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# The Successful Immediate Neonatal Transition to Extrauterine Life

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**Abstract**

**Purpose:** To define and describe the processes underlying the successful neonatal transition to extrauterine life and methods to assess the transition. **Method:** Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, Web of Science, and Google Scholar were searched using a combination of the key words *neonate*, *neonatal*, *newborn*, *transition*, *respiratory* OR *pulmonary*, *cardiac*, *metabolic*, *pH*, *umbilical cord*, and *assessment*. Articles in English and German were reviewed. The final sample of articles consisted of one randomized controlled trial, 30 observational studies using human neonates, one observational study using rabbit pups, one secondary analysis, three systematic reviews, and 23 review articles. **Major Findings:** The pertinent findings in regard to normal events in the respiratory, cardiovascular, and metabolic transitions are reviewed and summarized. We address the underlying factors necessary for the transition to extrauterine life, specify the consequences of a successful transition, and review common assessment approaches. **Conclusion:** Available evidence indicates that the successful immediate transition to extrauterine life should be completed within 1–3 hr after birth, though some adaptive processes can fail as late as 24–48 hr after birth. Further research is necessary to identify a feasible, easily used, noninvasive method to assess the status of a neonate's transition to extrauterine life.

**Keywords**
neonate, transition, successful, immediate

The successful immediate transition to extrauterine life is a complex process (Hillman, Kallapur, & Jobe, 2012). Nevertheless, 90% of all neonates successfully transition from intrauterine to extrauterine life without any or only limited assistance (American Academy of Pediatrics [AAP] & American Heart Association [AHA], 2011). The establishment of air breathing and the remodeling of the cardiovascular system to a postnatal circulation are the most immediate steps in the neonatal transition; however, all organ systems undergo changes in the process (Askin, 2009; Hillman et al., 2012). The successful immediate transition to extrauterine life is poorly defined and poorly understood, despite the fact that it is a normal physiological process.

The vast majority of neonates are able to tolerate stressful ante- and intrapartum events, maintain homeostasis, and transition successfully to extrauterine life. However, they may use significant resources, such as glucose stores, to maintain this homeostasis. Understanding the processes involved in the transition to extrauterine life will facilitate recognition of small differences in neonatal outcomes associated with ante- or intrapartum events and advance research efforts to examine the potential effects of common intrapartum management approaches on the neonate.

At the time of birth, neonates undergo many compulsory adaptations that allow them to survive outside the uterus. The cessation of placental blood flow, coupled with thermal and tactile stimuli, is necessary to initiate the steps essential to transition from the intrauterine to the extrauterine environment (Askin, 2002). While some of these changes occur immediately, others can take weeks to be completed (Friedman, 1993; Graves & Haley, 2013; Vyas, Field, Milner, & Hopkin, 1986).

The successful immediate transition to extrauterine life can be defined as the successful transition to air breathing, cardiovascular remodeling, and independent glucose/energy management. However, there is no clear standard as to when neonates should have completed this process. Researchers have explored many of the gross physiological changes necessary for the neonatal transition, mainly through animal studies. Nevertheless, many intricacies of the neonatal transition that occur on the molecular and biochemical level remain to be understood (Hillman et al., 2012). Neonatal oxygenation, as well as hemodynamic stability, is as important to neonatal transition as are

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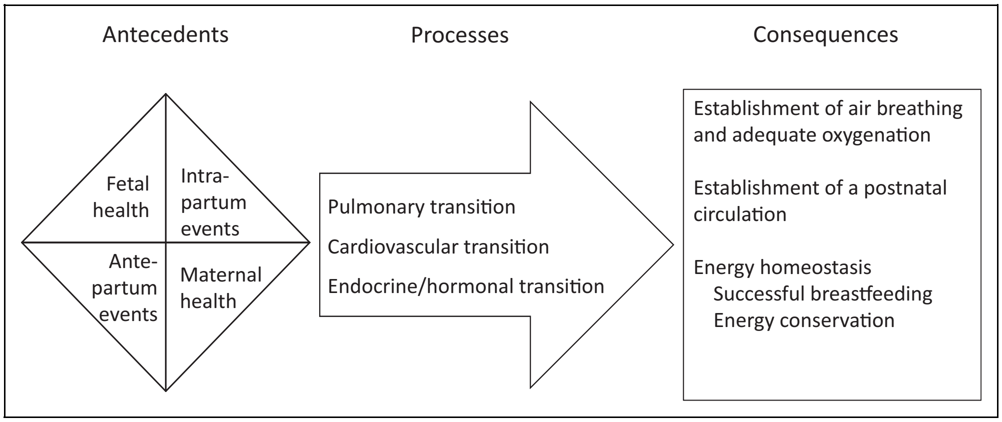


**Figure 1.** Neonatal transition to extrauterine life.

levels of hormones such as thyroid hormones, insulin, epinephrine, and cortisol. These factors influence and are coupled with others, including gestational age and mode of delivery. Furthermore, transitional events may affect levels of biomarkers such as cortisol and lactate, yet these biomarkers may also affect transitional events (Atasay, Ergun, Okulu, Akin, & Arsan, 2013; Duncan, 1999; Friedman, 1993; Janér, Pitkänen, Helve, & Andersson, 2011; Wiberg, Källén, Herbst, Åberg, & Olofsson, 2008). The purpose of this article is to describe the current scientific understanding of the processes comprising the successful immediate transition to extrauterine life, review potential antecedents, describe the consequences of these processes, and explore common approaches to assessing the neonate's transition (see Figure 1).

## Method

We searched Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, Web of Science, and Google Scholar using a combination of the key words *neonate*, *neonatal*, *newborn*, *transition*, *respiratory* OR *pulmonary*, *cardiac*, *metabolic*, *pH*, *umbilical cord*, and *assessment.* We reviewed articles addressing the immediate transition to extrauterine life written in either English or German. Initially, we considered both human and animal studies. Ultimately, we included only studies using human neonates with one exception (Lang et al., 2014). The final sample of articles consisted of one randomized controlled trial, 30 observational studies using human neonates, one observational study using rabbit pups, one secondary analysis, three systematic reviews, and 23 review articles.

## Findings

### *Respiratory Transition*

Hillman, Kallapur, and Jobe (2012) posited that the establishment of air breathing is the most critical element in the successful immediate transition to extrauterine life. The exact mechanism prompting neonates to take their first breath is unknown (van Vonderen, Roest, et al., 2014). It has been postulated that initiation of respirations is triggered by cessation of blood flow from the placenta and subsequent removal of circulating prostaglandins, tactile and thermal stimulation, and changes in partial pressure of oxygen and partial pressure of carbon dioxide levels. The neonate's initial step, beginning with the first breath, is to disperse the fluid that fills the fetal lungs prior to birth into the pulmonary interstitial spaces (te Pas, Davis, Hooper, & Morley, 2008). Continued breathing leads to development of functional residual capacity (FRC; Klaus, Tooley, Weaver, & Clements, 1962; Vyas et al., 1986) and an increase in peripheral capillary oxygen saturation ($SpO_2$; Rabi, Yee, Chen, & Singhal, 2006; Ullrich & Ackerman, 1972). These steps coupled with changes in the cardiovascular system are the basis for a successful immediate neonatal transition to extrauterine life.

In utero, the fetal lungs are fluid filled. Fetal lung fluid balance is controlled by multiple factors including corticosteroids, hypoxemia, and fetal breathing movements (Hooper & Harding, 1995). At the time of birth, fluid is cleared from the lungs, though the exact mechanisms for this process are unclear. Authors have presumed that a decrease in lung fluid secretion is combined with an increased expulsion of fluid via the trachea and absorption of the remaining lung fluid into interstitial lung tissue through sodium channels, leading to clearance of the lung fluid (Hooper, Siew, Kitchen, & te Pas, 2013; van Vonderen, Roest, et al., 2014). After birth, neonatal inspirations, crying, grunting, and braking maneuvers are thought to establish and maintain FRC. In their studies of rabbit pups, Lang et al. (2014) found that vascular changes in the lungs play a central role in the process of gas exchange with an increase in pulmonary perfusion with each breath after birth. With each subsequent breath, neonates dispel a little more fluid out of their lungs into the interstitial spaces until air reaches the distal alveoli and pulmonary gas exchange commences.

A neonate's first breath after birth is generally the longest and deepest breath (Fisher, Mortola, Smith, Fox, & Weeks, 1982). This first breath and the following two to three breaths require the most inspiratory work (Karlberg, Cherry, Escardó, & Koc, 1962). These breaths clear fluid out of the neonatal lungs and establish FRC (Helve, Pitkänen, Janér, & Andersson, 2009; Katz, Bentur, & Elias, 2011). In their study of 12,000 healthy neonates, Ersdal, Linde, Mduma, Auestad, and Perlman (2014) found that neonates initiated spontaneous respirations in 10.8 $\pm$ 16.7 s. This finding supported those from earlier studies of a mean time to first breath as 10.8 $\pm$ 8.9 s (Vyas et al., 1986) and time to first clinically visible breath of 0–16 s (Karlberg et al., 1962) in cohorts of 16 and 18 term healthy neonates born vaginally, respectively. Karlberg et al. described that some mothers received nitrous oxide during labor or chloroform shortly before giving birth that may have affected time to onset of respirations in the neonate. The FRC continues to increase over the next 30 min of life after the initial respirations (Klaus et al., 1962), though at a slower rate, after which it remains stable (Karlberg et al., 1962).

Neonates' respiratory rates and patterns following birth are highly variable. Fisher, Mortola, Smith, Fox, and Weeks (1982) recorded breathing patterns in 41 neonates birthed at term at 10, 60, and 90 min and 1 and 5 days of age. They noted that during the immediate period after birth, defined as 10–90 min, the neonates showed deep breaths combined with short periods of breath holding, a maneuver aimed at increasing FRC (Hooper et al., 2013). The authors also found that variability in the respiratory pattern was significantly greater at 10 min of life when compared to the variability in the pattern at 90 min of life and later ($p < .05$; Fisher et al., 1982).

Authors have estimated that human neonates take between 4 (about 20 s; Ullrich & Ackerman, 1972) and 11 breaths (about 30 s; Chou, Ullrich, & Ackerman, 1974) before adequate gas exchange is established as determined by serial cord-blood gas analysis. A. P. Harris, Sendak, and Dinham (1986) studied blood oxygen saturation using pulse oximetry levels in 32 term singleton neonates born vaginally in vertex presentation. They determined that the neonates had an oxygen saturation of 61 $\pm$ 5% at 1 min of life, which increased to 81 $\pm$ 2% around 7 min after birth. Using pulse oximetry, Rabi, Yee, Chen, and Singhal (2006) assessed the oxygen saturation of 45 neonates $\geq$35 weeks' gestation born vaginally and not requiring supplemental oxygen. These neonates reached median blood oxygen saturations measurements (interquartile range) of 91% (82–95%) at 8 min of life.

The most critical task of the immediate neonatal transition to extrauterine life is the clearance of lung fluid and the establishment of air breathing. Neonates take their initial breath within a few seconds after birth; however, it may take up to 30 min to establish a stable FRC. Furthermore, they need up to 90 min to establish a stable, regular respiratory pattern and rate. Therefore, neonates who achieve oxygen saturation levels >90% within the first 10 min of life and demonstrate adequate gas exchange, respiratory patterns, and respiratory rate within the first 90 min of life appear to have made a successful respiratory transition to extrauterine life.

## Cardiovascular Transition

The successful cardiovascular transition to extrauterine life includes the removal of the placenta and a shift from a parallel to an in-series circulation. Furthermore, the pulmonary vascular resistance decreases while the systemic vascular resistance increases. This shift is followed by the remodeling of the fetal circulation into a postnatal circulation through the closure of the fetal shunts, namely, the ductus arteriosus (DA), foramen ovale (FO), and the ductus venosus (DV). In utero, fetuses receive nutrients and oxygen from their mothers through placental exchange from maternal to fetal blood. About 50% of the oxygenated fetal blood returning to the fetus from the placenta flows past the fetal liver (DV) and through the inferior vena cava into the right atrium. Deoxygenated blood returned from the fetal head and extremities enters the right atrium through the superior vena cava, but flow patterns within the atrium prevent the blood from completely mixing. About two thirds of the blood in the atrium—mainly the oxygenated blood—is shunted through the FO to the left atrium and ventricle to perfuse the coronary arteries and the brain. The remaining blood flows into the right ventricle from where it is ejected toward the lungs. Due to vascular resistance in the pulmonary arteries, this blood flows through the DA into the descending aorta, circumventing the lungs (Friedman, 1993; Graves & Haley, 2013; van Vonderen, Roest, et al., 2014).

The transitional changes of the cardiovascular system, coupled with the pulmonary transitional events, lead to a change from placental gas exchange to pulmonary gas exchange and changes in heart rate (HR), stroke volume (SV), and left ventricular output (LVO; Azhibekov, Noori, Soleymani, & Seri, 2014; Friedman, 1993). The cardiovascular system has to remodel simultaneously with the respiratory system to balance oxygen delivery with the oxygen requirements of the tissues (Azhibekov et al., 2014). Some of these changes happen in the first few minutes of life, while others can take several days to complete (Hines, 2013; van Vonderen, Roest, et al., 2014).

In utero, the fetal DA and FO guide blood away from the lungs through the heart to the brain and back to the placenta, effectively bypassing the pulmonary circulation. As blood flow through the placenta ceases (i.e., through vascular constriction and/or cord clamping), the neonate's systemic vascular resistance increases while the pulmonary vascular resistance decreases—a mechanism necessary to facilitate pulmonary perfusion (van Vonderen, Roest, et al., 2014). These changes in pressure gradients lead to functional closure of the DA and FO.

Authors have presumed the DA's closure to be mediated by the increase in neonatal oxygenation and a withdrawal of prostaglandin E2, though the exact pathways are unknown (Coceani & Baragatti, 2012). DA closure begins shortly after birth with significant decreases in DA patency as early as 2–5 min after birth (van Vonderen, te Pas, et al., 2014), though it may still be patent at 4 hr of life (Alenick, Holzman, & Ritter, 1992; Popat & Kluckow, 2012). By 24−48 hr of life, the DA appears to have closed in almost all healthy neonates (Agata et al., 1991; Alenick et al., 1992; Walther, Benders, & Leighton, 1993).

Blood flow through the FO decreases immediately after birth (Alenick et al., 1992) due to an increase in left atrial volume caused by an increase in pulmonary venous return

(Friedman, 1993). It closes functionally when pressure in the left and right atria are approximately equal. Hannu, Pentti, Henrik, Markku, and Ilkka (1989) completed five serial cardiac ultrasounds in 37 healthy, term neonates over the first 48 hr of life. At 24 hr of age, 22 neonates continued to have a patent FO but did not have any differences in blood pressure, cardiac output, HR, or other hemodynamic variables compared to neonates without a patent FO. Follow-up examinations in 20 of these neonates showed that one had a structurally patent FO at 1 year of age without hemodynamic consequences.

The workload of the left ventricle increases immediately after birth while the workload of the right ventricle decreases as the right ventricular afterload lessens due to a decrease in pulmonary vascular resistance (van Vonderen, te Pas, et al., 2014). Researchers have observed significant increases in LVO within 2–5 min after birth (van Vonderen, te Pas, et al., 2014) with a peak in cardiac output around 1 hr of life (Agata et al., 1991; Walther et al., 1993) followed by a decrease and subsequent stabilization in LVO between 8 (Walther et al., 1993) and 24 hr of age (Agata et al., 1991).

A neonatal HR of 100 beats per minute (bpm) is considered the threshold for a successful immediate neonatal transition to extrauterine life and guides neonatal resuscitation (Apgar, 1953; Wyllie et al., 2010). However, the neonatal HR immediately after birth is affected by gestational age, mode of delivery, maternal anesthesia, and the timing of cord clamping (before or after onset of spontaneous respirations). It may take several minutes for a healthy neonate to achieve a HR of >100 bpm (Baik et al., 2015). This observation is supported by Dawson, Kamlin, Wong, and colleagues (2010), who assessed neonatal HR in 468 term and preterm neonates immediately after birth. Median (Interquartile Range [IQR]) HR for the full cohort was 96 bpm (65–127 bpm) at 1 min of life. It took neonates an additional 30–60 s to reach HRs of >100 bpm, especially if they were born preterm.

The DV closes passively within a few days after birth due to a decrease in venous return after the blood flow through the umbilical cord ceases (Friedman, 1993). The closure of this shunt has no known immediate effect on the cardiovascular transition to extrauterine life.

Multiple adaptive changes have to occur in the cardiovascular system to support the successful immediate neonatal transition to extrauterine life. In order to successfully transition, neonates must maintain a threshold HR of 100 bpm to adequately transport oxygenated blood to tissues (Wyllie et al., 2010). According to current practice, they are expected to achieve this HR at 1 min of life; however, this value has been set arbitrarily without supporting prospective clinical data. Another adaptation is the functional closure of the DA and the FO, as previously described, which is important for the neonate's hemodynamic stability. Healthy neonates are able to tolerate a delay in shunt closures as long as they are able to increase their cardiac output. Finally, LVO output is greatest at about 1 hr of life. Therefore, the immediate cardiovascular transition to extrauterine life appears to be completed around 1 hr after birth, although stabilization of cardiovascular function including functional closure of the fetal circulatory shunts continues for 24–48 hr after birth.

## Glucose/Energy Management During Transition

In utero, fetuses depend on maternal glucose supplies to provide adequate energy resources. With the cessation of placental blood flow, neonates are forced to balance their metabolism independently through calorie intake (e.g., via breast-feeding) to meet their energy needs (e.g., thermoregulation).

Neonatal body temperature may be an objective indicator of the successful neonatal transition to extrauterine life. Neonates function within a narrow range of body temperature; however, that range is specific to each individual neonate and can be affected by the neonate's behavioral state. Researchers have reported neonatal rectal and axillary temperatures to be 36.5–37.5 °C and 35.6–37.0 °C, respectively (Freer & Lyon, 2011). In order to maintain body temperature in this range, neonates depend on outside factors such as room temperature or maternal skin temperature but also on their ability to mobilize internal energy sources, such as glucose, lactate, or brown fat. Neonates use multiple interrelated fuel sources, including glucose, lactate, and pyruvate but also different fatty acids and ketones to maintain their metabolism (D. L. Harris, Weston, & Harding, 2015; Hawdon, Ward Platt, & Aynsley-Green, 1992).

Glucose and lactate are important fuel sources for all organ systems in the body. Glucose is a mandatory fuel source for the central nervous system, yet it is transformed into lactate during anaerobic conditions (D. L. Harris et al., 2015; Zanardo et al., 2015). Hypoglycemia at the time of birth and immediately thereafter may affect neurological and motor development (Adamkin, 2011; Boluyt, van Kempen, & Offringa, 2006). Neonatal glucose levels during the first few hours of life are associated with maternal glucose levels at the time of birth (Heck & Erenberg, 1987; Ward Platt & Deshpande, 2005). Srinivasan, Pildes, Cattamanchi, Voora, and Lilien (1986) reported mean neonatal glucose levels of 56 $\pm$ 19 mg/dl (17–119 mg/dl) at 1 hr of age in 52 neonates born vaginally to healthy mothers. Of the sample, $10-15\%$ were breast-fed, while the remaining neonates received 20 kcal/oz formula. All neonates in this study had glucose levels $\geq$40 mg/dl at 4 hr of age. Heck and Erenberg (1987) also reported low glucose values at 1 hr of life, with values between 36 and 99 mg/dl (5th–95th percentile) in 114 neonates, of which 95% were born vaginally and the remainder via Cesarean section. Glucose levels at the 5th percentile did not rise above 40 mg/dl until $20-28$ hr after birth. Of these neonates, 60 were breast-fed, while the remainder received 20 kcal/oz formula. Initial feedings were delayed 2 hr and 4 hr after birth, respectively.

The amount of energy needed to maintain homeostasis is different for each neonate and depends on a variety of factors including birth weight, gestational age, and energy usage during labor as well as other intrapartum and environmental factors. The individual variability in energy consumption and maintenance makes it difficult to assess the successful immediate neonatal transition to extrauterine life in regard to energy homeostasis. On the other hand, neonates who display behaviors such as jitteriness, tachypnea, poor muscle tone, lethargy, or poor feeding behavior may be hypoglycemic and thus having difficulty with energy homeostasis and their transition to extrauterine life (Adamkin, 2011; Jain et al., 2008).

Based on the available research, it is difficult to assign a specific timepoint at which a neonate should have successfully metabolically transitioned. As outlined above, neonatal glucose levels may nadir around 1–3 hr of life, but neonates are still at risk for developing hypoglycemia at 20–28 hr of life (Heck & Erenberg, 1987). Therefore, if neonates do not display behaviors indicative of neonatal hypoglycemia by 1−3 hr of life, it may indicate that the immediate transition to extrauterine life has been successful, though further observation is necessary.

## Antecedents to the Neonatal Transition

A multitude of additional factors, both internal and external to the neonate, may affect the successful transition to extrauterine life. These antecedent factors can be classified as maternal health, antepartum events, fetal health, and intrapartum events (Figure 1). We will touch on some of these factors briefly as a thorough review is beyond the scope of this article.

Maternal health before and during pregnancy is linked to neonatal outcomes. Maternal age, spacing of pregnancies, nutritional status, chronic conditions such as diabetes or hypertensive disorders, illicit or prescription drug use, alcohol use, tobacco use, maternal weight, as well as the presence of infection can affect fetal well-being (Bhutta, Lassi, Blanc, & Donnay, 2010; Lassi, Majeed, Rashid, Yakoob, & Bhutta, 2013). In a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health, Abalos et al. (2014) found that 2.73% of women were diagnosed with hypertensive disorders (chronic hypertension [2.16%], preeclampsia [0.28%], and eclampsia [0.29%]). Neonates of women diagnosed with preeclampsia or eclampsia were 4.51 (4.23−4.80) and 6.57 (5.60−7.71) more likely to be delivered preterm, respectively, than neonates born to women without these diagnoses. The odds ratios (*OR*s) for these neonates to be admitted to the Neonatal Intensive Care Unit (NICU) were 3.45 (3.21–3.71) and 7.83 (4.48–9.45), respectively. Another example of maternal health affecting the neonatal transition to extrauterine life is maternal diabetes. D. L. Harris, Weston, and Harding (2015) studied 35 hypoglycemic neonates. They found that neonates born to diabetic mothers were more likely than neonates born preterm or small for gestational age to have insulin concentrations larger than the median 1.2 μU/ml (78% vs. 26% vs. 40%, respectively, $p = .04$), thus putting them at higher risk for continued hypoglycemia than the remainder of the study sample.

Factors such as genetic anomalies, premature birth, and situational factors can also affect the transition to extrauterine life. A knot in the umbilical cord may increase the risk of premature birth and lower 1- and 5-min Apgar scores (ASs; Räisänen, Georgiadis, Harju, Keski-Nisula, & Heinonen, 2013). Another example is otherwise healthy neonates who are born prematurely. Depending on the level of prematurity, these neonates may not be able to increase their LVO or adequately oxygenate their blood as necessary for a successful cardiopulmonary transition (Azhibekov et al., 2014).

Finally, intrapartum events such as maternal breathing patterns and oxygenation status affect cord-blood oxygenation status (Roemer, 2007), mode of delivery (Cesarean section vs. vaginal birth) influences neonatal cortisol levels and thus ability to respond to stress (Olza Fernández et al., 2013), and exogenous oxytocin administration during labor alters breastfeeding behavior in the neonate (Olza Fernández et al., 2012). Even the timing of an intervention as routine as clamping the umbilical cord affects the neonatal transition, as outlined by Ersdal et al. (2014). The researchers found that clamping the umbilical cord before rather than after the onset of spontaneous respirations significantly increased the risk of neonatal death ($OR = 4.53$; 95% CI [1.92, 9.58], $p = .0005$). Smit et al. (2014) evaluated $SpO_2$ and HR values in 1-min intervals in 109 healthy neonates who transitioned normally without interventions other than routine care. The attending midwives delayed cord clamping and initiated immediate skin-to-skin contact between neonates and their mothers. The researchers noted significantly higher $SpO_2$ levels 1–3 min after birth ($p < .01$–$p < .001$) and significantly lower HR 2–10 min after birth (all $p < .001$) when compared to reference ranges defined by Dawson, Kamlin, Wong, et al. (2010) and Dawson, Kamlin, Vento, et al. (2010).

The neonatal transition to extrauterine life is dependent on a multitude of interconnected factors that may hinder or facilitate the transition. Researchers have focused on the unsuccessful transition to extrauterine life to provide a baseline understanding of when intervention is needed. However, understanding the consequences of a successful immediate transition will allow for recognition of a normal transition for which no intervention is required.

## Assessment of the Transition

A multitude of factors alone and in combination with each other can affect the immediate neonatal transition to extrauterine life. Researchers have explored many of the necessary adaptive processes through animal studies using rabbits and lambs, leaving open the question as to whether such findings are applicable to human neonates. The majority of human neonates, of course, are able to transition successfully.

There is currently no tool whose purpose is to assess the immediate neonatal transition to extrauterine life. The AS, a tool commonly and inappropriately used for this purpose, was originally developed to assess the neonatal response to resuscitation and was later used to assess a neonate's need for resuscitation (Apgar, 1953; Apgar, Holaday, James, Weisbrot, & Berrien, 1958). Clinicians no longer use the AS to determine the need for neonatal resuscitation (AAP & AHA, 2011), yet the score is routinely documented in the neonate's medical record at 1 and 5 min after birth.

As outlined above, HR is one noninvasive measure to assess the successful immediate neonatal transition to extrauterine life because it is an indicator of successful ventilation. A neonatal HR of 100 bpm is considered the threshold for a successful immediate neonatal transition and guides neonatal resuscitation (Apgar, 1953; Wyllie et al., 2010), although, as discussed above, this value may have been set arbitrarily. A rapid increase in HR over 30−45 s indicates effective ventilation in the neonate and should be used as the primary indicator to assess the need and the effectiveness of any resuscitative measure (Perlman, Kattwinkel, Wyllie, Guinsburg, & Velaphi, 2012; Wyllie et al., 2010).

Other noninvasive measures to assess the immediate transition to extrauterine life include neonatal oxygen saturation, cardiac output, SV, blood pressure, carbon dioxide production, end-tidal carbon dioxide levels, lung–tidal volumes, and tissue perfusion (van Vonderen, Roest, et al., 2014). For example, respiratory-function monitors in the delivery room may facilitate the assessment of tidal volumes, peak airway pressure, positive end expiratory pressure, and respiratory rate in ventilated as well as spontaneously breathing neonates (Schmölzer et al., 2010). However, factors such as gestational age, delayed lung fluid clearance, or neonatal sepsis may affect the result of the assessment tools (van Vonderen, Roest, et al., 2014). Furthermore, technical requirements may prevent the use of a particular assessment tool (e.g., echocardiography) in every delivery room (van Vonderen, te Pas, et al., 2014), making its clinical use to assess the transition to extrauterine life in healthy neonates impractical. Finally, it must be noted that noninvasive does not mean nonintrusive. Any equipment that requires moving healthy, normally transitioning neonates away from their mothers could interfere with the normal transition to extrauterine life and early bonding.

Currently, there are no nonintrusive, comprehensive, clinically usable tools that assess the successful immediate transition to extrauterine life other than general clinical observation. Imaging studies, like echocardiograms or X-rays, or assessment of biomarkers are potentially invasive, intrusive, and focus on isolated events in the neonatal transition. The ideal tool would be nonintrusive, so as not to distract mother or neonate immediately after birth, and be based on easily identifiable and recognizable neonatal behaviors.

## Conclusion

The successful neonatal transition to extrauterine life is a complex, yet obligatory, event in a human's life. Based on available evidence, the successful immediate transition to extrauterine life should be completed within 1–3 hr after birth, though some adaptive processes can fail as late as 24–48 hr after birth. However, due to the wide variability among neonates and within individual neonates, the expected range of normal for some transitional processes may not apply to all neonates. None of the processes or antecedent factors we have described in this article affects the neonatal transition in isolation. Rather, it is the combination of these processes and factors that either facilitates or hinders the neonatal transition to extrauterine life. The multitude of possible events makes it difficult to isolate a single factor responsible for a successful transition. Future research may provide an understanding of the relationships among biomarkers, physiological events, and neonatal behaviors that will facilitate recognition of the successful immediate transition to extrauterine life.

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