Transition from fetus to neonate

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Abstract

This article provides an overview of the key physiological changes that take place as the fetus transitions to neonatal life. It provides and an overview of fetal transition with a focus on respiratory and cardiovascular changes.

Keywords Catecholamines; cortisol; CPAP; ductus arteriosus; lung fluid; pulmonary blood flow; surfactant; transition

Introduction

Fetal transition is a dynamic process with profound changes in physiology involving all systems. The key change is the establishment of breathing which is accompanied by concurrent changes in pulmonary flow as the fetus to an independent existence.

Respiratory transition

The transition from fetal to neonatal life requires fluid-filled lungs to be aerated, followed by initiation of pulmonary gas exchange as well as the conversion of fetal circulation into the adult form. Complex changes to fetal physiology happen within minutes of birth.[1] The vast majority of infants make this transition without any clinical intervention with fewer than and happen unaided in the over 90% of infants. Fewer than 10% of babies require some form of support and <1% require extensive resuscitation (e.g. as chest compression).[1]

Respiratory transition includes three main events: clearance of lung fluid; initiation of breathing; and surfactant production and distribution. Infants born preterm pose additional challenges related to size and end organ immaturity.

Clearance of fluid

In utero, the airways are filled with liquid that is secreted by the fetal lung, which then effuses through the trachea. Fetal lung growth and airway development are stimulated by lung distension.

During fetal life, the lung epithelium is in a secretory mode, mainly caused by active secretion of chloride ions. At birth, there is an urgent need for the newborn to clear this liquid rapidly in order to allow air entry and trigger the onset of gas exchange.

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Both mechanical and cellular mechanisms are required to achieve rapid elimination of this lung fluid. Recent literature has identified three different mechanisms to be responsible for clearance of this fluid:[2]

1. Uterine contractions during labour play a vital role by increasing the fetal abdominal pressure and forcing the fetal diaphragm upwards resulting in an increase in airway pressure. This increase in pressure results clearance of lung fluid via the trachea.
2. The change in maternal fetal hormonal milieu associated with impending delivery, including an upsurge in hormonal concentrations of glucocorticoids and adrenaline, the latter being further increased by the labour. Adrenaline stimulates the Na^+ reabsorption mechanism from the airways via activation of epithelial apical sodium channels. Once sodium is in the epithelial cells, this Na^+ is actively pumped out into the interstitium by Na–K–ATPase pump. Cl^- ions and water passively follow Na^+ into the interstitium. The high osmolarity of the interstitial fluid may play a part as well.
3. Most importantly perhaps, recent studies have shown that rapid clearance of large volume of lung fluid is initiated by an increase in transpulmonary (i.e. across the airway wall) pressure generated during inspiration or lung inflation. This pressure, observed to act only in inspiratory phase, provides a hydrostatic pressure gradient that drives the intra-alveolar liquid to move from the airways and into the surrounding interstitial tissue. This movement has been observed in rabbit models to be as fast as 35 ml/kg/hour, a rate much higher than possible by epithelial Na^+ channels. Once this fluid has been pushed into the interstitial compartment, the pressure in that compartment remains increased for at least 4–6 hours and then gradually comes down, drained by pulmonary vasculature (mainly) as well as lymphatics (approximately 15%).[2]

High compliance of the chest wall plays two important roles in this transition. It allows for the pressure from uterine contractions to be transferred to the thoracic cavity, resulting in partial clearance of fluid from airways, and it helps to accommodate the rapidly shifting fluid into the pulmonary interstitium.

Surfactant

Surfactant plays an important role in lung inflation by counteracting the surface tension, and thereby preventing the alveoli from collapsing. The absence of sufficient surfactant leads to neonatal respiratory distress syndrome (NRDS) characterized by widespread collapse and diffuses atelectasis of the lung, with plain X-ray showing small volume 'whiteout' lungs in its severest form.

The incidence and severity of RDS are inversely proportional to the gestational age of the baby. Type II pneumocytes within the lungs start producing surfactant at 22 weeks of gestation and the surfactant pool increases in size with gestational maturity. This is exemplified by the fact that surfactant pool in preterm babies with RDS is approximately 5 mg/kg compared with term neonates who have a pool of 100 mg/kg. Surfactant present in preterm babies also has proportionally lower quantities of phosphatidylglycerol and surfactant proteins.[3]

Surfactant production by type 2 pneumocytes is induced by antenatal corticosteroids. Antenatal steroids in preterm babies

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also improve the lung mechanics-improving the overall lung volume and compliance, allowing a better gas exchange. Antenatal steroids also induce pulmonary beta receptors. Catecholamines released during labour act through these receptors and stimulate the release of surfactants as well upregulates epithelial Na^+ channels, important for absorption of lung fluid after birth.[4]

Initiation of breathing

During fetal life, the fetus breathes mainly during REM sleep phase.[4] The stimuli for initiation of spontaneous breathing are ill-defined and are thought to be due to a combination of the removal of placenta-derived rapidly catabolized prostaglandins as a result of cord clamping, a drop in ambient temperature, a rise in PCO_2 and a catecholamine surge.[5] Unless severely hypoxic, the fetus moves into a pattern of regular spontaneous breathing soon after birth.

The initial breaths in spontaneously breathing newborns generate very high inspiratory (mean = −52, maximum up to −105 cm H_2O) and expiratory (mean = +71 cm) pressures with the average inspiratory tidal volume of approximately 40 ml. To generate the lung volumes seen in stable term newborn, they often employ expiratory braking, which is attempted exhalation against partially closed glottis. Expiratory braking is also used during initial cry to aid lung recruitment.[5]

Clinical relevance

Application of positive end expiratory pressure (PEEP) assists by providing an opposing pressure within the airspaces which counterbalances the high interstitial tissue pressure, preventing fluid re-accumulating in the airways in the absence of PEEP. In babies, unstressed by labour such as those born by caesarean section as well as those preterm babies where adrenaline mediated sodium transport is minimally effective, there is relatively more fluid in the airway which needs to be moved into the interstitium during initial inspiratory breaths. The clearing of this extra fluid would need higher inspiratory pressures; however, this in turn may result in an increased amount of interstitial, forming perivascular cuffs and fluid in the fissures. This increases the likelihood of the fluid re-entering the airways during the expiratory phase. CPAP provides continuous positive pressure in both phases of breathing and this forms the basis of its effectiveness in the treatment of infants with transient tachypnoea of newborn.

Apart from having a smaller surfactant pool, the lungs in preterm infants are more immature with fewer airspaces as compared to overall lung volume. Prompt administration of appropriate level of delivery room CPAP cannot only prevent the collapse of alveoli but also prevents interstitial lung fluid from re-entering the alveolar cavity. Endocrine changes following the birth of the unlaboured fetus (catecholamine release) as well distension of alveolar cavity causing stretch-induced deformations of type 2 pneumocytes, leads to the release of surfactants. This now forms a thin but functional layer of surfactant over alveolar surface, which stabilizes the lung volume in conjunction with CPAP.[6]

The lungs of preterm infants are fragile and are prone to injury if over distended. Six large volume breaths may be sufficient to cause lung injury. The role of the use of surfactant is well established. However, recent evidence supports the use of CPAP in the first instance in spontaneously breathing preterm infants. Several recent trials using either CPAP alone or a combination of brief intubation and surfactant installation followed by CPAP have shown benefit in reducing long-term lung disease.[7] Meta-analyses have also shown that for every 25 babies treated with CPAP in delivery room versus intubation, one additional newborn would survive to 36 weeks without broncho-pulmonary dysplasia.[7]

Cardiovascular transition

Lung aeration plays a pivotal role in initiating the complex cascade of events in cardiovascular physiology that are vital to a smooth transition.

Fetal circulation

In fetal life, the ventricles of the fetal heart pump in parallel as the right and left ventricle both contribute predominantly to the systemic circulation. Pulmonary vascular resistance (PVR) of the fluid-filled lung field is high and pulmonary blood flow is only 10% of this combined ventricular output. After birth, the initiation of pulmonary gas exchange triggers a significant decrease in PVR and increase in pulmonary blood flow (PBF). Most of the right ventricular output (~90%) flows pass through the ductus arteriosus (an embryonic connection between the pulmonary artery and aorta) into the aorta, contributing to systemic blood flow. The low resistance placental circulation at least receives 30–50% of combined ventricular output and contributes in similar proportion to the venous return to right side of the fetal heart through the umbilical vein. Up to 30–50% of oxygenated umbilical venous (PaO_2 of 32 mmHg, highest in fetal circulation) blood flows through the ductus venosus (a fetal connection between the umbilical vein and IVC allowing shunting of the oxygenated blood from the placenta to bypass the liver), passes up the IVC and through the foramen ovale (embryological opening between the right atrium [RA] and left atrium [LA]) to directly enter the LA. This serves two purposes: it provides a left-sided preload, and it results in pre-ductal cerebral circulation to be preferentially more oxygenated as compared with the post ductal arteries.

In fetal life, there are four important shunts: placenta, ductus venous, foramen ovale and ductus arteriosus. As soon as the cord is clamped, the systemic resistance is increased as the low resistance placenta is removed. Functional closure of ductus venosus (DV) occurs soon after birth, whereas structural closure requires longer, about 3–7 days in a term baby. This anatomical patency of DV is key for successful umbilical venous catheterization during first week of life.

Once the cord is clamped, the foramen ovale still remains an opening within the atrial septum covered by a flap valve. Functional closure is brought about soon after birth as the pulmonary vascular resistance decreases to allow more blood in the LA through the pulmonary veins. The increased pressure in the LA 'presses' the flap valve and impedes any flow of blood from the right to left side of the atria.

The ductus arteriosus (DA) is the last of these embryological shunts and often remains patent in preterm babies postnatally. However, in term babies, DA closes functionally within 10–15 hours of birth, mainly as a response to postnatal increase in saturation (PaO_2 25 mmHg in fetal life to 50 mmHg in postnatal life). This oxygen responsiveness of ductal tissue is related to

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