# Decompression comparison of helium and hydrogen in rats

R. S. LILLO, E. C. PARKER, AND W. R. PORTER
*Diving and Environmental Physiology Department, Naval Medical Research Institute, Bethesda, Maryland 20889-5607*

**Lillo, R. S., E. C. Parker, and W. R. Porter.** Decompression comparison of helium and hydrogen in rats. *J. Appl. Physiol.* 82(3): 892–901, 1997.—The hypothesis that there are differences in decompression risk between He and $H_2$ was examined in 1,607 unanesthetized male albino rats subjected to dives on 2% $O_2$-balance He or 2% $O_2$-balance $H_2$ (depths ≤ 50 ATA, bottom times ≤ 60 min). The animals were decompressed to 10.8 ATA with profiles varying from rapid to slow, with up to four decompression stops of up to 60 min each. Maximum likelihood analysis was used to estimate the relative decompression risk on a per unit pressure basis (termed "potency") and the rate of gas uptake and elimination, both factors affecting the decompression sickness risk, from a specific dive profile. $H_2$ potency for causing decompression sickness was found to be up to 35% greater than that for He. Uptake rates were unresolvable between the two gases with the time constant (TC) estimated at ~2–3 min, leading to saturation in both cases in <15 min. Washout of both gases was significantly slower than uptake, with He washout (TC ~1.5–3 h) substantially slower than $H_2$ washout (TC ~0.5 h). It is unknown whether the decompression advantage of the faster washout of $H_2$ or the disadvantage of its increased potency, observed in the rat, would be important for human diving.

decompression sickness; diving; hyperbaric; inert gases

COMPRESSED AIR is a satisfactory breathing gas for almost all shallow water diving and is widely used. Beyond 5 ATA, however, $N_2$ narcosis begins to significantly impair an air diver's performance, and working dives much below 6 ATA are prohibited by narcosis (8). To avoid this problem, divers generally breathe binary mixtures of He and $O_2$. However, the deeper dives are complicated by *1*) long decompression schedules; *2*) reduced work capacity due to the increased work of breathing a dense, highly compressed gas (21); and *3*) a variety of neurological symptoms collectively known as the high-pressure nervous syndrome (HPNS; Ref. 2). Small amounts of $N_2$ have been added experimentally to He-$O_2$, which have reduced some of the pronounced HPNS symptoms, but breathing resistance is increased and the potential for $N_2$ narcosis recurs. Based on the rationale that *1*) $H_2$ also has some narcotic potency that could antagonize, hence lessen, HPNS and *2*) $H_2$ is one-half as dense as He and should be easier to breathe, the use of $H_2$ as a complete or partial substitute for He has been proposed (4). The recent interest in $H_2$ as a diving gas has coincided with the development of technology that overcomes the danger of $H_2$ flammability, particularly at great depths where low percentages of $O_2$ are used in breathing mixtures (9). These gas mixtures have been safely tested starting in the 1980s during experimental dives in Europe, particularly France, and were reasonably successful (13).

An important consideration for using $H_2$ for diving is the decompression characteristics of this gas and how it compares to He. Research and experience indicate that there can be significant differences in risk among gases for causing decompression sickness (DCS; Refs. 17, 18). Given the role that bubbles appear to play in DCS, these differences have been generally attributed to differences in gas properties such as tissue solubility and diffusivity. For $H_2$, however, there is an additional consideration of reactivity within the body. Typical "inert" diving gases such as $N_2$ and He are generally considered to be chemically nonreactive with the tissues. On the other hand, the conversion of $H_2$ to water through enzymatic oxidation may be possible (13). Such a process would not only reduce the decompression time by chemical removal of the gas from the body but also might increase cold-water tolerance by enhancing body heat production. However, a recent study suggests that mammalian tissues do not metabolize $H_2$ even in a hyperbaric environment (14). Limited experience with human decompression after $H_2$ diving suggests that decompression requirements for He and $H_2$ may be similar (6, 13).

This investigation responds to the need to examine critically the decompression aspect of $H_2$ by comparing the decompression risk of He and $H_2$ in rats with the maximum likelihood technique (7), which is well suited for analyzing binary data such as decompression outcome. Based on differences between the properties of the two gases, the study hypothesis was that there would be differences in the risk of DCS between He and $H_2$.

## METHODS

### *Summary*

Rats were subjected to simulated dives on 2% $O_2$-balance He or 2% $O_2$-balance $H_2$ at depths up to 50 ATA and bottom times up to 60 min. They were then decompressed with various profiles to 10.8 ATA and observed for signs of DCS. The maximum likelihood technique was used to fit mathematical models, which predict the risk of DCS, to the data.

The experiments reported herein were conducted according to the principles set forth in the *Guide for the Care and Use of Laboratory Animals* [DHEW Publication No. (NIH) 86-23, Revised 1985].

### *Experimental Protocols*

Male albino rats (*Rattus norvegicus*, Sprague-Dawley strain) weighing ~200–300 g were obtained from a local supplier and housed in the Institute's Animal Care Facility for at least 1 wk before use. The animals were allowed access to food and water up until immediately before the dive began.

*Diving procedures.* The experiments were conducted in a facility equipped with special safety features designed for small-animal diving with $H_2$ and He at pressures up to ~60

ATA. The animals were dived on one of two gas mixtures: *1*) 2% $O_2$-balance He or *2*) 2% $O_2$-balance $H_2$. Both dive mixtures were obtained either commercially or prepared in-house and were confirmed to be within 2.0–2.2% $O_2$ for use.

Immediately before each dive, five animals were individually weighed on a triple-beam balance to the nearest gram and placed in a cylindrical cage (56 cm long, 23 cm diameter), which was then loaded into a hyperbaric chamber (Bethlehem model 183160 HP, Bethlehem, PA). The air-filled chamber was sealed and pressurized with pure He to 10.8 ATA, resulting in an $O_2$ concentration of ~2%. Immediately on reaching 10.8 ATA, a gas switch was made by venting the chamber over a 5-min period with ~6,000 standard liters of one of the two dive mixtures, holding the depth constant. After the switch, a delay of 4.5 min was allowed for sampling of the chamber atmosphere for gas analysis. Compression to the final depth, up to 50 ATA, was then begun with the dive mixture. Clocking of bottom time, which ranged up to 60 min, started as soon as the final depth was reached. All compression was done at 1.8 ATA/min. The animals were held at that depth for up to 60 min and were then decompressed with varying profiles back to 10.8 ATA. They were then observed for 30 min for signs of DCS, as described previously (18).

Throughout the dive and postdecompression period, the animals were exercised by rotating the cage at a perimeter speed of ~3 m/min to ensure that all animals sustained a similar level of activity and to facilitate DCS scoring. For data analysis, decompression results were recorded as no DCS symptoms, obvious DCS, or death. Therefore, the category DCS included the subset category of death. Two different scorers were involved in these experiments, although only one scorer participated in any one dive. After the 30-min postdecompression period, all surviving animals were killed by flushing the chamber at 10.8 ATA with $CO_2$. The chamber was then decompressed to the surface, and the animals were again weighed.

Three series of dives were performed (details in APPENDIX).

SATURATION (SAT) DIVES. This series compared the decompression risk of He and $H_2$ while minimizing the confounding issues of gas uptake and washout. All dives were done with a 60-min bottom time. The dive depth was varied to produce a range in incidence levels from 0 to 100% for both DCS and death for each gas. Experience has shown that this wide range in incidence is necessary for effective modeling. Based on prior work (17), the 60-min time at depth should produce saturation for He, although the model used for analysis and described in *Data Analysis: the Model* does not assume this. All dives were decompressed rapidly (<1 min) to 10.8 ATA to minimize gas washout.

VARIABLE TIME-AT-DEPTH (TD) DIVES. This series examined the rates of gas uptake of He and $H_2$ by allowing a variable amount of time for gas to enter the animal while minimizing gas washout during decompression. Bottom time was varied from 0 (immediate decompression on reaching depth) to 20 min followed by rapid decompression, with the goal again to generate the full range of incidences for both DCS and death.

VARIABLE DECOMPRESSION (VD) DIVES. These dives compared the rates of gas elimination of He and $H_2$ by varying the decompression time primarily via the length and number of stops during ascent rather than via travel rate. The animals were decompressed with a number of different profiles varying from rapid (<1 min) to slow (0.9 or 1.8 ATA/min), with as many as four stops of up to 60 min each.

The three dive series were conducted in sequential order over a period of 3 yr. After preliminary experiments to define the appropriate range in dive profiles for a specific series, the dives were conducted in random order, generally with two or three dives per day. A specific dive profile (i.e., identical depth, time at depth, and decompression) was replicated up to 6 times, resulting in up to 30 rats exposed to the same pressure history. Depth vs. time records of each dive were recorded on a personal computer with the PC-ACQUISITOR data-acquisition system (Dianachart, Rockaway, NJ) to confirm the profile accuracy. Actual depth at any time was generally within 0.05 ATA of the expected value.

When at depth, no venting of the chamber was done to remove $CO_2$ or add $O_2$. Gas (dive mixture) was added only to compensate for any very minor leakage that occurred to maintain depth. Soda lime on a tray below the animal cage was used to absorb $CO_2$. $CO_2$ levels were not measured routinely during the actual experiments. However, previous experience at shallower depths (i.e., 5–8 ATA) indicated that $CO_2$ should be effectively removed this way and kept below 1% surface equivalent. This was confirmed several times for the present dives by drawing samples in gastight syringes from the chamber and analyzing them. During the postdecompression period at 10.8 ATA, the chamber was vented for 20 s with the dive mixture at 5, 15, and 25 min to slow the decline in $O_2$. During the experiments, $O_2$ was observed to fall by up to 0.1% from the starting concentration of 2.0–2.2%, resulting in a lower $O_2$ limit of 1.9%.

At depth, the chamber atmosphere was kept at 30.0 ± 1.5°C by means of a heating-cooling system built into the chamber and regulated by a temperature controller (Omega CN9000A series miniature autotune temperature controller, Omega Engineering, Stamford, CT). During compression, the chamber atmosphere increased by 3–5°C. However, this temperature change was transient, and the atmosphere generally returned to 30°C in <5 min. During the rapid ascent, the temperature dropped to 2–13°C but returned to 30°C in <1 min. During the slow ascent (0.5–1 ATA/min), little deviation from the desired temperature was observed.

The dive profiles used reflect several requirements. For safety reasons, the maximum percentage of $O_2$ in $H_2$ in the chamber atmosphere was limited to 2%. This is well below the flammability limits of 3.5–4% $O_2$ for $H_2$ mixtures reported over a large range of pressures (11, 25). It was also arbitrarily decided to perform the gas switch during compression at the same depth where the animals would be decompressed at the end of the dive. This decompression depth (10.8 ATA) would be the lowest possible pressure while still maintaining normoxia (0.21 ATA $O_2$) at the lower limit of 1.9% $O_2$.

*Gas analysis.* An automated gas chromatograph (Shimadzu model GC-9A, Shimadzu, Columbia, MD) with thermal conductivity detection and pneumatic sampling valves was used to analyze the chamber atmosphere once every 9 min for He, $H_2$, $N_2$, and $O_2$. Ar was used as the carrier gas to allow analysis of both He and $H_2$ with a molecular sieve 5A packed column (⅛ inch OD by 12 foot length, 60/80 mesh; Supelco, Bellefonte, PA). Current of the thermal conductivity detection was set at 75 mA, and both column and reference gas flows were 50 ml/min. Analysis was done isothermally at 60°C. Peak analysis and quantitation were performed with a Shimadzu CR601 chromatopac integrator based on a one-point calibration with a gravimetric primary standard obtained commercially and certified to ±1% relative to the stated value: *1*) 2% $O_2$-2% $N_2$-4% He-balance $H_2$ for $H_2$ dives and *2*) 2% $O_2$-2% $N_2$-balance He for He dives. These standards were selected to be very close to the actual composition of the chamber atmosphere to enhance analytic accuracy. Accuracy of analysis was estimated at ±2% relative to both $O_2$ and residual He (for $H_2$ dives) and ±5% relative to residual $N_2$.

*Data Analysis: the Model*

A dose-response model predicting the probability of DCS in rats was fit to all three series of data by the technique of maximum likelihood (7). Parameter values of the model were adjusted to maximize the log likelihood (LL) of the model with a modified Marquardt nonlinear estimation algorithm (22). The likelihood ratio (LR) test was used to evaluate the significance of parameters based on improvement in "goodness of fit" (15). The shape of the likelihood surface near the converged parameters was used to estimate the precision of the parameter values.

All DCS cases were treated equally, with no allowance in the model for grades in severity. The only accommodation for differences in response was to model all DCS cases (including fatalities) and then to repeat the modeling with only cases of death. The dose-response model used for this analysis was the Hill equation

$$\text{probability (DCS)} = \text{dose}^n/\text{dose}^n + P_{50}^n \qquad (1)$$

where $P_{50}$ represents the dose at which there is a probability of 50% for the occurrence of DCS, and the exponent $n$ is the order of the Hill equation that controls the steepness of the central portion of the sigmoidal curve.

The dose in *Eq. 1* represents a measure of decompression stress and was defined in a manner similar to previous reports (17, 18) based on the traditional idea of total gas supersaturation. In the present experiments, the possible gases contributing to the decompression response are He, $H_2$, $N_2$, and $O_2$; $CO_2$ is ignored. To allow for possible differences in gases, each partial pressure is multiplied by a relative potency (RP) value that weights each gas according to risk on a per unit pressure basis. The resulting equation for dose, in ATA, is

$$\text{dose (in ATA)} = [(\text{Pti}_{\text{He}} \cdot \text{RPHe}) + (\text{Pti}_{\text{H}_2} \cdot \text{RP}_{\text{H}_2}) + (\text{Pti}_{\text{N}_2} \cdot \text{RP}_{\text{N}_2})] - 10.8 \qquad (2)$$

where $\text{RP}_{\text{He}}$, $\text{RP}_{\text{H}_2}$, and $\text{RP}_{\text{N}_2}$ are RP values for He, $H_2$, and $N_2$, respectively, and $\text{Pti}_{\text{He}}$, $\text{Pti}_{\text{H}_2}$, and $\text{Pti}_{\text{N}_2}$ are the tissue partial pressures (Pti) of He, $H_2$, and $N_2$, respectively, in absolute atmospheres in the animal immediately on reaching the decompression depth (10.8 ATA). Because $O_2$ was a fixed percentage (2%) of the diving mixtures used, the effect of this gas could not be determined, because its potency would be directly correlated with depth. Thus a contribution of $O_2$ to the dose was not included. The subtraction of 10.8 ATA defines the amount of supersaturation postdecompression. In addition to potency, the model also included a second way to allow for gas differences by using separate exponents for He ($n_{\text{He}}$) and $H_2$ ($n_{\text{H}_2}$) in place of the single exponent $n$ to define the steepness of the Hill equation response slope.

The tissue partial pressures of He, $H_2$, and $N_2$ in the animal were obtained with single-exponential kinetics, assuming a single compartment (i.e., whole rat) even though real tissues need a more complex model (12, 23). After a step change in partial pressure of one gas at *time 0* ($T_0$), the Pti of the gas at *time T* can be described by the following equation for $T > T_0$

$$\text{Pti} = (\text{Pam}_i - \text{Pti}_0) \cdot [1 - e^{-(t-t_0)/\text{TC}_i}] + \text{Pti}_0 \qquad (3)$$

where $\text{Pam}_i$ is the ambient partial pressure at *time T*, $\text{Pti}_0$ is the initial Pti, $\text{TC}_i$ is the time constant affecting the rate of gas uptake or washout, and $i$ is the reference to each gas.

The situation becomes more complicated when calculating Pti during actual dives where the ambient gas partial pressures change in a nonstepwise manner (e.g., during compression, gas switching, or decompression). The solution used in the present analysis was to treat each dive as a series of partial pressure ramps that describe the pressure history of the dive. Partial pressures of individual gases at the beginning and ending of each ramp were estimated by multiplying the chamber pressure by the percentage of each gas as measured by gas chromatography. Once 10.8 ATA were reached during compression, $O_2$ was assumed to stay constant at 2.0% for the rest of the dive. For $H_2$ dives, the partial pressure of the residual He after the shift to $H_2$ at 10.8 ATA was calculated at two points: *1*) immediately after the gas switch and *2*) at the depth just before the start of decompression. In these cases, He pressure was assumed to decline linearly from the time when the depth was first reached to the start of decompression.

For calculation purposes, each ramp was subdivided into a number of smaller time intervals, and *Eq. 3* was used to successively compute Pti values at each interval along each ramp until decompression was completed. This procedure was performed for each of the gases that was being considered, in this case He, $H_2$, and $N_2$. Separate TCs for the uptake ($\text{TC}_{\text{in}}$) and washout ($\text{TC}_{\text{out}}$) of each gas allowed for the possibility of asymmetry in gas kinetics. This was implemented by taking the Pti for each gas and comparing it to the $\text{Pam}_i$ for that gas. When $\text{Pti}_0 > \text{Pam}_i$ in *Eq. 3*, the $\text{TC}_{\text{in}}$ was replaced with the $\text{TC}_{\text{out}}$. This situation generally occurred some time after decompression began, although in the case of He washout during a $H_2$ dive, $\text{TC}_{\text{out}}$ for He was used even while $H_2$ was still washing in.

Gas kinetics in *Eq. 3* assume that, at equilibrium, the partial pressures in the animal become equal to those in the chamber. This assumption avoids the difficult task of choosing a more complicated model based on inadequate knowledge of tissue-blood relationships. Because decompression data often do not allow resolution of very different models, simpler models frequently fit the data as well as, or better than, more complex ones. Although *Eq. 3* models gas kinetics in the rat, it is important to emphasize that gas uptake and washout were not actually measured. Consequently, what is being modeled is the animal response. The TCs that are being estimated define the rates of change in processes that affect the probability of DCS or death, although interpretation in terms of gas kinetics is made in this report.

The premise behind the definition of dose was that the gas supersaturation existing immediately at the completion of decompression is the measure of insult, leading to the development of DCS. Thus the model estimates the risk of DCS that starts to develop immediately on surfacing and assumes that there is no risk of DCS before this. Problems related to this assumption are discussed below.

The partial pressures of the gases are reported in absolute atmospheres. To estimate the RP values, one of the potencies had to be fixed so that the other potencies could be calculated in relation to it. The $\text{RP}_{\text{He}}$ value was arbitrarily set at 1.0 so that the $P_{50}$ would be expressed in terms of the partial pressure of He in absolute atmospheres. The effect of this weighting calculation was to convert exposures of $H_2$ and $N_2$ into equivalent He exposures.

Because animal weight has a significant effect on the decompression outcome, a weight correction term for dose was included in the model, as previously done, with a power function (17, 18). Animal weight (Wt), normalized to a weight (260 g) close to the average weight of all animals (258 g), was raised to an exponent denoted as the weight factor (WtF). Consequently, the final expression for dose was

$$\text{Dose (Wt corrected)} = \text{dose (Wt/260)}^{\text{WtF}} \qquad (4)$$

Postdive weights were used for all analyses because a few predive weights were missing due to procedural error.

The three dive series were initially analyzed separately. Parameter estimation began with the simplest possible model: $P_{50}$, $n$, and symmetrical gas kinetics, with a single TC for all inert gases. Each subsequent level of complexity of the model, with all possible combinations of estimated parameters, was evaluated by at least five different sets of starting parameter values to ensure that the maximum LL found was a global and not a local maximum. Parameter combinations that showed promising improvement to the fit were explored with many more starting values so that, overall, several thousand separate starting parameter sets were evaluated.

The next step was to perform an LR test to determine whether the data sets were combinable

$$LR = 2 \cdot [LL_{1+2} - (LL_1 + LL_2)] \quad (5)$$

where $LL_1$ and $LL_2$ are the LLs of the same model fit to *data sets 1* and *2* separately and $LL_{1+2}$ is the LL fit to the combined data sets. Dive series found combinable by these criteria were subsequently modeled together.

In summary, this model *1*) predicts the probability of DCS in rats subjected to dives on 2% $O_2$-balance He or 2% $O_2$-balance $H_2$; *2*) assumes that the decompression response is dependent on the degree of supersaturation of the gases He, $H_2$, and $N_2$ in the animal; and *3*) is used to estimate the parameters governing the location and shape of the dose-response curve, the RP values of the gases, the exponent correcting for animal weight, and the $TC_{in}$ and $TC_{out}$ values of the individual gases.

## RESULTS

Table 1 presents a summary of the decompression results from 1,607 dives with the rats that were used for modeling. Detailed results of these data are given in the APPENDIX. Data include results from all workup dives that were done to define the experimental profiles for each dive series. Overall incidence was 82.0% for DCS and 23.4% for death. The incidence rates were similar for He and $H_2$ dives (83.4 and 79.1%, respectively, for DCS; 24.1 and 22.0%, respectively, for death).

Table 1. *Summary of decompression results*

| | Weight Postdive, g | %DCS | %Death | No. of Rats |
|---|---|---|---|---|
| | | *Saturation* | | |
| He | 242 ± 16 | 82.5 | 23.2 | 211 |
| $H_2$ | 247 ± 14 | 83.6 | 39.0 | 146 |
| Total | 244 ± 16 | 82.9 | 29.7 | 357 |
| | | *Variable time at depth* | | |
| He | 249 ± 20 | 82.2 | 24.6 | 460 |
| $H_2$ | 248 ± 16 | 83.7 | 18.5 | 325 |
| Total | 249 ± 18 | 82.8 | 22.0 | 785 |
| | | *Variable decompression* | | |
| He | 250 ± 14 | 85.4 | 24.1 | 390 |
| $H_2$ | 261 ± 11 | 50.7 | 4.0 | 75 |
| Total | 252 ± 14 | 79.8 | 20.9 | 465 |
| | | *Overall* | | |
| He | 248 ± 16 | 83.4 | 24.1 | 1,061 |
| $H_2$ | 250 ± 18 | 79.1 | 22.0 | 546 |
| Total | 249 ± 17 | 82.0 | 23.4 | 1,607 |

Values are means ± SD. DCS, decompression sickness.

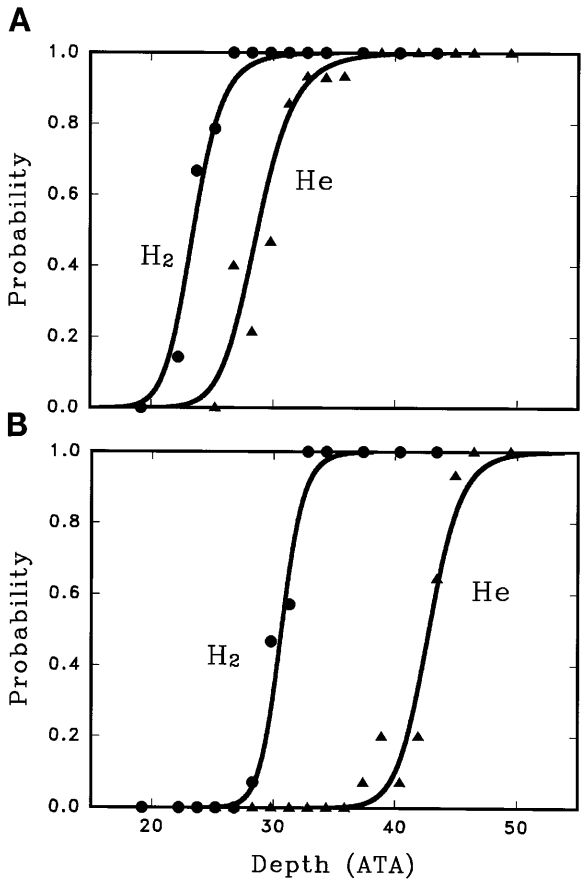


Fig. 1. Decompression sickness (DCS; *A*) and death (*B*) incidences in rats increase with saturation (Sat) depth for both He (▲) and $H_2$ (●), both 2% $O_2$. Shallower dives were needed for $H_2$ compared with He to produce similar incidence levels. This reflects greater DCS potency of $H_2$. Decompression was rapid (<1 min) to 10.8 ATA. Values are experimentally observed incidence values based on 4–15 animals (see APPENDIX). Curves are predictions from Sat + time-to-depth (TD) dive models (Sat + TD; see Table 2), with animal weight set at 260 g.

Rat weights before diving ranged from 192 to 318 g with a mean of 258 ± 17 (SD) g. The animals experienced a mean drop of 9 ± 3 g by the end of the experiments. Gas-switching effectiveness varied with the specific series, with the postswitch residual He concentration ranging from 1.8 to 4.8% for the Sat series, 5.3 to 10.6% for the TD series, and 11.2 to 13.2% for the VD series. These gas-switch differences among series are thought to reflect plumbing changes that were made to the inside of the chamber over the course of the investigation, which affected the flow of gas during the switching procedure.

Although the three dive series will be briefly described here, conclusions regarding the decompression differences between He and $H_2$ will be based on the model analysis of the combined data discussed in *Model Analysis*.

### *Sat Dives*

The DCS and death incidences increased with saturation depth for both He and $H_2$ (Fig. 1). Deeper dives were needed for He compared with $H_2$ to produce

similar incidence levels, suggesting a greater $H_2$ potency for causing DCS. For example, $H_2$ dives at depths from 19 to 27 ATA produced DCS incidences from 0 to 100%, whereas He dives required depths from 25 to 37 ATA to span the same range. To produce death, the corresponding depth range was 27–33 ATA for $H_2$ compared with 36–46 ATA for He.

*TD Dives*

These dives were done at 28–47 ATA for He and 27–33 ATA for $H_2$, again indicating that deeper dives were needed with He than with $H_2$ to produce similar incidence rates. Incidence levels for both gases tended to increase similarly, with increasing bottom time, until a plateau was reached that suggested comparable rates of gas uptake for the two gases (Fig. 2).

*VD Dives*

Difficulty was encountered during initial He dives in defining the profiles that produced a low incidence of DCS. To reduce the DCS risk, the decompression time was increased by inserting additional decompression stops, particularly at relatively deep depths. Surprisingly, this approach appeared to have little effect on the incidence of DCS. However, as a result, the majority (84%) of dives in this series were done on He before finishing up with a small number of $H_2$ dives, all at the same depth. In contrast to He, the DCS incidence appeared to decline with an increasing amount of decompression time when using $H_2$.

For the VD dives, there were 80 cases where DCS symptoms were observed during ascent before reaching 10.8 ATA. All but three of these dives were on He. For He, 25 of these 77 early cases died; none of the 3 rats showing early symptoms on $H_2$ died. Although these DCS cases violate the assumption that there is no DCS risk until the observation depth is reached, treating these "early" DCS cases as having occurred before arrival at that depth results in censored data. For the purposes of this study, we will consider all animals on a common pressure exposure to have been given the same dose.

The large number of different dive profiles in this series makes it difficult to evaluate how the gas washout rates of the two gases compare without modeling.

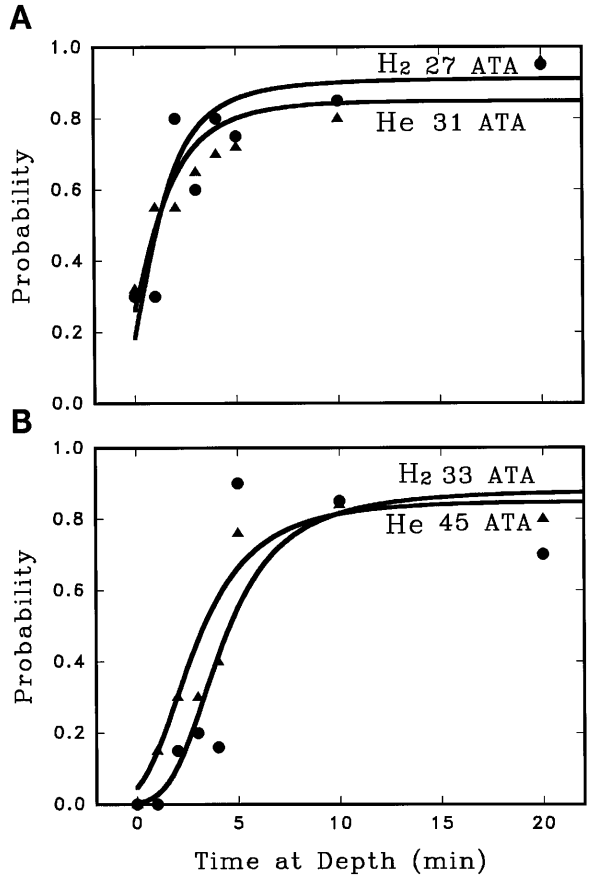


Fig. 2. DCS (*A*) and death (*B*) incidences in rats increase with TD similarly for He (▲) and $H_2$ (●), both 2% $O_2$ with saturation achieved in <15 min. Data and plots for He are for deeper dives than those for $H_2$ to produce similar incidence rates, again reflecting greater DCS potency of $H_2$. Decompression was rapid (<1 min) to 10.8 ATA. Values are experimentally observed incidence values based on 5–25 animals (see APPENDIX). Curves are predictions from Sat + TD models (see Table 2), with animal weight set at 260 g.

*Model Analysis*

Model parameters were estimated separately for DCS and death with the model described by *Eqs. 1–4* (Table 2). Only parameters found to be significant at the 0.05 level are included. Sat and TD dives were found combinable by LR testing. Thus parameters for the combined model (Sat + TD) are given. The VD dives were not combinable with either or both of the other two series; thus the parameters for the VD dives are presented separately.

*Sat + TD.* The model allowed for different $TC_{in}$ and $TC_{out}$ values. However, because only rapid decompression procedures were used for Sat + TD, the data did not provide sufficient information on washout to estimate $TC_{out}$ values. Consequently, $TC_{out}$ was set equal to $TC_{in}$ for each gas, so only $TC_{in}$ values are given in Table 2.

*VD.* Because VD dives had relatively long bottom times, these profiles were not well suited for estimating $TC_{in}$ values. Thus it was not unexpected that $TC_{in}$ values in the VD1 model, which estimated all parameters, were very poorly defined. This model was also accompanied by $RP_{H_2}$ values with very large standard errors. This undoubtedly is partly due to the strong correlation observed between $RP_{H_2}$ and $TC_{out}$ for $H_2$ because the dose can be altered by adjusting either parameter or some combination of the two. Such problems did not occur with the Sat and TD data because the $TC_{in}$ is well determined by the TD data and $RP_{H_2}$ can be estimated, independently of the kinetics, from the Sat data.

To try to improve the model estimates for VD, $TC_{in}$ values were fixed at the values estimated for Sat + TD, and the model was reestimated. This reduced the error in $RP_{H_2}$ and $TC_{out}$ values. This model is denoted VD2. Standard errors for the $H_2$ $TC_{out}$ values were further reduced by refitting the model, again after fixing both $RP_{H_2}$ and $TC_{in}$ at values estimated for Sat + TD. This model is called VD3. In both the VD2 and VD3 models,

Table 2. *Estimated model parameters for Sat + TD and VD dives*

| | Sat + TD ($n$ = 1,142) | | VD1 ($n$ = 465) | | VD2 ($n$ = 465) | | VD3 ($n$ = 465) | | VD4 ($n$ = 465) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | DCS | Death | DCS | Death | DCS | Death | DCS | Death | DCS | Death |
| $P_{50}$ | 15.3 ± 0.22 | 27.2 ± 0.18 | 17.7 ± 0.95 | 31.0 ± 0.96 | 17.7 ± 0.95 | 31.0 ± 0.96 | 17.7 ± 0.96 | 31.1 ± 0.92 | 5.22 ± 0.69 | 24.6 ± 0.82 |
| $n$ | 12.6 ± 1.3 | 26.5 ± 2.4 | 6.21 ± 1.12 | 10.3 ± 1.5 | 6.22 ± 1.11 | 10.3 ± 1.5 | 6.11 ± 1.04 | 10.3 ± 1.4 | 2.05 ± 0.34 | 4.72 ± 0.67 |
| $RP_{H_2}$ | 1.20 ± 0.01 | 1.34 ± 0.09 | 1.02 ± 0.73 | 1.19 ± 1.94 | 1.12 ± 0.14 | 1.30 ± 0.09 | 1.20 F | 1.34 F | 1.20 F | 1.34 F |
| $TC_{in}$ (He and $H_2$) | 2.45 ± 0.25 | 3.45 ± 0.21 | 0.07 ± 17.2 | 0.03 ± 62.3 | 2.45 F | 3.45 F | 2.45 F | 3.45 F | He: 32.2 ± 4.0<br>$H_2$: 2.84 ± 1.47 | 26.1 ± 3.4<br>15.1 ± 5.4 |
| $TC_{out}$ (He) | * | * | 187.9 ± 50.0 | 85.1 ± 22.5 | 185.7 ± 48.8 | 84.6 ± 22.4 | 190.8 ± 51.4 | 86.8 ± 22.7 | * | * |
| $TC_{out}$ ($H_2$) | * | * | 46.7 ± 35.9 | 48.9 ± 128.4 | 46.4 ± 32.4 | 44.4 ± 42.0 | 33.8 ± 7.3 | 36.3 ± 23.0 | * | * |
| WtF | 0.40 ± 0.13 | 0.22 ± 0.07 | NS | NS | NS | NS | NS | NS | NS | NS |
| LL | 277.2 | 245.7 | 168.5 | 137.4 | 168.6 | 137.8 | 168.8 | 138.0 | 186.2 | 155.6 |

Values are means ± SE; $n$, no. of rats. Sat + TD, models for combined saturation and variable time-at-depth dives; VD1–VD4, models for variable decompression dives; $P_{50}$, dose at which 50% probability of event occurs (in ATA of gas); $n$, exponent of Hill equation; $RP_{H_2}$, relative potency of $H_2$; $TC_{in}$, uptake time constant (in min); $TC_{out}$, washout time constant (in min); WtF, weight factor; LL, log likelihood; F, fixed parameter; NS, not significant. *Value same as $TC_{in}$.

the parameters $P_{50}$ and $n$ did not change appreciably from the initial VD1 model in which $TC_{in}$ and $RP_{H_2}$ values had been estimated.

*Model VD4* was a test for the significance of asymmetrical kinetics as estimated in VD1–VD3. In this version, the $TC_{out}$ parameters were set equal to the $TC_{in}$ values, resulting in symmetrical gas uptake-washout. This produced much poorer fits as indicated by the LL value, which is ~17 LL worse for both DCS and death in VD4 than in VD3 for the same number of parameters. The symmetrical kinetic TCs estimated in VD4 are intermediate in value between the previously estimated uptake and washout values (VD3). This test (VD4) supports the strong asymmetry estimated in VD1–VD3.

All VD models are included in Table 2. *Model VD1* is included to show the changes that occurred going from this model to VD2 and VD3. *Models VD2* and *VD3* are similar, with the main difference being the greater precision associated with the $H_2$ $TC_{out}$ estimates for VD3.

### *Parameter Estimates (Models Sat + TD and VD2–VD3)*

In comparing the models for DCS and death, the $P_{50}$ values for death were larger, as would be expected, because a higher dose is required to cause death. The exponent defining the degree of slope of the central portion of the response curve was larger for Sat + TD vs. VD, particularly in the case of death. None of the models required separate exponents for He and $H_2$ or a nonzero potency term for $N_2$. The latter was not surprising because gas switching during compression generally removed all detectable $N_2$ from the chamber atmosphere. Therefore, little information was available to estimate $N_2$ potency.

The potency of $H_2$ was estimated at ~10–20% greater than that of He for causing DCS overall and ~30–35% greater than He for death. Predictive response curves (Fig. 1) illustrate the differences in potency and model agreement with the Sat data. Uptake rates were unresolvable between the two gases, so a single $TC_{in}$ value was used that was estimated at ~2–3 min, leading to saturation in <15 min (Figs. 2 and 3). Washout of both gases was over an order of magnitude slower than uptake, with He washout (TC ~1.5–3 h) substantially slower than $H_2$ washout (TC ~0.5 h; Fig. 3). This would necessitate a much longer decompression time to avoid DCS when using He. He washout was approximately twice as slow for DCS vs. death.

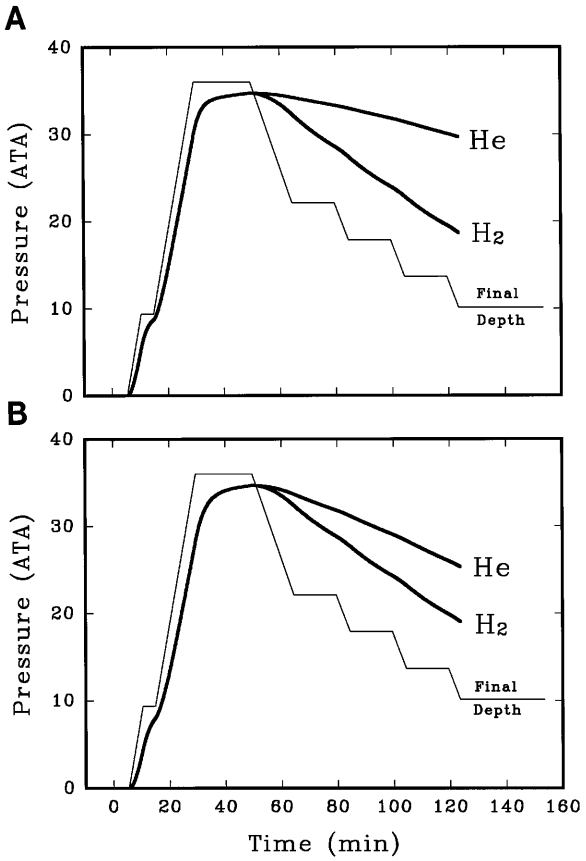


Fig. 3. Predicted partial pressure changes in rats are similar for He and $H_2$ (thick lines) (both 2% $O_2$) during a 20-min dive at 37.4 ATA but diverge later in a 3-stop decompression. *A*: DCS. *B*: death. Thin lines, total chamber pressure. Predicted pressures are from variable decompression models (VD3), with animal weight set at 260 g.

For Sat + TD, inclusion of a weight correction (the parameter WtF) in the model produced a significant improvement in fit for both DCS and death. This was not the case for VD.

*Effectiveness of the Model*

The ability of the models to describe the wide range of dive profiles was examined by plotting the difference between model prediction and observed incidence vs. total decompression time for each different dive profile (Fig. 4). All the data were used in this exercise, with the observed values being the mean incidence rates of the dive profiles. The predictive values were derived from the reported best fit model for Sat + TD for those sets of dives and the *model VD3* for those dives. Animal weight was set at 260 g in all model predictions. The scatter of points around zero illustrates that the models predict DCS or death without significant bias and generally equally well regardless of total decompression time.

## DISCUSSION

This investigation supported the initial hypothesis that there are differences in the risk of DCS between He and $H_2$ and demonstrated differences between He and $H_2$ in both potency for causing DCS and in the estimated washout rate in the whole rat. Here, potency defines the level of risk based on the estimated Pti values of the gases. Exchange rates (gas uptake or washout) govern the rate of change in the Pti values of the gases with time. Gas kinetics were extrapolated from rate constants estimated from the changes in DCS risk rather than determined from the direct measurement of gas uptake and washout. Both potency and rate constants interact to affect the degree of risk associated with a specific dive profile.

Previous work has suggested that the greater potency of "riskier" gases may be due to larger volumes of gas evolving during decompression (20). These gas volumes would be expected to be affected by differences among gases in tissue solubility and/or diffusivity and in rates of bubble development. With the use of published data on gas properties, some simple comparisons can be made, although it should be emphasized that it is unknown how well such data relate to actual tissues under pressure. Coefficients for $H_2$ and He solubility in water at 37°C (0.0185 and 0.0099 ml gas/ml fluid, respectively; Ref. 24) are in the relative proportion of 1.9 for $H_2$-to-He. A similar ratio for the $H_2$-to-He solubility in oil (0.0495 and 0.0168 ml gas/ml fluid, respectively; Ref. 24) is 2.9. These solubility ratios are considerably higher than the observed potency differences (i.e., up to 35% or a ratio of 1.35), although this was also the case when He, $N_2$, and Ar were similarly compared previously (20). However, the greater solubility of $H_2$ in both water and oil would support the greater potential gas volume-greater risk hypothesis.

The rates of gas exchange of animals or humans are also believed to depend on solubility and diffusivity properties as well as on the partial pressure gradients and on factors such as the relative importance of gaseous diffusion and blood perfusion. In examining the rate constants estimated here, several observations are particularly interesting in light of previous work with rats at depths up to 9 ATA (17–19). First, at the shallower depths, the rate of gas uptake was similar to that of gas washout for both $N_2$ (17, 19) and He (R. S. Lillo, unpublished data). However, $N_2$ was approximately three times slower than He in both cases. This is in contrast to the much slower (over an order of magnitude) washout compared with uptake seen here

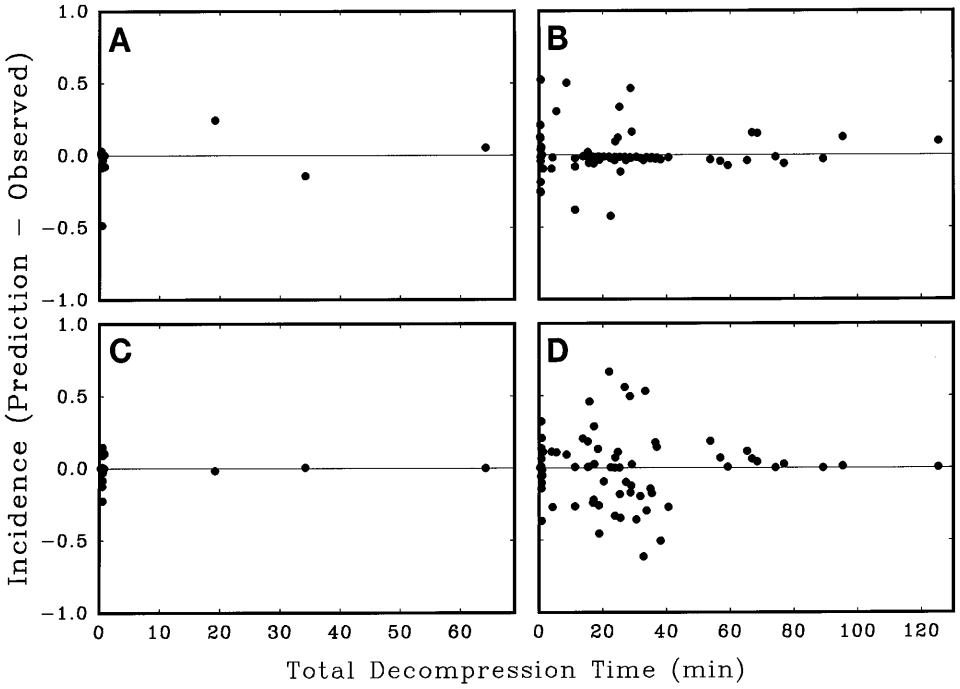


Fig. 4. Maximum likelihood models predict DCS or death without significant bias and generally equally well regardless of total decompression time, shown by plotting difference between model prediction (Sat + TD or VD3) and observed incidence vs. total decompression time of each dive. *A*: $H_2$ DCS. *B*: He DCS. *C*: $H_2$ death. *D*: He death. Each symbol represents value associated with a different dive profile based on 4–30 animals (see APPENDIX). All dives from study are included.

at the greater depths for He and $H_2$. Second, although the uptake rates reported here for He and $H_2$ are indistinguishable and similar to those found before for He (17), the washout rates for these two gases during decompression are very different.

Despite previous reports of reduced rates of inert gas elimination during decompression due to cardiovascular changes or bubble development (5, 10), the magnitude of slowing estimated here was unexpected. This suggests the possibility that the increased depth of the present dives may be affecting washout. Another explanation may be that the risk of DCS becomes uncoupled from the gas load in the animal at greater depths, so that risk remains elevated long after most excess gas has been eliminated. A recent examination of the time course of predicted bubble evolution with predicted DCS risk in humans has suggested that gas-phase dynamics may not fully explain persistent DCS risk (1).

These experiments do not specifically model a type of human DCS. Rather, we take a simplistic approach with these dives in terms of gas loading and elimination and how these processes relate to DCS. In this way, we avoid having to make assumptions regarding the etiology of DCS that is not well understood and is probably very complex and varies depending on the tissues involved. Whether these findings relating to a very severe type of DCS have an application to DCS in humans is unknown. Obviously, the scaling effect going from a rat to a human would prevent use of absolute gas rate constants (3, 16). Thus it is unknown whether the decompression advantage of the faster washout of $H_2$ or the disadvantage of its increased potency, observed in the rat, would be important for human diving. However, these findings raise the possibility of exploiting such differences between He and $H_2$ to manipulate the DCS risk after saturation diving with humans.

## APPENDIX

*Dive profiles and results*

| Gas | Depth, ATA | Bottom Time, min | Decompression Profile | Mean Postdive Weight, g | %DCS | %Death | No. of Rats |
|---|---|---|---|---|---|---|---|
| | | | *Saturation* | | | | |
| $H_2$ | 19.2 | 60 | 99 | 242 | 0.0 | 0.0 | 4 |
| $H_2$ | 22.2 | 60 | 99 | 251 | 14.3 | 0.0 | 14 |
| $H_2$ | 23.7 | 60 | 99 | 250 | 66.7 | 0.0 | 15 |
| $H_2$ | 25.2 | 60 | 99 | 244 | 78.6 | 0.0 | 14 |
| $H_2$ | 26.8 | 60 | 99 | 240 | 100.0 | 0.0 | 15 |
| $H_2$ | 28.3 | 60 | 99 | 255 | 100.0 | 7.1 | 14 |
| $H_2$ | 29.8 | 60 | 99 | 245 | 100.0 | 46.7 | 15 |
| $H_2$ | 31.3 | 60 | 99 | 253 | 100.0 | 57.1 | 14 |
| $H_2$ | 32.8 | 60 | 99 | 247 | 100.0 | 100.0 | 15 |
| $H_2$ | 34.3 | 60 | 99 | 246 | 100.0 | 100.0 | 14 |
| $H_2$ | 37.4 | 60 | 99 | 247 | 100.0 | 100.0 | 4 |
| $H_2$ | 40.4 | 60 | 99 | 236 | 100.0 | 100.0 | 4 |
| $H_2$ | 43.4 | 60 | 99 | 247 | 100.0 | 100.0 | 4 |
| He | 25.2 | 60 | 99 | 262 | 0.0 | 0.0 | 4 |
| He | 26.8 | 60 | 99 | 235 | 40.0 | 0.0 | 15 |
| He | 28.3 | 60 | 99 | 231 | 21.4 | 0.0 | 14 |
| He | 29.8 | 60 | 99 | 252 | 46.7 | 0.0 | 15 |
| He | 31.3 | 60 | 99 | 242 | 85.7 | 0.0 | 14 |
| He | 32.8 | 60 | 99 | 231 | 93.3 | 0.0 | 15 |
| He | 34.3 | 60 | 99 | 235 | 92.9 | 0.0 | 14 |

*Dive profiles and results—Continued*

| Gas | Depth, ATA | Bottom Time, min | Decompression Profile | Mean Postdive Weight, g | %DCS | %Death | No. of Rats |
|---|---|---|---|---|---|---|---|
| He | 35.8 | 60 | 99 | 242 | 93.3 | 0.0 | 15 |
| He | 37.4 | 60 | 99 | 251 | 100.0 | 7.1 | 14 |
| He | 38.9 | 60 | 99 | 246 | 100.0 | 20.0 | 15 |
| He | 40.4 | 60 | 99 | 246 | 100.0 | 7.1 | 14 |
| He | 41.9 | 60 | 99 | 238 | 100.0 | 20.0 | 15 |
| He | 43.4 | 60 | 99 | 241 | 100.0 | 64.3 | 14 |
| He | 44.9 | 60 | 99 | 246 | 100.0 | 93.3 | 15 |
| He | 46.5 | 60 | 99 | 250 | 100.0 | 100.0 | 14 |
| He | 49.5 | 60 | 99 | 235 | 100.0 | 100.0 | 4 |
| | | | *Variable time at depth* | | | | |
| $H_2$ | 32.8 | 0 | 99 | 261 | 100.0 | 0.0 | 20 |
| $H_2$ | 32.8 | 1 | 99 | 238 | 100.0 | 0.0 | 20 |
| $H_2$ | 32.8 | 2 | 99 | 236 | 100.0 | 15.0 | 20 |
| $H_2$ | 32.8 | 3 | 99 | 240 | 100.0 | 20.0 | 20 |
| $H_2$ | 32.8 | 4 | 99 | 237 | 100.0 | 16.0 | 25 |
| $H_2$ | 32.8 | 5 | 99 | 263 | 100.0 | 90.0 | 20 |
| $H_2$ | 32.8 | 10 | 99 | 265 | 100.0 | 85.0 | 20 |
| $H_2$ | 32.8 | 20 | 99 | 243 | 100.0 | 70.0 | 20 |
| He | 44.9 | 0 | 99 | 259 | 100.0 | 0.0 | 20 |
| He | 44.9 | 1 | 99 | 240 | 100.0 | 15.0 | 20 |
| He | 44.9 | 2 | 99 | 248 | 100.0 | 30.0 | 20 |
| He | 44.9 | 3 | 99 | 249 | 100.0 | 30.0 | 20 |
| He | 44.9 | 4 | 99 | 242 | 100.0 | 40.0 | 20 |
| He | 44.9 | 5 | 99 | 252 | 100.0 | 80.0 | 20 |
| He | 44.9 | 10 | 99 | 264 | 100.0 | 85.0 | 20 |
| He | 44.9 | 20 | 99 | 251 | 100.0 | 75.0 | 20 |
| $H_2$ | 26.8 | 0 | 99 | 242 | 30.0 | 0.0 | 20 |
| $H_2$ | 26.8 | 1 | 99 | 245 | 30.0 | 0.0 | 20 |
| $H_2$ | 26.8 | 2 | 99 | 255 | 80.0 | 0.0 | 20 |
| $H_2$ | 26.8 | 3 | 99 | 256 | 60.0 | 0.0 | 20 |
| $H_2$ | 26.8 | 4 | 99 | 251 | 80.0 | 0.0 | 20 |
| $H_2$ | 26.8 | 5 | 99 | 254 | 75.0 | 0.0 | 20 |
| $H_2$ | 26.8 | 10 | 99 | 243 | 85.0 | 0.0 | 20 |
| $H_2$ | 26.8 | 20 | 99 | 250 | 95.0 | 0.0 | 20 |
| He | 31.3 | 0 | 99 | 254 | 35.0 | 0.0 | 20 |
| He | 31.3 | 1 | 99 | 245 | 55.0 | 0.0 | 20 |
| He | 31.3 | 2 | 99 | 242 | 55.0 | 0.0 | 20 |
| He | 31.3 | 3 | 99 | 248 | 65.0 | 0.0 | 20 |
| He | 31.3 | 4 | 99 | 248 | 70.0 | 0.0 | 20 |
| He | 31.3 | 5 | 99 | 246 | 80.0 | 0.0 | 20 |
| He | 31.3 | 10 | 99 | 251 | 85.0 | 0.0 | 20 |
| He | 31.3 | 20 | 99 | 249 | 95.0 | 0.0 | 20 |
| He | 46.5 | 15 | 99 | 257 | 100.0 | 100.0 | 5 |
| He | 46.5 | 10 | 99 | 251 | 100.0 | 100.0 | 5 |
| He | 46.5 | 5 | 99 | 256 | 100.0 | 100.0 | 5 |
| He | 46.5 | 0 | 99 | 263 | 100.0 | 80.0 | 5 |
| He | 44.9 | 20 | 99 | 243 | 100.0 | 100.0 | 5 |
| He | 44.9 | 10 | 99 | 228 | 100.0 | 80.0 | 5 |
| He | 44.9 | 5 | 99 | 232 | 100.0 | 60.0 | 5 |
| He | 44.9 | 0 | 99 | 226 | 100.0 | 0.0 | 5 |
| He | 43.4 | 15 | 99 | 266 | 100.0 | 60.0 | 5 |
| He | 43.4 | 10 | 99 | 263 | 100.0 | 80.0 | 5 |
| He | 43.4 | 5 | 99 | 259 | 100.0 | 40.0 | 5 |
| He | 41.9 | 20 | 99 | 261 | 100.0 | 0.0 | 5 |
| He | 41.9 | 10 | 99 | 259 | 100.0 | 20.0 | 5 |
| He | 41.9 | 5 | 99 | 248 | 100.0 | 20.0 | 5 |
| He | 37.4 | 20 | 99 | 247 | 100.0 | 0.0 | 5 |
| He | 37.4 | 10 | 99 | 257 | 100.0 | 0.0 | 5 |
| He | 37.4 | 5 | 99 | 252 | 100.0 | 0.0 | 5 |
| He | 37.4 | 0 | 99 | 268 | 100.0 | 0.0 | 5 |
| He | 31.3 | 20 | 99 | 239 | 100.0 | 0.0 | 5 |
| He | 31.3 | 10 | 99 | 238 | 60.0 | 0.0 | 5 |
| He | 31.3 | 5 | 99 | 242 | 40.0 | 0.0 | 5 |
| He | 31.3 | 0 | 99 | 268 | 20.0 | 0.0 | 5 |
| He | 28.3 | 20 | 99 | 252 | 60.0 | 0.0 | 10 |
| He | 28.3 | 5 | 99 | 229 | 60.0 | 0.0 | 5 |
| He | 28.3 | 0 | 99 | 244 | 0.0 | 0.0 | 15 |

*Dive profiles and results—Continued*

| Gas | Depth, ATA | Bottom Time, min | Decompression Profile | Mean Postdive Weight, g | %DCS | %Death | No. of Rats |
|---|---|---|---|---|---|---|---|
| | | | *Variable decompression* | | | | |
| $H_2$ | 28.3 | 20 | 1 | 261 | 100.0 | 20.0 | 10 |
| $H_2$ | 28.3 | 20 | 2 | 260 | 53.3 | 6.7 | 15 |
| $H_2$ | 28.3 | 20 | 3 | 263 | 60.0 | 0.0 | 25 |
| $H_2$ | 28.3 | 20 | 5 | 259 | 20.0 | 0.0 | 25 |
| He | 37.4 | 20 | 1 | 259 | 100.0 | 0.0 | 10 |
| He | 37.4 | 20 | 2 | 258 | 70.0 | 0.0 | 10 |
| He | 37.4 | 20 | 4 | 267 | 86.7 | 0.0 | 15 |
| He | 37.4 | 20 | 5 | 256 | 73.3 | 0.0 | 30 |
| He | 37.4 | 20 | 6 | 250 | 70.0 | 0.0 | 30 |
| He | 49.5 | 60 | 20 | 253 | 100.0 | 60.0 | 5 |
| He | 49.5 | 60 | 21 | 247 | 100.0 | 0.0 | 5 |
| He | 49.5 | 60 | 22 | 254 | 100.0 | 100.0 | 5 |
| He | 49.5 | 60 | 23 | 245 | 100.0 | 0.0 | 5 |
| He | 49.5 | 60 | 24 | 256 | 100.0 | 0.0 | 5 |
| He | 49.5 | 60 | 25 | 261 | 100.0 | 20.0 | 5 |
| He | 49.5 | 60 | 26 | 256 | 100.0 | 60.0 | 5 |
| He | 49.5 | 60 | 27 | 256 | 100.0 | 80.0 | 5 |
| He | 49.5 | 60 | 28 | 262 | 100.0 | 80.0 | 5 |
| He | 49.5 | 60 | 60 | 267 | 100.0 | 60.0 | 5 |
| He | 49.5 | 60 | 30 | 259 | 100.0 | 60.0 | 5 |
| He | 49.5 | 60 | 31 | 252 | 100.0 | 100.0 | 5 |
| He | 49.5 | 60 | 32 | 254 | 100.0 | 100.0 | 5 |
| He | 49.5 | 60 | 33 | 256 | 100.0 | 80.0 | 5 |
| He | 37.4 | 60 | 26 | 255 | 40.0 | 0.0 | 5 |
| He | 37.4 | 60 | 60 | 242 | 40.0 | 20.0 | 5 |
| He | 37.4 | 60 | 36 | 272 | 60.0 | 0.0 | 5 |
| He | 37.4 | 60 | 37 | 271 | 100.0 | 40.0 | 5 |
| He | 37.4 | 60 | 38 | 231 | 100.0 | 0.0 | 5 |
| He | 37.4 | 60 | 66 | 230 | 80.0 | 0.0 | 5 |
| He | 31.3 | 15 | 50 | 231 | 70.0 | 0.0 | 10 |
| He | 31.3 | 15 | 2 | 233 | 60.0 | 0.0 | 10 |
| He | 31.3 | 15 | 49 | 245 | 60.0 | 0.0 | 10 |
| He | 31.3 | 30 | 50 | 256 | 100.0 | 0.0 | 5 |
| He | 31.3 | 30 | 2 | 249 | 100.0 | 0.0 | 5 |
| He | 49.5 | 60 | 66 | 254 | 100.0 | 100.0 | 5 |
| He | 49.5 | 60 | 58 | 254 | 100.0 | 80.0 | 5 |
| He | 44.9 | 15 | 54 | 251 | 100.0 | 80.0 | 5 |
| He | 44.9 | 15 | 55 | 251 | 100.0 | 0.0 | 5 |
| He | 44.9 | 15 | 56 | 250 | 100.0 | 60.0 | 5 |
| He | 44.9 | 15 | 57 | 250 | 100.0 | 20.0 | 5 |
| He | 44.9 | 15 | 58 | 239 | 100.0 | 80.0 | 5 |
| He | 44.9 | 10 | 30 | 235 | 100.0 | 80.0 | 5 |
| He | 44.9 | 10 | 60 | 224 | 100.0 | 80.0 | 5 |
| He | 43.4 | 60 | 66 | 232 | 100.0 | 40.0 | 5 |
| He | 43.4 | 60 | 64 | 246 | 100.0 | 10.0 | 10 |
| He | 43.4 | 60 | 65 | 262 | 100.0 | 80.0 | 5 |
| He | 40.4 | 60 | 64 | 265 | 100.0 | 20.0 | 5 |
| He | 40.4 | 60 | 65 | 263 | 100.0 | 40.0 | 5 |
| He | 38.9 | 60 | 66 | 244 | 80.0 | 0.0 | 5 |
| He | 31.3 | 60 | 28 | 269 | 60.0 | 0.0 | 5 |
| He | 28.3 | 60 | 60 | 237 | 40.0 | 0.0 | 5 |
| He | 28.3 | 60 | 25 | 253 | 0.0 | 0.0 | 5 |
| He | 46.5 | 60 | 70 | 233 | 100.0 | 0.0 | 5 |
| He | 46.5 | 60 | 71 | 242 | 100.0 | 0.0 | 5 |
| He | 46.5 | 60 | 72 | 239 | 80.0 | 0.0 | 5 |
| He | 46.5 | 20 | 73 | 244 | 80.0 | 0.0 | 5 |
| He | 46.5 | 60 | 74 | 248 | 100.0 | 0.0 | 5 |
| He | 46.5 | 60 | 75 | 239 | 80.0 | 0.0 | 5 |
| He | 46.5 | 60 | 76 | 249 | 80.0 | 0.0 | 5 |
| He | 46.5 | 60 | 77 | 234 | 100.0 | 0.0 | 5 |
| He | 46.5 | 60 | 78 | 245 | 100.0 | 100.0 | 5 |
| He | 46.5 | 60 | 79 | 246 | 100.0 | 20.0 | 5 |
| He | 46.5 | 60 | 80 | 256 | 100.0 | 60.0 | 5 |
| He | 46.5 | 60 | 66 | 260 | 100.0 | 60.0 | 5 |

DCS, decompression sickness.

*Decompression profile descriptions*

| Profile No. | Decompression Description |
|---|---|
| *1* | 31 ATA/min; no stops |
| *2* | 0.9 ATA/min; no stops |
| *3* | 0.9 ATA/min; stop at 14.6 ATA for 15 min |
| *4* | 0.9 ATA/min; stops at 28.3 and 19.2 ATA for 15 min each |
| *5* ($H_2$) | 0.9 ATA/min; stops at 23.7, 19.2, and 14.6 ATA for 15 min each |
| *5* (He) | 0.9 ATA/min; stops at 28.3, 19.2, and 14.6 ATA for 15 min each |
| *6* | 0.9 ATA/min; stops at 28.3, 23.7, 19.2, 14.6 ATA for 15 min each |
| *20* | 1.8 ATA/min; no stops; change travel rate at 16.2 ATA* |
| *21* | 1.8 ATA/min; stop at 16.2 ATA for 10 min* |
| *22* | 1.8 ATA/min; no stops; change travel rate at 19.2 ATA* |
| *23* | 1.8 ATA/min; stop at 19.2 ATA for 5 min* |
| *24* | 1.8 ATA/min; stop at 19.2 ATA for 10 min* |
| *25* | 1.8 ATA/min; stop at 19.2 ATA for 20 min* |
| *26* | 1.8 ATA/min; no stops; change travel rate at 22.2 ATA* |
| *27* | 1.8 ATA/min; stop at 22.2 ATA for 5 min* |
| *28* | 1.8 ATA/min; stop at 22.2 ATA for 10 min* |
| *30* | 1.8 ATA/min; no stops; change travel rate at 25.2 ATA* |
| *31* | 1.8 ATA/min; stop at 25.2 ATA for 5 min* |
| *32* | 1.8 ATA/min; stop at 25.2 ATA for 10 min* |
| *33* | 1.8 ATA/min; stop at 25.2 ATA for 20 min* |
| *36* | 1.8 ATA/min; no stops; change travel rate at 28.3 ATA* |
| *37* | 1.8 ATA/min; stop at 28.3 ATA for 20 min* |
| *38* | 1.8 ATA/min; no stops; change travel rate at 31.3 ATA* |
| *49* | 34.5 ATA/min; no stops |
| *50* | 1.8 ATA/min; no stops |
| *54* | 1.8 ATA/min; stop at 43.4 ATA for 30 min* |
| *55* | 1.8 ATA/min; stop at 40.4 ATA for 30 min* |
| *56* | 1.8 ATA/min; stop at 37.4 ATA for 30 min* |
| *57* | 1.8 ATA/min; stop at 34.3 ATA for 30 min* |
| *58* | 1.8 ATA/min; stop at 31.3 ATA for 30 min* |
| *60* | 1.8 ATA/min; stop at 22.2 ATA for 20 min* |
| *64* | 1.8 ATA/min; stop at 31.3 ATA for 10 min* |
| *65* | 1.8 ATA/min; stop at 28.3 ATA for 10 min* |
| *66* | 1.8 ATA/min; stop at 31.3 ATA for 20 min* |
| *70* | 1.8 ATA/min; stop at 37.4 ATA for 20 min and 22.2 ATA for 20 min* |
| *71* | 1.8 ATA/min; stop at 37.4 ATA for 30 min and 19.2 ATA for 20 min* |
| *72* | 1.8 ATA/min; stop at 37.4 ATA for 30 min and 19.2 ATA for 50 min* |
| *73* | 1.8 ATA/min; stop at 37.4 ATA for 50 min and 19.2 ATA for 60 min* |
| *74* | 1.8 ATA/min; stop at 34.3 ATA for 30 min and 16.2 ATA for 30 min* |
| *75* | 1.8 ATA/min; stop at 34.3 ATA for 30 min and 16.2 ATA for 20 min* |
| *76* | 1.8 ATA/min; stop at 34.3 ATA for 30 min and 13.1 ATA for 20 min* |
| *77* | 1.8 ATA/min; stop at 31.3 ATA for 20 min and 16.2 ATA for 20 min* |
| *78* | 1.8 ATA/min; no stop; change travel rate at 40.4 ATA* |
| *79* | 1.8 ATA/min; stop at 37.4 ATA for 10 min* |
| *80* | 1.8 ATA/min; stop at 34.3 ATA for 10 min* |
| *99* | 40.0 ATA/min |

*Travel rate from final stop depth to 10.8 ATA is 34.5 ATA/min.

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Address for reprint requests: R. S. Lillo, Code 0541, Diving and Environmental Physiology Dept., Naval Medical Research Institute, 8901 Wisconsin Ave., Bethesda, MD 20889-5607.

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## REFERENCES


1. **Ball, R., J. Himm, L. D. Homer, and E. D. Thalmann.** Does the time course of bubble evolution explain decompression sickness risk? *Undersea Hyper. Med*. 22: 263–280, 1995.
2. **Bennett, P. B., and J. C. Rostain.** The high pressure nervous syndrome. In: *The Physiology and Medicine of Diving* (4th ed.), edited by P. B. Bennett and D. H. Elliott. London: Saunders, 1993, p. 194–237.
3. **Berghage, T. E., T. D. David, and C. V. Dyson.** Species differences in decompression. *Undersea Biomed. Res.* 6: 1–13, 1971.
4. **Brauer, R. W.** (Editor). *Hydrogen as a Diving Gas. 33rd Undersea and Hyperbaric Medical Society Workshop*. Bethesda, MD: Undersea and Hyperbaric Medical Society, 1987.
5. **D'Aoust, B. G., H. T. Swanson, R. White, R. Dunford, and J. Mahoney.** Central venous bubbles and mixed venous nitrogen in goats following decompression. *J. Appl. Physiol.* 51: 1238–1244, 1981.
6. **Edel, P. O., J. M. Holland, C. L. Fischer, and W. B. Fife.** Preliminary studies of hydrogen-oxygen breathing mixtures for deep sea diving. In: *Symposium Proceedings of the Working Diver*. Washington, DC: Marine Technology Society, 1972, p. 257–270.
7. **Edwards, A. W. F.** *Likelihood*. London: Cambridge Univ. Press, 1972.
8. **Fowler, B., K. N. Ackles, and G. Porlier.** Effects of inert gas narcosis on behavior: a critical review. *Undersea Biomed. Res.* 12: 369–402, 1985.
9. **Gortan, C., and H. G. DeLauze.** System design and safety considerations for "Hydra" experiments. In: *Hydrogen as a Diving Gas. 33rd Undersea and Hyperbaric Medical Society Workshop,* edited by R. W. Brauer. Bethesda, MD: Undersea and Hyperbaric Medical Society, 1987, p. 227–244.
10. **Hills, B. A.** Effect of decompression per se on nitrogen elimination. *J. Appl Physiol.* 45: 916–921, 1978.
11. **Holmstedt, G. S.** The upper limit of flammability of hydrogen in air, oxygen, and oxygen-inert mixtures at elevated pressures. *Combust. Flame* 17: 295–301, 1971.
12. **Homer, L. D., P. K. Weathersby, and S. Survanshi.** How countercurrent blood flow and uneven perfusion affect the motion of inert gas. *J. Appl. Physiol.* 69: 162–170, 1990.
13. **Imbert, G.** Safe deep sea diving using hydrogen. *Mar. Technol. Soc. J.* 23: 26–33, 1989.
14. **Kayar, S. R., M. J. Axley, L. D. Homer, and A. L. Harabin.** Hydrogen gas is not oxidized by mammalian tissues under hyperbaric conditions. *Undersea Hyper. Med.* 21: 265–275, 1994.
15. **Kendall, M. G., and A. Stewart.** *The Advanced Theory of Statistics* (4th ed.). London: Haffner, 1979, vol 2, p. 38–180.
16. **Kindwall, E. P.** Metabolic rate and animal size correlated with decompression sickness. *Am. J. Physiol.* 203: 385–388, 1962.
17. **Lillo, R. S.** Effect of $N_2$-He-$O_2$ on decompression outcome in rats after variable time-at-depth dives. *J. Appl. Physiol.* 64: 2042–2052, 1988.
18. **Lillo, R. S., Flynn, E. T., and L. D. Homer.** Decompression outcome following saturation dives with multiple inert gases in rats. *J. Appl. Physiol.* 59: 1503–1514, 1985.
19. **Lillo, R. S., and M. E. MacCallum.** Decompression comparison of $N_2$ and $O_2$ in rats. *Undersea Biomed. Res.* 18: 317–331, 1991.
20. **Lillo, R. S., M. E. MacCallum, and J. M. Caldwell.** Intravascular bubble composition in guinea pigs: a possible explanation for differences in decompression risk among different gases. *Undersea Biomed. Res.* 19: 375–386, 1992.
21. **Maio, D. A., and L. E. Farhi.** Effect of gas density on mechanics of breathing. *J. Appl. Physiol.* 23: 687–693, 1967.
22. **Marquardt, D. W.** An algorithm for least-squares estimation of non-linear parameters. *J. Soc. Ind. Appl. Math.* 11: 431–441, 1963.
23. **Novotny, J. A., D. L. Mayers, Y.-F. J. Parsons, S. S. Survanshi, P. K. Weathersby, and L. D. Homer.** Xenon kinetics in muscle are not explained by a model of parallel perfusion-limited compartments. *J. Appl. Physiol.* 68: 876–890, 1990.
24. **Weathersby, P. K., and L. D. Homer.** Solubility of inert gases in biological fluids and tissue: a review. *Undersea Biomed. Res.* 7: 277–296, 1980.
25. **Zalosh, R. G.** Hydrogen flammability and ignitability in deep diving atmospheres. In: *Hydrogen as a Diving Gas. 33rd Undersea and Hyperbaric Medical Society Workshop,* edited by R. W. Brauer. Bethesda, MD: Undersea and Hyperbaric Medical Society, 1987, p. 213–225.