Imaging Lung Aeration at Birth Identifies Better Strategies for Ventilating Very Premature Babies

The transition to air-breathing at birth is crucial for the survival of all newborn infants. To make this transition, the liquid that fills the airways during fetal life must be cleared to allow the entry of air and the onset of pulmonary ventilation [1]. However, a thin film of liquid must remain to protect the inner surface of the lung from desiccation, leading to the formation of an air/liquid interface and the creation of surface tension within the lung which increases lung recoil. This process initiates many changes in lung physiology that allow it to become the sole organ of gas exchange [2]. For instance, the onset of pulmonary ventilation is closely associated with a dramatic increase in pulmonary blood flow (PBF) and the closure of vascular shunts that allow blood to by-pass the lungs during fetal life [2]. However, airway liquid clearance is restricted in infants that are born very preterm (<28 weeks of gestation) and, therefore, these infants commonly suffer from airway liquid retention. This reduces the lung's gas volume, increases the risk of lung injury and impedes the changes required for the lung to transform into an efficient gas exchange organ. It is not surprising, therefore, that respiratory failure at birth is the greatest cause of morbidity and mortality in newborn infants.

Despite the fundamental importance of lung aeration to survival at birth, little is known about this process because until recently, it could not be observed or measured. As a result, the ventilation procedures that most effectively aerate the lung are unknown, although this information is vital for the resuscitation and ventilation of infants that are born preterm. Using phase contrast (PC) X-ray imaging we can now observe and measure the rate and pattern of lung aeration from birth. PC X-ray imaging utilises refractive index variations (phase information) in addition to conventional absorption information to greatly improve image contrast of the lung [4,5]. As the air-filled lung is predominantly comprised of air (~80% by volume), surrounded by thin tissue structures (predominantly water), a marked difference in refractive index exists between the airways and surrounding tissue. When X-rays pass through the lung, the refractive index differences between air and water cause phase shifts in the propagated wavefronts and a change in their direction. The phase shifted wavefronts interfere with adjacent waves producing strong edge enhancement of the boundaries between air and tissue [4]. As the fetal lung is liquid-filled, it is not visible using phase contrast X-ray imaging, but rapidly becomes visible as the lung aerates after birth.

Our aim was to identify ventilation procedures that promote uniform lung aeration and facilitate pulmonary ventilation without causing injury to the very immature lung. In particular, we have examined the benefits of applying a positive end expiratory pressure (PEEP) to the lungs immediately following birth during the resuscitation period. Although the international guidelines for the resuscitation of very preterm infants does not recommend the application of PEEP, we hypothesised that PEEP is essential for proper lung aeration.

Rabbit pups were delivered prematurely (at 27 days of a 32 day gestation) by Caesarian Section, placed in a water-filled plethysmograph (head out) and were imaged while they were being ventilated. Pups were ventilated from birth using a set peak inspiratory pressure (PIP) and either no PEEP or a PEEP of 5 cmH_2O. The increase in tidal volume and lung gas volume at end expiration were observed and measured using PC X-ray imaging and plethysmography. In the absence of PEEP, all pups gradually developed an increasing tidal volume, but no pups were able to accumulate an end expiratory gas volume within their lung during the period examined (10-15 mins) (Figs. 1 and 2). As a result, the lungs collapsed at the end of each

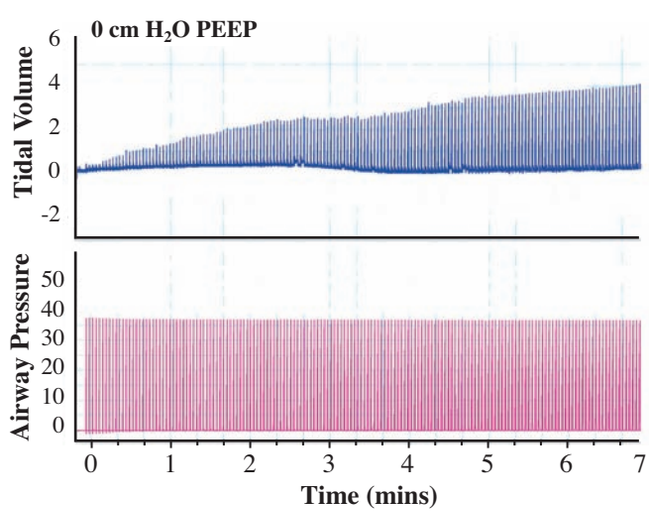

Fig. 1. Change in lung gas volume (top panel), measured using a water-filled plethysmograph, from birth in a mechanically ventilated prematurely delivered newborn rabbit pup. The pup was ventilated with a peak inspiratory pressure (PIP) of 35 cmH_2O and no (0 cmH_2O) positive end expiratory pressure (PEEP; bottom panel).

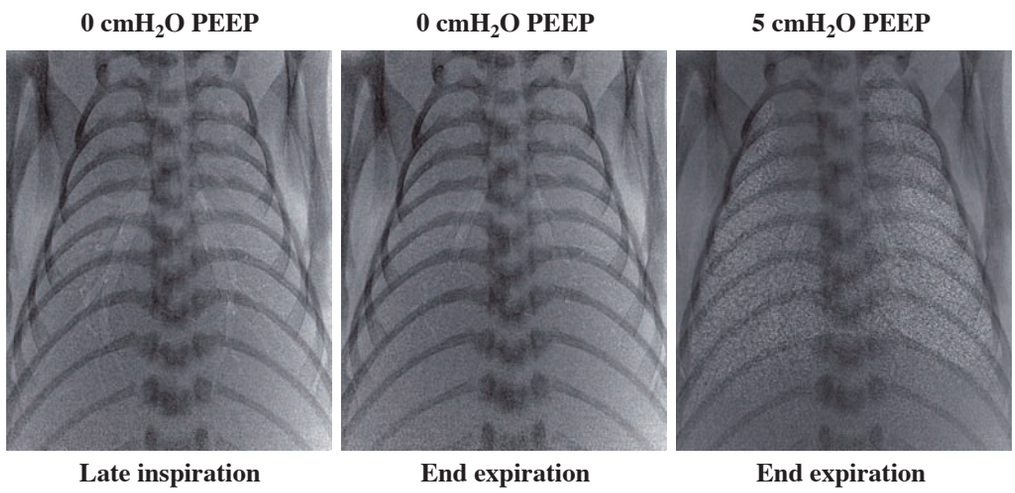

Fig. 2. Phase contrast X-ray images of prematurely delivered newborn rabbits mechanically ventilated from birth using a peak inspiratory pressure of 35 cmH_2O and either no (0 cmH_2O) positive end expiratory pressure (PEEP; left and middle images) or 5 cmH_2O of PEEP (right image). The two images (let and middle) acquired from a pup ventilated with 0 cmH_2O of PEEP where acquired at late inspiration (left) and end expiration (middle) and demonstrate lung collapse at the end of each breath.

expiration which is known to be very injurious to the lung; closure of the airways at end-expiration (vs mid inspiration) is clearly evident in the PC images (Fig. 2). In contrast, all pups ventilated with 5 cmH_2O of PEEP gradually accumulated an end-expiratory gas volume within the lung and, importantly, the lungs did not collapse at end expiration (Figs. 2 and 3); the increase was very similar to the increase measured previously in spontaneously breathing term pups [5].

Our observations demonstrate that the application of PEEP to very preterm infants that require ventilation at birth prevents lung collapse at end-expiration and, therefore, is less injurious to the lung than the application of no PEEP. These data will be used to change the International guidelines for the resuscitation and ventilation of very preterm infants.

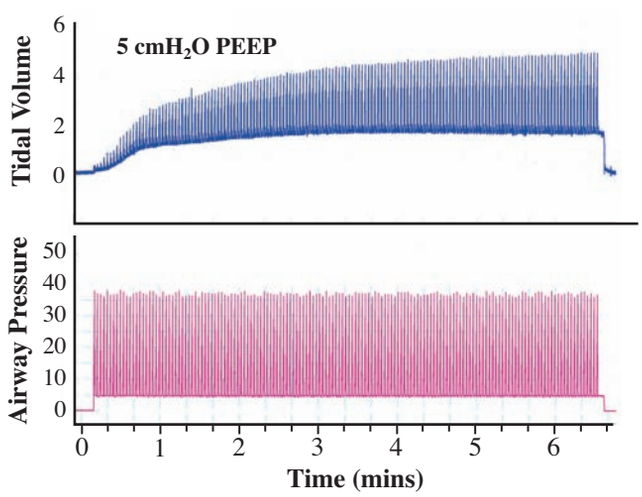

Fig. 3. Change in lung gas volume (top panel), measured using a water-filled plethysmograph, from birth in a mechanically ventilated prematurely delivered newborn rabbit pup. The pup was ventilated with a peak inspiratory pressure (PIP) of 35cmH_2O and 5 cmH_2O positive end expiratory pressure (PEEP; bottom panel)

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