# STATISTICALLY BASED DECOMPRESSION TABLES IX:

# PROBABILISTIC MODELS OF THE ROLE OF OXYGEN

# IN HUMAN DECOMPRESSION SICKNESS

E. C. Parker
S. S. Survanshi
E. D. Thalmann
P. K. Weathersby

Naval Medical Research
and Development Command
Bethesda, Maryland  20889-5606

Bureau of Medicine and Surgery
Department of the Navy
Washington, DC  20372-5120

19960515 034

## NOTICES

The opinions and assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the naval service at large.

When U. S. Government drawings, specifications, or other data are used for any purpose other than a definitely related Government procurement operation, the Government thereby incurs no responsibility nor any obligation whatsoever, and the fact that the Government may have formulated, furnished or in any way supplied the said drawings, specifications, or other data is not to be regarded by implication or otherwise, as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto.

Please do not request copies of this report from the Naval Medical Research Institute. Additional copies may be purchased from:

<div align="center">

Office of the Under Secretary of Defense (Acquisition & Technology)
Defense Technical Information Center
8725 John J. Kingman Road, Suite 0944
Ft. Belvoir,  VA 22060-6218

</div>

Federal Government agencies and their contractors registered with the Defense Technical Information Center should direct requests for copies of this report to:

## TECHNICAL REVIEW AND APPROVAL

## NMRI  96-05

The experiments reported herein were conducted according to the principles set forth in the current edition of the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council.

This technical report has been reviewed by the NMRI scientific and public affairs staff and is approved for publication. It is releasable to the National Technical Information Service where it will be available to the general public, including foreign nations.

THOMAS J. CONTRERAS
CAPT, MSC, USN
Commanding Officer
Naval Medical Research Institute

# REPORT DOCUMENTATION PAGE

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

| 1. AGENCY USE ONLY (Leave blank) | 2. REPORT DATE<br>March 1996 | 3. REPORT TYPE AND DATES COVERED<br>TECHNICAL 1/91 – 12/93 |
|---|---|---|

**4. TITLE AND SUBTITLE**
Statistically based decompression tables IX: Probabilistic models of the role of oxygen in human decompression sickness.

**5. FUNDING NUMBERS**

PE - 63713N
PR - M0099
TA - .01A
WU - 1002

**6. AUTHOR(S)**
Parker, E.C., S.S. Survanshi, E.D. Thalmann, P.K. Weathersby

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**
Naval Medical Research Institute
Commanding Officer
8901 Wisconsin Avenue
Bethesda, Maryland 20889-5607

**8. PERFORMING ORGANIZATION REPORT NUMBER**

NMRI 96-05

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**
Naval Medical Research and Development Command
National Naval Medical Center
Building 1, Tower 12
8901 Wisconsin Avenue
Bethesda, Maryland 20889-5606

**10. SPONSORING / MONITORING AGENCY REPORT NUMBER**

DN177792

**11. SUPPLEMENTARY NOTES**

**12a. DISTRIBUTION / AVAILABILITY STATEMENT**

Approved for public release; distribution is unlimited.

**12b. DISTRIBUTION CODE**

**13. ABSTRACT (Maximum 200 words)**

While probabilistic models of human decompression sickness (DCS) have been successful in describing both the level and timing of DCS risk in a wide variety of $N_2$-$O_2$ data, they have failed to account for the observed DCS risk in the currently available collection of dives with significant periods of 100% oxygen breathing. The best model to date, calibrated with over 2300 air and $N_2$-$O_2$ dives, under-predicts the DCS risk of these $O_2$ dives by 60%, whether $O_2$ is breathed during in-water decompression or during surface decompression procedures. This overestimation of the benefit of $O_2$ is due to an exaggerated acceleration of $N_2$ wash-out during $O_2$ breathing. Seven-hundred and twenty-nine $O_2$ decompression and surface decompression dives were added to the calibration data set. Fitting the existing 'base' model to the new combined data set resulted in some improvement in DCS prediction in $O_2$ data, but DCS predictions remained about 30% below the observed level. Three classes of $O_2$-specific modifications to the 'base' model were proposed: 1) modification of inert gas kinetics as a function of $O_2$ pressure, 2) direct contribution of DCS risk as a function of either $O_2$ pressure or fraction, 3) a separate $O_2$ risk compartment with independent $O_2$ wash-in and wash-out kinetics. Each of these modifications attempts to include $O_2$ as an explicit contributor to DCS risk, where the 'base' model considers only $N_2$ as risk producing. Six of the resulting seven models slightly improved the fit to the data, with only the separate $O_2$ compartment model resulting in a significant improvement in fit. The estimated $O_2$ time constant for this model is very short at 0.4±0.3 minutes. This model is a good predictor of DCS incidence in both the original $N_2$-$O_2$ and the new $O_2$ data. In contrast to the 'base' model, this $O_2$ model is able to distinguish between $O_2$ dives of different risk level. The success of this '$O_2$ Compartment' model suggests that $O_2$ may contribute to DCS risk over short intervals following exposure to high levels of $PO_2$.

**14. SUBJECT TERMS**
decompression, modeling, oxygen

**15. NUMBER OF PAGES**
35

**16. PRICE CODE**

| 17. SECURITY CLASSIFICATION OF REPORT<br>Unclassified | 18. SECURITY CLASSIFICATION OF THIS PAGE<br>Unclassified | 19. SECURITY CLASSIFICATION OF ABSTRACT<br>Unclassified | 20. LIMITATION OF ABSTRACT<br>Unlimited |
|---|---|---|---|

# TABLE OF CONTENTS

## LIST OF TABLES

# LIST OF FIGURES

# ACKNOWLEDGEMENTS

**INTRODUCTION**

Probabilistic models of human decompression sickness (DCS) have been successful in describing the occurrence, and even the time of occurrence, of DCS (5,12,16,17,19,20). The successful models thus far have not dealt explicitly with $O_2$, but have considered $N_2$ or He to be the only contributor to DCS risk. Such models have not performed well in prediction of DCS in dives that use a high fraction (40 - 100%) of oxygen in the breathing gas during decompression (12). Occurrence of DCS in these dives is systematically under-predicted by about 60%.

Previous models have been fitted to a collection of over 2300 well documented experimental Air and $N_2$-$O_2$ dives (12,18). While the majority of these dives use compressed air (21% $O_2$, regardless of pressure), there are also a large number of dives with enriched oxygen atmospheres, either as a constant partial pressure of oxygen ($PO_2$), usually 0.7 ata, or as a constant fraction ($\leq$40%) of $O_2$ ($F_2$). For this study, 729 dives using $\approx$100% $O_2$ during in-water or surface decompression are added to the data set, for a total of 3112 dives. A wide variety of dives are represented in this expanded data set, including single, repetitive, multi-level, surface decompression and multiple day, or saturation, dives. Important time of symptom information (18,19) is included for all DCS and many marginal cases.

The emphasis of this study is a set of modifications to the previous 'base' model in an attempt to identify a specific oxygen effect in the accumulation of DCS risk. The ideal modification would improve, or leave undisturbed, the 'base' model's success with $N_2$-$O_2$ data while achieving a similar ability to describe the $O_2$ decompression data. Simply fitting this 'base' model to the combined data set, although an improvement, does not achieve the desired result. The oxygen effects explored here are of three forms: 1) a $PO_2$-dependent alteration of the inert

1

gas wash-in/wash-out kinetics (1), 2) a direct contribution to the $N_2$ tissue tension as a function of either $PO_2$ or $FO_2$ (2,3,15), and 3) a parallel, independent wash-in and wash-out of $PO_2$. Models similar to some of those explored here have been previously described (21), but were fitted to sub-sets of the current data, with a limited range of both $FO_2$ and $PO_2$.


## DATA

The data sets used in fitting models in this report were taken from the dive data we have described in detail elsewhere (18). The dives used here are from carefully controlled and well documented experimental dives conducted in the U.S., Canada, and Great Britain. The basic data set, **A** in Table 1, used in the development of the 'base' model (12), contains 2383 dives. The data set with ≈ 100% $O_2$ breathed during decompression included in this analysis, **B** in Table 1, contains 729 dives, all from the Defense and Civil Institute for Environmental Medicine (DCIEM), Toronto, Ontario, Canada (7-9,11).

From the basic set of dives in data set **A** there are 131 DCS and 75 marginal cases, giving an overall DCS incidence of 5.8%. The $O_2$ decompression data contain 17 DCS and 4 marginal cases, for an incidence of 2.4%. Marginal cases are taken to be equal to 0.1 DCS case. For a discussion of the importance of the value assigned to marginal symptoms, see Parker et al. (12). Table 1 gives the distribution of dive types and the number of dives and DCS cases for each data category.

| Data Set | Category | Dives | # DCS | Marg[*] | % DCS | $PO_2$ Range (ata) | $FO_2$ Range (%) |
|---|---|---|---|---|---|---|---|
| | Single - Air | 876 | 45 | 9 | 5.2 | 0.21-4.0[†] | 0.21 |
| | Repet - Air | 194 | 14 | 0 | 7.2 | 0.21-1.3 | 0.21 |
| A | Single - non Air | 772 | 29 | 18 | 4.0 | 0.19-1.5 | 0.10-0.70 |
| | Repet - non Air | 239 | 11 | 0 | 4.6 | 0.21-0.7 | 0.21-0.70 |
| | Saturation - $N_2$-$O_2$ | <u>302</u> | <u>32</u> | <u>48</u> | <u>12.2</u> | 0.21-1.5 | 0.09-0.21 |
| | *Subtotal* | 2383 | 131 | 75 | 5.8 | | |
| | $O_2$ Decompression | 302 | 6 | 3 | 2.1 | 0.21-2.1 | 0.21-0.99 |
| B | $O_2$ Sur-D | <u>427</u> | <u>11</u> | <u>1</u> | <u>2.6</u> | 0.21-2.6 | 0.21-0.98 |
| | *Subtotal* | 729 | 17 | 4 | 2.4 | | |
| | *Total* | 3112 | 148 | 79 | 5.0 | | |

\* Marginal DCS = 0.1 DCS case[(12)]

† $PO_2$ > 1.5 ata in Single Air dives have a duration < 1 min.

## Table 1. Summary of Data

While the majority of data set **A** consists of air dives, about 40% are dives that used an enriched oxygen atmosphere. About half of these dives used a constant $PO_2$ of 0.7 ata, either throughout the dive or with periods of air breathing (14,15). Some used a range of constant fractions of oxygen (10-40%), in order to obtain $PO_2$ values from 0.21 to 1.5 ata (21).

The high $PO_2$ values, up to 4.0 ata, in the Single Air category come from a few short (<5 min) dives from a submarine escape experiment (18) in which these pressures are never present for more than 1 min. Without these profiles, the $PO_2$ range for this category would be 0.21 to 1.5 ata.

The $O_2$ decompression dives being added here are of two types: air dives that use ≈100% $O_2$ during decompression and air dives followed by ≈100% $O_2$ during surface decompression procedures. To allow for inevitable imperfections in the delivery of $O_2$ to the diver, our data represent immersed and dry divers as having breathed 99.5% and 98% $O_2$, respectively. Among these data, the range of $PO_2$ is 0.21 to 2.6 ata, with the majority of the $O_2$ exposures at 1.9 or 2.2 ata, corresponding to 30 and 40 fsw decompression stop depths.

Time of DCS occurrence is included for all DCS cases and for most of the marginal cases. The time of symptom occurrence is represented in the data as an interval (T1-T2) over which symptoms appeared. T1 is taken to be the last known time the diver was entirely free of symptoms and T2 is the time at which definite symptoms were reported. The methods and rules of establishing the T1-T2 times for most reported dives are described in detail elsewhere (18).

**MODELS**

The best fitting model from our most recent $N_2$-$O_2$ modeling effort (12) will be used as the 'base' model for this study. This model allows for exponential wash-in and a mixed exponential-linear wash-out in each compartment (12,14). Risk accumulation for this model is characterized by an instantaneous risk proportional to the sum of the risks of each of its three parallel compartments;

$$r = \sum_{i=1}^{3} A_i \left( \frac{P_{tis}i - Pamb - Thr_i}{Pamb} \right) \quad ; \quad r \geq 0 \qquad (1)$$

where; $A_i$ is a scale factor, $P_{tis}i$ is the tissue gas pressure for the $i$th compartment and is a function of a time constant, $\alpha_i$, and a linear-exponential kinetic crossover parameter, $PXO_i$ and includes the contribution of metabolic gases (12). $Pamb$ is the ambient pressure and $Thr_i$ is the risk threshold parameter (5,17) for the $i$th compartment. Tissue pressure must exceed ambient plus the threshold in order for that compartment to generate a non-zero instantaneous risk and no compartment may make a negative contribution to risk.

This 'base' model, when fitted to the original $N_2$-$O_2$ data set, has been shown to be successful in predicting the DCS incidence in those data (12). However, the 'base' model's prediction of DCS incidence in the $O_2$ decompression data is consistently and substantially low. Table 2 lists the observed DCS cases for each of the data categories, along with the number of cases predicted by the 'base' model. The first column of predicted DCS is for the 'base' model fitted to the original $N_2$-$O_2$ data set (A). This data/model combination results in a 60% under-prediction of DCS for the $O_2$ data. Note that the under-prediction of DCS occurrence is essentially equal in both $O_2$ Decompression and $O_2$ Surface-Decompression (Sur-D) data. The second column of predicted DCS is the result of adding the $O_2$ dives to the fitting data set (A+B). This new fit raises the 'base' model's prediction of DCS for the $O_2$ data considerably, so that it is now a 30% under-prediction. However, the observed DCS incidence for the $O_2$ dive data remain outside the propagated 95% confidence limits of the predictions (6), making this data/model

5

combination a statistical "failure". It is interesting to note that while the 'base' model fitted to A+B moderately over-predicts DCS risk overall in data set A, it does a slightly better job of predicting DCS risk in three of the five categories of data set A than when fitted to A alone.

| Data Set | | DCS Cases Observed | DCS Cases Predicted by Base Model: Fitted to A | Fitted to A+B |
|---|---|---|---|---|
| | Single Air | 45.9 | 40±7 | 42±7 |
| | Repetitive Air | 14.0 | 13±3 | 14±3 |
| | Single non-Air | 30.8 | 31±6 | 35±6 |
| A | Repetitive non-Air | 11.0 | 15±3 | 16±3 |
| | Saturation | 36.8 | 40±12 | 36±9 |
| | *Total* | 138.5 | 139±23 | 144±22 |
| | $O_2$ Decompression | 6.3 | 2±1 | 4±1 |
| B | $O_2$ Surface Decom. | 11.1 | 4±3 | 9±2 |
| | *Total* | 17.4 | 6±4 | 13±4 |

**Table 2.  Base Model prediction of DCS incidence (±95% confidence limits).**

For two of the model's three compartments, the estimated parameter values (time constants, thresholds, etc.) for the 'base' model's fits to data set A and to A+B are the same, within their estimated confidence limits.  The exceptions, with substantial changes in estimated values, are the time constant, $\alpha_3$, and the threshold, $Thr_3$, both from the third compartment.  This time constant (407±22 min), estimated by the fit to A+B, is 16% shorter than that fitted to A alone

(488±41 min), and the threshold is 75% smaller (0.44±0.3 versus 1.75±0.7 fsw). Although the shorter time constant will result in faster inert gas wash-out, it will mean faster gas uptake as well, potentially resulting in higher overpressures, depending on the specifics of the dive. For example, for saturation dives, the shorter time constant results in a lower prediction of DCS occurrence because only wash-out is affected; in saturation dives this compartment's gas uptake is saturated for either time constant.

The more important difference, for a majority of the dive data, is the lower absolute supersaturation threshold, which allows a greater risk accumulation for almost all dives. It is this lower estimated threshold that accounts for much of the increased DCS incidence predicted for both **A** and **B** by the fit to **A+B** shown in Table 2.
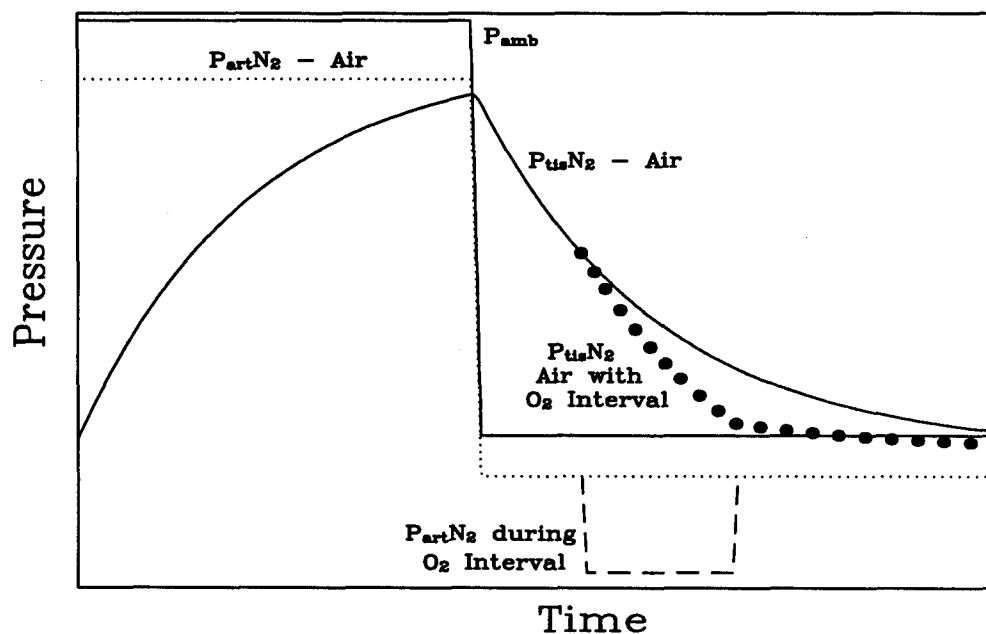


**Figure 1. Accelerated N$_2$ washout during O$_2$ breathing.**

Figure 1 illustrates the underlying reason for the 'base' model's under-prediction of DCS risk in the $O_2$ decompression data. In the hypothetical dive profile shown, two possible washout curves are plotted: one for a diver who breathes Air (solid curve) during the decompression stop, another for a diver who breathes 100% $O_2$ (dotted curve) during a portion of the stop. The duration of the $O_2$ period is indicated by the drop in arterial $N_2$ ($P_{art}N_2$) level below that for breathing Air. During the $O_2$ breathing period tissue $N_2$ wash-out accelerates because the asymptote for the model's calculated $N_2$ tissue pressure, $P_{art}N_2$, is then essentially zero. Since the model considers DCS risk to be proportional to the area between the $N_2$ tissue pressure curve and ambient pressure, risk is reduced, both in magnitude and duration, due to the $O_2$ breathing period.

While this reduction in risk is in qualitative agreement with the idea that breathing $O_2$ during decompression reduces the risk of DCS, the effect is exaggerated in the 'base' model when compared to the observed DCS incidence in the available $O_2$ decompression data. We need to modify the 'base' model either to reduce the $N_2$ wash-out rate during $O_2$ breathing periods, or to introduce a specific $O_2$-based risk contribution.

Three types of modifications to the 'base' model are proposed in this study, each with the aim of better describing the DCS risk observed in the $O_2$ decompression data while maintaining the model's ability to describe the $N_2$-$O_2$ data set as a whole. These modifications to the 'base' model attempt to involve either the partial pressure or the fraction of oxygen present during the dive in the accumulation of DCS risk. We seek to accomplish this through **a)** modification of inert gas wash-in/wash-out kinetics, **b)** direct $PO_2$ or $FO_2$ contribution to risk, or **c)** a $PO_2$ based kinetic risk compartment.

## Kinetic Modifications

The first class of modifications (Models 1 & 2) attempts to include the effect of breathing high pressures of $O_2$ by altering the inert gas kinetic time constants for each compartment as a function of $PO_2$. This class of modifications is based on experimental results in which a reduction of whole body $N_2$ washout is observed with exposure to increasing $PO_2$ (1). This reduced $N_2$ wash-out is attributed to simultaneously observed reductions in cardiovascular parameters, including heart rate, perfusion, and blood flow, the combined effects of which we can model as slower kinetic time constants.

In Model 1, the modified time constant for each compartment is defined as

$$\alpha_i = \alpha_{0_i} \cdot \left(1 + \left(k_1 \cdot PO_2\right)^{k_2}\right) \tag{2}$$

where $\alpha_{0i}$ is the unmodified inert gas time constant for the $i$th compartment, to be estimated by fitting to data, $PO_2$ is the oxygen pressure during the time of interest, and $k_1$ and $k_2$ are parameters to be estimated from the data. Model 1 adds up to two parameters per compartment to the 'base' model.

In Model 2, the modified compartment time constant is defined as

$$\alpha_i = \alpha_{0_i} \cdot \left(\left(\frac{PO_2}{P_{surf}O_2}\right)^{k1}\right) \tag{3}$$

with the terms defined as for Model 1, above. The term $P_{surf}O_2$ is the $PO_2$ of blood at 1 ata of air. Model 2 adds only one parameter to be estimated per compartment.

Figure 2 shows a range of effects that Models 1 and 2 might have on an $N_2$ kinetic time constant, for several values of $k_1$ and $k_2$, over the $PO_2$ range contained in the data. The value on the y-axis in these plots is the exchange retardation factor within parentheses in equations (2) and (3).
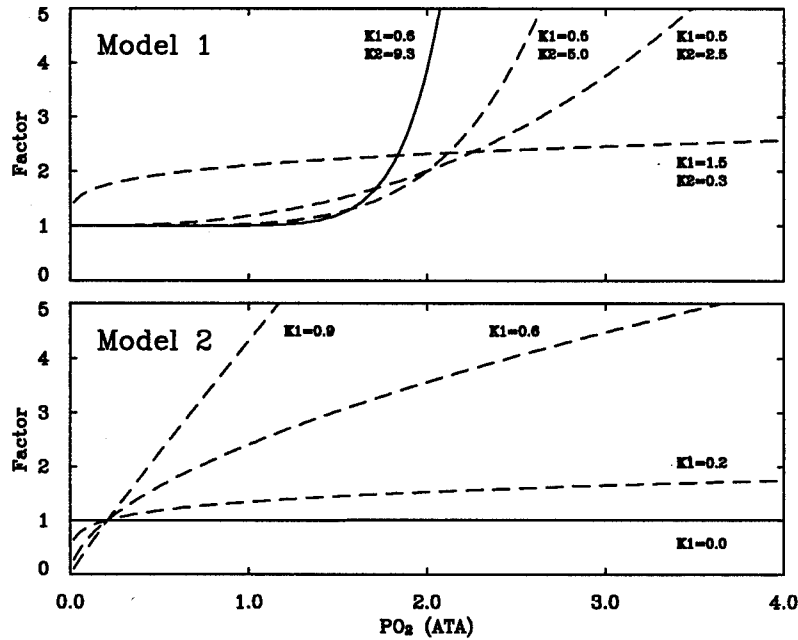


**Figure 2. Range of responses for Models 1 and 2**

It is clear that a wide range of kinetic modifications are possible with these functions, producing from subtle to pronounced effects, depending on the values of the parameters $k_1$ and $k_2$. In particular, Model 1 is capable of producing a seemingly desirable modification that has virtually no effect on $\alpha_0$ for values of $PO_2$ generally observed in the air dives ($PO_2$ usually below 2.0 ata), and an increasing effect on $\alpha_0$ for higher $PO_2$ levels.

10

*Direct Risk Contribution*

The second class of modifications (Models 3 - 6) proposes a direct addition to the instantaneous risk, as a function of either the $PO_2$ or $FO_2$ level in the breathing gas. These modifications are based on the idea that at certain high levels of $O_2$ exposure, some of the $O_2$ present acts essentially as an inert gas and may therefore contribute to DCS risk (2-4,13,15,21).

For Models 3 through 6, an "$O_2$ effect" is added to the instantaneous risk function, Equation (1), to make;

$$r = \sum_{i=1}^{3} A_i \left( \frac{P_{tis}i - Pamb - Thr_i + EFO_{2i}}{Pamb} \right) \; ; \quad r \ge 0 \tag{4}$$

As for Equation (1), the term inside the summation must be greater than zero, i.e., no compartment may make a negative risk contribution.

*Pressure-based Direct Contribution*

In Model 3, the $O_2$ contribution to instantaneous risk is a function of the pressure of oxygen present beyond that in air on the surface. We restrict the risk contribution to $PO_2$ values greater than $P_{surf}O_2$ so that no DCS risk accumulates while breathing air on the surface.

$$EFO_{2_i} = \left( k_1 \cdot (PO_2 - P_{surf}O_2) \right)^{k_2} \tag{5}$$

In Model 4, only the pressure of oxygen present beyond a $PO_2$ threshold, $O_2$thr, contributes to DCS risk. The value of $O_2$thr was set at 1.5 ata for this study, based on the range of $PO_2$ in the current data set. As seen in Table 1, 1.5 ata is the upper limit of $PO_2$ in the non-$O_2$

11

data sets (with the exception of a few deep submarine escape exposures of short duration in the Single Air category).

$$EFO_{2_i} = \left( k_1 \cdot (PO_2 - O_2 thr) \right)^{k_2}$$ (6)

Figure 3 shows a range of possible functionalities by which Models 3 and 4 can contribute to the DCS risk. Note that, depending on the values of $k1$ and $k2$, either model can vary its response greatly, from a gentle increase in $EFO_2$ as $PO_2$ increases to a sudden increase over a small $PO_2$ interval. Also note the restricted range of $PO_2$ in which Model 4 can contribute risk due to the selected value of its $O_2 thr$ parameter.
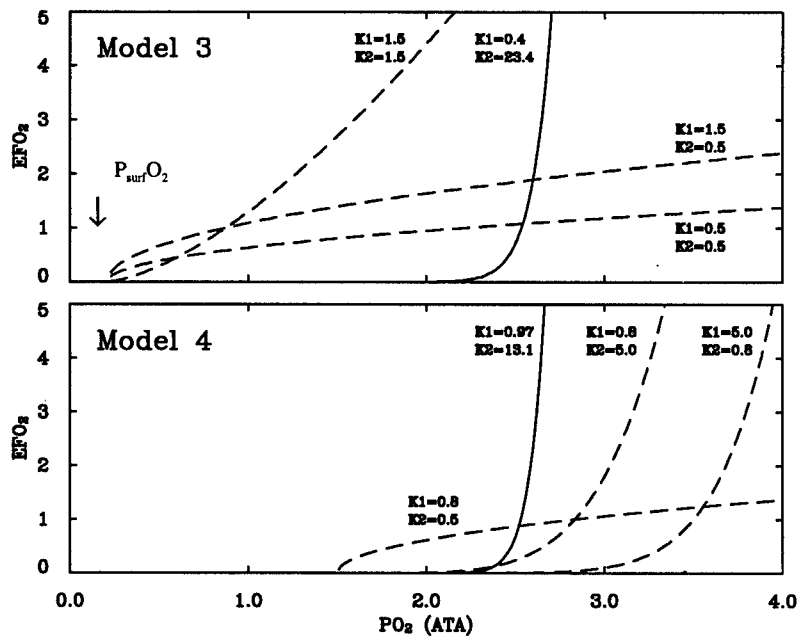


Figure 3. Range of responses for Models 3 and 4

12

## Fraction-based Direct Contribution

In Table 1 we made a distinction between the $O_2$ decompression dives and the remaining data on the basis of $PO_2$, although there is some overlap in $PO_2$ between the two types. This indefinite boundary allows any $PO_2$-based risk contribution to be implemented not only for the $O_2$ data sets, where it is needed, but also for some parts of the remaining data, where it may not be needed. A clearer distinction can be made between these data sets on the basis of the fraction of $O_2$. Although the dives in data set **B** use air at depth, their subsequent exposure to 100% oxygen makes these dives clearly different from the others. Since it is during these $O_2$ exposures that the 'base' model fails to accumulate sufficient risk, we can attempt to make an $O_2$-based risk contribution only during these high $FO_2$ exposures.

Model 5 is based on the fraction of $O_2$ present and uses the parameter $k_2$ as a threshold of $O_2$ fraction below which no contribution is made to risk.

$$EFO_{2_i} = \left( k_1 \cdot (FO_2 - k_2) \right) \qquad (7)$$

Model 6 is similar to Model 3, but uses the fraction, rather than the pressure, of $O_2$ present in excess of the fraction of $O_2$ present on the surface (breathing air), in determining its risk contribution.

$$EFO_{2_i} = \left( k_1 \cdot (FO_2 - F_{surf}O_2) \right)^{k_2} \qquad (8)$$

Figure 4 shows a range of possible contributions that Models 5 and 6 can make to DCS risk for the range of $FO_2$ values found in the current data.

**Model 5**

EFO₂

K1=0.5
K2=0.2

K1=1.0
K2=0.2

K1=1.0
K2=0.0

K1=3.0
K2=0.7

**Model 6**

K1=0.1
K2=0.1

EFO₂

K1=0.5
K2=0.5

K1=0.65
K2=0.63

0.0    0.2    0.4    0.6    0.8    1.0

FO₂ (ATA)
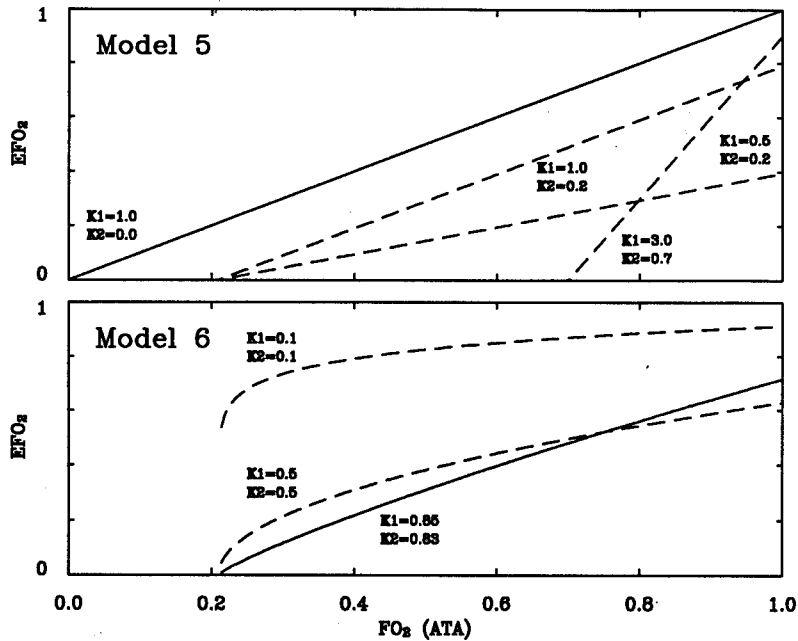
**Figure 4. Range of responses for Models 5 and 6**

Each of the modifications in this direct risk contribution class (Models 3 - 6) increases the number of parameters per compartment to be estimated from the data by two; $k_1$ and $k_2$. The effect of the modifications of Models 1 - 6 can each be nullified simply by setting the parameter $k_1$ to 0, simplifying in every case to the 'base' model.

## $O_2$ Kinetic Compartment

The third class of modification (Model 7) adds a fourth parallel risk compartment in which $Ptis_4$ is based on $PO_2$ rather than $PN_2$ and uses only single exponential kinetics for gas wash-in and wash-out. This model should have the ability to isolate the risk contribution due to high pressures of oxygen in this fourth compartment, while leaving the $N_2$-based risk accumulation relatively undisturbed in the three original compartments of Equation 1.

14

$$r_4 = A_4 \left( \frac{P_{tis}O_2 - Pamb - Thr_4}{Pamb} \right) \quad ; \quad r_4 \geq 0 \qquad (9)$$

In order to get an overpressure, and therefore a risk contribution from this compartment, the 'tissue pressure' of oxygen, $P_{tis}O_2$, must exceed ambient pressure. For Air dives, it is not possible to obtain this much overpressure with bottom depths shallower than about 5 ata (about 132 fsw). Risk on deeper air dives would require rapid decompression either to a shallow stop or the surface so that sufficient overpressure was established before the 'tissue pressure' kinetics of $O_2$ washout $P_{tis}O_2$ below ambient pressure. The constant $PO_2$ dives prevalent in the non-Air portion of data set **A** will never invoke an overpressure in this compartment because they maintain a fixed $PO_2$ of 0.7 ata. The primary source of potential overpressures in this fourth compartment are the periods of 100% $O_2$ breathing in data set **B**.

## PARAMETER ESTIMATION

The parameters for each model are estimated from the data using a modified Marquardt (11) nonlinear estimation routine. The probability of each outcome, needed for the estimation, comes from the following:

if DCS *is not* observed;

$$P(no\ DCS) = e^{-\int_0^{+24hrs} r\,dt} \qquad (8)$$

if DCS *is* observed in the interval T1 - T2:

$$P(DCS) = \left( e^{-\int_0^{T1} r\,dt} \right) \cdot \left( 1 - e^{-\int_{T1}^{T2} r\,dt} \right) \qquad (9)$$

15

The calculation of P(DCS) combines the probability of not observing DCS over the interval from 0 to T1 with the probability of observing DCS over the interval T1 to T2. Any risk remaining after T2 in this case is ignored, where in the case of no DCS, all risk out to 24 h (48 h for saturation dives) after surfacing is included.

Since each of the proposed models is a modification of, and can be simplified to, the 'base' model, a likelihood ratio test (5,6) can be used to test for the significance of the added parameters contained in each modification. A proposed model will have a significantly improved fit to the data compared to the 'base' model, if its LL increases by more than 2 for 1 added parameter, or by 3 for 2 added parameters.

Each model, including the 'base' model, is fitted to the combined data set (A+B). Models 1 through 6 allow for up to 6 new parameters (2 per kinetic compartment) to be estimated, in addition to the 'base' model's kinetic time constants, scale factors, thresholds, and linear-exponential crossover parameters. Some or all of the added parameters may not add significantly to the improvement of the fit, as judged by the likelihood ratio test. In order to arrive at the form for each model that would maximize the improvement in LL with the fewest added parameters, each model was fitted to the data with incremental addition of estimated parameters.

Each of Models 1 through 6 allows for all three kinetic compartments to use the same fitted $k_1$ and $k_2$ values, or for each compartment to have independently fitted $k_1$ and $k_2$ values. Using Model 1 as a typical example, the fewest possible additional fitted parameters is two: one $k_1$ and one $k_2$ parameter applied to all three compartments. Application of the modification to only one compartment, setting $k_1 = 0$ for the other two compartments, also results in two added estimated parameters. If the modification is applied to two or three compartments independently, there will be 4 or 6 added estimated parameters, respectively. Model 2 contains only a $k_1$ parameter, so it will add 1, 2, or 3 estimated parameters, as above.

The added parameters of Model 7 pertain only to a fourth kinetic compartment, and will add at least two estimated parameters, a time constant and scale factor. A threshold may be included for this compartment if found to be significant.

## RESULTS OF FITTING

After fitting each model to the data set by incrementally adding estimated parameters by the above procedure, the best fit of each model was found to add no more than two estimated parameters to the 'base' model, which contains eight estimated parameters (12). Model 1 and Models 3 through 6 each add two estimated parameters, $k_1$ and $k_2$, but only for the third compartment; the $k_1$ and $k_2$ parameters for the first and second compartments proved not to significantly improve the fit. This $O_2$ effect emphasis on the third (longest time constant) compartment is not surprising, since the long-lasting overpressure that this compartment can provide will be useful in adding the necessary risk accumulation. No improvement of fit was found for any value of $k_1$ in Model 2.

Table 3 lists the LL values and the number of additional estimated parameters found for the best fit of each model to data set **A+B**. Only Model 7 produced a significant improvement in the fit to the data, with a likelihood improvement of 4.2 for 2 added parameters.

| | Models | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **Base** | **(1)** | **(2)** | **(3)** | **(4)** | **(5)** | **(6)** | **(7)** |
| **LL** | -813.3 | -810.8 | -813.3 | -811.7 | -811.4 | -810.8 | -811.3 | -809.1 |
| **# of Added Parameters** | - | 2 | 0 | 2 | 2 | 2 | 2 | 2 |

**Table 3. Log Likelihood Results for Fitting to Data Set A+B**

Table 4 lists the best fit parameters and standard errors estimated for each model by fitting to data set **A+B**. The estimated parameter values for all seven models are listed here, regardless of whether a model achieved a significant improvement of fit to the data compared to the 'base' model. We show "less than significant" parameter estimates since they may still suggest something about the nature of an $O_2$ effect in the data.

Parameters in the upper section of Table 4 are those found to be significant in fitting the 'base' model: For example, only $PXO_2$ is listed since the PXO parameters for compartments 1 and 3 did not significantly improve the fit. Those parameters in the lower section of the table are the added $O_2$ effect parameters as they apply to Models 1 - 7. The $k_1$ and $k_2$ values listed for Model 1 and Models 3 through 6 apply only to compartment 3, since these parameters did not improve the fit when applied to Compartments 1 and 2.

| | Models | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **Base** | **(1)** | **(2)** | **(3)** | **(4)** | **(5)** | **(6)** | **(7)** |
| $\alpha_1$ | 1.07 (0.50) | 1.09 (0.52) | 1.07 (0.50) | 3.82 (3.50) | 3.99 (3.82) | 0.97 (0.49) | 0.98 (0.51) | 1.14 (0.57) |
| $\alpha_2$ | 26.6 (11.4) | 44.4 (18.6) | 26.6 (14.4) | 27.2 (10.9) | 27.3 (11.0) | 25.2 (11.0) | 25.3 (11.1) | 26.8 (10.3) |
| $\alpha_3$ | 404.5 (21.3) | 443.1 (37.4) | 404.5 (21.3) | 405.2 (21.3) | 405.3 (21.2) | 404.9 (22.0) | 403.2 (23.7) | 411.6 (22.4) |
| $A_1$ | 6.1E-3 (5.1E-3) | 5.9E-3 (5.0E-3) | 6.1E-3 (5.1E-3) | 8.6E-4 (9.7E-4) | 8.1E-4 (9.3E-4) | 7.0E-3 (6.4E-3) | 6.8E-3 (6.2E-3) | 5.4E-3 (4.8E-3) |
| $A_2$ | 5.1E-5 (2.3E-5) | 9.1E-5 (4.0E-5) | 5.1E-5 (2.3E-5) | 4.9E-5 (1.5E-5) | 4.9E-5 (1.5E-5) | 4.5E-5 (1.5E-5) | 4.5E-5 (1.5E-5) | 5.0E-5 (1.5E-5) |
| $A_3$ | 1.0E-3 (1.5E-4) | 9.9E-4 (1.7E-4) | 1.0E-3 (1.5E-4) | 1.0E-3 (1.5E-4) | 1.0E-3 (1.5E-4) | 1.0E-3 (1.5E-4) | 1.0E-3 (1.5E-4) | 9.7E-4 (1.5E-4) |
| $PXO_2$ | 0.0 (Fixed) | 1.00 (0.94) | 0.0 (F) | 0.0 (F) | 0.0 (F) | 0.0 (F) | 0.0 (F) | 0.0 (F) |
| $Thr_3$ | 0.44 (0.30) | 1.04 (0.59) | 0.44 (0.30) | 0.43 (0.30) | 0.43 (0.30) | 6.39 (2.81) | 0.41 (0.31) | 0.41 (0.31) |
| $k_1$[†] | | 0.56 (0.09) | | 0.43 (0.07) | 0.97 (0.29) | 0.97 (0.46) | 0.85 (0.91) | |
| $k_2$[†] | | 9.30 (8.30) | | 23.4 (8.8) | 13.1 (5.4) | 0.0 (F) | 0.83 (0.57) | |
| $\alpha_4$ | | | | | | | | 0.40 (0.30) |
| $A_4$ | | | | | | | | 0.12 (0.35) |

**Table 4. Estimated Parameters (and SE) for Models fitted to Data Set A+B**

† k parameter applied to third compartment only.

Several parameter values are shown with a value of 0.0 and a standard error of (F). In these cases, the estimated value of the parameter is very close to zero and has a large standard error, giving a confidence limit range which includes zero. This results from the estimation

routine's handling of very small optimal parameter values. We fix these parameters to 0.0, with no degradation in fit. This commonly occurs in the case of $PXO_2$, for which a value of 0.0 indicates that linear kinetics are present for any inert gas supersaturation in the second compartment.

Ideally, the $O_2$ effect parameters of any model would describe the added $O_2$ data, **B**, and allow the basic parameters to better describe the data in **A**. The estimated parameters for Model 1 suggest that it has had some success toward this end. Each of the basic parameters estimated for Model 1 is within the standard error of that parameter's value in the 'base' model fit. However, parameter values for Model 1 are very similar to those estimated by the 'base' model when fitted only to the original data set, **A** (12), suggesting that the influence of the added data, **B**, is at least partly being accounted for by the added $k_1$ and $k_2$ parameters. The estimated $k_1$ and $k_2$ values indicate one type of $O_2$ effect which seems to fit the combined data set; little alteration of the $N_2$ based kinetics for values of $PO_2$ below 1.5 ata, but a rapidly increasing effect for higher values of $PO_2$, up to an exchange retardation factor of almost 50 at 2.6 ata. The curve for these estimated parameter values is shown as the solid line in the upper plot of Figure 2.

The estimated parameters for Model 2 are the same as those for the 'base' model. The estimated $k_1$ parameter value is 0, so that the base time constant is multiplied by 1.0 (Eqn. 3) and no $O_2$ effect is present. The lack of an exchange retardation effect for Model 2 is shown as the flat line at Factor = 1.0, in the lower plot of Figure 2.

Models 3 and 4 share nearly identical estimated basic parameters. Their estimated $k_1$ and $k_2$ values result in very similar $O_2$ effect curves, shown as solid lines in Figure 3. While the 'added-risk' type of $O_2$ effect in these models is quite different from the time constant alteration

20

of Model 1, the nature of the $PO_2$ dependence is essentially the same: no effect for low values of $PO_2$, then an abrupt increase in effect over a short interval of higher $PO_2$. In Model 1, this $O_2$ effect jump takes place at the upper boundary of $PO_2$ seen in the non-$O_2$ data, so that there is little or no effect for Air and other $N_2$-$O_2$ data and a large effect for the $O_2$ decompression data. In Models 3 and 4 the jump takes place near the upper boundary of $PO_2$ seen in the $O_2$ data, so that there is little effect for any but the most extreme $PO_2$ exposures.

With the exception of their risk thresholds, Models 5 and 6 also have nearly identical basic parameters. There is a strong correlation between the $Thr_3$ and $k_2$ parameters in Model 5, so that any change in one is directly reflected in the other. Since a smaller value of $k_2$ results in a larger $O_2$ effect risk contribution for any given $FO_2$, the threshold correspondingly increases to reduce risk accumulation. In the range of about 1 to 7 fsw, the specific value of $Thr_3$ has little effect on the fit to these data, as long as the $k_2$ value is allowed to adjust in the corresponding range of about 0.2 to 0.0 ($FO_2$). For values of $k_2$ above 0.2 the strong correlation with $Thr_3$ vanishes, suggesting that the correlation results primarily from the Air data, which requires the higher threshold to eliminate the added and, for Air dives unneeded, $O_2$ effect risk. However, the overall fit of Model 5 is substantially poorer at values of $k_2$ above 0.2.

The estimated $O_2$ effect curves for Models 5 and 6, shown as solid lines in Figure 4, have a relatively gentle linear increase of effect over the $FO_2$ range, not the sudden jump in effect seen in Models 1, 3, and 4 for $PO_2$ dependency.

The estimated $N_2$ kinetic parameters for Model 7 are essentially unchanged from those of the 'base' model. The time constant estimated for the $PO_2$ risk compartment is short at 0.4 min, while its scale factor is over 20 times larger than the largest $N_2$ compartment scale factor.

21

This leads to $O_2$-based overpressures of short duration, but which are capable of substantial risk contributions.

The standard errors are large (75 and 300%) on Model 7's $O_2$ compartment parameter estimates because of the limited contribution this compartment makes to the overall DCS risk: barely 3% of the total risk accumulation for the whole data set. The fact that the confidence limits for this compartment's scale factor ($A_4$) include zero suggests that eliminating the $O_2$ compartment would not alter the fit. However, fixing $A_4$ to zero results in exactly the 'base' model fit, which is more than 4 LL units worse. Thus, even though the contribution this compartment makes is small, it allows Model 7 to better fit the data than the other models, as reflected in both the LL improvement as well as the DCS risk predictions described below.

**PREDICTION OF DCS**

Table 5 lists the DCS occurrence estimated by each of the models for the data used in fitting, divided into data sets A ($N_2$-$O_2$), and B ($O_2$ decompression) as listed in Table 1.

| | OBS DCS | Base | (1) | (2) | (3) | (4) | (5) | (6) | (7) |
|---|---|---|---|---|---|---|---|---|---|
| **A** Total | 138.5 | 144±22 | 140±22 | 143±22 | 144±22 | 142±22 | 142±22 | 143±22 | 140±22 |
| **B** Decom | 6.3 | 4±1 | 4±2 | 4±1 | 4±1 | 4±1 | 5±2 | 5±2 | 6±2 |
| Surd-D | 11.1 | 9±2 | 12±5 | 9±2 | 9±3 | 9±3 | 9±3 | 9±3 | 11±4 |
| Total | 17.4 | 13±4 | 16±6 | 13±4 | 13±4 | 13±4 | 14±4 | 14±4 | 17±6 |

**Table 5. Prediction of DCS Occurrence for all Models (fit to A+B)**

From the results listed in Table 5, it is clear that only Models 1 and 7 have the specific behavior we are looking for; prediction of DCS occurrence in data set **A** centered more nearly on the observed value *and* prediction of DCS occurrence in data set **B**, which includes the observed value within its confidence limits, preferably centered on the observed value.

For data set **B** as a whole, Model 1 has the type of result desired, but since its improvement of the fit to the data was not significant as measured by LL, it cannot be considered a total success. Additionally, its predicted DCS incidence for the $O_2$ Decompression subset of data set **B** is unchanged from that of the 'base' model and falls short of the observed value.

Since this model was intended to incorporate the experimental observations of Anderson et al. (1), we might learn something about our models and data by comparing the behavior of Model 1 with those observations. They report 9% and 17% reductions in the volume of $N_2$ elimination, compared to normoxic levels, over 2 hours at $PO_2$ levels of 2.0 and 2.5 ata, respectively. Model 1 (Eqn. 2; using the best fit parameters shown in Table 4) yields kinetic retardation factors of 2.02 and 11.11 at $PO_2$ of levels of 2.0 and 2.5 ata, respectively. This retardation applies only to the slowest of the three compartments, giving $N_2$ wash-out time constants of 895 or 4923 min for these two $PO_2$ levels. Over a two-hour wash-out period these retarded time constants would result in 12.8% and 21.8% reductions in $N_2$ elimination compared to the unmodified time constant of 443 min. Since we make no distinction of the inert gas volume represented by each compartment, it is impossible to make a direct comparison between the reported (1) and this calculated decrease in $N_2$ volume elimination. However, we find a reasonable match with the reported values if we assume that the third compartment of Model 1 represents about 70% of the total inert gas volume: the calculated reductions in $N_2$ wash-out

23

would give whole body reductions of 9% and 15% for $PO_2$ levels of 2.0 and 2.5 ata, respectively. We will retain Model 1 as a promising candidate for fitting to larger data sets as they become available.

Models 3 and 4 show no improvement in predictive ability over the 'base' model. While Models 5 and 6 contain the observed value within the confidence limits of their DCS prediction for **B**, they retain some of the 'base' model's overprediction of occurrence in data set **A**. This modest overprediction, together with the failure of either of these models to achieve a significant improvement in the fit to the data, makes them less than successful.

Model 7 exhibits a prediction of DCS in data set **A** nearly identical to that of the 'base' model when fitted only to **A** (see Table 2). In addition, Model 7 is a good predictor of DCS occurrence in the $O_2$ decompression data, **B**. This, combined with the fact that it significantly improves the fit to **A**+**B** over the 'base' model, makes Model 7 a success by these three important measures. Note that, in contrast to Model 1, Model 7 achieves its good prediction of the overall level of DCS incidence in data set **B** by correctly predicting the incidence level in both subsets of **B**.

Table 6 shows another measure of the improvement that Model 7 provides in our ability to describe, with a single model, DCS incidence in both the original $N_2$-$O_2$ data set as well as the $O_2$ decompression data. In this test a model is used to group the dives in a data set by its estimation of each dive's risk level, and the observed and predicted DCS incidence for each group is compared. For example, in the first group of three columns of the lowest risk category row, 0 to 2.5%, the 'base' model fit to **A** is used to select those dives that it predicts to belong in this risk group. This set of dives is observed to have an average DCS incidence of 2.6%, while the

24

model predicts 1.8%; this group of dives is somewhat riskier than this model predicts. However, it can be seen that there is generally good agreement, with each higher risk level group corresponding to a higher observed and predicted incidence.

The model which we have set out to improve upon, the 'base' model fitted to data set **A**, is generally able to distinguish between dives of different risk level within data set **A**, but fails in this regard when applied to data set **B**, as shown on the right side of Table 6. Our best candidate to accomplish the desired improvement, Model 7 fitted to the combined **A+B** data set, retains much of the 'base' model's ability to distinguish the risk level of dives in data set **A**, and is also able to do so for the dives of data set **B**.

The unmodified 'base' model, when fitted to the combined **A+B** data set, gives a result intermediate between those shown in Table 6; some degradation of the prediction of DCS incidence in data set **A** and only moderate improvement in DCS prediction for data set **B**.

| | Data Set A | | | | | | Data Set B | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 'Base' Model (fit to A) | | | Model (7) (fit to A+B) | | | 'Base' Model (fit to A) | | | Model (7) (fit to A+B) | | |
| Risk Level | n | Obs | Pred | n | Obs | Pred | n | Obs | Pred | n | Obs | Pred |
| 0.0-2.5% | 535 | 2.6% | 1.8% | 630 | 2.7% | 1.6% | 708 | 2.5% | 0.9% | 550 | 1.9% | 1.7% |
| 2.5-5.0 | 614 | 3.6 | 3.7 | 474 | 3.1 | 4.0 | 21 | 0.0 | 2.9 | 179 | 4.0 | 3.2 |
| 5.0-7.5 | 643 | 4.3 | 6.2 | 652 | 4.4 | 6.2 | | | | | | |
| 7.5-10. | 298 | 10.6 | 8.5 | 363 | 10.8 | 8.5 | | | | | | |
| 10.-100. | 293 | 14.8 | 14.1 | 264 | 14.8 | 12.7 | | | | | | |

**Table 6. Prediction of DCS by risk level.**

25

## SUMMARY AND CONCLUSIONS

The 'base' model, while quite successful in describing DCS occurrence in a wide range of $N_2$-$O_2$ data, both within the fitted dives and for other dives, fails to accurately describe DCS occurrence in a data set of $O_2$ decompression dives. The substantial underprediction of DCS incidence in these dives, due to accelerated $N_2$ wash-out during $O_2$ breathing, is only modestly improved by fitting the 'base' model to the combined data set. The remaining discrepancy between observed and predicted incidence requires that $O_2$ itself contribute to the DCS risk. The degree of suggested effect, however, is much greater than that measured in human whole-body wash-out experiments (1) and is near the limit of possible conclusions from a human dive trial specifically designed to elicit the role of $O_2$ in DCS (21).

Alteration of the inert gas kinetic time constants based on $PO_2$, as tested in Model 1, shows some promising qualities, but is not statistically successful with the current available data set. Further explorations with this type of modification to the 'base' model may be profitable when more $O_2$ data become available.

Direct contribution to DCS risk, based on either $PO_2$ or $FO_2$ present, results in little or no improvement for the current combined data set.

Addition of a separate, parallel risk compartment based on $PO_2$, rather than $PN_2$, overpressure (Model 7) is the only modification of the 'base' model explored in this study that results in a significant improvement in the fit to the combined data set. The time constant estimated for this single exponential kinetic compartment is very short at 0.4 min. This brief duration of risk accumulation is offset by an unusually large estimated scale factor, which causes the $O_2$ supersaturation to make a large risk contribution. This model results in a nearly exact

26

prediction of DCS occurrence in the $O_2$ dives, whether looked at as a whole, separated by type of decompression (Table 5), or ranked by risk level (Table 6).

The failure of the 'base' model to describe DCS risk in a large set of $O_2$ decompression dives lead us to explore the idea that $O_2$ itself contributes to DCS risk when present in high pressures or fractions. The success of Model 7 in increasing the risk accumulated during these $O_2$ dives while retaining, or improving upon, the desirable behavior of the 'base' model on all other dives, suggests that $O_2$ can be considered to independently contribute to DCS risk over short durations following exposure to high $PO_2$.

# REFERENCES

1.  Anderson, D., Nagasawa, G., Norfleet, W., Olszowka, and A., Lundgren, C., " $O_2$ pressures between 0.12 and 2.5 atm abs, circulatory function, and $N_2$ elimination." Undersea Biomedical Research, Vol. 18, No. 4, pp. 279-292, 1991.

2.  Donald, K.W., "Oxygen Bends." Journal of Applied Physiology, Vol. 7, pp. 639-644, 1955.

3.  Eaton, W.J. and Hempleman, H.V., The Role of Oxygen in the Aetiology of Acute Decompression Sickness. Report 12-73, Royal Navy, Alverstoke, UK, 1973.

4.  Forest, T.W. and Ward, C.A., "Effect of dissolved gas on the homogeneous nucleation pressure of a liquid. Journal of Chemistry and Physics, Vol. 66, pp. 2322-2330, 1977.

5.  Hays, J.R., Hart, B.L., Weathersby, P.K., Survanshi, S.S., Homer, L.D., and Flynn, E.T., Statistically Based decompression tables IV. Extension to air and $N_2O_2$ saturation diving. NMRI Technical Report No. 86-51, Naval Medical Research Institute, Bethesda, Maryland, 1986.

6.  Kendall, M.G., and Stewart, A., <u>The Advanced Theory of Statistics.</u> 4th ed. Vol. 2. London: Haffner, p. 38-180, 1979.

7.  Lauckner, G.R., Nishi, R.Y., and Eatock, B.C., <u>Evaluation of the DCIEM 1983 decompression model for compressed air diving(Series A-F).</u> DCIEM Report 84-R-72, Defence and Civil Institute of Environmental Medicine, Toronto, Canada, Oct 1984.

8.  Lauckner, G.R., Nishi, R.Y., and Eatock, B.C., <u>Evaluation of the DCIEM 1983 decompression model for compressed air diving (Series G-K).</u> DCIEM Report 84-R-73, Defence and Civil Institute of Environmental Medicine, Toronto, Canada, Nov 1984.

9.  Lauckner, G.R., Nishi, R.Y., and Eatock, B.C., <u>Evaluation of the DCIEM 1983 decompression model for compressed air diving (Series L-Q).</u> DCIEM Report 85-R-18, Defence and Civil Institute of Environmental Medicine, Apr 1985.

10. Marquardt, D.W., "An algorithm for least-squares estimation of non-linear parameters." <u>Journal of the Society of Industrial and Applied Mathematic,</u> Vol. 11, pp. 431-441, 1963.

11. Nishi, R.Y., Lauckner, G.R., Eatock, B.C., Hewitt, J.T., Oxygen decompression techniques for compressed air diving using the XDC-2 decompression computer programmed with the Kidd-Stubbs 1971 model. DCIEM Report 84-R-19, Defence and Civil Institute of Environmental Medicine, June 1984.

12. Parker, E.C., Survanshi, S.S., Weathersby, P.K., and Thalmann, E.D., Statistically based decompression tables VIII: Linear-exponential kinetics. NMRI Technical Report No. 92-73, Naval Medical Research Institute, Bethesda, Maryland, 1992.

13. Rashbass, C. and Eaton, W.J., The Effect of Oxygen Concentration on the Occurrence of Decompression Sickness. Report 10-57, Royal Navy, Alverstoke, UK, 1957.

14. Thalmann, E.D., Phase II testing of decompression algorithms for use in the U.S. Navy underwater decompression computer. NEDU Technical Report, No. 1-84, Navy Experimental Diving Unit, Panama City, Fla., 1984.

15. Thalmann, E.D., Air-$N_2O_2$ Decompression Computer Algorithm Development. NEDU Technical Report, No. 8-85, Navy Experimental Diving Unit, Panama City, Fla., 1985.

16. Tikuisis, P., Weathersby, P.K., and Nishi, R.Y., "Maximum Likelihood Analysis of Air and $HeO_2$ Dives." Aviation, Space, and Environmental Medicine, Vol. 62, pp. 425-31, 1991.

17. Weathersby, P.K., Survanshi, S.S., Homer, L.D., Hart, B.L., Nishi, R.Y., Flynn, E.T., and Bradley, M.E., <u>Statistically Based decompression tables I. Analysis of standard air dives: 1950 - 1970.</u> NMRI Technical Report No. 85-16, Naval Medical Research Institute, Bethesda, Maryland, 1985.

18. Weathersby, P.K., Survanshi, S.S., Nishi, R.Y., Thalmann, E.D., <u>Statistically Based decompression tables VII. Primary data for testing human $N_2O_2$ decompression models.</u> NSMRL Report No. 1182 and NMRI Technical Report No. 92-85, Naval Submarine Medical Research Laboratory, Groton, CT, 1992.

19. Weathersby, P.K., Survanshi, S.S., Homer, L.D., Parker, E.C. and Thalmann, E.D., "Predicting the time of occurrence of decompression sickness," <u>Journal of Applied Physiology</u>, Vol. 72, No. 4, pp.1541-1548, 1992.

20. Weathersby, P.K., Survanshi, S.S., and Nishi, R.Y. "Relative decompression risk of dry and wet chamber air dives." <u>Undersea Biomedical Research,</u> Vol. 17, No. 4, 1990.

21. Weathersby, P.K., Hart, B.L., Flynn, E.T., and Walker, W.F. "Role of oxygen in the production of human decompression sickness." <u>Journal of Applied Physiology,</u> Vol. 63, No. 6, pp. 2380-2387, 1987.