

EDITORIAL



# The baby lung and the COVID-19 era

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The concept of the baby lung was born in 1987 [1] when quantitative CT scan analysis demonstrated that, in severe ARDS, the amount of the ventilatable lung tissue of an adult was similar to that of a 6-year-old healthy child. We called it a “baby lung.”

Three features seemed apparent: (1) The baby lung was anatomically located in the non-dependent lung regions (parasternal, when supine), while the radiological densities were primarily located in the dependent regions (paravertebral); (2) the respiratory system compliance was a useful tool with which to estimate the baby lung size [1]. Indeed, compliance was not an inverse function of the amount of non-aerated tissue, but instead correlated strongly with the amount of well-aerated lung. In other words, measured compliance characterizes only those lung units that receive the gas volume. This finding changed a prevailing concept of ARDS important to its management: The lung was not stiff, as commonly believed at that time, but small; (3) the specific compliance (i.e., respiratory system compliance measured in the ventilating circuit normalized to the size of the baby lung) was similar for healthy individuals and ARDS patients. That fact does not necessarily mean that the baby lung is healthy, but does indicate that its mechanical characteristics are preserved, exclusive of the possible presence of fibrosis or deficit of surfactant.

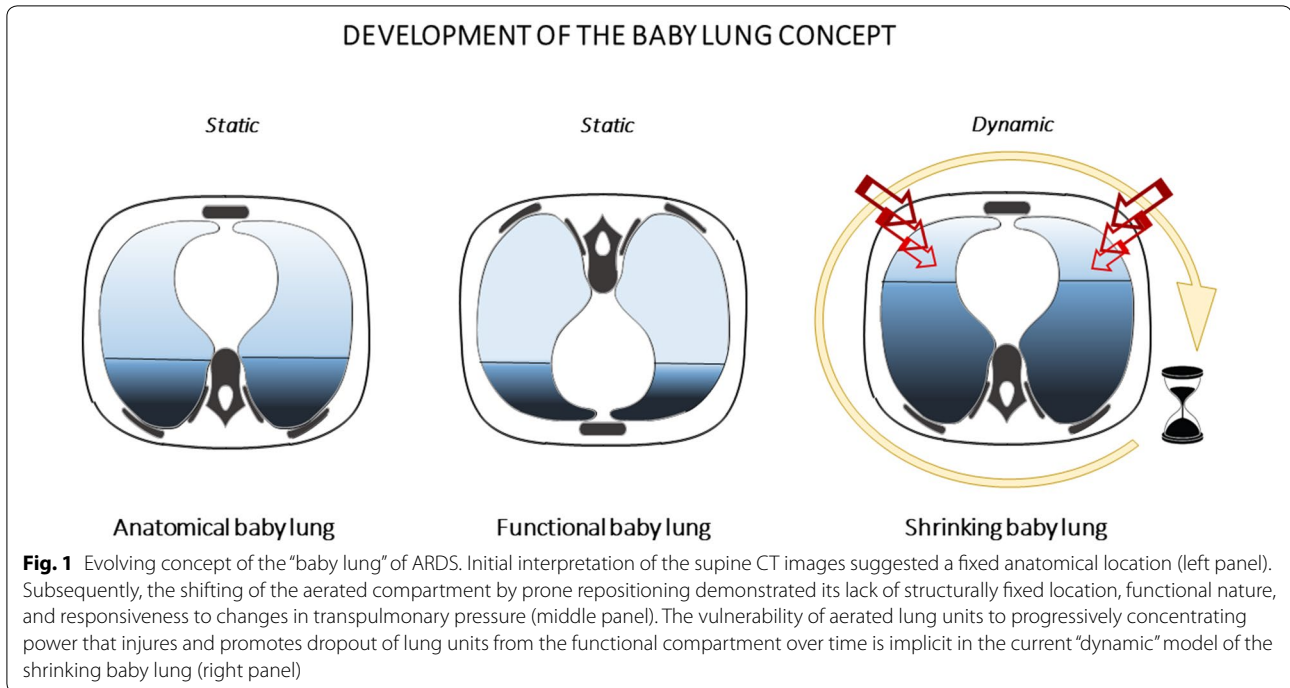
The anatomical location of the baby lung led us to introduce the prone position as a treatment for ARDS [2]. Indeed, we thought that the anatomically situated parasternal baby lung should be better perfused in the prone position, with resulting improvement in oxygenation and possibly a decrease in PaCO<sub>2</sub>. Actually, an increase in oxygenation *was* observed in the majority of patients,

with PaO<sub>2</sub> increasing even more than 100 mmHg for the same FiO<sub>2</sub>. However, almost one year later, we also took a CT scan in the prone position, and to our surprise, we found that the anatomically envisioned baby lung disappeared in the parasternal regions, while a new baby lung appeared in the dorsal zone [3]. This finding convincingly negated the concept of the *anatomical* baby lung and replaced it with the concept of the *functional* baby lung. Understanding the mechanism behind this positional switch implied the need to perform and compare regional analyses of CT in both supine and prone positions. Doing so led to the model of the “sponge lung” [4]. Indeed, the densities in the dependent lung regions, whether in supine or prone positions, were primarily due to superimposed hydrostatic pressures that compress the lung along the vertical gravitational axis. More importantly, it appeared evident that the densities were not due to the movement of edema but instead due to squeezing gas from the alveoli by compressive forces. This led also to a revised hypothesis for the mechanism of PEEP's benefit, which now would act as a counterforce against superimposed pressure, thereby preventing the expulsion of alveolar gas and atelectasis.

This model, actually without significant changes, held reasonably true until the COVID-19 era [5]. Several COVID patients at hospital presentation met the broad ARDS definition criteria. Indeed, the hypoxemia qualifies, on the basis of PaO<sub>2</sub>/FiO<sub>2</sub>, and bilateral infiltrates on chest X-ray are present. However, even though many authors continue to characterize this presentation as “ARDS” (which is a syndrome) and proceed accordingly, it must be recognized that, in many cases, we deal with an atypical ARDS [6]. Indeed, at the beginning this atypical syndrome does not show a baby lung, but as measured by the quantitative CT scan an “adult lung,” with normal mechanics and normal specific compliance [7]. It would be interesting to know, however, if and how the adult lung of early or mild COVID-19 pneumonia transitions to a baby lung. Is this due only to disease progression or

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also to inappropriate treatment which, in the absence of interventions, forces the adult lung to shrink progressively and deteriorate through a sort of “VILI vortex” [8] of concentrating injurious mechanical power [9]?

After becoming infected, only a minority of COVID patients develop bilateral pneumonia and hypoxemia [10]. The radiological lesions present initially as “ground glass” infiltrates located primarily near the visceral pleura. This location is similar to the one we found in experimental animals when VILI is produced with high tidal volume [11]. In these patients, the hypoxemia is primarily due to the VA/Q maldistribution caused by the loss of the lung perfusion regulation. Respiratory drive is highly activated because of hypoxemia, infection, and possibly direct presence of virus in the central nervous system. High tidal volume follows (increased strain) in association with higher transpulmonary pressure (stress). If this increase in stress and strain remains without correction, patient self-inflicted lung injury develops, causing overt lung edema [12]. Dependent regions of the lung then tend to collapse due to the increased hydrostatic superimposed pressure [13], and the lung transitions from the adult size to the baby lung size, with a parallel decrease in respiratory system compliance. If the conditions leading to increased stress and strain remain unchecked, the VILI vortex develops. Indeed, for any increase in edema and reduction in the lung size, stress and strain are more concentrated in a smaller lung and promote a vicious cycle. It is therefore

mandatory to interrupt this sequence of events which cause the baby lung to shrink and become more vulnerable. For many authors, the concept of VILI does not include the vascular side of the alveolus which is, in our opinion, of similar importance as the gas side, particularly in COVID. Indeed, the forces of mechanical power (a function of strain, stress, and respiratory rate) are primarily applied to the extracellular matrix to which both the epithelial and *endothelial* cells are anchored. The strain of these two cell populations contributes through a cytokine release to a further recruitment of inflammatory cells. Although the lung mechanics of the baby lung are not dramatically changed, the reaction to and tolerance of repeated cycles of high stress and strain is profoundly altered by the inflammatory reaction. This effect has been shown in CT-PET studies in which the inflammation was often recognized in the well-aerated tissue compartment [14].

It is beyond the purpose of this paper to discuss the therapy of COVID-19. At its core, however, is the prevention/interruption/reduction of the VILI vortex, keeping well in mind that PEEP modifies both stress and strain and contributes to the applied mechanical power [15].

In summary (Fig. 1), the baby lung concept evolved from a static representation (“anatomic entity located in the non-dependent lung”) to a static functional model (“sponge lung”) to dynamic entity subject over time to the VILI vortex if not maintained and preserved.

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### Compliance with ethical standards

### Conflicts of interest

The authors declare that they have no conflict of interest.

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