Hyperoxia and acute lung injury

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TO THE EDITOR: The review by Matute-Bello et al. (15) has misleading and potentially dangerous statements concerning the role of hyperoxia in human acute lung injury (ALI). Table 4 states “in normal human lungs, 100% oxygen has not induced lung injury...” The text states that most mammalian species develop respiratory distress and die with exposure to 100% oxygen, but the “same findings have not been reproduced in humans with normal lungs...” That statement is essentially true (fortunately) but mainly because very few studies of potentially lethal hyperoxia have been carried out in individuals with normal lungs, for obvious reasons. The one study referenced in the review (1) was carried out in patients with reversible brain injury, which may have influenced the pulmonary response to hyperoxia, and indeed a subsequent similar study demonstrated significant lung injury (13). Studies of normal individuals exposed experimentally to 100% oxygen at normal pressure (i.e., 1 ATA) have shown evidence of tracheobronchitis and changes in vital capacity, diffusing capacity, and lung permeability (2–5, 7, 17). Inadvertent exposure of patients with normal lungs to prolonged hyperoxia resulted in clinical findings compatible with oxygen toxicity (12). Exposure of normal humans to oxygen at elevated pressure (that is, greater than 1 ATA O2) has indicated a shorter duration of exposure for equivalent pulmonary symptoms and function changes (8, 10, 16, 18). Pulmonary-related death has been reported for one patient in the normobaric O2 exposure group (12) and another with hyperbaric exposure (9). Thus evidence of lung abnormalities with severity proportional to the partial pressure of oxygen has been demonstrated in normal human lungs similar to the findings with experimental animals. It is known that different species, and indeed strains of the same species as well as individuals from the same strain, show varying sensitivity to the toxic effects of oxygen (11). Rats exposed to 0.8 ATA O2 become tolerant to 1 ATA O2 but uniformly die when subsequently exposed to higher (1.5 ATA) O2 partial pressures (14), emphasizing the importance of O2 “dose.” Parenthetically, the dose range for lethality (approximately 0.8–1.5 ATA) is quite narrow compared with many toxicants where dose sensitivity of various species may vary by more than an order of magnitude. So the important question is, what is the dose range for human pulmonary oxygen toxicity? Based on the limited number of human studies but with analogy to nonhuman primates (6), the “average” human might require O2 at 1.1 or 1.2 ATA to reach a lethal concentration. If that is the case, a large segment of the human population might be spared ALI and lethality with 100% oxygen at 1 ATA. However, that concentration of oxygen could prove to be lethal for that fraction of the population whose resistance to oxidant stress is less than the population mean. All indications are that hyperoxia in animals (with appropriate consideration of dose) does serve as a model for human ALI associated with oxidant stress, although probably not for ALI associated with inflammation, and that due diligence is necessary when humans are exposed to elevated partial pressures of O2.

REFERENCES