TINY BUBBLES

Richard T. Mahon

Undersea Medicine Department, Naval Medical Research Center, Silver Spring, MD
and
Uniformed Services University of the Health Sciences, Bethesda, MD

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Address for Correspondence:
Richard T. Mahon, CDR, MC, USN
Naval Medical Research Center
Undersea Medicine Department
503 Robert Grant Avenue
Silver Spring, MD 20910-7500
Ph: 301.319.7317
Fax: 301.319.7378
E-mail: Richard.Mahon@med.navy.mil
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Since decompression sickness (DCS) was first described the elusive nature of its pathophysiology has been a challenge. It is generally thought that intravascular and extravascular bubbles are responsible for a host of downstream effects that cause the constellation of clinical findings known as DCS. Through the years, theories of gas exchange and bubble formation have been hypothesized, tested and modified to increase safety and performance in hypo and hyperbaric decompression excursions. While perhaps not ideal, this approach has been necessary given the technical limits in a growing field that needs real-time application. In this issue, Wilbur, et. al. present what could potentially provide a technical solution to the long hypothesized but ultimately evasive micronuclei. This unique blend of theory and empiricism has certainly advanced the field, but large gaps in our understanding of the basic mechanisms of bubble formation (and hence DCS) remain.

Early studies in decompression theory demonstrated that supersaturation (even at extreme changes in ambient pressure) alone was insufficient to generate bubbles. As early as 1912 Hill postulated the need for weak “points” in a fluid for bubbles to form (7). Through the years these weak “points” evolved through observations and sound research into the micronuclei concept. Currently, micronuclei are defined as a small particle less than ten microns in diameter that is filled with gas. These small bubbles would satisfactorily explain larger bubble formation at relatively small pressure changes observed in decompression. If bubbles then need micronuclei to form their origin, the micronuclei should present an ideal therapeutic target in the prevention of DCS (8).

Since its theoretical inception, a vast body of sound investigations has strongly supported the micronuclei concept, but reliably fallen short of actually proving its existence. The reliance of a basic theory of bubble formation on a theoretically necessary entity that has not been conclusively demonstrated has been an interesting story in decompression research. Initially, studies applied to inanimate fluids, excised tissue and ex vivo blood supported the existence of micronuclei. The observation that fewer bubbles were formed in a liquid that had been subjected to “denucleation” (such as centrifugation to “crush the nuclei”) compared to a liquid that had not been denucleated, was not only encouraging, but established a rationale for whole animal testing.

Evans utilized translucent shrimp to validate and strengthen the micronuclei case by demonstrating a significant reduction in bubble formation when shrimp were compressed to 400 atmospheres of pressure prior to decompression (6). Vann then provided further evidence of micronuclei in rats by rapidly compressing air breathing rats to 1000 fsw prior to decompression after 2 hours at 240 fsw. Vann’s results demonstrated significantly less DCS with this strategy, supporting the existence of the micronuclei and, more importantly, presenting a potential therapeutic target in other mammalian species (8).

In the current millennium experiments directed at the micronuclei concept have yielded authentic practicality, in enhancing the safety and performance capacity of pressure excursions. The potential of micronuclei as a therapeutic target has been hypothesized and examined in oxygen pre-breathing, exercise and nitric oxide donors.
Recognizing that micronuclei depleting pressure excursions are not easily feasible or even desired, alternative methods to limit micronuclei through gas-changing techniques have been tested. If micronuclei are gas filled, then it stands to reason that a change in its surrounding gas partial pressure (such as using high fractions of inspired oxygen) would favor the shrinking and dissolution of the micronuclei. In small animal models, surface and hyperbaric oxygen used prior to full compression and decompression have decreased bubbles (2) and decreased evidence of spinal cord injury in the rat (1).

Theories of exercise in relation to bubble formation and DCS could certainly benefit from proving the existence of micronuclei. It has been well-established that strenuous exercise 24 hours before an 18 meter dive significantly decreases intravascular bubbles in man (5). Whereas strenuous exercise closer to dive time, or more than 48 hours from dive time, confers no benefit in the way of decreasing bubbles. And exercise immediately prior to diving appears to worsen the bubble load in hypobaric excursions (4). The micronuclei (or changes in rheologic properties) has been invoked to explain the nature of the benefit (or harm) in this fairly precise timing of exercise relative to dive time.

Finally, observations regarding the timing of exercise in both humans and animals before diving have lead to simple pharmacologic manipulation in the form of nitric oxide donors that have decreased bubble counts in humans (and presumably decreased DCS risk) (9).

In this issue Wilbur, et. al. describe the technique of dual frequency ultrasound (DFU) in recognizing signals consistent with micronuclei after normobaric exercise. The availability of a technique that could potentially shed much needed light on bubble formation is welcomed. A technique that could quantiﬁy anticipated bubble formation would be downright dazzling.

Certainly much work remains to be done. The signals reported here by Wilbur, et. al. may have alternative explanations, such as lipid transport, and need to be conﬁrmed with other techniques. If these signals are in fact gas ﬁlled micronuclei, their composition and distribution would also be of more than curious interest (3). Lastly, the demonstration that recent experiments designed speciﬁcally to examine micronuclei have, in fact, decreased micronuclei quantities could lead to entirely new directions for decompression research.

I am (cautiously) optimistic that the signals reported are gas ﬁlled micronuclei. If such is the case, it would be a facile leap to envision improved decompression schedules as a result of this work and may signiﬁcantly move the ﬁeld of decompression theory beyond the comfortable and well-worn empiricism we all know too well.

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