Point: Counterpoint: Pulmonary edema does/does not occur in human athletes performing heavy sea-level exercise

POINT: PULMONARY EDEMA DOES OCCUR IN HUMAN ATHLETES PERFORMING HEAVY SEA-LEVEL EXERCISE

My colleagues (25) have a difficult task, because it is easier to prove a positive than a negative. A 1978 case report documents two athletes that presented, after running the Comrades marathon, with shortness of breath, cough productive of blood tinged and/or pink frothy sputum, crepitations on auscultation, and chest radiograph findings of pulmonary edema (18). There can be no doubt that these athletes had pulmonary edema, and although the Comrades marathon represents an extraordinary exercise task because of its length (90 km), the elevation of the route never exceeded 1,000 m. In addition, there are numerous reports in the literature that document the presence of pulmonary edema after exercise. These include cases of pulmonary edema occurring as a result of swimming (1), as distinct from pulmonary edema associated with diving, i.e., immersion pulmonary edema (26), as well as cases of overt edema occurring during sexual intercourse (29) and heavy or/prolonged exercise with very modest altitude exposure (2, 17) in otherwise healthy people. Consequently these case reports prove that pulmonary edema occurs during heavy sea-level exercise and this debate could stop here.

However, given the sporadic nature of these reports, perhaps a better question is why don’t more athletes develop alveolar flooding during exercise? While the healthy human lung is overbuilt for a sedentary existence, during maximal exercise it is subjected to substantial physiological stressors. In particular, ventilation and cardiac output greatly increase and pulmonary blood volume and capillary blood volume rise (16). Even during submaximal exercise, pulmonary arterial and occlusion pressures (i.e., left atrial pressure) approximately double from rest, cardiac output increases approximately fourfold (13), and microvascular pressures rise. Starling’s law is thought to apply to the lung microvasculature (see Ref. 28 for review), and thus fluid balance in the lung reflects the interplay of hydrostatic pressures and colloid osmotic pressures in the lung microvasculature and surrounding interstitium. Increases in microvascular pressure, combined with a greater surface area for fluid filtration are expected to increase fluid exchange between the lung vascular space and the interstitium (28). Given this, it is not difficult to imagine that lung fluid balance might be altered, without completely overwhelming the lymphatic drainage, resulting in alveolar flooding. There are animal data supporting this idea. In dogs, when the capillary pressure is increased, a distinct pattern of edema formation emerges (Fig. 1). First, there is extravasation of fluid into the interstitial space surrounding the conducting vessels and airways (27). Following this, if the rise in pressure is prolonged, alveolar wall fluid is increased and then finally overt alveolar flooding, gas exchange defects, and possibly alveolar collapse occur (27). In keeping with this idea, lung lymphatic flow increases rapidly after the onset of exercise in sheep and further increases with increasing exercise duration (5, 20). On this basis it is to be expected that fluid balance in the human lung is likely to follow a similar pattern. However severe pulmonary edema with alveolar flooding has been documented during heavy sea-level exercise only under conditions where the development is exacerbated by factors such as very prolonged exercise (18), psychological stress (1), cold (29), moderate altitude exposure (2, 17), and water immersion (1, 26). This suggests that the normal lung has a large safety margin preventing the development of alveolar flooding except in the most extreme cases. However, interstitial edema is more likely.

In humans, the evidence for the development of interstitial edema is indirect, but very consistent. As seen in Fig. 1, interstitial edema would be expected to compress small air-
ways and blood vessels, potentially affecting ventilation-perfusion (V\textsubscript{A}/Q\textsubscript{O}) matching. In many humans, V\textsubscript{A}/Q\textsubscript{O} mismatch increases with exercise (6, 8, 9, 13, 14, 21, 22) and the pattern is consistent with the cause being interstitial edema. For example, those subjects who increase V\textsubscript{A}/Q\textsubscript{O} mismatch during exercise, have greater V\textsubscript{A}/Q\textsubscript{O} mismatch in recovery than those subjects that do not show an increase. This difference persists beyond the point at which ventilation and cardiac output normalize to pre-exercise levels (24). Exercise in normobaric hypoxia causes a greater increase in V\textsubscript{A}/Q\textsubscript{O} mismatch than in normoxia, and this increase is relieved by breathing 100% oxygen (9). Since hypoxia and hyperoxia alter pulmonary perfusion inequality in normal humans during exercise at sea level and simulated altitude. J Appl Physiol 58: 978–988, 1985.


Point:Counterpoint

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COUNTERPOINT: PULMONARY EDEMA DOES NOT OCCUR IN HUMAN ATHLETES PERFORMING HEAVY SEA-LEVEL EXERCISE

The arterial partial pressure of oxygen (PaO₂) can be reduced by as much as 30 mmHg and oxyhemoglobin saturation (SaO₂) by 15% below resting levels in some aerobically trained athletes exercising at high intensities (3). Some have hypothesized that mild interstitial edema could develop and, through changes in local compliance (e.g., alveolar wall edema) or resistance (e.g., perivascular or bronchial edema), affect the distribution of ventilation or blood flow. However, the measurement of lung density in humans in vivo is not possible, so any discussion of whether transient pulmonary edema exists is dependent on the validity and sensitivity of the tools used to estimate the change in lung water. One must also consider the pathophysiology, or at least the physiology, that would lead to pulmonary edema in human athletes at sea level. Possible mechanisms in this population are limited but include 1) increased pulmonary capillary permeability secondary to leakage (starling forces) or damage (capillary stress failure); 2) increased pulmonary capillary surface area; 3) increased pulmonary capillary hydrostatic pressure; and 4) lymphatic insufficiency. Others have argued that it is unlikely that exercise at sea level would result in pulmonary edema because there are important “edema safety factors” that exist to oppose it’s formation (16, 19). Here we present the relevant studies that have been unsuccessful in documenting pulmonary edema.

Repeate exercise. Repeated heavy exercise does not worsen gas exchange (13, 18) in athletes. In fact, gas exchange impairment can be lessened by prior exercise (18). This shows that impairments to gas exchange are not caused by a mechanism that persists after the initial exercise period and is not aggravated by subsequent exercise, as would be expected of structural alterations to the blood-gas interface.

Transthoracic electrical impedance. Reductions in transthoracic electrical impedance (TEI) following exercise have been reported as related to the accumulation of lung water (1). The physiological importance of these findings remain unclear, because the measurement of TEI is nonspecific, it does not explain the source of hindered impedance, and may be due to elevated intravascular volume not interstitial edema. Furthermore, others (15) have reported increased TEI following maximal exercise.

Chest radiography. There are reports of pulmonary edema in two athletes competing in a 90-km running race (12). While the clinical manifestations of pulmonary edema appear present, two points should be emphasized. First, the pulmonary pressures would not be significantly elevated during this type of exercise and the possibility of “stress failure” is low. Second, ultra-distance running races occur worldwide without widespread reports of pulmonary edema, suggesting that the presence of edema was more likely to be related to undiagnosed pathology. Chest radiographs were scored following three sets of 5-min of heavy cycle exercise with an increase in a semiquantitative edema score (20). However, the pre-exercise values were not zero (i.e., no edema present) and calls into question the meaningfulness of the scale. Changes in the magnitude of extravascular water needs to be ~35% to be detected by chest radiography (17), implying a pathology not seen in a healthy, athletic population.

99mTc-labeled diethylenetriaminepentaacetic acid. Usage of 99mTc-labeled diethylenetriaminepentaacetic acid (99mTc-DTPA) is a sensitive method for detecting lung pathology. Edwards et al. (4) found that pulmonary clearance of 99mTc-DTPA after maximal cycle exercise was unchanged. Furthermore, there was no relationship between pulmonary clearance and the fall in PaO₂ (−27 mmHg), suggesting that hypoxemia occurs despite maintenance of alveolar epithelial integrity. Conversely, following 6 min of maximal rowing, clearance appears to be increased (6). However, this is not direct evidence of edema. Rather, it could reflect a change in epithelial permeability, meaning that the blood-gas barrier is simply more permeable or it may be attributable to an increase in pulmonary capillary blood volume and the associated increase in pulmonary surface area.

Computed tomography. Computed tomography (CT) allows a rapid image of the lung, but because it exposes the subjects to ionizing radiation, it’s usefulness as a research tool in healthy, young athletes is limited. Following completion of a triathlon race, CT scans revealed a 19 and 21% increase in lung density and mass, respectively (2). However, heart rate was higher during post-race scans and the number of veins and venules was increased reflecting increases in pulmonary blood flow. Also, visual analysis of CT scans did not reveal an obvious image of acute pulmonary edema. We recently conducted two studies (5, 11) where the exercise protocol was...