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The first breaths of life: imaging studies of the human infant during neonatal transition

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EDUCATIONAL AIMS

The reader will appreciate the importance of imaging studies during neonatal transition with regard to:

- Facilitating our understanding of adaptive physiology during the birth process.
- Increasing our knowledge of the mechanisms of lung recruitment in the newborn.
- Assessing the benefit of neonatal interventions such as positive end expiratory pressure and surfactant administration.

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SUMMARY

The neonatal transition during birth is characterized by major physiological changes in respiratory and hemodynamic function, which are predominantly initiated by labor, lung aeration and clamping of the umbilical cord. Lung liquid clearance and lung aeration are not only important for the establishment of functional residual capacity, but these events also trigger the significant decrease in pulmonary vascular resistance and increase in pulmonary blood flow. Clamping the umbilical cord also contributes to these hemodynamic changes by increasing the systemic vascular resistance and sudden loss of a large proportion of venous return. This results in blood flow changes both through the foramen ovale and ductus arteriosus and eventually leads to closure of these structures and the separation of the pulmonary and systemic circulations. Most of the early theories describing neonatal transition are based on imaging studies of human infants from the 1900s. Some of these theories have been disproven in more recent studies using more accurate and non-invasive imaging techniques. This review will provide an overview of the theories suggested to explain the process of liquid clearance and lung recruitment and also addresses new findings in this field of research.

INTRODUCTION

Before birth the lungs are entirely filled with liquid, which is secreted by the pulmonary epithelium [1]. The lungs are not needed for gas exchange and the pulmonary vascular resistance (PVR) is high and pulmonary blood flow is low [2,3]. During labor the lung liquid will be partly reabsorbed as the release of adrenaline will activate the epithelial sodium channels and reverse the Na^+ flux and the osmotic gradient across the epithelium [4]. These epithelial sodium channels were also held responsible for lung liquid clearance right after birth for many years, but this has been challenged by recent studies [5].

At birth onset of breathing has to occur, characterized by large initial breaths followed by regular breathing, which are completely different from fetal breathing movements before birth. The lung liquid needs to be cleared and the lung aerated as functional residual capacity (FRC) is established [6]. Lung aeration triggers a decrease in pulmonary vascular resistance (PVR) leading to a sudden increase in pulmonary blood flow (PBF). Both the establishment of FRC and increase in PBF are needed for adequate gas exchange.

From the 1900s onwards X-ray imaging of human infants at birth has been used to investigate and explain the neonatal transition. Recently this field of research has been rediscovered

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[2,7] and imaging has been developed further to increase our understanding [8]. In this review we will provide an overview of these theories suggested to explain the process of liquid clearance and lung recruitment. Also, we will discuss recent imaging techniques that led to new insights into transition at birth.

PIONEERS IN PULMONARY IMAGING AT BIRTH

Between the 1850s and 1900s, X-ray imaging was used to investigate the mechanism of birth and the physiological changes that take place during this process [9,10]. Olshausen performed X-rays of infants passing through the birth canal and observed that the thorax is compressed in the birth canal which would cause expulsion of lung liquid [9]. In 1918, Warnerkros repeated this and verified that the thorax was indeed compressed during delivery [10]. The Swedish investigators Borell *et al.* [11] and Karlberg *et al.* [12] improved the imaging techniques and further developed theories to explain transition. Like Warnerkros, Borell described the shape and size of the fetal thorax and confirmed that thoracic compression takes place when the fetal thorax passes through the birth canal and the trunk is flexed. This has been named "the vaginal squeeze" and the increase in intrathoracical pressure would cause liquid removal through nose and mouth [11].

Currently, there is still a common belief among caregivers that the vaginal squeeze is important for lung recruitment [13]. However, the little resistance that the chest offers when it follows the head through the birth canal makes it unlikely that 'vaginal squeeze' significantly influences liquid clearance [14,15]. Postural changes during labor can cause lung liquid loss [16] and flexion of the fetal trunk during delivery, which causes an increase of abdominal pressure and elevation of the diaphragm, are more likely to cause liquid expulsion [11,13].

Many explanations of how air enters the lungs at birth have been suggested. After compression of the thorax in the birth canal, the release at birth would then cause a recoil of the chest and lungs as was suggested by Olshausen [9] and Borell [11]. The effect of this "thoracic recoil" on lung aeration has been visualized using X-ray imaging by Karlberg et al. [12] and simultaneously the volume displacement was measured using reversed plethysmography. The thoracic recoil directly after birth then would provide up to one third of the total FRC the infant needed for adequate gas exchange. The X-rays taken during and shortly after birth showed that aeration starts at the oropharynx followed by the lungs and this aeration was concordant with the "thoracic recoil" [12] (Figure 1) However, Saunders and Milner suggested that these observed volume changes may have been the initial breaths that were missed within seconds of delivery [17].

The idea of lung aeration, originating from the oropharynx, has been described by Bosma *et al.* as "frog breathing" or "glossopharyngeal breathing" [18]. Using "high speed" X-ray imaging directly after birth Bosma et al. noted distinct movements of the larynx and pharynx. He showed that after each breathing movement, which he described as an "engulfment of air", more gas was visible in the upper airways until it creates a positive pressure in the lungs and thereby causes lung aeration and increase of FRC [18]. The "glossopharyngeal breathing" could not be confirmed by Milner and Vyas who showed that a number of infants generated positive intrathoracic pressure prior to their first breath [19]. Although glossopharyngeal breathing has never been formally rejected as a potential mechanism, it is considered too slow and inefficient to make a substantial contribution to lung gas volumes.

After using an experimental setting with excised lungs, von Basch suggested in 1891, [20] that the increase in pulmonary blood flow after birth would cause "capillary erection" and this would be responsible for lung aeration at birth [21,22]. However, this was contradicted by Lind et al. showing that the first breath caused a marked chest movement associated with a sudden air filling of the lungs [23]. Using a radio-opaque substance administered through an IV-line and X-ray imaging he visualized that as soon as the lungs were recruited pulmonary blood flow increased [23]. However, experimental studies using a lamb model which was infused with marked spheres before birth [24,25] have shown that pulmonary vasodilation actually occurs in response to lung aeration, leading to a gradual reduction in pulmonary arterial pressure. This was confirmed by more recent research using a rabbit pup model and phase contrast X-ray imaging simultaneously with angiography and in lambs using flow probes around the pulmonary artery [8,26]. In these experiments it was shown that lung aeration triggers the increase in PBF [8,26].

Fawcitt et al. showed that the first inspiration of air resulted from contraction of the diaphragm, which was associated with dilation of the intrathoracic trachea and the movement of air into the posterior portions of the lung [27]. During expiration, some air remained in the lungs, and some closure of the pharynx-larynx was observed. Similar observations were made by Karlberg who described the first breaths as initially large inspirations, followed by a braked and slow expiration [28]. Research using imaging of fetal rabbit pup-models (described below) and observations in newborn infants [5,29,30] have confirmed these older observations. This breathing pattern is currently described as an "expiratory braking maneuver" [6,29]. This expiratory breaking is now known as an important mechanism for maintaining the FRC after birth. As the infants expires slowly across nearly closed vocal cords the pressure is increased in the lungs, which will prevent lung liquid from returning into the airways. te Pas et al. has recently shown that expiratory breaking is a mechanism which is frequently used, mostly by preterm born neonates, to enable them to defend the FRC gained during expiration [29,30]. Other breathing patterns such as crying and grunting are similar ways to slow down expiration and increase intrathoracic pressure [30].

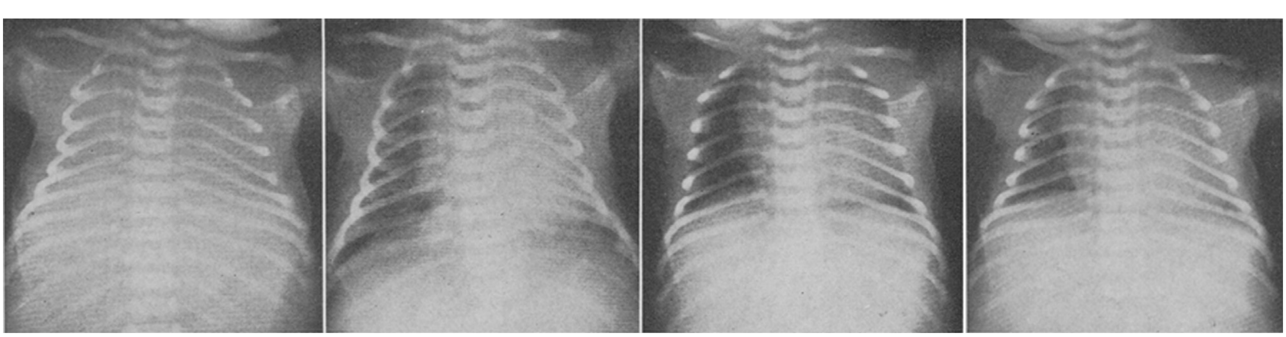

Figure 1. X-ray of aeration of the lungs during the first breaths of a term born infant [23].