From Liquid to Air: Breathing after Birth

Arjan B. te Pas, MD, Peter G. Davis, MD, Stuart B. Hooper, PhD, and Colin J. Morley, MD

The first breaths after birth are characterized by a rapid transition from liquid- to air-filled lungs. Air is drawn into the lung during inspiration, and some remains at end expiration to establish an end-expiratory gas volume or functional residual capacity (FRC). This is usually marked by a cry, often misinterpreted as a protest from the baby. Some infants, especially those born preterm, require respiratory support during this transitional phase. To do this effectively, we need to understand the normal physiological processes occurring at this time.

Sometimes it can be difficult to aerate the lungs of preterm infants with intermittent positive pressure ventilation with pressures recommended in international guidelines, particularly when the infant does not breathe and aeration is completely dependent on the inflation pressures. Studies have shown that intermittent positive pressure ventilation should be performed without high tidal volumes to avoid damaging the lung while establishing the FRC.[1,2] However, since the use of antenatal steroids, more very preterm infants breathe spontaneously at birth, only requiring support from nasal continuous positive airway pressure.

Understanding the normal spontaneous breathing pattern after birth is essential for developing safe, efficient ventilatory strategies when breathing is inadequate. Numerous physiological studies immediately after birth of spontaneously breathing infants were published between 1960 and 1986.[3-10] However, little new data are currently available on this topic, reflecting the difficulties of performing these studies. This review will discuss what happens during the first breaths of air with the emphasis on where the liquid goes and the current knowledge about the spontaneous breathing pattern adopted by infants immediately after birth.

CLEARING LUNG LIQUID

In utero the lungs are filled with a liquid that is secreted by the lung epithelium. The volume of liquid in the lung before birth is controversial, but the available evidence indicates that it is greater than the FRC measured soon after birth.[11] The high prenatal lung volume is due to adduction of the glottis restricting lung liquid efflux promoting its accumulation within the airways and increasing lung expansion. The high degree of lung expansion provides an essential physiological stimulus for fetal lung development.[12]

Although the precise mechanisms for airway liquid clearance at birth are unclear, the process starts just before or with the onset of labor.[13] It is well established that limited intrauterine space (as occurs during labor), impose changes in fetal posture that alter fetal chest wall configuration, increase transpulmonary pressure, and lead to the loss of large volumes of liquid from the lung.[14] In addition, a large release of fetal adrenaline occurs late in labor, which stimulates pulmonary epithelial cells to stop secreting and start reabsorbing lung liquid as a result of the activation of luminal surface sodium channels.[15,16]

Many studies have focused on the role of epithelial sodium channels in lung liquid reabsorption, and they have been the subject of several reviews.[16-19] At birth the pulmonary epithelium switches from facilitated Cl^- secretion to active Na^+ reabsorption with the opening of amiloride-sensitive Na^+ channels on the apical surface. This is believed to reverse liquid movement across the pulmonary epithelium, promoting liquid uptake from the airways into the interstitium.[20] Diminished activity or immaturity of this process may reduce the adaptation of the newborn lung to air breathing, contributing to wet lung syndrome and hyaline membrane disease.[17,18] However, the specific role of Na channel activation in lung liquid reabsorption at birth is still unclear. In animal studies, the blockade of epithelial Na^+ channels with amiloride and selective inhibition of β adrenergic receptors (proposed mechanism for Na^+ channel activation) reduces or delays, but does not prevent, lung liquid clearance at birth.[21] Similarly, although deletion of the gene encoding αENaC (but not βENaC or γENaC) impairs lung liquid clearance, as indicated

FRC	Functional residual capacity	NCPAP	Nasal continuous positive airway pressure

From the Division of Newborn Services, Royal Women's Hospital (A.T., P.D., C.M.), Carlton, and the Department of Physiology, Monash University (S.H.), Melbourne, Victoria, Australia.

Supported by a Ter Meulen Fund grant for working visits, Royal Netherlands Academy of Arts and Sciences, The Netherlands.

Submitted for publication Jul 5, 2007; last revision received Sep 19, 2007; accepted Oct 24, 2007.

Reprint requests: Arjan B. te Pas, The Division of Newborn Services, Royal Women's Hospital,132 Grattan Street, Carlton, Victoria 3053, Australia.

J Pediatr 2008;152:607-11

0022-3476/$ - see front matter

10.1016/j.jpeds.2007.10.041

by high lung water contents, the αENaC −/− neonates must establish some pulmonary gas exchange as they survive for up to 40 hours after birth.[22] Recent commentaries have highlighted the considerable evidence supporting a role for Na^+ uptake in alveolar fluid clearance, particularly under stimulated conditions, and the role of glucocorticoids, catecholamines, and oxygen in regulating the activity of this uptake.[18] But it has also been noted that additional mechanisms, independent of amiloride-sensitive Na^+ uptake are likely to be involved.[18]

Mechanical forces aid lung liquid clearance during labor. In 1917, Warnekros[23] used radiography to show that the thorax is compressed and stretched as the fetus is forced through the distal part of the birth canal. In 1962, Borell and Fernstrom[24] concluded that compression of the thorax and abdomen during birth must reduce lung volume and cause lung liquid expulsion. Between 1935 and 1956, German textbooks stated that as the respiratory tract is suddenly exposed at birth to the lower pressure outside the uterus, a jet of liquid is forced from the nose and mouth.[25] Measurements during delivery indicated that 25% to 33% of lung liquid could be expelled in this way.[26,27] Vyas et al[9] measured intrathoracic pressures during birth and found the maximum pressure averaged 145 cm H_2O (range 88 to 265 cm H_2O) but failed to show any loss of lung liquid. However, they reported that liquid escaped from the mouth before they could place a mask on the infant's face. They also compared infants born by elective caesarean section and vaginal delivery and found the esophageal pressure changes were halved during caesarean section. Furthermore, although the initial inspiratory volumes recorded in the 2 groups were similar, significantly fewer infants born by caesarean section retained air at the end of their first breath. This may reflect greater liquid retention within a lung of an infant born by caesarean section that had not been exposed to labor, thereby limiting the entry of air into the lower airways.[7]

Most early studies suggested that "vaginal squeeze" during the progression of the chest through the birth canal was the predominant mechanical factor influencing lung liquid loss at birth. However, uterine contractions during labor impose fetal postural changes, leading to compression of the thorax, which could account for the high intrathoracic pressures measured previously,[9] causing expulsion of lung liquid early in labor. Indeed, large volumes of lung liquid can be lost shortly after the first signs of labor, before the onset of the second stage.[13]

Whatever the mechanism for removal of liquid from the airways before birth, liquid still fills the airways after birth until the infant takes its first breath. A recent study used phased-contrast X-ray imaging to observe the rate and spatial pattern of lung aeration at birth in rabbit pups delivered by caesarean section.[28] The distal movement of the air/liquid interface only occurred during inspiration, indicating that the transpulmonary pressure generated by inspiratory efforts also plays a critical role in airway liquid clearance. Thoracic volume increased during lung aeration, indicating that the gas volume of the lung increased faster than the liquid could be cleared from the thorax. The conclusion was that the transpulmonary pressure gradient during inspiration promoted the movement of liquid into the interstitial tissue compartment from which it was gradually cleared, probably by the pulmonary circulation and lymphatic vessels. This suggestion is consistent with the finding that interstitial tissue pressures transiently increase at birth[29] and accounts for the increase in thoracic lymph flow observed in immature and term fetal sheep after the initiation of ventilation.[30,31]

CREATING AND SUSTAINING AN END-EXPIRATORY GAS VOLUME (FRC)

The normal FRC of about 30 mL/kg body weight is usually achieved within hours of birth,[32] taking 2 to 3 hours in vaginally delivered term infants and 5 to 6 hours in infants delivered by caesarean section.[33,34] Many explanations of how air enters the lungs at birth have been suggested. In 1901, Olshausen[35] suggested that thoracic recoil, caused by passive expansion of the chest at delivery, drew air into the lungs. This was supported by Warnekros[23] and Karlberg et al,[26] who measured inspiratory volumes of up to 29 mL before the first obvious spontaneous breath. However, Saunders and Milner[27] suggested that these observed volume changes may have been the initial breaths that were missed within seconds of delivery. Other proposed mechanisms include erection of the pulmonary capillaries leading to lung expansion and active inflation through contraction of pharyngeal muscles (glossopharyngeal respiration, "frog breathing").[36-39] However, the capillary erection theory was disproved by the finding of an immediate and dramatic decrease in pulmonary vascular resistance with inflation.[40] In addition, although glossopharyngeal breathing has never been formally rejected as a potential mechanism, it is too slow and inefficient to make a substantial contribution to lung gas volumes.

To understand the mechanics of creating and maintaining end-expiratory gas volumes in the lung, cineradiography[38,41] and recordings of breathing patterns[4,10,42] were performed in full-term infants. Fawcitt et al[41] 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. During expiration, some air remained in the lungs, and some closure of the pharynx-larynx was observed.[38,41] These studies and the more recent phase-contrast X-ray imaging of the lung[28] have demonstrated that the entry of air into the lung is dependent on the generation of a transpulmonary pressure created by inspiratory efforts; this mainly results from contraction of the diaphragm.

Measurements of respiratory activity in healthy term infants at birth indicate that it can take up to 30 seconds before the infant takes its first breath.[4,9,10,42] The first breaths tend to be deeper and longer than subsequent breaths and are characterized by a short deep inspiration followed by a prolonged expiratory phase. Commonly, expiratory flow is interrupted by a period of low or zero flow, ending in a short