Amelia Earhart, alveolar mechanics, and other great mysteries

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ALTHOUGH THE DISAPPEARANCE of Amelia Earhart on her 1937 attempt to fly around the world is still considered one of the world’s great mysteries, the mystery was actually solved in 1940. According to the Discovery News, skeletal remains and other physical evidence were discovered by Richard Gillespie on a tiny coral atoll, Nikumaroro, about 300 miles southeast of Earhart’s target destination of Howland Island. Unlike the Earhart mystery the mechanism by which the lung inflates at the alveolar level still eludes scientists today.

The use of in vivo $^3$He lung morphometry via MRI utilized by Hajari et al. (4) in this issue of the Journal of Applied Physiology is an exciting new tool to unearth the mysteries of alveolar mechanics (i.e., the dynamic change in alveolar size, shape, and number with lung inflation).

There is no consensus on how the lung changes volume at the alveolar level. Proposed models include 1) isotropic expansion and contraction of alveoli, 2) expansion and contraction of alveolar ducts with little change in alveolar volume, 3) successive alveolar recruitment, 4) alveolar coupling and uncoupling (like a paper bag), and 5) pleating and unpleating of alveolar corners (3). In this study Hajari et al. (4) demonstrated, using the $^3$He MRI technique, that the healthy human lungs inflate primarily by alveolar recruitment combined to a lesser extent with anisotropic expansion of alveolar ducts. The elegance of this technique is that it measures the dynamic change in alveolar volume and number in vivo, and it can be performed in humans.

The inconsistencies in findings related to alveolar mechanics using fixed lung tissue may be explained by the differences in experimental preparations and the relative insensitivity of morphometric techniques. Lungs have been fixed for morphometric study by vascular perfusion, formalin vapor, rapid freezing, and by instillation of fixative (3). Fixation is also associated with artifacts caused by tissue shrinkage and distortion and the possibility of operator-related variability. A second major problem with fixed tissue is that the lung can only be studied at one volume/animal, and thus to measure dynamic changes in alveolar mechanics lungs from different animals at different volumes must be compared.

Although there are still many inconsistencies in the literature I believe the conclusion of Hajari et al. (4) that lung inflation is secondary to opening of new alveoli rather than alveolar enlargement is solid and confirmed by multiple studies (1, 2, 6–9). The hypothesis that the lung inflates by alveolar recruitment is not a new concept. In 1950 Macklin (7) demonstrated histologically that there was little change in alveolar size with lung volume change, which suggested that alveolar ducts and sacs may be the structures that change size. These data were supported by Radford (9) in 1962 using direct visualization of subpleural alveoli, who found that alveolar diameter either increased minimally or decreased with lung inflation. Radford’s conclusion from these data was that lung inflation is caused by alveolar recruitment. These studies were further confirmed by Carney et al. (1), who used in vivo microscopy to measure the size and number of subpleural alveoli as the lung was inflated from 20–80% of total lung capacity. Carney concluded that the majority of lung inflation was secondary to alveolar recruitment. Using a unique monodispersed aerosol technique in excised lungs, Smaldone et al. (10) observed the aerosol’s gravitational deposition at zero air flow during a fixed breath hold. The fraction of deposited aerosol reflects the cross-sectional geometry of the air spaced with particle deposition inversely proportional to the mean linear intercept (MLI). Repeated measures of the MLI demonstrated that the lung inflates by progressive recruitment of alveoli. Lum (6) used cord length-frequency distribution analysis of freeze-dried lung sections at different lung volumes and also concluded that lung inflation is the result of alveolar recruitment. Namati et al. (8) developed an optical confocal process to evaluate alveolar dynamics in fresh intact mouse lung and found that alveoli become smaller and more numerous with lung inflation, supporting the hypothesis that the lung inflates by alveolar recruitment. Last, Escolar (2) used analysis of the pressure/volume curves of the morphometric changes in the size and number of alveoli with lung inflation and deflation and concluded that alveolar recruitment is the microscopic expression of pulmonary hysteresis. Combined, these studies suggest the normal lung inflates primarily by a mechanism of alveolar recruitment.

Fig. 1. Computer simulation of a single alveolus (A) and 4 alveoli forming an alveolar duct (B) with changing lung volume. The alveolar mouth (black) changes size greatly with only a moderate change in alveolar size with lung deflation (A). As the collective mouths of the 4 alveoli comprising the alveolar duct contract, the size of the duct decreases in size dramatically (B). The white bar is the size of the alveolar duct at full inflation (B, far left) and used to highlight the large change in duct size with lung deflation. [Adapted with kind permission from Springer Science + Business Media B.V. (5).]
Anatomy of the alveolus and alveolar duct. Kitaoka et al. (5) developed a four-dimensional (4-D) alveolar model by combining springs and hinges, corresponding to elastin fibers at the alveolar mouths and junctions of alveolar septa. Their dynamic model of the alveolus and duct features the majority of change in the alveolus during ventilation being secondary to large changes in the size of the alveolar mouth (Fig. 1A). Clusters of these alveoli are combined to form an alveolar duct (Fig. 1B). As the mouths of these alveoli change in unison during lung inflation, the size of the duct would change greatly (Fig. 1B). This mechanistic model of alveolar and alveolar duct mechanics could explain the findings of Hajari et al. (4). Kitaoka’s alveolar model features minimal change in alveolar size during ventilation with a change in alveolar duct size (5), similar to Hajari’s findings (4). The Kitaoka model also has a mechanism for alveolar collapse and reopening (image not shown) explaining the finding by Hajari et al. that the majority of lung inflation is caused by alveolar recruitment. Thus this dynamic alveolar model fits nicely with the biological findings of alveolar recruitment as a major mechanism of lung inflation.

In conclusion, the mechanism of lung volume change at the alveolar level is essential to understanding and preventing ventilator-induced lung injury (VILI). Further experimentation to understand dynamic alveolar mechanics both in the normal and acutely injured lung will guide our protective ventilator modes of the future.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES