq. 3 and enter on line 15.

The normalized O_2 window: Changes of bubble size due to diffusion depends not only on movement of molecules across the bubble interface but also on the effect those molecules have on the bubble size. In the present context, the rate of diffusion of molecules depends on the magnitude of the O_2 window, since the O_2 window is tantamount to a difference of P_{N_2} between the inside and outside of a bubble. The effect of a certain number of molecules on bubble size depends on barometric pressure; when the bubble is under pressure, it takes a loss of more molecules to decrease its radius by a given amount. According to a derivation from the basic principles of diffusion (17,20), the rate of change of radius of a spherical bubble is proportional to a ratio which involves $P_{bub}N_2$ and P_{AN_2}:

$$dr/dt = \frac{K \cdot (P_{bub}N_2 - P_{AN_2})}{P_{bub}N_2} \qquad \text{Eq. 8}$$

For simplicity, actions of several variables are incorporated into the proportionality value, K. The normalized O_2 window on line 16 of Table II is calculated by dividing the O_2 window by the denominator of Eq. 8:

$$P_{W_{norm}} = P_W/P_{bub}N_2 = (P_{bub}N_2 - P_{AN_2})/P_{bub}N_2 \qquad \text{Eq. 9}$$

RESULTS AND DISCUSSION

The contentions that follow ensue from seven tables, counterparts of Table II, for various combinations of R, arteriovenous O_2 difference, and breathing of air or pure oxygen. Arteriovenous O_2 difference of 5 vol% and R of 0.85 for Table II are traditional whole-body values in normal resting man. When P_B decreases (read right to left in Table II), inspired P_{O_2} decreases in proportion to barometric pressure and, of course, P_{AO_2} decreases as well (line 3). The lowering of P_{ACO_2} in the several columns at the left on line 4 is brought about by increasing ventilation to compensate for hypoxia (15).

Tissue P_{O_2} and P_{CO_2} (lines 11 and 12) are graphed in Fig. 2A; if alveolar P_{CO_2} were shown on the graph, it

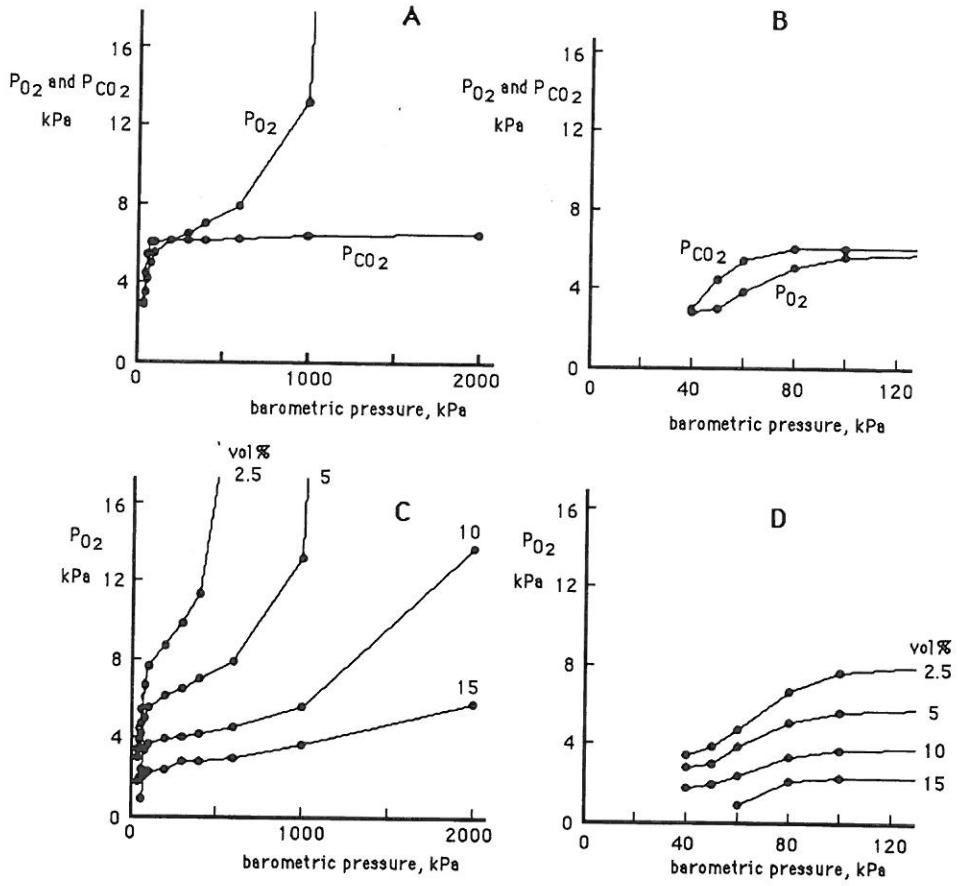

Fig. 2. A. Partial pressures of O_2 and CO_2 in tissue (venous blood) as functions of barometric pressure; air breathing, R = 0.85; arteriovenous O_2 difference = 5 vol%. B. Expanded scale showing values from Fig. 2A in the hypobaric region. C. Impact of O_2 extraction on tissue P_{O_2}; air breathing, R = 0.85. The designation "vol%" indicates the magnitude of the arteriovenous difference. D. Expanded scale showing values from Fig. 2C in the hypobaric region. The two left-hand points are missing from the vol% = 15 trace because the arterial blood contained less than 15 vol% at these low barometric pressures. In Fig. 2–4, the dots show calculated results for the particular barometric pressures chosen.

would be a few kPa below the tissue values over the entire pressure range, but alveolar P_{O_2} would rise very steeply on the scale of Fig. 2A. On the left side of Fig. 2A, tissue P_{O_2} has a relatively shallow upslope between 100 and 600 kPa, a consequence of the oxygen-hemoglobin carriage by blood. An expanded scale shows the trend of tissue P_{O_2} and P_{CO_2} in the hypobaric region (Fig. 2B). The location and level of the relatively flat region depends on the O_2 extraction (Fig. 2C); tissues that extract little oxygen, such as the kidney cortex, have a small flat region, as with the 2.5 vol% curve, but the flat region extends to hypobaric pressures for all four isopleths (Fig. 2D). The tissues with a large flat region may have very high metabolic activity with high blood flow, such as exercising muscle, or very low blood flow relative to their metabolic activity; perhaps connective tissue is in this category. According to the concept of "equivalent air depth" (4), oxygen enrichment in inspired air cuts down the risk of DCS. However, the rising curves in Fig. 2A and 2C show the limits to the benefit of oxygen; if added O_2 brings tissue P_{O_2} above the relatively flat region on the traces, O_2 can play a role in bubble dynamics as if it were an inert gas.

The oxygen window: The calculated values of the O_2 window in Fig. 3A show the trend which was presented before (18,21): the window rises in proportion to the barometric pressure until it levels off when both arterial and venous O_2 are above the range of the hemoglobin-oxygen dissociation curve, so that metabolic needs are completely met by oxygen in physical solution. The window also tends to level off as barometric pressure decreases in the hypobaric range (Fig. 3B) because low P_{O_2}, P_{CO_2} combinations occur in hypoxia. Changing R from 0.7 to 1.0 made no appreciable difference to the O_2 window in the hyperbaric region, but R = 1.0 gave window values as much as 30% higher than R = 0.7 in the hypobaric region.

The normalized form shown in Fig. 3C and 3D, where the window is divided by the P_{bubN_2}, is more closely related to the actual effect on bubble absorption rate and DCS symptoms than the presentation as kPa in Fig. 3A and 3B. The shapes of the traces in Fig. 3C imply that in most tissues shrinkage of size of gas bubbles of an air-breathing person is positively related to the barometric pressure of the person's environment up to P_B of 500 kPa. In tissues having low O_2 extraction, the benefit diminishes with further increases of P_B. When the O_2 requirements are completely met by physically dissolved O_2, there is a constant O_2 window, as seen in Fig. 3A, so rate of exit of N_2 molecules is constant, and the effect on size change is diminished by increasing pressure. The high rate spans a greater P_B range for tissues with greater O_2 extraction.

In the hypobaric range (Fig. 3D), the normalized O_2 window is comparatively low, indicating that change of bubble size due to the O_2 window in air-breathing persons at altitude would be slower than in air-breathing persons at normal or hyperbaric pressures; this is because partial pressures of O_2 for both arterial and venous blood are in the steep part of the O_2-Hb dissociation curve so there is a small P_{O_2} difference between the two.

When a person breathes pure O_2 long enough that the N_2 in alveolar gas and tissues is zero, the normalized O_2

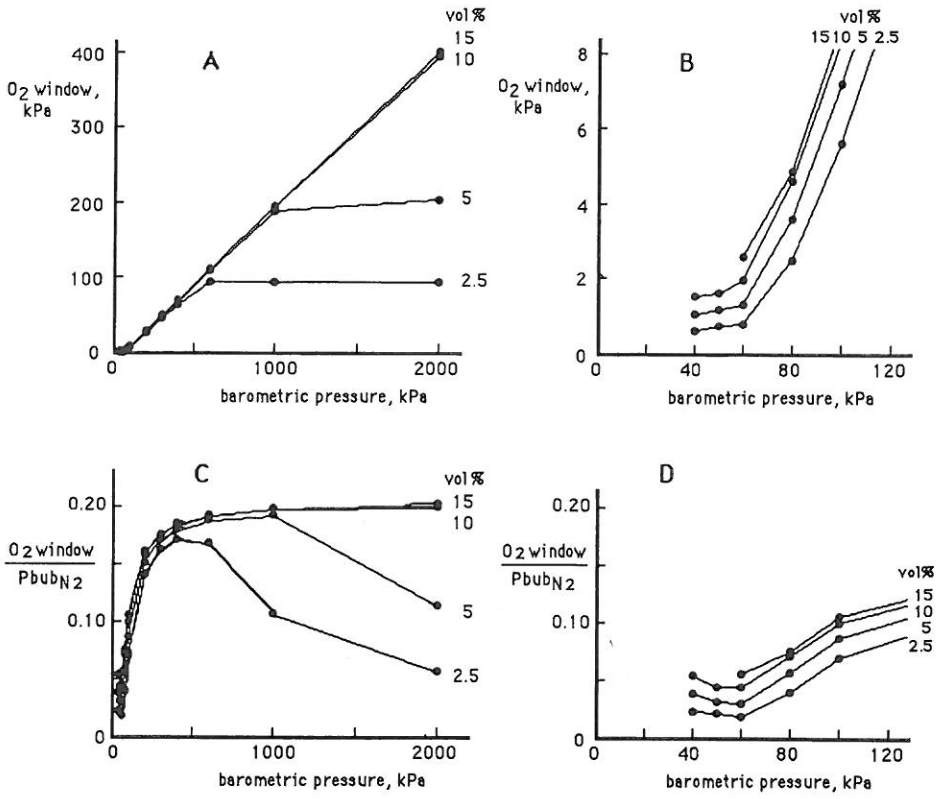

Fig. 3. A. Oxygen window vs. P_B for various arteriovenous O_2 differences; air breathing, R = 0.85. B. Expanded scale showing values from Fig. 3A in the hypobaric region. C. Same values as in Fig. 3A, but O_2 window has been normalized by division by $P_{bub}N_2$. D. Expanded scale showing values from Fig. 3C in the hypobaric region.

window equals 1.0 for a bubble that contains N_2 (see Eq. 9). This provides a convenient point of reference; it sets the maximal rate for absorption of a bubble in any particular situation and gives meaning to the y-axes of Fig. 3C and 3D. Thus the plateau of the normalized O_2 window in Fig. 3C is 20% of the maximal rate that could be attained with O_2 breathing, and the left side of Fig. 3D shows that the rate when breathing air in extreme hypobaric environments occurs well below 10% of the rate that could occur with O_2 breathing.

Oxygen breathing makes for a much larger O_2 window at any given barometric pressure (Fig. 4A). When a person breathes O_2-enriched gas rather than pure O_2, the O_2 window is proportionately less than shown. When the arteriovenous difference is small, the window is as much as 50 times greater when breathing O_2 than with air (Fig. 4B). The peak difference between air and O_2 breathing is at about 60 kPa where P_{O_2} is low but the physiological response to low inspired O_2 has not yet caused a fall in P_{CO_2} (see Fig. 2B). The advantage achieved by switching from breathing of air to oxygen may not be as great as indicated on Fig. 4B if the switch is accompanied by a change of local blood flow (2), which would change the O_2 extraction of the tissue.

Review of Assumptions

In what follows, we discuss uncertainties that accompany use of our estimates of the oxygen window in practical situations or in simulations of bubble dynamics (17,20,22). In addition to lack of knowledge about where damaging bubbles are located in the body and where they arise, there are important uncertainties inherent in our calculations.

Three questionable assumptions underlie estimates of P_{O_2} and P_{CO_2} in tissue and values derived from them:

a) The "average P_{O_2} in tissue" is assumed to be a useful concept. Since O_2 diffuses from blood vessels to the sites in cells where oxidations take place, there may be large variations from point to point in the tissue, with

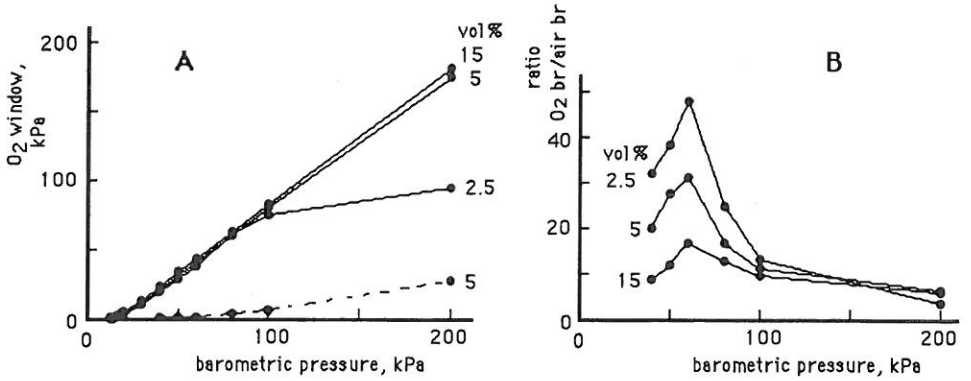

Fig. 4. A. Solid traces are the oxygen window during oxygen breathing vs. P_B; R = 0.85, three arteriovenous oxygen differences. Dashed trace is for air breathing; arteriovenous O_2 difference = 5 vol%. The O_2-breathing trace is displaced to the left because the person can survive barometric pressures lower than 20 kPa whereas the cutoff for air breathing is about 40 kPa. B. The O_2 window ratio (O_2 breathing/air breathing) from data of Fig. 4A.

locations near arteries having P_{O_2} nearly the same as P_{AO_2}, and locations far from arteries, veins, and capillaries having low or zero P_{O_2} (11). Further, the partial pressure field within a tissue probably varies with time as local blood flow and local metabolism change. The idea of an average tissue P_{CO_2} is less tenuous because of the high effective solubility of CO_2 and the relatively small P_{CO_2} difference between arteries and veins.

b) Values of P_{O_2} and P_{CO_2} in venous blood from a particular tissue are often assumed to be acceptable approximations of P_{O_2} and P_{CO_2} in that tissue. The assumption that there are no important gradients for these gases from point to point within the tissue is perhaps reasonable on a gross scale, but is certainly invalid on a microscopic scale, especially for O_2 as pointed out in a) above.

c) Values of P_{O_2} and P_{CO_2} in alveolar gas are often assumed to be acceptable approximations of P_{O_2} and P_{CO_2} in arterial blood. This disregards extensively studied complications of pulmonary gas exchange such as heterogeneous distribution of ventilation and perfusion in various parts of the lung, and the possibility that O_2 and CO_2 in arterial blood may not be completely equilibrated with their counterparts in the alveolar gas.

Calculations of values for bubble variables involve additional assumptions:

a) In a steady state, the P_{N_2} outside a gas bubble or incipient bubble (gas nucleus) is assumed to be equal to the P_{N_2} in arterial blood, which in turn is assumed equal to P_{N_2} in alveolar gas. This would be true if the temperature in the tissue were the same as in the lung. If tissue temperature were less, for instance, the higher solubility of N_2 in cold liquid would cause P_{tisN_2} to tend to be less than P_{aN_2}.

b) We assumed that the P_{O_2} and P_{CO_2} inside a bubble are equilibrated with P_{O_2} and P_{CO_2} in surrounding tissue. This is demonstrably invalid because when the bubble is decreasing in size, P_{O_2} and P_{CO_2} must have a diffusion gradient from inside to outside (16). Corrections can be applied, but for our calculations the approximations are probably close enough, considering the other uncertainties.

c) An important assumption is that tissue metabolism and tissue blood flow behave as expected. If quantities of acid were produced by anaerobic metabolism, for example, there could be large amounts of CO_2 liberated from bicarbonate stores of blood and tissue. The resulting high P_{CO_2} could lead to bubble growth. This idea can be amplified by reference to Eq. 1 and 3. If P_{tisCO_2} is high, P_w could be zero or negative; the high P_{CO_2} in tissue and bubble would lower P_{N_2} inside so that N_2 would enter, causing bubble growth.

Other influences: For our graphs and tables, we assumed that many variables which could act on a bubble are zero. Consider five matters of definition:

a) Total pressure inside a bubble is the sum of barometric pressure and additional pressures. The additional category may include pressure due to elastic forces exerted by the tissue; pressure due to surface tension at the bubble/tissue interface; pressure due to the additional hydrostatic head of blood pressure if a bubble is in blood or of a water column if the bubble is above or below the level of the lungs or if the body is immersed; and pressure due to other unnamed forces on the bubble, if any exist.

b) Partial pressure of N_2 inside a gas bubble is diminished by partial pressures of any other gases which are present in the bubble, in addition to O_2, CO_2, and water vapor.

c) The P_{N_2} in alveolar gas is diminished by any other gases that are present in the alveolar gas, in addition to O_2, CO_2 and water vapor.

d) The P_{N_2} in the tissue around the bubble is less than the alveolar P_{N_2} by any loss of N_2 which occurs between alveolar gas and the tissue in which the bubble resides.

e) The P_{O_2} and P_{CO_2} have small diffusion gradients across the walls of bubbles when the bubbles are being absorbed (18).

The driving force for outward diffusion of inert gas from the bubble can be greater or less than the O_2 window if some of the 9 additional variables listed above are appreciable (P_{el}, P_γ, P_{hy}, P_{other}, P_{bubU}, P_{AU}, ΔP_{N_2}, ΔP_{O_2}, and ΔP_{CO_2}—see Appendix A). Our justification for assuming that these variables are zero is partly ignorance of the values they might have in a particular situation and partly expediency in order to be able to discuss decompression bubbles in the context of the O_2 window at all. In particular, our assumption that pressure due to surface tension is unimportant is clearly invalid for small bubbles; if surface tension is 50 dynes/cm, surface tension pressure is 100 kPa or more when the radius is 1.0 μm or less.

Perspective: Any calculations about the growth or decay of decompression bubbles require assumptions about the magnitudes of the P_{O_2} and P_{CO_2} in tissue that are the basis of the O_2 window. Simplified statements about the window are that: a) gas bubbles in the body should eventually be absorbed; b) the oxygen window and its effect on rate of change of bubble size is dependent on oxygen extraction by tissue; c) the window is smaller for air-breathing persons at altitude than when decompression is from depth, even though O_2 and CO_2 make up large fractions of the contents of bubbles at altitude; d) the relative benefit of switching breathing gas from air to pure O_2 is much greater at altitude than at depth; and e) in order to characterize the absorptive tendency in terms of bubble size, it is necessary to use the normalized O_2 window.

APPENDIX A: COMPREHENSIVE EQUATION FOR P_{N_2} DIFFERENCE BETWEEN THE INSIDE AND OUTSIDE OF A BUBBLE.

A. Basic Statements

Total pressure inside a bubble can be written in terms of a sum of hydrostatic pressures and in terms of a sum of partial pressures:

$$P_{tot} = P_B + P_{el} + P_\gamma + P_{hy} + P_{other} \quad \text{Eq. 10}$$

$$P_{tot} = P_{bubN_2} + P_{bubO_2} + P_{bubCO_2} + P_{H_2O} + P_{bubU} \quad \text{Eq. 11}$$

In alveolar gas, total pressure (barometric pressure) equals partial pressures of the component gases:

$$P_B = P_{AN_2} + P_{AO_2} + P_{ACO_2} + P_{H_2O} + P_{AU} \quad \text{Eq. 12}$$

For algebraic manipulation, it is convenient to lump several variables:

$$\text{Let } A = P_{el} + P_\gamma + P_{hy} + P_{other}$$
$$\text{so that } P_{tot} = P_B + A \quad \text{Eq. 10'}$$

$$\text{Let } B = P_{bubO_2} + P_{bubCO_2} + P_{H_2O} + P_{bubU}$$
$$\text{so that } P_{tot} = P_{bubN_2} + B \quad \text{Eq. 11'}$$

$$\text{Let } C = P_{AO_2} + P_{ACO_2} + P_{H_2O} + P_{AU}$$
$$\text{so that } P_B = P_{AN_2} + C \qquad \text{Eq. 12'}$$

Partial pressure of N_2 in the tissue where the bubble resides differs from alveolar P_{N_2} by a term which accounts for the following: a) changes of P_{N_2} due to alveolar-to-arterial exchange; b) changes which occur due to blood's traversal of the circulatory tree to the tissue; and c) excess dissolved N_2 in the tissue before washout has been completed.

$$P_{AN_2} = P_{tisN_2} + \Delta P_{N_2} \qquad \text{Eq. 13}$$

B. The Comprehensive Equation

To obtain Eq. 15, the "comprehensive" equation for P_{N_2} difference which drives diffusion between inside and outside of a bubble, set Eq. 10' and 11' equal to each other; substitute Eq. 12' for P_B, substitute Eq. 13 for P_{AN_2}, and solve for $(P_{bubN_2} - P_{tisN_2})$:

$$P_{bubN_2} - P_{tisN_2} = \Delta P_{N_2} + A - B + C \qquad \text{Eq. 14}$$

Finally, substitute definitions of A, B, and C back into Eq. 14 for the final result:

$$P_{bubN_2} - P_{tisN_2} = \Delta P_{N_2} + P_{el} + P_\gamma + P_{hy} + P_{other} - P_{bubO_2} - P_{bubCO_2} - P_{bubU} + P_{AO_2} + P_{ACO_2} + P_{AU} \qquad \text{Eq. 15}$$

C. Comprehensive Equation and the O2 Window

To relate Eq. 15 to the oxygen window, recall that in Eq. 1 the O_2 window can be defined as the difference in partial pressure between the barometric pressure and the sum of partial pressures of all gases in the tissue:

$$P_w = P_B - (P_{tisN_2} + P_{tisO_2} + P_{tisCO_2} + P_{tisU} + P_{H_2O}) \quad \text{Eq. 1}$$

Account for diffusion gradients, inside the bubble to outside, of O_2, CO_2, and other gases:

$$P_{tisO_2} = P_{bubO_2} - \Delta P_{O_2} \qquad \text{Eq. 16}$$
$$P_{tisCO_2} = P_{bubCO_2} - \Delta P_{CO_2} \qquad \text{Eq. 17}$$
$$P_{tisU} = P_{bubU} - \Delta P_U \qquad \text{Eq. 18}$$

Substitute Eq. 16 through 18 into Eq. 1:

$$P_w = P_B - (P_{bubO_2} - \Delta P_{O_2} + P_{bubCO_2} - \Delta P_{CO_2} + P_{tisN_2} + P_{bubU} - \Delta P_U + P_{H_2O}) \qquad \text{Eq. 19}$$

$$\text{Let } D = P_{bubO_2} - \Delta P_{O_2} + P_{bubCO_2} - \Delta P_{CO_2} + P_{bubU} - \Delta P_U + P_{H_2O} \text{ so that}$$
$$P_w = P_B - P_{tisN_2} - D \qquad \text{Eq. 19'}$$

Next, substitute for P_B with Eq. 10'; in the result substitute for P_{tot} with Eq. 11', and solve for $(P_{bubN_2} - P_{tisN_2})$:

$$P_{bubN_2} - P_{tisN_2} = P_w + A - B + D \qquad \text{Eq. 20}$$

Finally, substitute back the identities of A, B, and D and remove items that cancel each other:

$$P_{bubN_2} - P_{tisN_2} = P_w + P_{el} + P_\gamma + P_{hy} + P_{other} - \Delta P_{O_2} - \Delta P_{CO_2} - \Delta P_U \qquad \text{Eq. 21}$$

It is clear from Eq. 21 that the O_2 window is only one of several items that determine the P_{N_2} difference for causing diffusion of N_2 out of a gas bubble. The magnitudes of ΔP_{O_2} and ΔP_{CO_2} are small relative to P_w (18), but the other items may be large or small depending on the size of the bubble, where it is located, and other circumstances. For the calculations presented in the figures and tables, we assumed the 7 right-hand items of Eq. 21 to be zero.

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