Acclimation to decompression sickness in rats

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Decompression sickness (DCS) occurs when divers who have incurred an excess inert gas load under hyperbaric conditions ascend to the surface (decompress) too rapidly, allowing inert gas bubbles to form in the blood and tissues. Tissues typically affected include joints, skin, lungs, and the central nervous system. Severity can range from trivial to fatal.

Acclimation is the phenomenon by which an organism develops functional compensation, over a period of days to weeks, in response to a specific environmental factor (12). Although acclimation is well documented in certain environmental conditions (such as thermal and altitude stress), there is scant literature that rigorously supports the occurrence of acclimation in response to hyperbaric/decompressive stress (6, 8). This is despite the fact that there is a body of colloquial diving lore that supports the perception that the risk of DCS decreases as more sequential hyperbaric exposures are undertaken (8, 20, 34).

Most of the literature addressing this question has come from anecdotal and retrospective studies of caisson workers. In general, these reports support the existence of an acclimation phenomenon whereby the incidence of DCS declines with repeated exposures to hyperbaric environments and rises again after periods of no exposure. In 1910, McWhorter reported (28) that previously exposed (“old”) workers working under the East River in New York City experienced a lower risk of DCS than “green” workers. Walder and coworkers’ analysis of data (14, 37) from caisson workers on the Tyne Tunnel during the years 1948–1950 and of other data from construction of the Dartford Tunnel suggests that acclimation occurred (~50% reduction in DCS incidence), that decreased incidence of DCS is probably not solely due to progressive “selecting-out” of susceptible individuals, and that the half-time for acclimation was 7 ± 4 days. However, these studies suffer from several shortcomings typical of retrospective studies: ascertainment is unclear, parameters reported are ill-defined, reporting of DCS was largely subjective, and there is the potential for selection bias, the possibility that individuals especially susceptible to DCS may self-select out early in the course of a series of exposures, leaving only those individuals with intrinsic resistance to DCS to complete the study.

A retrospective study of diver health scores in human divers (6) and a prospective study of humans compressed in a hyperbaric chamber primarily relying on Doppler ultrasound detection of venous bubbles as an index of DCS risk (8) both yielded equivocal results regarding the existence of acclimation to decompression. Others have inferred that acclimation with respect to DCS occurs, but without rigorously demonstrating its existence (16, 19, 33, 39). In an altitude acclimation study, Fang and Chen (11) exposed rats to hypobaria (and hypoxia) for 30 min/day for 84 days followed by a single explosive decompression to simulated altitude and showed that preexposed animals had fewer and milder pulmonary hemorrhages than nonpreexposed control animals, but they did not assess the animals for DCS.

The aim of the present research was to prospectively determine whether acclimation to decompression from hyperbaric exposure occurs and, if so, to determine possible contributing factors such as pressure and number of hyperbaric exposures. Experiments reported here were performed in two phases.

Phase 1 experiments were designed to address the following questions: Do prior hyperbaric/decompressive exposures protect against DCS or death from subsequent exposures (i.e., does acclimation occur)? Given that acclimation occurs, can differences in acclimation effectiveness be demonstrated by varying the number of daily acclimation dives or the depth of the acclimation dive?

Phase 2 experiments were designed to employ the most successful acclimation regimen from phase 1 to explore the following questions: Which is the more important determinant of acclimation: 1) exposure to hyperbaric stress, that stress produced by being at pressure which is assumed to increase as...
the duration and depth of the acclimation exposure increase, or 2) exposure to decompressive stress, that stress which presumably increases with the severity of the decompression procedures, resulting in increased amounts of evolved gas in the body? Can acclimation be produced with a single hyperbaric/decompressive exposure?

METHODS

Animals

Male Sprague-Dawley rats (Rattus norvegicus) were procured in groups of 30 at weights of ~155 (range 150–161) g on day of receipt, with each group constituting one “test cycle.” All animals were examined on receipt by the veterinary staff and were housed in an Association for Assessment and Accreditation of Laboratory Animal Care International-accredited, professionally staffed animal care facility. Animals were stabilized for 5 days before experimentation and maintained under a 12:12-h light-dark cycle with access to food and water ad libitum. Animals were weighed daily at midday (before any acclimation exposure on that day) and were weighed immediately before and immediately after the test dive on the final day (day 17). On the first experimental day (day 6), the 5 animals with the greatest weight differences (outliers) were culled from each cycle of 30 to allow for the tightest range of weights at the time of the test dive to minimize the influence of weight on DCS outcome. Power analysis indicated that detection of a 15–20% absolute decrease in DCS incidence from the targeted baseline value of 60% (i.e., decreased to 40–45% incidence) with 95% confidence would require ~50 (34–60) animals per group. Ten test cycles were performed in phase 1 and ten more cycles in phase 2.

All experiments were conducted according to the principles set forth in the Guide for the Care and Use of Laboratory Animals (Institute of Laboratory Animal Resources, National Research Council, National Academy Press, 1996). Before the experiments commenced, the Institutional Animal Care and Use Committee reviewed and approved all aspects of this protocol.

Hyperbaric Chambers

Hyperbaric exposures were conducted in two identical 5-ft³ chambers. Identical operator panels were connected to a common gas supply line from the facilities gas farm. CO₂ and O₂ levels in each chamber were monitored with portable gas analyzers (model HB 1.2, Geotechnical Instruments, Leamington Spa, UK) calibrated daily. Internal chamber temperatures were monitored via a Cole Parmer Digi-Sense (model 89000-10) Temperature Controller. Each chamber was fitted with a Freon-based internal heat exchanger, allowing for both heating and cooling of the chamber atmospheres. Chamber temperatures were held at 28°C (±1.5°C) for the exposures. Four cylindrical drum cages were custom fabricated for use in the chambers and on the bench, with each cage divided into five separate compartments accommodating five rats per exposure. Each animal compartment was ~3.5 in. wide × 9 in. in diameter. Each cage was rotated to exercise the rats with Superior Slo-Syn stepper motors (type MIII-FF-206) and an Applied Motion Products Step Motor Driver (PDO-5580), controlled by a variable-speed rheostat controller.

Dive Profiles

All dives began by compression at a rate of 1 ft of seawater (fsw)/s directly to depth.

Acclimation dives were done at a depth of either 70 or 40 fsw for 30 min (i.e., “bottom time,” as measured from the time depth was first reached), followed in most cases by rapid decompression to the surface in <20 s (see Fig. 1A). The only exception to rapid decompression was one group of 70-fsw acclimation dives that used staged decompression, traveling at 1 fsw/s from 70 fsw first to 30 fsw for 15 min, then to 15 fsw for another 15 min, before rapidly decompressing in <10 s to the surface (see Fig. 2).

Test dives were done at the end of the acclimation period to estimate susceptibility to DCS. These dives were at 175 fsw for 60 min, followed by rapid decompression in ~20 s to the surface (see Fig. 1B). This profile was selected to produce a target incidence of ~60% (estimated range 50–70%) of severe cardiopulmonary DCS (often with spinal involvement) in unacclimated rats of equivalent weight range as predicted from previous experience (22).

Dive Sequence

Five rats per exposure were individually placed in one of the cages in the wire mesh cylindrical drum. The drum was then placed in one of two hyperbaric chambers, and drum rotation was started. Immediately after decompression from each acclimation and test dive, the rotating drum was removed from the hyperbaric chamber and rotation was continued on the bench. Ambulatory behavior and survival of all
Acclimation and test regimens for each experimental group

<table>
<thead>
<tr>
<th>Phase</th>
<th>Group</th>
<th>Days 1–5 (stabilization period—no dives)</th>
<th>Days 6–10 (daily 30-min acclimation dives)</th>
<th>Days 11 and 12 (no dives)</th>
<th>Days 13–16 (daily 30-min acclimation dives)</th>
<th>Day 17 (test dive)</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
<td>0 fsw (sham)</td>
<td>0 fsw (sham)</td>
<td></td>
<td>70 fsw</td>
<td>70 fsw</td>
<td>Negative controls</td>
</tr>
<tr>
<td></td>
<td>L70</td>
<td>70 fsw</td>
<td>70 fsw</td>
<td></td>
<td>70 fsw</td>
<td></td>
<td>Nine deep acclimation exposures</td>
</tr>
<tr>
<td></td>
<td>S70</td>
<td>0 fsw (sham)</td>
<td>0 fsw (sham)</td>
<td></td>
<td>70 fsw</td>
<td></td>
<td>Four deep acclimation exposures</td>
</tr>
<tr>
<td></td>
<td>L40</td>
<td>40 fsw</td>
<td>40 fsw</td>
<td></td>
<td>40 fsw</td>
<td></td>
<td>Nine shallower acclimation exposures</td>
</tr>
<tr>
<td></td>
<td>S40</td>
<td>0 fsw (sham)</td>
<td>0 fsw (sham)</td>
<td></td>
<td>40 fsw</td>
<td></td>
<td>Four shallower acclimation exposures</td>
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<td>2</td>
<td>Control</td>
<td>0 fsw (sham)</td>
<td>0 fsw (sham)</td>
<td></td>
<td>70 fsw</td>
<td></td>
<td>Within-phase negative controls</td>
</tr>
<tr>
<td></td>
<td>L70</td>
<td>70 fsw</td>
<td>70 fsw</td>
<td></td>
<td>70 fsw</td>
<td></td>
<td>Comparison of effectiveness of rapid vs. staged decompression</td>
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<tr>
<td></td>
<td>L70-St</td>
<td>70 fsw—staged decompression</td>
<td>70 fsw—staged decompression</td>
<td></td>
<td>70 fsw—staged decompression</td>
<td></td>
<td>Effective of single acclimation exposure</td>
</tr>
<tr>
<td></td>
<td>SS70</td>
<td>0 fsw (sham)</td>
<td>0 fsw (sham)</td>
<td></td>
<td>0 fsw (sham) (days 13–15), 70 fsw (day 16)</td>
<td></td>
<td></td>
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</tbody>
</table>

See text for group descriptions. Test dives on day 17 were at 175 ft of seawater (fsw) × 60 min.
forelimb and/or hindlimb paralysis, rolling, seizures, or death. These symptoms have been extensively used, and proven to be reliable criteria, to evaluate in rats the presence of severe cardiopulmonary DCS, often with spinal involvement (22, 23). Time (nearest 30 s) of onset of DCS and/or death was recorded.

Statistical Analyses

Comparisons of DCS incidences and death rates among experimental groups are based on odds ratios generated with a logistic regression model that controls for predive and postdive weights. Mean group dive weights just before the test dive on day 17 were compared by analysis of variance (ANOVA).

RESULTS

A total of 435 rats were entered into the studies reported here, 250 in phase 1 and 185 in phase 2. Because weight is a strong determinant of DCS risk in rats (22, 30), careful attention was paid to weight gains over the course of the experiments and to weight on the day of the test dive (day 17). Data from three rats in phase 1 were excluded from analysis because of pre-test dive weights that fell more than three standard deviations below the group mean, and data from six rats in phase 2 were excluded from analysis because of errors in experimental procedure. An additional 65 rats were included in phase 2 in groups not reported on here.

Mean weight of all 426 remaining animals (all acclimation regimens) on day 17 before the test dive was 291 ± 18 (SD) g. Baseline DCS incidence (all 89 control rats) was 66% (close to the targeted 60%), and baseline death rate (same cohort) was 38%. There were no instances of DCS or death during any acclimation regimen. All animals that died within the 30-min postdive observation period following the test dive on day 17 were diagnosed with DCS.

Phase 1

Mean ± SD weights (in g) of all groups just before the test dive on day 17 were as follows: phase 1—Control 292 ± 20 (n = 50), L70 292 ± 19 (n = 50), S70 291 ± 21 (n = 49), L40 292 ± 18 (n = 48), S40 294 ± 17 (n = 50); phase 2—Control 289 ± 17 (n = 39), L70 287 ± 15 (n = 50), L70-St 289 ± 14 (n = 55), S70 288 ± 15 (n = 35). There were no significant differences among the group mean weights within each phase or across all nine groups (ANOVA).

Figure 3 depicts the percentage of rats in each phase 1 group that exhibited evidence of DCS or died during the 30-min postdive observation period following the test dive on day 17. Table 2 summarizes the corresponding odds ratio analysis of significance for DCS and death in these groups. In general, the deeper (70 fsw) acclimation dives were more successful than the shallower (40 fsw) acclimation dives at protecting against DCS and death. Also, the longer the acclimation regimen (i.e., the greater the number of daily acclimation dives), the greater the protection. The L70 acclimation regimen significantly (P = 0.0107) decreased the odds for DCS incidence by 66% relative to sham-acclimated control animals, with a relatively narrow 95% confidence interval. The S70 acclimation regimen was also effective at a P < 0.05 significance level, but not as effective as the L70 regimen. The protective effects of all other acclimation regimens followed the general trends cited above but did not reach the P < 0.05 significance level.

Mortality followed a similar pattern across acclimation regimen groups, but the differences between mortality odds ratios did not reach statistical significance at the P < 0.05 level.

Phase 2

Staging of decompression and prolonging the total time at elevated pressure from acclimation dives did not significantly alter the protective effect of the L70 acclimation regimen when results from the L70-St experimental group are compared with those from the L70 and Control groups performed during phase 2 (Fig. 4B). In contrast to phase 1, the protection provided by the L70 regimen did not reach statistical significance compared with control animals, nor did the L70-St regimen—perhaps because the size of the phase 2 Control group was smaller than that of the phase 1 Control group (n = 39 vs. 50). If, however, the results from the Control and L70 groups performed during phase 2 are augmented with results from the respective groups performed in phase 1, thereby increasing the n of these groups, then the L70 (but not the L70-St) regimen’s protective effect regains statistical significance versus control animals (odds ratio 0.43, P = 0.0051; see Fig. 4C and Table 3). However, the 7% difference (51% vs. 44%) between the protective effects of L70 versus L70-St regimens when phase 1 and phase 2 data are combined does not reach statistical significance.

A single acclimation dive to 70 fsw on the day preceding the test dive (SS70) provided no apparent protection against either DCS or death (Fig. 5).

DISCUSSION

To our knowledge this is the first study to prospectively rigorously demonstrate that acclimation to hyperbaric/decompressive stress actually occurs. Some previous studies have retrospectively attempted to discern an acclimation effect, but these studies, while suggestive, are subject to inherent biases. Other studies, accepting the results of retrospective analyses, have attempted to determine a mechanism of acclimation without rigorously establishing its existence.

In our studies, the 70-fsw acclimation dives were selected to produce 0% DCS incidence for rats of the weight range being...
used but near the inflection point on the dose-response curve where risk of DCS was predicted to become greater than zero, thus providing as much decompression stress as possible during acclimation procedures without causing DCS. The 40-fsw dives were selected to provide less decompression, thereby providing a “low-stress” comparison to the 70-fsw “high-stress” acclimation procedure. Thus our acclimation dive profiles were designed to minimize the risk of incurring DCS during the acclimation regimen, and they were successful in doing so (no animals contracted DCS from the acclimation dives). The deepest dives (70 fsw) provided statistically significant protection against DCS. Deeper acclimation dives (70 fsw) were more protective than shallower (40 fsw) acclimation dives, and among the deeper dives (70 fsw) there was a trend toward the longer regimen (9 daily acclimation dives) being more protective than the shorter regimens (4 daily acclimation dives or a single acclimation dive) (odds ratios of 0.34 vs. 0.39 and 0.51, respectively). This pattern is consistent with general concepts of acclimation (13).

The acclimation profiles that were protective against DCS were not significantly effective in reducing mortality. The differences between mortality odds ratios of the L70 and Control groups was nearly significant ($P = 0.0578$), but the analogous group comparison from phase 2 data was less pronounced. The observed trend suggests that a larger sample size might have elicited a statistically significant difference in mortality. However, the discrepancy in the magnitude of the effect of acclimation on DCS incidence versus mortality is not unexpected because death rates in rats with DCS have commonly been observed to go up with the more severe DCS that usually accompanies higher rates of DCS incidence, indicating that DCS and death are not strongly correlated in some situations and thus may be affected differently by acclimation.

Because of the nature of hyperbaric exposure, it is difficult to determine whether the stressor that triggers the acclimation process is hyperbaric exposure or decompression, since all animals were exposed to both during each acclimation dive. In phase 2, we attempted to separate the effects of these two factors. We chose the acclimation dive regimen from phase 1 that was most successful in protecting against DCS (the L70 regimen). We compared the results from a new group of rats exposed to this regimen to those from a group exposed to a similar regimen, but in which decompression from acclimation dives was done more slowly (L70-St). The staged decompression profile introduced two stops during decompression, each for 15 min, a time that approximates published estimates for the time constant for uptake and elimination of N2 as it relates to DCS in rats (23). The staged group would thus have a longer

### Table 2. Odds ratio analysis of differences in DCS incidence and mortality of each phase 1 acclimation regimen compared with sham-acclimated control animals

<table>
<thead>
<tr>
<th>Comparison</th>
<th>DCS Odds ratio</th>
<th>95% Confidence interval</th>
<th>$P$ value</th>
<th>Death Odds ratio</th>
<th>95% Confidence interval</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>L70 vs. Control</td>
<td>0.34</td>
<td>0.15–0.78</td>
<td>0.0107*</td>
<td>0.42</td>
<td>0.17–1.03</td>
<td>0.0578</td>
</tr>
<tr>
<td>S70 vs. Control</td>
<td>0.39</td>
<td>0.17–0.91</td>
<td>0.0291*</td>
<td>0.52</td>
<td>0.22–1.24</td>
<td>0.1388</td>
</tr>
<tr>
<td>L40 vs. Control</td>
<td>0.55</td>
<td>0.24–1.26</td>
<td>0.1578</td>
<td>0.55</td>
<td>0.23–1.32</td>
<td>0.1813</td>
</tr>
<tr>
<td>S40 vs. Control</td>
<td>0.53</td>
<td>0.23–1.21</td>
<td>0.1313</td>
<td>0.62</td>
<td>0.27–1.46</td>
<td>0.2763</td>
</tr>
</tbody>
</table>

DCS, decompression sickness. Asterisks indicate statistical significance.
hyperbaric exposure than the other 70 fsw groups, but presumably substantially less decompression stress, with the additional time allowed for N₂ off-gassing, permitting examination of the relative roles of decompression versus hyperbaric stress in any acclimation process. Thus, as depicted in Fig. 2, L70 animals were exposed to less hyperbaric stress but were decompressed more strenuously than L70-St animals; in contrast, L70-St animals were exposed to more hyperbaric stress (kept at depth longer) but were decompressed less strenuously than L70 animals. We predicted that if decompressive stress was the more critical inducer of acclimation, then the L70 group would be more protected than the L70-St group. Conversely, if hyperbaric stress was more critical, then the L70-St group would be more protected. Unfortunately, we were unable to detect any difference in protective effect between the two groups in phase 2. However, if group n values are augmented with results from identically treated Control and L70 animals from phase 1, a trend can be detected toward decompression stress being the more critical inducer of acclimation.

Our inability to detect a statistically significant difference between the protective effects of these two acclimation regimens in phase 2 may have one or more of several causes. First, it may be that there is no difference, and either both are equally critical or some other, unmeasured factor is most critical. Second, differences between the hyperbaric stresses and the decompressive stresses of the two groups may not have been adequately large. If so, the use of a more gentle and prolonged decompression profile for the L70-St group might have been adequate to segregate the effects. Finally, group sizes (n) may have been insufficient to reach significance. That this may be the case is suggested by the appearance of a trend when the n values of the Control and L70 groups were augmented with results from phase 1. A post hoc power analysis indicates that if the observed trend were to continue [44% DCS incidence for the L70 regimen and 51% incidence for the L70-St regimen (Fig. 4C)], a total n of 629 animals per group would be necessary to detect a difference between groups at an α < 0.05 with 80% power.

Possible mechanisms for acclimation to decompression have been divided into two categories: 1) mechanisms that reduce bubble formation and 2) mechanisms that reduce the body’s response to bubbles (6, 8).

A leading hypothesis in the first category is that repeated dives eliminate bubble-precursor micronuclei, thereby decreasing the likelihood that a subsequent decompression will produce clinically relevant bubbles. The mechanism of micronucleus elimination most commonly hypothesized is via “crushing” during the earliest compressions in an exposure sequence, but an alternative hypothesis is that they are eliminated via off-gassing during sequential decompressions.

Harvey (15) showed that pretreating inanimate fluids with exposure to extreme pressures (≥1,000 atm) rendered them resistant to bubble formation. Similar experiments on excised mammalian tissues resulted in bubble formation in some cases but are difficult to interpret since no controls (not pressurized) were reported (15). In 1969, Evans and Walder (10) showed that similarly extreme pressures (389 ATA) protected against bubble formation in subsequently decompressed shrimp. They appear to be the first to have hypothesized that this phenomenon might account for “acclimatization” against DCS. Others have also demonstrated that extremes of pressure pretreatment (in excess of 20 atm) can decrease the ease of bubble formation or the number of bubbles formed during subsequent decompressions in water (21), in gelatin (32), and in invertebrates (5) and can prevent death, presumably from DCS, in rats (36). Crustacea replete their bubble-forming capacity within 16 h of a high-pressure exposure, suggesting that micronuclei regenerate within that time frame (5).

McDonough and Hemmingsen have presented data from crustacea that question whether micronuclei are responsible for the bubbles produced during decompression (27) and whether precompression to extreme pressure decreases subsequent decompression bubble formation (26). Wisloff and Brubak (40) showed that an aerobic training regimen lasting 2 or 6 wk before a test dive decreased bubble scores (and incidence of severe DCS and death) in rats. They postulated that the exercise regimen might be protective via elimination of bubble micronuclei. However, the possibility that their observations...
represent an acclimation (or cross-acclimation) phenomenon similar to the one we report is minimized by the complexity of the time course of exercise-induced protection. In the same study, a single acute bout of exercise 1 day before a test dive was as effective as the 2-wk exercise regimen, and the 6-wk regimen was less effective than the 2-wk regimen. Furthermore, a subsequent study indicated that an acute bout of exercise 30 min before the test dive could eliminate the protection provided by exercise on the previous day (25). Van Liew (35) has commented on the paucity of evidence that micronuclei are important in mammalian DCS, that they are crushable, and that any crushing effect persists long enough to influence DCS risk from dive to dive. The high pressures that seem necessary to crush micronuclei, and the relatively short time course of the effect, suggest that the crushing of micronuclei is not a likely explanation for the acclimation effect we have demonstrated.

Nonetheless, Lin et al. (24) have presented data indicating a temperature-dependent decrease in bubble formation in decompressed rats following a previous decompression ~24 h earlier. These results could conceivably be attributed to either micronuclear crushing or micronucleus elimination during the initial decompression.

The second category of hypotheses, that acclimation is due to host responses to bubble formation, takes several forms, including physical, immunologic, and genomic/proteomic. Hills (16) studied the mechanical relaxation properties of ex vivo tendon and cartilage and concluded that pain-only DCS could be explained by a theory of simple mechanical hysteresis, whereby alternating expansion and contraction of bubbles produced progressively lower pain-inducing gas-tissue pressure differentials. Ward and colleagues (38) demonstrated that individual men with highly activatable endogenous complement levels also exhibited increased susceptibility to DCS. Decomplementation of DCS-susceptible rabbits with a cobra venom extract “deacclimatized” them to DCS for the 3-day duration of their decomplementation (39). However, Broome et al. (3) were unable to diminish DCS risk in rats by inactivating complement by administration of a soluble complement receptor. Detection of complement activation via measurement of rabbit and/or human serum anaphylatoxin C5a indicates that complement activation exhibits pronounced intraindividual temporal variability and does not appear to correlate with the presence of bubbles (2). Furthermore, complement activation did not change in the serum of divers exposed to three repeated dives, nor did it correlate with the occurrence of DCS (17). Ersson et al. (9) found that humans exposed to daily dives for 2 mo developed alterations in certain interleukin and immune system signaling proteins that they deemed consistent with “compensated activation of the inflammatory defense mechanisms without loss of homeostasis of the inflammatory system.” However, the cohort they studied was simultaneously undergoing a physical conditioning regimen, and no control group was followed for this potentially confounding factor. Nonetheless, they speculate that their findings may be integral to an acclimation process.

While not studying acclimation processes directly, a handful of investigations suggest the possibility that hyperbaric/decompression stress may be amenable to cross-acclimation or cross-tolerance, a phenomenon whereby exposure to one stress induces tolerance to a different stress (13). Daily administration of endotoxin to spontaneously hypertensive rats for 4 days protects them against DCS during subsequent hyperbaric exposures (7). In another study, exercise-conditioned pigs were protected against DCS independent of age, adiposity, or weight (4). The phenomenon of cross-acclimation suggests that there may be one or more common pathways that mediate acclimation to a variety of stressors (18, 29, 31).

Our phase 2 experiments were designed to try to distinguish between the two categories of mechanistic hypotheses (decreasing bubble formation vs. increasing host responses). The L70 regimen, with daily exposures to decompressive stress, would be expected to maximize bubble formation and trigger a greater host response than the more gentle decompression of the L70-St regimen. On the other hand, the L70-St regimen, with its more prolonged durations at pressure and more gentle decompression, would be expected to minimize bubble formation and growth while minimizing the stimulation of host responses. While the trend we observed toward greater effectiveness of the L70 regimen might argue in favor of a host-response mechanism and against the micronucleus compression hypothesis, the data, as noted, are not strong enough to draw this conclusion.

To examine the hypothesis that acclimation results from activation of unknown genomic and/or proteomic factors, we have performed experiments similar to those described in this study in rats that were euthanized after acclimation, but without exposure to a test dive, and have collected tissue samples for genomic and proteomic analysis. These data will be presented in a subsequent publication.

Conclusions

Protection against DCS can be attained by prior acclimating exposures to daily dives that do not themselves cause DCS. Within the parameters used in these experiments, the effectiveness of the acclimation process is increased with increased depth of the acclimation dives and at the most effective depth tended to be increased with increased number of daily acclimation dives. The critical stressor for inducing acclimation may be the decompressive stress, as opposed to the hyperbaric stress, to which these animals were exposed, but our data on this issue did not reach statistical significance.

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REFERENCES


ACCLIMATIZATION TO DECOMPRESSION SICKNESS IN RATS


