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Neonatal Transitional Physiology: A New Paradigm

Judith S. Mercer

Rebecca L. Skovgaard

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Early clamping of the umbilical cord at birth, a practice developed without adequate evidence, causes neonatal blood volume to vary 25% to 40%. Such a massive change occurs at no other time in one's life without serious consequences, even death. Early cord clamping may impede a successful transition and contribute to hypovolemic and hypoxic damage in vulnerable newborns. The authors present a model for neonatal transition based on and driven by adequate blood volume rather than by respiratory effort to demonstrate how neonatal transition most likely occurs at a normal physiologic birth. Key words: *capillary erection, cardiopulmonary adaptation, the first breath, hypovolemia, neonatal blood volume, neonatal transition, nuchal cord, placental transfusion, polycythemia, postpartum placental respiration, umbilical cord clamping*

Judith S. Mercer, CNM, DNSc, FACNM
Associate Clinical Professor
University of Rhode Island
Kingston, Rhode Island

Rebecca L. Skovgaard, CNM, MS
Associate in the Department of
*   Obstetrics and Gynecology*
University of Rochester at Highland
*   Hospital*
Rochester, New York
Assistant Professor in the School
*   of Nursing*
University of Rochester
Editorial Staff, Strong Perifax

CURRENT ANALYSIS OF knowledge related to neonatal transitional physiology reveals that early cord clamping may interfere with completion of a normal physiologic neonatal transition. An end result of this interference with transitional physiology is a 25% to 40% reduction in the neonate's blood volume.[1,2] In other circumstances over the life span, such a massive restriction in blood volume would result in severe consequences, even death. Human babies are remarkably adaptable, and in most cases no apparent harm is initially evident. However, practitioners are obligated to establish a rationale for early neonatal management and then to apply it in practice. The existing evidence suggests that the intervention of early cord clamping evolved without adequate evidence-based rationale and, accordingly, is deserving of careful scientific review.[3] The debate remains: what is optimal care—what do all babies need initially? Do some babies experience

harm because of inadequate blood and red cell volume? Synthesizing knowledge from several disciplines, this article presents a new model for explaining physiologic neonatal transition that promotes an alternative view about placental transfusion and the importance of delayed cord clamping in the first minutes of life. The application of this model to practice may lead to benefits for all newborns and may be especially important for compromised infants who do not have adequate perfusion.

Two factors, the singular role of the red blood cell (RBC) in the body and the idea that a significant reduction in RBCs at birth does no harm, must be explored in examining any relationship between neonatal transition and cord clamping interval. In recent years, advances in physiological measurement tools and understanding of physiologic and pathologic processes have been made that may substantiate the evidence against early cord clamping. Application of this new knowledge to the issue of fetus-to-neonate transition argues for a reformulation of current practice and presents a rational basis for optimal clinical practice. Of key importance are these two facts: that the only oxygen-carrying component in the body is the RBC,[4] and that, in a typical approach to early neonatal management today, immediate cord clamping, a reservoir of RBCs is routinely, according to tradition, discarded with the placenta. The problem occurs when oxygen delivery is the primary concern in neonatal illness. These include respiratory distress syndrome, persistent pulmonary hypertension, necrotizing enterocolitis, and hypoxic-ischemic encephalopathy. Discovery of any potential relationship of the pathologic processes of these conditions to essential hypovolemia in the newborn has been hampered by the fact that there is no reliable, available, clinically useful measure for RBC or blood volume in the neonate.[2] The lack of evidence to guide practice, the assumption that early cord clamping can "do no harm," and the relative connection that the RBC is the only transporter of oxygen lead to the conclusion that reexamination of the consequences of early versus delayed cord clamping is warranted.

The second key issue in explaining the normal neonatal transition is the rationale for the establishment of breathing. Traditional views for causality of first breath have focused exclusively on the respiratory and neurological system.[5–8] These theories have claimed asphyxia at birth, touch, cold and sensory stimulation, frog breathing, and chest recoil as potential explanations for the first breath.[7,8] These theories were developed prior to the discovery that fetuses perform breathing movements in utero. None of these explanatory theories have held up to scrutiny upon closer examination.[9] While early cord clamping appears to hasten an infant's first breath, severely depressed babies do not breathe spontaneously—an interesting paradox worthy of investigation. Alternate analysis and synthesis of current knowledge can produce a more plausible model for the pathways to successful extrauterine respiration.

LITERATURE REVIEW

In the last decade, there has been a resurgence of interest in the issue of optimal cord clamping time and its effect on neonatal transition. Recent studies show the benefits of delayed cord clamping as improving the neonate's cardiopulmonary adaptation,[10] blood

Table 1. Effects of placental transfusion on human neonatal systems in the first 6 hours after birth

Blood volume/Component measures	
• Blood volume[17–21]	+
• Red cell mass[17–21]	+
• Plasma volume[17–19,21]	+
• Hematocrit[15,16,21–24]	=, +
Vascular pressures	
• Atrial pressure[25]	+
• Pulmonary artery[26]	+
• Systolic blood pressure[11,12,23]	+
Blood flow	
• Right and left ventricular output[21]	=
• Renal blood flow[27]	+
• Cutaneous blood flow (skin temperature)[28]	+
• Systemic and pulmonary resistance[10,29]	+
• Blood viscosity[10,21,30]	+
• Vascular hinderance[10]	−
• Red blood cell flow[10]	+
• Cerebral red blood cell flow[10]	+
• Gastrointestinal red blood cell flow[10]	+
Other cardiac effects	
• Heart rate[26,31]	=
• Cardiac size[23]	+
• EKG signs of cardiac load[22]	+
• Preejection period[22,32]	+
• Murmurs[23]	−
Renal function	
• Effective renal blood flow[27]	+
• Glomerular filtration rate[27]	+
• Urine flow[27]	+
• Urinary sodium excretion[27]	−
Respiration	
• Respiratory rate[31,33]	+
• Lung compliance[33,34]	−
• Function residual capacity[33,34]	−
• Expiratory grunting[31]	+

Key: + = increased; − = decreased; = = no change found.

pressures,[11–13] oxygen transport and red blood cell flow,[10,14] days on oxygen and ventilation,[15] and anemia.[16] Earlier studies demonstrated consistent physiological effects in newborns.[17–34] Table 1 summarizes the findings.

What is not agreed upon by clinicians and researchers is the meaning of the

findings—are they harmful or beneficial? Delayed cord clamping seems to prevent shock-like parameters and anemia (refer to Table 1). However, concerns exist about volume overload and polycythemia.[35–37] Unfortunately, the wide range of study designs and definitions of variables prevents a meaningful meta-analysis of the studies. An additional shortcoming is that few studies evaluate outcomes beyond the first few hours after birth. The volume of diverse studies and the lack of an organizing framework for understanding this research thwart any attempt to synthesize the literature or direct further knowledge development. A theoretical model for the transition from fetus to neonate is essential to establish the blueprint for understanding this critical physiologic process. A gap exists because no current model for neonatal transition adequately explains the relationships among oxygen transport, RBC volume, and initiation of breathing, or predicts the effects of early versus delayed cord clamping.

The goal of a theoretical model is to connect and find meaning in a group of related concepts for the purpose of understanding, describing, or explaining a phenomenon.[38] Such models provide and dictate hypotheses for research. Testing and further development may lead to prediction of outcomes and prescription for practice. Clinical sciences need prescriptive models to guide interventions and to provide underlying rationale for

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practice.[39] The development and use of models to direct research reduces the risk that a single factor, examined out of context, will direct interventions. The following situation-specific model presents a description of and explanation for the physiologic processes of normal neonatal transition.

The hypothesis proposed is that a successful neonatal transition is dependent upon a newborn having an adequate *blood* volume to recruit the lung for respiratory function through capillary erection and an adequate *red cell* volume to provide enough oxygen delivery to stimulate and maintain respiration. The mechanism that initiates fetal breathing in utero is currently unknown, but it is thought to be sensitive to oxygen.[9,40] This same oxygen-sensitive mechanism is the more likely candidate to begin and maintain neonatal breathing at birth. Capillary erection may also be important for other vulnerable structures in the neonate's body. The explanation of origins for this model rests upon the development of an adequate blood volume in the neonate—a substantially greater blood volume than is necessary for the fetus during intrauterine life, when maternal "life support" obviates the need for much fetal organ function.

This model for successful neonatal transition takes into account the research findings related to timing of cord clamping and the evidence for physiological mechanisms underlying this dramatic transition to life after birth. The model is diagrammed and the relevant documentation to support the model is summarized.

OVERVIEW OF THE MODEL

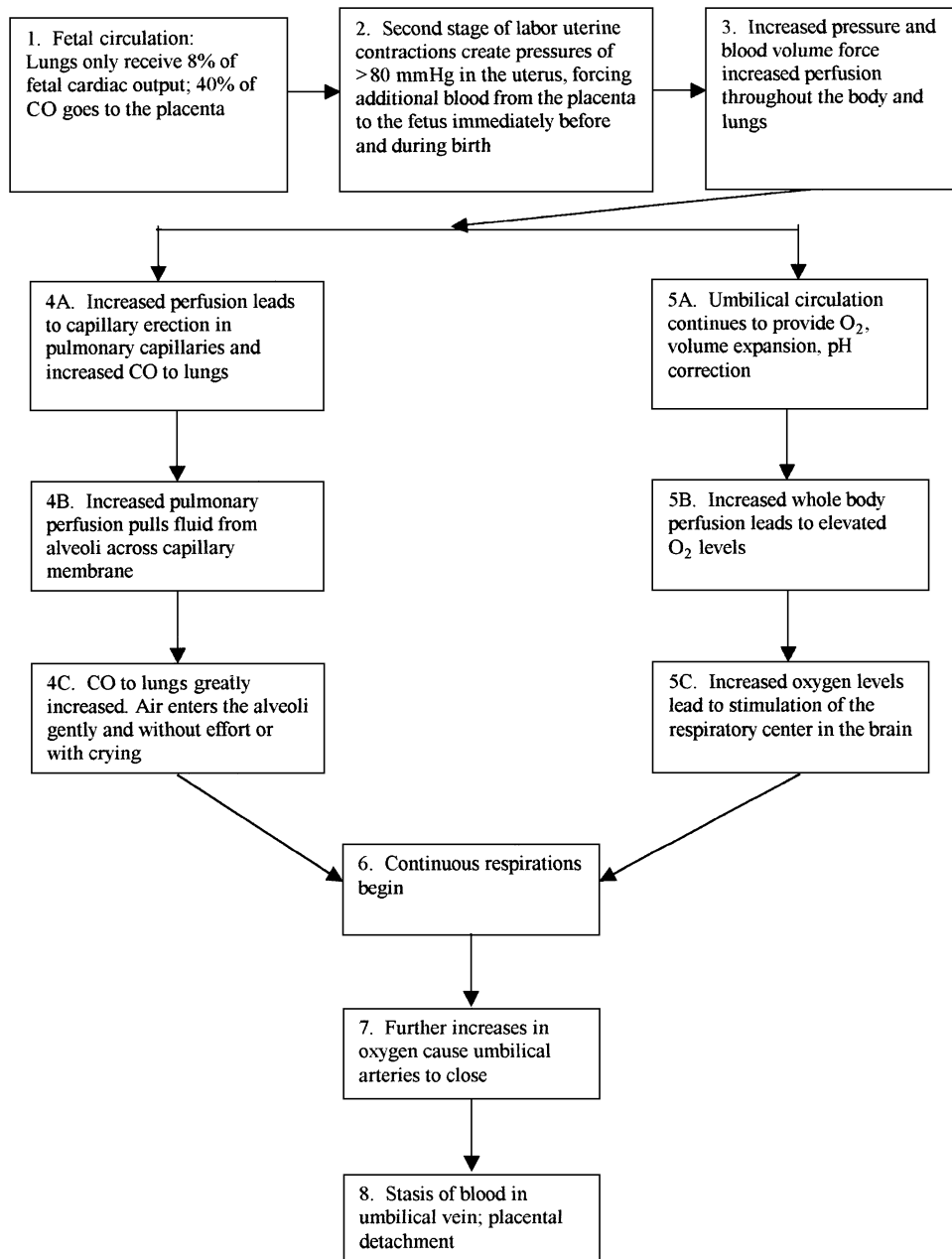Figure 1 presents an overview of the Blood Volume Model for physiologic

| 1. Fetal circulation: Lungs only receive 8% of fetal cardiac output; 40% of CO goes to the placenta | 2. Second stage of labor uterine contractions create pressures of >80 mmHg in the uterus, forcing additional blood from the placenta to the fetus immediately before and during birth | 3. Increased pressure and blood volume force increased perfusion throughout the body and lungs |

| 4A. Increased perfusion leads to capillary erection in pulmonary capillaries and increased CO to lungs | 5A. Umbilical circulation continues to provide O_2, volume expansion, pH correction |

| 4B. Increased pulmonary perfusion pulls fluid from alveoli across capillary membrane | 5B. Increased whole body perfusion leads to elevated O_2 levels |

| 4C. CO to lungs greatly increased. Air enters the alveoli gently and without effort or with crying | 5C. Increased oxygen levels lead to stimulation of the respiratory center in the brain |

6. Continuous respirations begin

7. Further increases in oxygen cause umbilical arteries to close

8. Stasis of blood in umbilical vein; placental detachment

Fig 1. The blood volume model for physiologic neonatal transition.

neonatal transition. The following paragraphs detail the processes summarized in the model.

In the fetal state, one third to one half of the fetal-placental blood volume is in the placenta (Step 1). The essential process of respiration, gas exchange, takes place in the placenta. Within the fetus, the pulmonary circulation receives only 8% of the cardiac output (CO). The vast majority of blood volume contained within the fetus supports systemic circulation. There is no apparent indication that demands for systemic circulation decrease at the time of birth. In fact, the opposite is most likely true, as the gut and all other organs gain increased function at birth. A dramatic increase in pulmonary circulation occurs, demanding 40% to 55% of the neonatal CO for extrauterine respiration. This transition requires a redirection of the CO and an increase in blood volume if adequate perfusion to other vital structures is to be maintained.

During birth, the uterine myometrium contracts around the emptying uterine cavity, causing compression of the placenta and transfer of blood to the fetus/neonate (Step 2). Second stage contractions generate intrauterine pressures of 80 to 100 mmHg and force blood from the placenta to the fetus. This process is dependent on three factors: (1) a patent umbilical vein; (2) a decrease in the blood volume remaining in the placenta; and (3) an increase in the corporal fetal/neonatal blood volume, blood pressure, and oxygen levels. The rise in fetal/neonatal blood pressure (due to increased blood volume, Step 3) overrides the high pulmonary vascular resistance to begin the process of lung recruitment via capillary erection (Step 4). Increased blood pressure and blood flow cause the erection of alveolar capillaries that support the alveolar structure and recruit the lung tissue.[41] Essentially, a capillary network surrounds each alveolus as a collapsed, fluid-filled sphere in the fetal state. When the capillary network is perfused at birth, hydrostatic pressure expands the sphere secondary to increased pressure from full expansion (erection) of the capillary plexuses covering each alveolus. Each alveolus, attached to the capillary network through elastic fibers in the extracellular matrix, is passively pulled open to an expanded state (see Fig 2) allowing effortless entry or air (Step 4C).[42]

The alveolus is further made ready for the first breaths as lung fluid diffuses across the alveolar-capillary membranes, driven by the higher colloid concentration within the capillaries (Step 4B). When the unclamped umbilical cord continues to pulsate, it allows the newborn to equilibrate blood volume, oxygen levels, and pH through ongoing placental exchange (Step 5A). The increased red blood cell flow raises the level of oxygen (Step 5B), stimulating the respiratory center to initiate breathing—exactly the same mechanism used to initiate fetal breathing movements in utero (Steps 5C and 6). Compression of the placenta continues as the uterus empties, transferring more of the placental-fetal blood to the baby. Gas exchange and acid-base adjustment may continue during this transition. When the oxygen level in the newborn's venous blood is elevated from 15 mmHg (fetal levels) to 36 mmHg, the normal extrauterine level, the umbilical arteries close, shutting down any further blood flow from the infant's body to the placenta (Step 7). The next few uterine contractions may squeeze a small amount of additional remaining blood through the umbilical vein to the infant, ensuring maximum RBCs for oxygenation and normal infant blood volume.
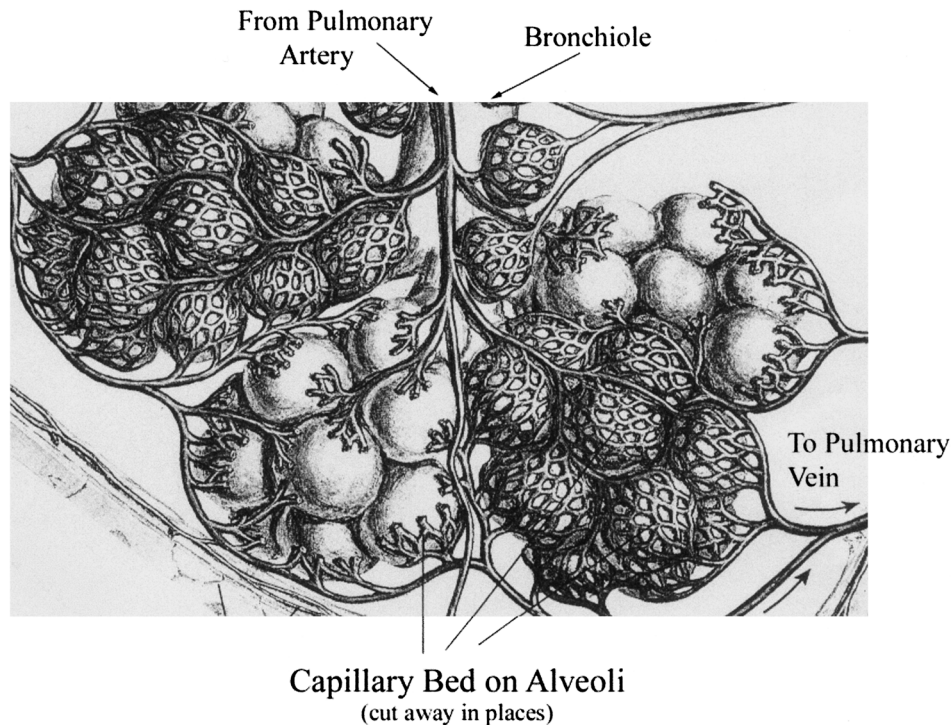
Fig 2. Schema of respiratory unit: relationship of alveoli and capillary plexuses. *Source*: Copyright, 1999. Icon Learning Systems, LLC, a subsidiary of Hava MediMedia USA Inc. Reprinted with permission from ICON Learning Systems, LLC, illustrated by Frank H. Netter, MD. All rights reserved.

Documentation and support for each step in the model follow.

Documentation and References for Model

The following section presents the rationale, documentation, and references for the processes in the model shown in Figure 1. Each process in the model is reiterated before discussion. Although creation of a model allows for conjecture, most of the concepts included here are well documented in published studies. By necessity, each step in the model is discussed as though it happens in linear order, although, in fact, the model functions in a recursive pattern until equilibrium is reached.

Step 1: In the fetal state, 40% of the CO goes to the placenta while only 8% goes to the fetal lungs.

In the fetal state, one third (full-term) to one half (pre-term) of the blood in the fetal-placental circulation (FPC) at any point in time is in the placenta fulfilling the respiratory function of gas exchange.[2,17] Within the fetus, the circulation to the lungs receives 8% to 10% of the CO. A dramatic increase of 32% to 47% in respiratory circulation occurs at birth, demanding 40% to 55% of the CO. Adequate perfusion of both the respiratory and systemic circulations in the neonate requires a partial transfusion of the placental blood volume to the neonate.

Step 2: Second stage uterine contractions create pressures of 80 mmHg or more in the uterus, transferring blood volume to the fetus.

Caldeyro-Barcia and colleagues[43] documented uterine contractions of approximately 80 mmHg pressure within the uterine cavity as the fetus descends into the birth canal. This pressure, exerted intermittently on the placenta acts to force additional placental blood into the fetus during contractions before and immediately after birth while still allowing for fetal-maternal exchange between contractions.[44] As the uterus extrudes the fetal head (one fourth of fetal mass) and body, it effectively compresses the placenta, causing more of the fetal-placental blood volume to transfer to the infant. The pressure of 80 mmHg is equal to Jaykka's findings that pressures of 80 mmHg are required to overcome the pulmonary vascular resistance in cadaverous fetal lungs[45,46] (see below).

Step 3: Increased pressure on the placenta forces increased perfusion and begins to open the pulmonary vessels.

Increased uterine pressures of second stage labor and birth may begin the process of increasing perfusion.[43] Yao, Hirvensalo, and Lind documented increased placental transfusion in babies after maternal contractions.[44] Higher atrial and pulmonary artery pressures were found in late-clamped (LC) versus early-clamped (EC) infants in the first few hours after birth, demonstrating increased perfusion and more pulmonary capillary filling in the LC infants.[25,26]

Step 4A: Increased perfusion leads to capillary erection in the pulmonary vessels.

Jaykka's[45,46] physiologic adaptation theory of capillary erection in the lungs offers a logical explanation for the phenomenon of lung recruitment at birth.

Jaykka concluded that, at birth, the sudden entry of blood under pressure into the pulmonary capillaries that surround each alveoli causes the alveoli to become individually symmetrically erect (recruited), thus easing entry of air. Jaykka designed an experiment to test the process of inflation using accompanying microscopic anatomy of the lung from stillborn infants and fetal lambs. He tested the effect of inflation alone, the effect of forcing dye through the pulmonary artery to mimic pulmonary perfusion, and a combination of these two methods.
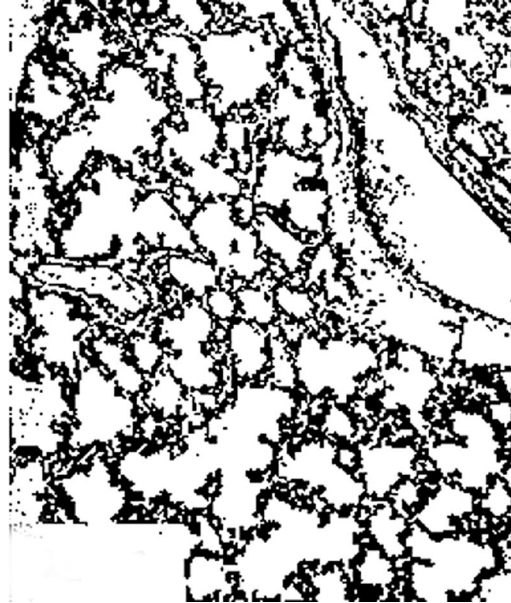
First, he inflated the lungs with air alone and found that the expansion did not proceed uniformly. He had difficulty injecting the India ink to mimic capillary circulation when he attempted to do so after the inflation. On microscopic examination, alveolar walls were found to be irregular and thin in shape and stretched around globular air spaces with considerable areas remaining unstained (unrecruited), as demonstrated in Figure 3. Next, in other lungs, he forced India ink in the pulmonary artery at 80 mmHg pressure and found that the capillary system in the excised lung became rigid or erect from the liquid forming a framework that supported the respiratory unit. The resulting microscopic picture resembled that of a normal aerated lung (see Fig 4). Last, he injected the India ink under pressure first and then inflated the lungs. He needed much less pressure to inflate the lungs when the vascular system was already distended with the India ink. With these "perfused" lungs, he was able to inflate so much air that the lungs became buoyant. The microanatomical picture of these lungs resembled those of a normally aerated lung and was similar to the lung that had been
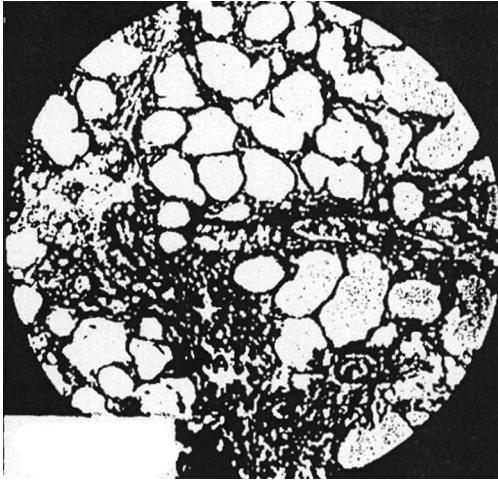
Fig 3. Inflation with air. Note irregular distension with over-distended alveoli in one area and atelectasis in other areas. *Source*: Reprinted with permission from *Acta Paediatr*; 47, Jaykka S. Capillary erection and the structural appearance of fetal and neonatal lungs, 484–500, 1958.

Fig 4. Thin section from lung with forced capillary distension using India ink. *Source*: Reprinted with permission from *Acta Paediatr*; 47, Jaykka S. Capillary erection and the structural appearance of fetal and neonatal lungs, 484–500, 1958.

experimentally treated with only liquid injected into the vascular system under pressure (refer to Fig 5). He concluded that this process of *capillary erection* is an essential step in normal neonatal cardiopulmonary adaptation. In a modification of this experiment, Avery[47] also found that lungs were easier to inflate at lower pressures if they were first perfused. These studies support the concept that the establishment of normal neonatal respiration is based on the adequate flow of blood into the lung bed.

Recent studies detailing ultrastructural development of the lung in rats from fetal through neonatal stages seem to verify Jaykka's work and, if anything, suggest that adequate pulmonary blood flow maintains an important role in effective respiratory function from birth to some time after.[48] In the rat lung, which is often used as

a model for the study of human lung structure and function, three morphological phases precede the development of a mature, alveolar lung. At term and for the first few days after birth, the terminal lung is in a saccular phase, with relatively smaller air spaces and thick intrasaccular septa containing multiple capillaries (see Fig 6). Not until seven days of life does the typical alveolar structure begin to develop, with thin intra-alveolar septa in which there lies a single capillary in contact with the air space on each side of the septum. The thick, vascular septa present at birth and for the following week may play an important role in the structural support of respiratory function in early neonatal life and may be similar to what Jaykka saw
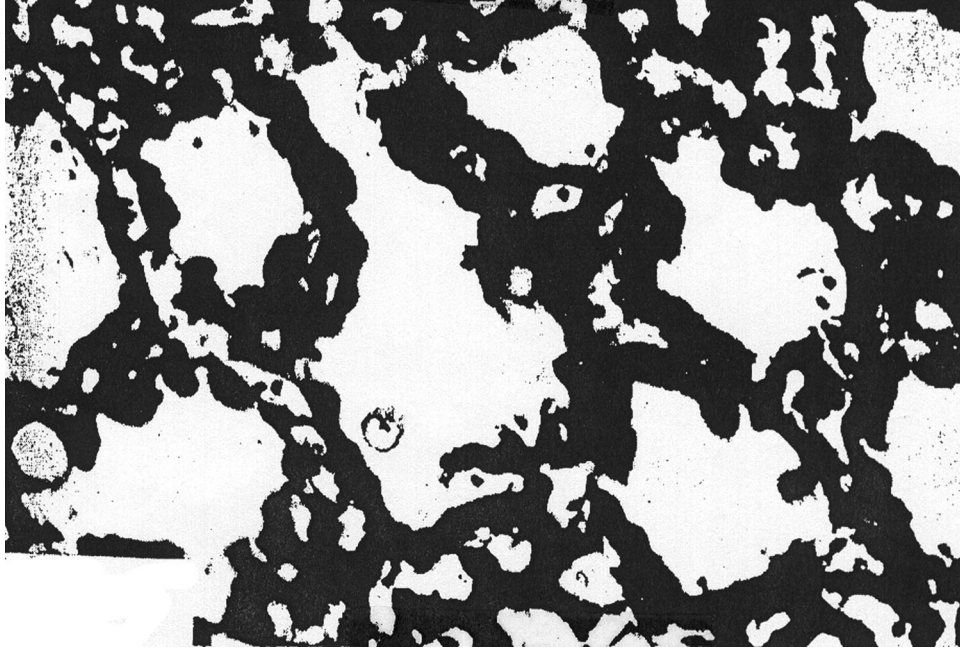
Fig 5. Capillary erection. Note distended, full capillaries bulging into the alveolar spaces. *Source*: Reprinted with permission from *Acta Paediatr*; 47, Jaykka S. Capillary erection and the structural appearance of fetal and neonatal lungs, 484–500, 1958.

in his experiments (refer to Fig 4 and Fig 5). Progress to normal alveolar structure and function may rest upon adequate pulmonary blood flow. Further, the efficiency of gas exchange across the thick intrasaccular septa would necessarily be lower than that in a mature alveolar lung and would likely function best in the presence of generous pulmonary blood volume.

Step 4B: Increased pulmonary perfusion pulls lung fluid from the alveoli across the capillary membrane.

Fetal lung fluid, which is in essence amniotic fluid, contains very little protein and has a low colloid osmotic pressure. Once the capillaries are filled with blood, which has a high colloid osmotic pressure, the alveolar fluid is rapidly absorbed into the pulmonary capillaries. The fluid has to cross only one alveolar cell and one blood capillary cell, constituting a distance of less than 2 μm (refer to Fig 2).[49] Thus, the process of capillary erection is probably an essential part of the rapid change from the "wet" lung of the fetus to the "dry" lung needed by the neonate for gas exchange. Capillary erection may be the stimulus for the lung to change both structure and function immediately at birth

> *Capillary erection may be the stimulus for the lung to change both structure and function immediately at birth from an organ of fluid secretion to an organ of gas exchange.*
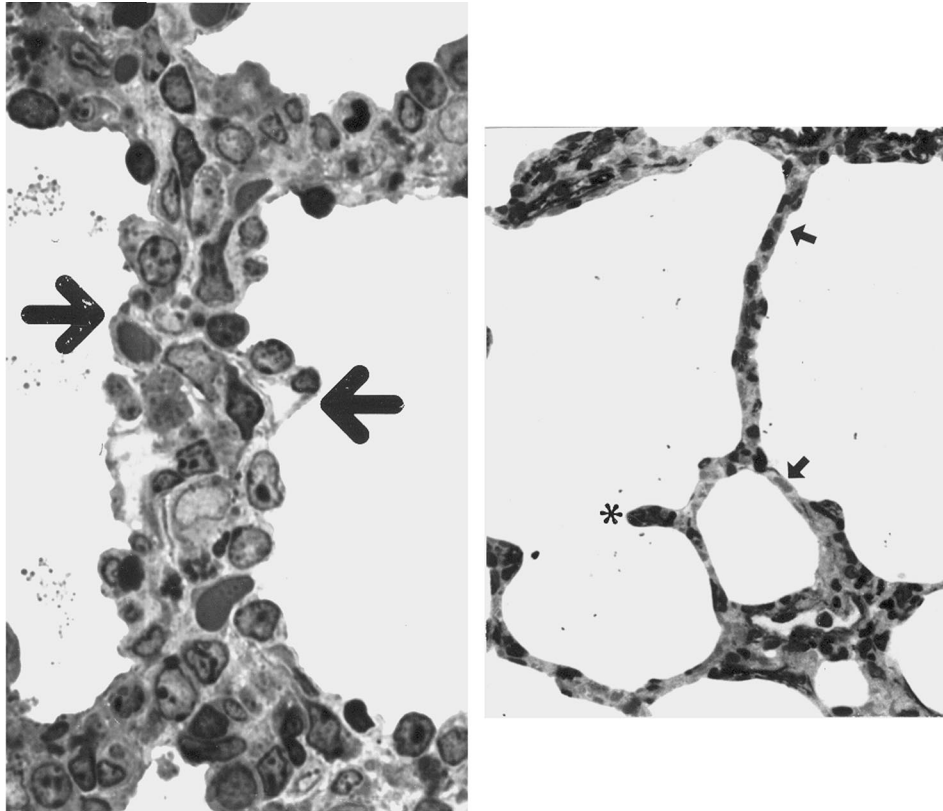
Fig 6. Left: the lung of a 2-day-old rat newborn with saccular structure. Intrasaccular septa are thick with capillaries located on both sides of the septa (large arrows). Right: Lung of a 21 day old rat newborn with alveolar structure. Alveolar septa are mainly thin; they accommodate only one capillary (small arrows). Original magnification X 400. *Source*: Reprinted with permission from *Folia Histochemica et Cytobiologica*, 36(1). Wasowicz M, Biczysko W, Marszalek A, Yokoyama S, Nakayama I. Ultrastructural studies on selected elements of the extracellular matrix in the developing rat lung alveolus, 3–13, 1998.

from an organ of fluid secretion to an organ of gas exchange.[9]

Step 5A: Umbilical circulation continues to provide oxygenation, volume expansion, and pH correction.

Significant blood flow in the umbilical cord after birth can be palpated easily and has been documented. Stembera and colleagues[50] developed a unique method to study the actual volume of blood flow through the human umbilical cord in the first few minutes after birth. From 113 measurements of thermodilution taken between 20 and 265 seconds after birth in 17 neonates, they were able to document blood flow of 248 mL/min in the average 3 kg newborn (approximately 75 ± 7 mL/min per kilogram). In the first 100 to 120 seconds, the rate of flow did not change in comparison with the first

reading at approximately 20 to 40 seconds. After 1.5 to 2 minutes, they found a marked decrease of flow in most, but not all, cases. In distressed infants, they recorded a flow of 50 mL/min per kilogram.[51] This study supports the idea that the transition to extrauterine respiration may be made gradually and without undue stress, as the neonate is able to rely on blood flow through the placenta for oxygenation during the first minutes of life while blood volume is equilibrating.

Yao and Lind[18] clearly documented the increased blood volume that occurs when the umbilical circulation is left intact. They estimated that 50% of the transfusion occurs within one minute if the infant is at the level of the introitus and 100% by 3 minutes. Lowering the baby at least 30 cm speeds the transfusion so that maximum transfusion occurs in 1 minute. This additional blood volume has been shown to increase perfusion,[52] raise blood pressure,[11,12] and increase RBC delivery to the vital organs.[10] Higher blood pressures have been consistently documented in preterm and full term babies with delayed cord clamping by several sources in older[23,24] and more recent studies.[11,12] Arcilla et al[26] have shown higher pulmonary artery pressures along with higher blood pressures in babies with delayed clamping.

Steps 5B and C: Increased systemic perfusion leads to elevated oxygen levels that initiate continuous respiration.

Increased perfusion leads to better capillary distention,[52] higher blood pressure,[11–13] and additional RBCs to carry maximum oxygen.[18] Increased oxygen levels have been shown to stimulate continuous fetal breathing movements in utero while the administration of low oxygen gas mixtures to the ewe caused fetal breathing to cease.[40] Ventilation of fetal lambs with 100% oxygen initiated continuous breathing.[9] "Breathing [movements] can occur in the fetus [lamb] in the absence of transient hypoxemia to stimulate the chemoreceptors and without any of the sensory stimuli thought to be important for the establishment of continuous breathing at birth."[9(p 1122)] It is probable that this adaptive process continues after birth to assist in initiating breathing in the neonate. Babies who are well-perfused breathe spontaneously while pale, limp infants require resuscitation and often intubation. While this information appears counterintuitive, suppression of breathing by low oxygen levels may be a physiologic response in a stressed infant, assuming uninterrupted umbilical circulation. In this circumstance, the infant can rely on the placenta for essential oxygenation while circulatory corrections are made to establish adequate pulmonary perfusion effecting capillary erection before breathing.

Steps 4C and 6: Air enters erect alveoli gently or with crying and continuous respirations begin.

With placental gas exchange supporting the neonate immediately after birth, the first breathing efforts may develop gradually and gently. Immediate cord clamping may stimulate earlier, more aggressive breathing efforts; however, these efforts are likely to be ineffective at gas exchange and in fact may be counterproductive.[53]

A major hypothesis of this paper is that time to accomplish capillary erection is essential for adequate lung perfusion. Capillary erection appears to be essential to the process of establishing extrauterine respiration. This is consistent with the finding that babies with delayed cord clamping have been found to take the first breath later than babies with early cord clamping.[54] Evidence for this

hypothesis is found in the work of Marquis and Ackerman,[53] who devised a technique to examine placental respiratory function in the immediate neonatal period. They clamped one umbilical artery (UA) immediately after birth and measured blood gases. They clamped the second UA up to 37 seconds after birth and found no change in the blood gases, even though several babies had breathed over six times. They concluded that little gas exchange takes place in the neonate's first few breaths. Dunn[55] reported higher 5-minute Apgar scores in a group of babies with delayed clamping when compared to a similar group who had early clamping. Thus, when the cord is left intact, the baby's first cry may not occur until there has been adequate transfer of blood volume to recruit the lung, fully perfuse the body, and stimulate the respiratory center with the higher oxy-gen levels. Even in babies who cry earlier, the first breaths are not effective at gas exchange.[53]

Step 7: Increased oxygen levels cause closure of umbilical arteries and umbilical circulation ceases.

The umbilical arteries, but not the vein, are sensitive to oxygen and will close when adequate oxygenation is achieved. Figure 7 compares cross sections of early and late clamped umbilical cords showing closure of the umbilical arteries after cord clamping at 3 minutes.[56] McGrath et al[57] examined sections of the umbilical cord exposed to oxygen and found that the arteries, but not the vein, were sensitive to oxygen at 36 mmHg. After birth, oxygen tension in the venous circulation (umbilical arteries) increases from the fetal level of 15 mmHg to the neonatal level of 40 mmHg. This rise in venous oxygen
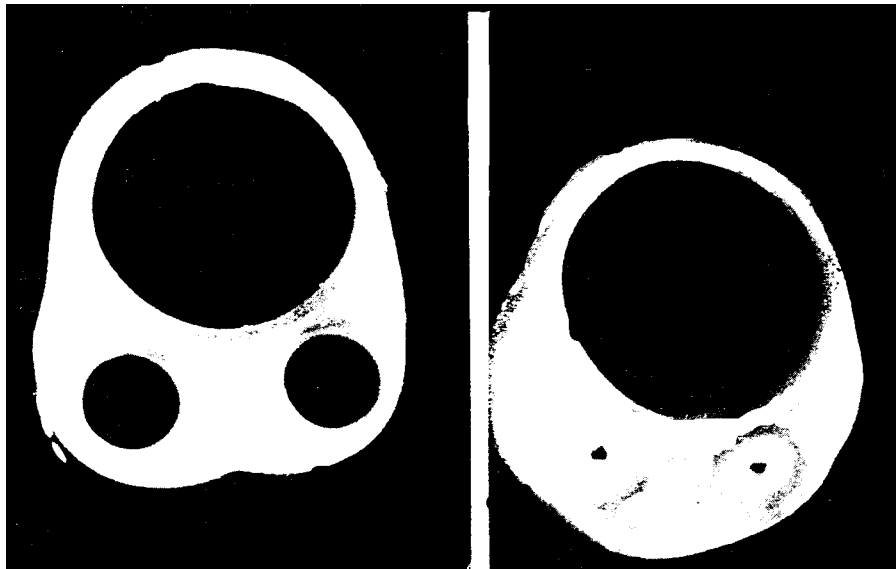
Fig 7. Cross section of early clamped umbilical cord on the left (within 10 sec) and late-clamped cord (over 3 min postpartum) on the right. *Source:* Reprinted from *European Journal of Cardiology*, Vol. 5/3, Lind J, Human fetal and neonatal circulation, 265–281, © 1977; with permission from Elsevier Science.

is most likely an adequate stimulus to effect closure of the umbilical arteries. In the physiological range, increased oxygen did not contract the umbilical vein that carries oxygenated blood to the fetus/neonate.

It is likely that this same level of oxygenation also begins to close other similar oxygen-sensitive structures, such as the ductus arteriosus, thus promoting the transition to neonatal circulation and respiration. Buckels et al found murmurs in all 17 early clamped babies and none in the 15 late clamped babies they studied.[23] The increase in blood volume that follows physiologic closure of the umbilical vessels is also likely to contribute to neonatal circulatory changes. Linderkamp[19] states, "Studies in newborn lambs have shown that an increase of 50% in blood volume causes the ductus arteriosus to close as a result of decreasing pressure gradient between the aorta and arteria pulmonalis."[(p.580)] Thus, increased blood volume, with its higher oxygen delivery capacity, appears to support more successful neonatal transition.

Cord pulsations may continue for several minutes after birth and can be readily palpated. The flow slows immensely but does not close entirely in some cases, perhaps providing for further equilibration if needed.[50] Spontaneous closure of the umbilical arteries within a few minutes after birth may be a protective mechanism that would have guarded against unregulated blood loss in newborns in more primitive settings. The longer patency of the umbilical vein may serve to protect the most stressed infants and offer a small amount of additional RBCs and nutrients. Yao and colleagues[44] documented that maternal uterine contractions effected complete placental transfusion by approximately 3 minutes after birth. Third stage administration of oxytocic medica-tion reduces that time by half, confirming the role of the uterus in placenta transfusion.[44]

Step 8: Stasis of blood in the umbilical vein occurs; the placenta separates.

Typically, the placenta separates from the uterus within a few minutes after birth. In the 1930s, Brandt,[58] using dye and X-rays, documented that the placenta rarely separated before 3 minutes. While separation ends the exchange of gases within the placenta, blood volume is still available for the infant.

DISCUSSION

To date, our knowledge related to the physiology of neonatal transition has been segmented and scattered among different disciplines. The development of this model is an effort to synthesize what is known into a whole. Its core concept is that an uninterrupted umbilical circulation will assist in the establishment of an adequate blood volume to perfuse the body and an adequate RBC flow to oxygenate and stimulate the respiratory center.

The model underscores the value of maintaining umbilical circulation in the first minutes after birth. This approach provides for adequate neonatal blood volume and allows a gradual and gentle, but effective, physiologic transition to extrauterine breathing. This interpretation of the neonatal transition process runs contrary to some long-held beliefs of many obstetric and pediatric care providers. These beliefs often (and necessarily) have been based on limited or conflicting empirical data. Reasonable consideration of this model will require reevaluating current knowledge relevant to several related issues. These include beliefs about neonatal polycythemia and jaundice and issues related to neonatal resuscitation procedures.

Neonatal Polycythemia and Jaundice

The belief that delayed cord clamping causes polycythemia and jaundice will probably be the single greatest obstacle to research on and acceptance of this model. Currently, this belief is so prevalent that one often finds it stated in the literature as accepted unreferenced fact.[36,37,59] Concerns about the potential for polycythemia and neonatal jaundice when cord clamping is delayed were initially raised in publications by Saigal et al[60–61] who reported symptomatic polycythemia in 2 of 42 babies held 30 cm (12 in) below the perineum for 5 minutes. In contrast, there are larger studies from the 1960s and 1970s that report no symptomatic polycythemia when infants were held at the level of the perineum and cord clamping was delayed until pulsations ceased.[17,18,23–29] A comprehensive review of the literature on cord clamping shows that most recent controlled trials do not support this concern.[62]

Polycythemia has long been a perplexing disorder that is difficult to manage and even to diagnose. It does have associations that are clearly unrelated to the timing of cord clamping. Pregnancy complications such as preeclampsia/eclampsia, maternal diabetes, small or large for gestational age conditions, and fetal genetic abnormalities all bear increased risk for neonatal polycythemia.[37,38,63,64] Kurlat[63] found that the risk of polycythemia in appropriate size infants of hypertensive mothers was 12.6-fold greater than that of the general newborn population. In a study of diabetic mothers, 5% of infants had polycythemia.[65] Diagnostic difficulties have persisted due to problems related to the unreliability of laboratory indicators for blood volume and hemoconcentration.[65,66] The blood test most commonly used for diagnosis, the hematocrit, can be influenced by factors as simple as site of sampling or time of testing.[67,24]

One new hypothesis has been put forth that may better explain the pathophysiologic processes and lead to more effective treatment. Jones et al[65] and Wardrop et al[66] suggest that an elevated hematocrit occurs when hypoxia induces a failure of the vascular endothelial integrity, leading to capillary leakage. This failure of the endothelium allows components of plasma such as salt, water, and albumin to leak from the intravascular space, causing a secondary hemoconcentration and poor correlation between the hematocrit and blood volume.[65,66] Their findings raise doubts about the results of older studies that used albumin markers such as radioactive I^{125} to measure blood volumes.[17,19,60,61] Leakage of tracer attached to albumin across the capillary membranes would lead to falsely high blood volume results—especially in sick or hypoxic infants.[2,65,66]

Polycythemia appears to be a multifactorial problem—it occurs most often in babies who have other serious problems—yet it is often assumed to be the cause, rather than a result, of any overarching problem.[37] This scientific flaw, as Werner[37] so aptly points out, causes polycythemia to continue to vex the neonatologists.

Issues Related to Neonatal Resuscitation

This model raises several issues related to neonatal resuscitation. These include

> *The belief that delayed cord clamping causes polycythemia and jaundice will probably be the single greatest obstacle to research on and acceptance of this model.*

the development of techniques for bedside resuscitation that dispense with the need for immediate cord ligation, inquiry into the possible risks of ventilation efforts that precede adequate pulmonary perfusion, and the potential of placental transfusion for avoiding the need for volume expansion in resuscitative efforts.

Successful resuscitation can occur at the perineum with an intact umbilical cord. In many hospital settings, this would require a new, but perhaps beneficial, interdisciplinary team effort. A neonate can be kept warm and dry and monitored for respiratory effort, heart rate, and color on the bed nearly as easily as anywhere else. When indicated, equipment for positive pressure ventilation can be brought to the infant. Lowering the infant as much as cord length will allow for 30 to 60 seconds while drying the baby can speed placental transfusion and provide volume expansion before clamping the cord when it must happen quickly.[18] Optimal management in cases where meconium is present in amniotic fluid needs further investigation. Immediate clamping of the cord may be likely to induce a first breath prior to adequate suctioning after birth. A better approach may be to keep the baby unstimulated, with cord intact at the perineum, while the nasopharynx is carefully suctioned.

Jaykka's work decades ago suggested that forceful ventilation prior to recruitment of the lung brought about by pulmonary perfusion and capillary erection damaged the alveoli. Clark[68] suggests that the lungs of ventilated newborns are most damaged when the lung is recruited and derecruited with each breath—exactly what would happen without adequate support from the full capillary plexuses. Allowing time and blood volume for adequate capillary perfusion and erection to occur, even (or perhaps especially) in premature infants, may help protect the delicate tissue of the neonatal lung and promote effective respiratory function. The need for immediate intubation is under study for preterm infants.[69]

A poor response to resuscitative measures in the delivery room is often attributed to neonatal volume depletion.[70] The ideal volume expander, and the only one with oxygen-carrying capacity, is whole blood. If one places a pale, limp baby at the level of the perineum or lower, the baby will get about 10 mL/kg of whole blood while resuscitation is being performed, as long as the heart rate is good and the cord is pulsating.[1]

CONCLUSION

Since the beginning of mammalian life, young have been born attached to a lifeline which supports their transition to extrauterine life. The process of birth invariably involves a period of maternal and neonatal rest before any active measure results in a severing of the umbilical cord. There have been two exceptions to the normal recovery process: human birth in some settings of recent times, and the attended births of thoroughbred foals.

In 1959, equine researchers Mahaffey and Rossdale[71] reported on an often fatal "convulsive syndrome" in newborn thoroughbred foals that occurred only to "foals born indoors, under human supervision."[(p 1224)] Human supervision of foaling at that time included rapid cord clamping, contrary to natural (unsupervised) settings, in which a mare and foal typically rest for about a half hour. The cord is then broken when either the mare or the foal rises. Pathology findings from foals that died of convulsive syndrome included an absence of aeration of the alveoli, with lung tissue so dense that it

rapidly sank in fixative, and presence of hyaline structures.[72]

Foal or baby, "human supervision" at birth should, at the least, do no harm. While the United States remains at 25th[73] in the worldwide ranking of infant mortality, with little change in the past several years, we must consider all possible sources of potential harm to babies. A difference in blood volume of 25% to 40% is not insignificant. The current typical practice of immediate cord clamping, especially of those infants potentially in most need of additional red blood cells, needs to be reconsidered.[74] Examination of short-term and long-term neonatal outcomes with variations in cord clamping practices and methods of resuscitation is essential. These issues demand a better understanding of and respect for the normal physiologic processes involved in labor, birth, and the neonatal transition. Continued research on the issue of neonatal transition for full-term and premature infants and the effect of cord clamping timing is urgently needed.

In fact, the current knowledge base is limited even to the extent that typical practices and the beliefs on which they are based are mostly undocumented.

A survey of American certified nurse-midwives revealed that one-third feel strongly that clamping should be delayed until the newborn has completed a successful transition.[75] They believe that this delay allows time for the neonate to gently make the transition to extrauterine respiration and to self-regulate blood volume. Midwives who practice early clamping (26%) believe that delay has no benefit and often fear it will cause polycythemia and jaundice.[75] Similar descriptions of practices or beliefs among other groups of obstetric and pediatric practitioners are not available. International practices and experiences are not shared in the literature.

Research-based evidence for practice is lacking. Management of the umbilical cord at the time of birth is probably most frequently done without thought, and clamping of the cord is often seen as merely a task. The presentation of the blood volume model for neonatal transition is a framework presented as an alternative to commonly held beliefs. It is put forth in an effort to encourage the application of critical thinking to this potentially significant issue, and to foster and frame the research that will answer the questions raised.

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