INTRODUCTION

In 1975 I proposed the inferior colliculus as a possible locus of impairment in children with autism underlying both the language disorder and deficits in environmental awareness [1]. This theory has not attracted any interest, but I continue to find more evidence in its favor than in other explanations of how the brain might be impaired. Perhaps most important: Loss of function in this brainstem nucleus in infancy may prevent production of trophic transmitters required for normal maturation of the language areas of the temporal and frontal lobes [2].

The inferior colliculus is a small nucleus in the midbrain auditory pathway, but it is more than a mere way-station in the neural circuit conducting acoustic sensations to the cerebral cortex. The inferior colliculus is metabolically the most active site in the brain [3]; and it may be the vigilance center of the brain [4]. The auditory sense evolved as an alerting mechanism for visual attention, and has developed into an information-seeking system that enables continuous awareness of the environment, even during sleep [4, 5]. Language for the human species is the greatest refinement of this information-seeking instinct.

Autism is a neurological disorder; thus theories of causation must in the end describe how brain areas needed for language, environmental awareness, and social instincts are affected. The search for autism genes has recently been the focus of much research. A huge lay movement believes infant vaccinations are responsible for the increased prevalence of autism that has become evident since the early 1990s. Autism has been reported in children with fetal alcohol syndrome, prenatal exposure to valproic acid or thalidomide, and rubella infection during gestation.

How the brain might be affected by these various etiological factors receives very little discussion. I will discuss evidence that the inferior colliculus is vulnerable to all of the known genetic defects and environmental insults associated with autism.

Further, perinatal problems are frequently found as predispositions for autism. The greatest worry when complications of pregnancy and birth occur is the possibility of oxygen insufficiency. Infants are thought to be more resistant to oxygen lack than adults, but this may be a serious misconception. The infant heart is more resistant to damage, but not the brain [6].

Experiments with monkeys on asphyxia at birth were begun during the 1950s in an attempt to produce an animal model of cerebral palsy [6]. Asphyxia was inflicted by delivering the head of the infant monkey into a saline-filled sac and clamping the umbilical cord. Thus the onset of breathing was blocked, as was continuing respiration from the placenta. The surprise result was that the monkeys displayed only transient delay in developing control of motor functions, and initially no damage in the brain could be found. Damage was found only after members of the team of Landau et al (1955) suggested looking in the inferior colliculi (plural of colliculus). This was the site in the brain, where, to their great surprise, they had recently found the highest rate of blood flow [3].
The asphyxiated monkeys did not develop cerebral palsy, and eventually outgrew their initial developmental delays. However, residual lack of manual dexterity remained in monkeys that survived for several months or years [7]. Windle (1969) suggested the damage to the inferior colliculi and lesser degrees of injury in other brainstem nuclei might be the cause of what was then known as "minimal cerebral dysfunction" (MCD). Pervasive developmental disorder (PDD) has now replaced the designation MCD, and developmental language disorder is one of the most serious aspects of PDD.

The research on asphyxia at birth appears to be long forgotten; I will review several aspects of the experiments with monkeys, including what caused cerebral palsy. These are experiments than cannot be repeated because of regulations on use of laboratory animals. However, the data remain valid and merit reconsideration, particularly the prominent damage found in the inferior colliculi.

With the advent of magnetic resonance imaging (MRI) in the early 1990s, selective damage of the inferior colliculi has been reported in several case reports of people who lost the ability to comprehend spoken language after traumatic head injury or cancerous growth into the midbrain [8]. Deafness and “word deafness” was assumed to be a psychological reaction in some of these cases, until the small lesions in the inferior colliculi were found in MRI scans. If impairment of function in the inferior colliculi can have such a catastrophic effect on people without previous language problems, what should we expect when a child sustains damage to the inferior colliculi by asphyxia at birth?

I am therefore returning to the view I put forth in 1975, that impairment of function within the inferior colliculi may underlie the language disorder of children with autism. Evidence for this view is the focus of the chapters that follow.

My research on autism dates back to 1967 when my three-year-old son, Conrad was diagnosed as autistic. I began graduate studies in 1969 at the Boston University School of Medicine, and in October came across the article by William Windle on asphyxia at birth in the Scientific American. When I saw the big holes in the inferior colliculi caused by asphyxia, I knew this must be the cause of Conrad's problems learning to speak. He had to be resuscitated after a traumatic "face presentation" birth. Research on asphyxia became the focus of my graduate studies.

I began writing this book around 1997 - thirty years later, and two years after Conrad's death in a group home from a prescribed overdose of Thorazine. At the suggestion of a friend I posted a website in Conrad's memory in April 2000.

Many people who came across my website have contacted me. One of these was Dr. George Morley, a retired obstetrician, who asked me if I knew how soon after birth Conrad's umbilical cord had been clamped. Clearly, it was before he was breathing, and I still re-experience the sense of panic I felt, that my baby was on the other side of the room, pale and lifeless, surrounded by a team of people working to get him breathing.
My grief is great. I do believe now that he could have been resuscitated sooner with the umbilical cord left intact and functioning, and been saved from brain damage and autism. Over the past six years I have become more and more involved, with many others, trying to change the "written standard of care" mandated by the American College of Obstetrics and Gynecology, to clamp the umbilical cord within seconds after birth [9]. Silence is the only response we have received from the obstetric professionals.

Evidence seems abundant that clamping the umbilical cord is a medical error, and it goes against a long tradition of waiting at least for the first breath and preferably until pulsations in the cord cease. It is no doubt instinctive for most obstetricians and midwives to wait for the infant to be breathing before clamping the cord, but this is no longer explicitly stated in the written protocols. Impairment, if not gross damage, of the inferior colliculi may occur with only the briefest lapse in respiration at birth, and this could well underlie developmental language disorders in increasing numbers of children.

References
(Note: full citations are in the alphabetic bibliography)

1. Locus of impaired language and environmental awareness
   • Simon N (1975) Echolalic speech in childhood autism, consideration of possible underlying loci of brain damage.

2. Trophic transmitters guide maturation of the cerebral cortex

3. Highest rates of blood flow and aerobic metabolism
   • Landau WM et al. (1955) The local circulation of the living brain; values in the unanesthetized and anesthetized cat.

4. The inferior colliculus may be the vigilance center of the brain

5. The auditory sense is an information-seeking system, language its highest evolutionary stage
• Fisch L (1983) Integrated development and maturation of the hearing system. A critical review article.
• Angelo R (1985) Physiologic acoustic basis of speech perception.

6. Asphyxia at birth
• Windle WF (1969) Brain damage by asphyxia at birth.
• Myers RE (1972) Two patterns of perinatal brain damage and their conditions of occurrence.

7. Maturation of the cerebral cortex was not normal following asphyxia at birth
• Faro & Windle (1969) Transneuronal degeneration in brains of monkeys asphyxiated at birth.

8. Impaired speech comprehension following injury of the inferior colliculi

9. Umbilical cord clamping
1. ERRORS IN PERINATAL MEDICINE

1. Visible versus hidden procedures

"The transfer of respiratory function from the placenta to the lungs at birth stands out as the most dramatic, complex and important event in our lives." (Dunn 1966)

1 – Birth and neonatal care

Many if not most families have concerns about the safety of vaccines [1-5]. Vaccination is a highly visible procedure, and easily blamed following an adverse reaction. Childhood vaccinations have increased dramatically since 1970 and are given earlier in infancy [6-9]. Hepatitis B vaccine is given in the immediate neonatal period [9]. The need for this is highly questionable [7, 8]. Even more outrageous is when parents have explicitly requested that the hep B vaccine not be given, then find out later that it was given “as a routine measure” in the neonatal nursery.

Clamping the umbilical cord immediately at birth, unlike vaccinations, is not something everyone knows about. Or perhaps clamping the cord is taken for granted or perceived as natural. After all, the father is often handed the clamp as a way to involve him in the process of birth, and prospective parents are now inundated with information about umbilical cord blood banking. Despite the routine practice of umbilical cord clamping at birth, caution has been voiced over the procedures employed to maximize the amount of blood obtained for banking [10-13].

Dunn (1992) stated:

“The HUC [human umbilical cord] blood belongs to the baby, at least until adaptation to extrauterine life has taken place and umbilical pulsation has ceased. It is unethical to rely on permission obtained in advance from the mother to take the blood unless the critical importance of the transitional feto/placental circulation is not only fully explained to her but also is defended in practice by the birth attendants. Unfortunately, in many parts of the world the importance of perinatal feto/placental haemodynamics is poorly understood, as shown by the arbitrary way in which the cord is often triple-clamped at birth to obtain arterial and venous samples for blood gas and acid-base studies. This practice not only abruptly interrupts the umbilical circulation but may also deprive the newly born infant of an amount of blood equivalent to at least a third of its normal circulating volume.” [10, p309]

Diaz-Rossello (2006) commented:

“Although there is strong evidence of its adverse effects, and no evidence of its benefits, early clamping is a common practice in modern obstetrics, especially with respect to the harvest of neonatal blood for cord blood banking…

... Quality standards for cord blood collection are based on ensuring that the largest volume of neonatal blood is retained in the placenta and umbilical cord, which involves
clamping the cord as early and as close to the neonate as possible. If complete physiological redistribution of blood from the placenta to the infant’s body is allowed to take place, the cord becomes flaccid and pulseless, and the natural residual placental blood volume is insufficient for banking...

... I suggest that the timing (in seconds) of cord clamping should be recorded at every birth, and that cord-blood donors should have a special haematological follow up.” [11, p840]

Both the Royal College of Obstetrics and Gynecology (RCOG) and the American College of Obstetrics (ACOG) have issued warnings about collection of umbilical cord blood:

“Some evidence indicates that immediate cord clamping may be harmful to babies. However, delaying cord clamping can prevent a successful cord blood collection.” [12, p5]

“The collection should not alter routine practice for the timing of umbilical cord clamping.” [13, p476]

Hopefully a change in the protocol for umbilical cord clamping is forthcoming, and soon, before any more children and their families must endure the lifelong hardships that follow brain injury. The obstetric clamp is an instrument that should be scrapped.

Vaccination in the first neonatal hours may be especially dangerous in view of the obstetric protocol to clamp the umbilical cord immediately at birth. If the cord is clamped before the infant has taken its first breath, a lapse is respiration is likely. Lucey et al. (1964) and Lou et al. (1977, 1979) demonstrated that the blood-brain barrier (BBB) is impaired by even a brief lapse in oxygen at birth. Circulating substances like bilirubin or the thimerosal preservative from vaccines can then gain entry into neurons of the brain [14-16].

13. ACOG Committee on Obstetric Practice; Committee on Genetics (2008) ACOG committee opinion number 399, February 2008: umbilical cord blood banking.
15. Lou HC et al. (1977) Breakdown of blood/brain barrier in kernicterus.
16. Lou HC et al. (1979) Pressure passive cerebral blood flow and breakdown of the blood-brain barrier in experimental fetal asphyxia.

2 – Blood flow and respiration at birth
Circulation to and from the placenta continues after birth [1, 2]. Stembera (1965) concluded from his research on postnatal umbilical blood flow:

"... the first 100 seconds after birth is a period during which the flow and metabolic conditions in the maternal-placental-fetal system continue essentially in a manner similar to that in utero" [1, p573]

Measurements of blood remaining in the placenta after ligation of the umbilical cord, of weight changes in the newborn, or increased red blood cells when umbilical blood flow is allowed to continue, have demonstrated that the baby’s blood volume is increased by 30 percent or more if the cord is left intact until pulsations in it cease [3-16]. Note that the research evidence goes back more than 130 years [3, 4].

Budin (1875) measured the blood that drained out of the umbilical vessels when the cord was cut at varying intervals of time [3]. In 32 cases, the cord was not tied until pulsations had ceased, with an average yield of 11.2 cc of residual blood. In 30 cases, after immediate ligation of the cord, the average was 98.4 cc.

Schucking (1877) described the blood recovered in Budin's experiments as "reserve blood," which he said was intended to fill the pulmonary vessels [4]. This certainly makes intuitive sense because the most important transition from fetal to postnatal life is the transfer of respiratory function from the placenta to the lungs. Jäykkä (1957) eight decades later performed experiments that demonstrated that the alveoli expand not by inhalation of air with the first breath, but that the first breath takes place only after the capillaries that surround the alveoli fill with blood [17, 18]. Schucking weighed each infant at the time of delivery, then again after tying of the cord. Infants gained from 30 to 110 grams when the cord was not tied. Babies whose cords were tied immediately had a more rapid pulse and gained weight more
slowly, whereas those whose cords were tied late had a slower pulse and regained their birth weight in four to six days.

Schucking also commented that he observed no jaundice in the infants whose cords were tied late. The problem of kernicterus, associated with bilirubin staining of selective subcortical nuclei, was a subject already under discussion [19]. The experiments of Budin and Schucking are early examples of what are now referred to as "randomized controlled trials" or RCTs. That they assigned some infants to groups for early ligation of the umbilical cord, indicates that waiting for pulsations of the cord to cease was not universally practiced. Both Budin and Schucking concluded that it was best to wait for pulsations to cease.

Haselhorst (1929) recorded infant weight changes during the period of placental transfusion following birth, showing fluctuations between loss and gain during the period of strong pulsations of the umbilical arteries [7]. Strong pulsations are from the infant heart, pumping blood back to the placenta for oxygen, and following the exertion involved in being born, strong pulsations may be the equivalent of increased heart and respiratory rates following exercise.

Haselhorst's method was completely non-invasive, as he recorded the weights of all infants until pulsations ceased — until transition was complete from placental to pulmonary respiration. In 20 babies, the average overall gain was 114 grams, with the greatest weight gain taking place in the first few minutes. Blood flow into the infant continued for two to three minutes before tapering off. This approach fits the "Do no harm" ethic, far better than recent "randomized controlled trials" with human infants, in which infants are randomly assigned before birth to have the cord clamped immediately or after a delay of a few seconds or minutes.

Earlier studies by Haselhorst (1928) involved early ligation of the cord in cases where the cord had broken, become knotted, or damaged in some other way [5, 6]. Blood pressure changes on the placental side of the ligature were measured with third stage contractions but Haselhorst noted that the data gathered in these circumstances did not represent natural physiology. Haselhorst also investigated the effects of intravenous "hypophysin" on time of delivery of the placenta.

The research of Haselhorst, and of Budin and Schucking was also summarized in an English language paper by Frischkorn and Rucker (1939), which they cited for comparison with their data on the effect of umbilical cord clamping on red blood counts in infants [10].

Allmeling (1930) measured weight gain in 100 infants during the period of postnatal transfusion [8]. Allmeling, like Haselhorst, used a method for temporary interruption of umbilical cord blood-flow – a piece of soft rubber tubing with a clamp that could be removed after obtaining an initial weight of the infant. She noted that a large amount of placental blood can be transferred in the first 20 to 30 seconds after birth. This observation
may be the basis others have used in assuming that a 20 to 30 second delay in cord clamping is sufficient to allow a full (or nearly full) placental transfusion – a one size fits all mentality.

Haselhorst and Allmeling provided many other useful references to the older literature. As can be seen, much data was gathered in investigations of the early twentieth and nineteenth centuries. What I present here is by no means all that could be mined from research of the past.

Gunther (1957) measured weight changes in infants at birth during the transition from placental to pulmonary respiration [16]. Several minutes elapsed after birth of some of the babies before the first breath during her experiments. What would have been the fate of these infants if subjected to the policy 50 years later of clamping off the blood flow to and from the placenta within seconds following birth? Gunther confirmed the results of earlier studies and summarized her findings as follows:

“These records confirm once more that, if the cord is left untied, a baby will usually increase his blood volume by a significant amount. The weight of blood received by these babies, as in Haselhorst’s (1929) and Allmeling’s (1930) work, was roughly correlated to the baby’s weight... If the blood of the neonate weighs about 10% of the body-weight the amount of blood involved can be more than 40% of the baby’s blood volume.” [13, p1278]

Redmond et al. (1965) measured residual placental blood as an estimate of placental transfusion before and after onset of respiration [18]. In 55 infants, the cord was clamped before onset of respiration, and in 97 after the onset of respiration. The plot of residual blood to onset of respiration from the paper by Redmond et al. shows a dramatic drop in residual blood in cases where the cord was clamped after onset of respiration:

“Our data, obtained from normal uncomplicated pregnancies, clearly demonstrated that a placental transfusion is an inevitable physiological consequence of initial pulmonary expansion, over which obstetricians and paediatricians have little, if any, control...

...The tendency for some obstetricians to deliver the head, aspirate the nose and mouth, and slowly extract the remainder of the baby probably aids the transmission of placental blood to the infant.” [18, p284]

Redmond et al. concluded that placental transfusion is the result of taking the first breath, but the first breath may in fact be the result of the transfer of blood from the placenta to the lungs. In either case, shouldn’t the first breath be allowed before disconnecting a newborn infant from the placental support system? Are neonatal specialists overconfident that they can resuscitate a baby after clamping off continuing blood flow and oxygen delivery from the mother?
Jäykkä (1957) demonstrated that the alveoli expand after the capillaries that surround them fill with blood [15, 16]. Jäykkä further demonstrated that inflation by capillary filling is uniform throughout the lungs, in contrast to external ventilation with air produces patchy uneven inflation. Circulation from the placenta should not be cut off until the lungs are fully inflated and breathing clearly established.

The obstetric clamp is not a benign instrument. When first introduced at the beginning of the 20th century, it was with explicit instructions to apply the clamp after all pulsations in the umbilical cord had ceased [19, 20]. Birth is a momentous event. Why should it be rushed for any reason?

3. Budin, P (1875-1876) A quel moment doit-on pratiquer la ligature du cordan omibilical?
11. DeMarsh QB et al. (1941) The effect of depriving the infant of its placental blood; on the blood picture during the first week of life.
13. DeMarsh QB et al. (1948) Factors influencing the blood picture of the newborn; studies on sinus blood on the first an third days.
15. Colozzi AE (1954) Clamping of the umbilical cord; its effect on the placental transfusion.
20. Redmond A et al. (1965) Relation of onset of respiration to placental transfusion.

3 – Data from Almelling (1930) and Gunther (1957)

a) Data from Allmeling (1930)
Of her 100 cases, Allmeling presented 10 in a table showing maternal parity, gender of the
infant, initial birth weight, and weight fluctuations at 1-minute intervals up to 34 minutes.
Uterine contractions and time of cessation of pulsation in the umbilical cord were noted within
the 1-minute interval that they occurred. The end-weight, amount gained, and residual blood
left in the placenta are also shown, with observations on the length and appearance of the
umbilical cord, if it were around the neck, and breathing or crying behavior of the child.

To accommodate the 34-minute time span of the table it was presented in three sections,
which are reproduced below. Most important perhaps is illustration of the variable time span
for continuing pulsation of the cord (Nabelschnur), designated by N (highlighted by me). The W
designates Wehe (uterine contractions), showing their association with additional gains in
weight, which diminish after pulsations of the cord cease - pulsations of the cord, from the
infant heart, are the primary signal for continuing need of placental circulation.

Notice that cord pulsations ceased within the first minute after birth for two infants. For two
more, pulsations stopped within two minutes. After that pulsations continued for ten, twelve,
fifteen, nineteen, twenty-two, and twenty-five minutes after birth. Why should placental
circulation be arbitrarily cut off within 30 seconds for those infants who require up to 30
minutes continuing connection with their mother?

Figure 2: Almelling’s Table, part 1
Part 1 of Almelling’s table shows maternal parity, sex of infant, initial weight, and the course of
placental transfusion during the first eleven minutes after birth. As described above: N =
cessation of pulsations, W = uterine contraction.
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>550</td>
<td>F. I ♀</td>
</tr>
<tr>
<td>571</td>
<td>W. II ♀</td>
</tr>
<tr>
<td>582</td>
<td>B. I ♂</td>
</tr>
<tr>
<td>607</td>
<td>W. I ♀</td>
</tr>
<tr>
<td>627</td>
<td>S. II ♀</td>
</tr>
<tr>
<td>667</td>
<td>B. I ♀</td>
</tr>
<tr>
<td>668</td>
<td>B. I ♀</td>
</tr>
<tr>
<td>670</td>
<td>H. II ♂</td>
</tr>
<tr>
<td>710</td>
<td>G. III ♀</td>
</tr>
<tr>
<td>722</td>
<td>B. I ♀</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name, Parity, sex</th>
<th>Weight</th>
<th>Minutes after birth</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3690</td>
<td>+20</td>
</tr>
<tr>
<td></td>
<td>3040</td>
<td>+30</td>
</tr>
<tr>
<td></td>
<td>3265</td>
<td>+45</td>
</tr>
<tr>
<td></td>
<td>3005</td>
<td>+30</td>
</tr>
<tr>
<td></td>
<td>3555</td>
<td>+35</td>
</tr>
<tr>
<td></td>
<td>3640</td>
<td>+55</td>
</tr>
<tr>
<td></td>
<td>2970</td>
<td>+120</td>
</tr>
<tr>
<td></td>
<td>4075</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>3385</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>3510</td>
<td>+70</td>
</tr>
</tbody>
</table>

Differenz nach

W: Wetter

N: Noten
Figure 3: Allmeling’s Table, part 2

Part 2 of Allmeling’s table spans minutes 12 through 29 after birth.

Minutes after birth
12  13  14  15  16  17  18  19  20  21  22  23  24  25  26  27  28  29

<table>
<thead>
<tr>
<th>12'</th>
<th>13'</th>
<th>14'</th>
<th>15'</th>
<th>16'</th>
<th>17'</th>
<th>18'</th>
<th>19'</th>
<th>20'</th>
<th>21'</th>
<th>22'</th>
<th>23'</th>
<th>24'</th>
<th>25'</th>
<th>26'</th>
<th>27'</th>
<th>28'</th>
<th>29'</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5</td>
<td>-5</td>
<td>+10</td>
<td>+10</td>
<td>-10</td>
<td>-</td>
<td>+10</td>
<td>+15</td>
<td>-20</td>
<td>-</td>
<td>+25</td>
<td>+15</td>
<td>+10</td>
<td>-</td>
<td>+5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>-10</td>
<td>+5</td>
<td>+5</td>
<td>+10</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>+15</td>
<td>+10</td>
<td>-</td>
<td>+5</td>
<td>-</td>
<td>+10</td>
<td>+5</td>
<td>+5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>-</td>
<td>+5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>+65</td>
<td>+5</td>
<td>-25</td>
<td>-60</td>
<td>+75</td>
<td>+5</td>
<td>+10</td>
<td>+10</td>
<td>-</td>
<td>-</td>
<td>+20</td>
<td>+5</td>
<td>-</td>
<td>+5</td>
<td>+5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Figure 4: Allmeling’s Table, part 3

Part 3 of Allmeling’s table spans minutes 30-34 after birth, gives the final weight of the infant (following placental transfusion), the amount of weight gained from placental transfusion, and the residual blood remaining in the placenta. Additional observations and comments are also provided.

<table>
<thead>
<tr>
<th>Minutes after birth</th>
<th>30</th>
<th>31</th>
<th>32</th>
<th>33</th>
<th>34</th>
<th>Final weight</th>
<th>Weight gained</th>
<th>Blood residual</th>
<th>Observations/comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>W</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3800</td>
<td>110</td>
<td>—</td>
<td>Nabelschnur mäßig lang, dick, pulsiert sehr kräftig. Starke Wehen. Kind schreit kräftig</td>
</tr>
<tr>
<td>2</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3130</td>
<td>90</td>
<td>—</td>
<td>Nabelschnur sehr lang und dick, nicht gewunden, pulsiert sehr kräftig. Häufige starke Wehen. Kind schreit kräftig</td>
</tr>
<tr>
<td>3</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3330</td>
<td>65</td>
<td>—</td>
<td>Nabelschnur sehr lang, knötzig, 1× um den Hals, leicht abstreifbar, pulsiert sehr schwach. Kind schreit kräftig</td>
</tr>
<tr>
<td>4</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3050</td>
<td>45</td>
<td>—</td>
<td>Nabelschnur kurz, mäßig dick. Sehr kräftige Pulsation. Kind schreit wenig</td>
</tr>
<tr>
<td>5</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3640</td>
<td>85</td>
<td>—</td>
<td>Nabelschnur sehr lang, dick. Sehr kräftige Pulsation. Kind schreit gut</td>
</tr>
<tr>
<td>6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3800</td>
<td>160</td>
<td>—</td>
<td>Nabelschnur kurz, dick. Kräftige Pulsation. Kind atmet gut, schreit nicht</td>
</tr>
<tr>
<td>7</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3120</td>
<td>150</td>
<td>—</td>
<td>Nabelschnur lang, dünn, nicht gewunden, 1× um den Hals, leicht abstreifbar. Pulsation kaum zu fühlen. Kind schreit kräftig</td>
</tr>
<tr>
<td>8</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>4150</td>
<td>75</td>
<td>—</td>
<td>Nabelschnur mäßig lang und dick, 1× um den Hals, leicht abstreifbar. Keine Pulsation. Kind schreit sehr kräftig</td>
</tr>
<tr>
<td>9</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3520</td>
<td>135</td>
<td>—</td>
<td>Nabelschnur sehr lang, mäßig dick. Sehr schwache Pulsation. Kind schreit kräftig</td>
</tr>
<tr>
<td>10</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3700</td>
<td>190</td>
<td>—</td>
<td>Nabelschnur kurz, mäßig dick, pulsiert anfangs schwach, später kräftig. Kind schreit kräftig</td>
</tr>
</tbody>
</table>

Note, I copied the 3-part table from Allmeling’s paper published in the Zentralblatt für Gynäkologie 1930; 54(14):850-860, pages 854, 855, and 856. I highlighted the N (for cessation of umbilical cord pulsations) for each infant summarized in the table, and comments about cord pulsations in part 3 of the table. I noted with arrows that pulsations of the cord of babies 1, 2, 4, 6, and 10 (all female) continued for 25, 15, 19, 12, and 22 minutes respectively. I could request this volume of the journal from the Harvard depository again and try to make cleaner copies, but decided my annotations might possibly be useful for others.

b) Data from Gunther (1957)
Most interesting of Gunther's findings were the annotations of the weight gain/loss tracings. In figure 5 (Gunther’s figure 1) postnatal activity and weight profile are shown for a baby who started crying only 9 minutes after birth, and with pulsations of the cord continuing for 19 minutes after birth. What would have been the Apgar scores and fate of this child had the cord been cut within the first minute after birth?

Likewise, in figure 6 (Gunther’s figure 3), resuscitation was started within one minute on an infant described as "slow to cry." Crying began more than 6 minutes after birth following a uterine contraction and additional weight gain from placental blood. Pulsations of the cord continued throughout the 10 minute interval shown in the graph. This would surely have been another infant described as severely depressed by Apgar, and with an ominous outcome.
Figure 5: Figure 1 from Gunther (1957)

Fig. 1—Weight changes in baby lying at level of vulva, with cord pulsating for 19 minutes. Note weight changes induced by uterine contraction and relaxation.

Figure 6: Figure 3 from Gunther (1957)

Fig. 3—Large early weight gain succeeded by loss and small gain. Cord pulsating throughout. Baby at level of vulva.
**4 – Oxygen exchange for carbon dioxide**

Respiration is delivery of oxygen in exchange for carbon dioxide, the metabolic end-product of aerobic metabolism. This exchange is accomplished by the hemoglobin molecule. As a student, I was inspired by my chemistry teacher’s explanation of hemoglobin as one of nature’s most elegant mechanisms in support of life in multicellular organisms. Recent textbooks tend to gloss over (or become too immediately technical) describing how and why hemoglobin mediates respiration. Following is from my old textbook of biochemistry by White, Handler, and Smith (1968):

"Primitive organisms rely on diffusion through their environmental media to provide the oxygen needed for their metabolism and to remove the carbon dioxide produced.

The active metabolism of mammalian tissues remote from the atmosphere is possible because of a mechanism which provides constant delivery of oxygen and removal of carbon dioxide. The magnitude of this task may be appreciated from the fact that a man oxidizing 3000 Cal. Of mixed food per day uses about 600 liters of oxygen (27 moles) and produces about 480 liters of carbon dioxide (22 moles).

Through the action of hemoglobin, oxygen is abstracted from the air, carried within a few seconds to the most distant parts of the body, and delivered to the tissues at a pressure only slightly less than that which it existed in the atmosphere.

The CO₂ produced daily by the tissues becomes H₂CO₃, an acid, in an amount equivalent to 2 liters of concentrated hydrochloric acid; yet all this acid normally pours from the tissues, through the blood, and out of the lungs with a change in the pH of blood of no more than few hundredths of a pH unit."

[1, p758 – Chapter 32. Chemistry of Respiration]

The delivery of oxygen by hemoglobin in exchange for the metabolic end-product carbon dioxide is known as the "Bohr Effect" [2, 3]. Christian Bohr (1857-1911) was the father of Nils Bohr, who determined the electron-proton structure of hydrogen, for which the Nobel Prize was awarded. Discovery of how hemoglobin mediates aerobic metabolism was as great a scientific achievement.
During prenatal life the fetal heart pumps deoxygenated carbon dioxide laden blood to the placenta, where oxygen is received in exchange for the carbon dioxide and delivered via the umbilical vein to the developing child. A fetal form of hemoglobin accomplishes this [4, 5].

The lungs are dormant during fetal life receiving circulation sufficient only for development and growth. Following birth the lungs must take over the function of respiration and this can only occur after the alveoli are supplied with blood, and shunts in the heart (the foramen ovale and ductus arteriosus) must close for full redirection of respiration from placenta to the lungs. These changes are not best promoted by swift clamping off continuing circulation to and from the placenta. Respiration via gas exchange in the placenta must continue until the alveoli are able to release carbon dioxide in exchange for oxygen.

Ventilation of the lungs was shown by Jäykkä (1957) to produce patchy inflation of the alveoli nearest the trachea and failure of aeration of distal lobes of the lungs [6]. Without blood in surrounding capillaries the alveoli have no way of obtaining oxygen. Allowing time after birth for the capillaries to fill brings carbon dioxide laden hemoglobin to the alveoli. Release of carbon dioxide into the alveoli may stimulate exhalation as an event preceding the first breath.

References
2. Bohr C et al. (1904) Über einen in biologischer Beziehung wichtigen Einfluss, den die Kohlensäurespannung des Blutes auf dessen Sauerstoffbindung ubt.

5 – Origin of fetal blood and circulation
The fetal heart is the earliest organ to become functional, and between the fourth and fifth weeks of development begins circulating erythrocytes produced in the embryonic yolk sac [1, 2]. The placenta becomes a major component of the cardiovascular system between the eighth and tenth weeks [2, 3]. Blood is pumped by the fetal heart through the umbilical arteries to the placenta, where replenished with oxygen and nutrients it returns via the umbilical vein [3, 4]. Placental blood is therefore part of the fetal circulatory system, as much as pulmonary blood is after birth.

Windle (1941) described the sequence of events in blood formation as follows:

“Genesis of red blood eells occurs shortly after the formation of the germ layers. It starts in the wall of the embryonic yolk sac and persists there until the second month. Blood formation begins to shift to the body mesenehyme and blood vessels about the fifth week. The liver starts to produce red blood cells in the sixth week, soon becomes the most active erythropoietic organ, and remains so until midfetal life. Erythropoiesis is initiated in the spleen at the end of the second month, and in the bone marrow during the third month. The activities of the various organs overlap and most loci of erythropoiesis are transient. Even in the liver, formation of blood elements stops at birth. Only the bone marrow normally carries it on into postnatal life.” [1, p538]

Windle then discussed development of red blood corpuscles from proerythroblast stem cells and the appearance of hemoglobin in these cells during the first six weeks of embryonic development. By two months of gestation these precursor cells have differentiated in several stages to true red blood corpuscles and the spleen and bone marrow as they develop become organs of hematopoiesis.

Fetal blood develops in the fetal organs and is pumped by the fetal heart to the placenta for oxygenation and nourishment. Erasmus Darwin, grandfather of Charles Darwin wrote in 1796:

"The placenta is an organ for the purpose of giving due oxygenation to the blood of the fetus; which is more necessary, or at least more frequently necessary, than even the supply of food." [5, p350]

Placental blood is not extra blood that can be discarded or collected for blood banks. Windle was adamant on this point saying:
“In view of the facts that the placenta contains one-fifth to one-fourth of the
total fetal blood at birth and that all this blood does not pass into the infant at
birth until after uterine contractions have had a chance to compress the
placenta, we believe that the rather common practice of pro.raptly clamping the
cord at birth should be condemned. Of course this will make it impossible to
salvage placental blood for "blood banks." However, the collection of usable
quantities of placental blood robs the newborn infant of blood which belongs to
him and which he retrieves under natural conditions...

... Immediate clamping of the cord is comparable to submitting the infant to a
rather severe hemorrhage. It appears to result in increased erythropoiesis which
is reflected in an increase in circulating reticulocytes.” [1, p546]

Windle’s paper was a publication of an address he gave in November 1940 at a meeting of the
American Academy of Pediatrics. Discussion following his presentation is also of interest, for
example the following two questions indicate that clamping the umbilical cord had become a
common practice even though textbook teaching was to wait for pulsations in the cord to
cease, as emphasized by Windle:

“QUESTION. -- How long should clamping of the cord be delayed?
DR. WINDLE.--Until the pulsation has ceased, and until tile placenta has separated from the
uterus...

QUESTION.--Is there any objection by the obstetrician to delay in clamping of the cord?
DR. WINDLE.--I have not heard any objection, directly from obstetricians. It is not too much to
expect them to wait a short period of time ten or fifteen minutes under ordinary conditions
and especially when they have adequate help in the operating room.” [1, p548]

References
1. Windle WF (1941) Round table discussion on anemias of infancy (from the proceedings
of the tenth annual meeting of the American Academy of Pediatrics Nov18-20, 1940)
2. Mäkikallio K et al. (1999) Yolk sac and umbilicoplacental hemodynamics during early
human embryonic development.
5. Darwin E (1796) Zoonomia; or, The Laws of Organic Life, Vol 1, Section XXXVIII.
2. Childbirth tradition

1 – Early understanding
William Harvey (1578-1657) through dissection of cold- and warm-blooded animals observed the circulation of blood, and that this was the result of the pumping action of the heart [1, 2]. He stated:

"It is absolutely necessary to conclude that the blood is in a state of ceaseless motion; that this the act or function which the heart performs by means of its pulse; and that is the sole and only end of the motion and contraction of the heart."

This description predated the discovery of oxygen by more than a century [3]. In his investigations into the origins of life and fetal development, Harvey further pointed out the meaning and importance of pulsations of the umbilical cord:

"Moreover, it is a sure way to know whether the Infant that sticketh in the birth be alive, or not, by the pulsation of the Vmbilical Arteries. But most certain it is, that those Arteries are not moved by the virtue or operation of the Mothers, but of his own proper Heart: For they keep a distinct time and pawze, from the Mothers pulse: which is easily experimented, if you lay one hand upon the Mothers wrest, and the other on the Infants Navel-string. Nay in a Casarean Section, when the Embryo's have been yet involved in the membrane called Chorion, I have oftentimes found (even when the Mother was extinct, and stiffe almost with cold) the Vmbilical Arteries beating, and the Foetus himself lusty."

Jakob Rüff (1500-1558) of Zürich instructed midwives to cut the umbilical cord with clean scissors (Ich schneid das Nabelgerthlien des Kindes mit einem sauberen Scherlin auf 4 Zwerchfinger ab nahe beý dem Kind...) [4]. Rüff's work was translated and printed in English in 1637 [5]. The translation does not mention scissors, but after cutting the cord four fingers from the belly of the child, to then bind it with a double thread as near to the child's belly as possible. That there is no mention of bleeding suggests that waiting for pulsations in the cord to cease was implied.

Figure 8 is a drawing from Rüff's work, in which he also described the secundine (amniotic membranes and placenta) and its attachment to the womb "with veins and arteries, by which it attracts and draws blood for the nourishment of the fetus, being attracted to the infant by his navel," thus showing already in the sixteenth century (a century before Harvey) some understanding of the function of blood. This knowledge was in part handed down from texts dating back to ancient Greece [2].

References
1. Harvey, William (1653) *Anatomical exercitations concerning the generation of living creatures to which are added particular discourses of births and of conceptions, &c.*
5. Rüff, Jakob (1637) *The Expert Midwife*

2 – Childbirth before anesthesia
Anesthesia was first used in surgery in 1846, and a year later to ease the pain of childbirth. Chloroform was administered to Queen Victoria for the birth of Prince Leopold in 1853, and use of anesthesia in childbirth became more widespread after that. Obstetric textbooks continued to advocate waiting for pulsations in the cord to cease before cutting it. However, tying the cord early also has a long tradition, otherwise admonitions against it would not have been made by Charles White in 1773 and Erasmus Darwin in 1801 quoted below.

White (1773)
Charles White (1728-1813) clearly understood that during gestation circulation to the lungs is sufficient for growth and development, and that shunt valves in the heart (the foramen ovale and ductus arteriosus) maintain circulation for respiration to and from the placenta during fetal life. Closure of these shunts must take place at birth for successful transition to pulmonary respiration. White (1773) pointed out that this cannot be expected to happen instantaneously. Circulation to the placenta should be allowed to continue until the alveoli of the lungs have sufficient blood supply to begin to receive oxygen in exchange for carbon dioxide.

White asked the question all prospective parents should ask their obstetrician or midwife:
"Can it possibly be supposed that this important event, this great change which takes place in the lungs, the heart, and the liver, from the state of a foetus, kept alive by the umbilical cord, to that state when life cannot be carried on without respiration, whereby the lungs must be fully expanded with air, and the whole mass of blood instead of one fourth part be circulated through them, the ductus venosus, foramen ovale, ductus arteriosus, and the umbilical arteries and vein must all be closed, and the mode of circulation in the principal vessels entirely altered - Is it possible that this wonderful alteration in the human machine should be properly brought about in one instant of time, and at the will of a by-stander?" [1, p45]

**Darwin (1801)**

Erasmus Darwin (1731-1802) was the grandfather of Charles Darwin, and he asked another question prospective parents should ask their obstetrician or midwife:

"Why is not the foetus in the womb suffocated for want of air, when it remains there even to the tenth month without respiration: yet, if it be born in the seventh or eighth month, and has once respired, it becomes immediately suffocated for want of air, if its respiration be obstructed?"

This was a question posed by William Harvey, and following the discovery and importance of oxygen, Erasmus Darwin was able to provide the answer:

"The placenta is an organ for the purpose of giving due oxygenation to the blood of the fetus; which is more necessary, or at least more frequently necessary, than even the supply of food."

Darwin also pointed out the error of tying off the umbilical cord too soon:

"Another thing very injurious to the child, is the tying and cutting of the navel string too soon; which should always be left till the child has not only repeatedly breathed but till all pulsation in the cord ceases. As otherwise the child is much weaker than it ought to be, a portion of the blood being left in the placenta, which ought to have been in the child." [2, p321]

Prospective parents need to ask why this understanding of basic physiology is no longer part of the standard of care in obstetrics. In 10th grade biology class (in my day at least) we were taught much of what Harvey, White, and Darwin had come to understand. It was with a sense of awe from learning about such developmental changes that some of us chose biological science as the field we wanted to pursue. What has happened? Is our educational system at fault? Gathering new “evidence” by experimentation is nothing more than reinventing the wheel if all learning of the past is ignored or forgotten.

Following are quotes from two textbooks of obstetrics (or midwifery) that predate widespread use of anesthesia in childbirth.
Meigs (1842)
"The head is born: perhaps the cord is turned once, or even more than once around the child’s neck, which it encircles so closely as to strangulate it. Let the loop be loosened to enable it to be cast off over the head. ... [or] by slipping it down over the shoulders. ... If this seems impossible, it should be left alone; and in the great majority of cases, it will not prevent the birth from taking place, after which the cord may be cast off. ... Should the child be detained by the tightness of the cord, as does rarely happen, ... the funis may be cut ... Under such a necessity as this, a due respect for one’s own reputation should induce him to explain, to the bystanders, the reasons which rendered so considerable a departure from the ordinary practice so indispensable. I have known an accoucheur’s capability called harshly into question upon this very point of practice. I have never felt it necessary to do it but once. ... The cord should not be cut until the pulsations have ceased." [3, p192]

Churchill (1850)
“#181 The umbilical cord, funis, or navel string ... After birth of the child, the pulsation ceases in about fifteen or twenty minutes, and that portion of the cord which remains attached to the umbilicus dies, and gradually withers, until it falls off, in the majority of cases, on the fifth or sixth day.” [4, p91]

“...in ordinary cases, if we find that the cord is twisted around the neck, all we need do is to draw down more of the cord, and either slip the lop over the head or shoulders. If we cannot do this, we must loosen the cord as much as we can, so as to prevent the strangulation of its vessels, and wait for the uterus to expel the child.” [4, p131]

“If the child be healthy, and not have suffered from pressure, &c. it will cry as soon as it is born, and when respiration is established, it may be separated from its mother...” [4, p132]

References

3 – Introduction of the clamp as a hygiene measure
On a page reporting new aseptic instruments in the Lancet for May 20, 1899, Magennis (1899) described both a traditional method for tying and ligating the umbilical cord and his invention of a clamp with knife blades to simplify the procedure. Note from the excerpt in figure 9 below that Magennis’ clamp was reported as part of a brief summary of new aseptic instruments.
Magennis’ description is excerpted from the article above, which may be too small to be read easily, but his description for use of his new clamp should be carefully noted, that it was intended to be used only after the cord had ceased to pulsate:

“In the old method of dividing the umbilical cord the accoucheur after tying the first thread pressed the blood in the vessels some distance along the cord which was then held by an assistant until the second thread was tied, the object being to avoid the escape of blood on to the bed-clothes. This part of the accoucheurs work may, however, be accomplished more conveniently by making use of a clamp which I have designed and which is represented open in Fig. 1 and closed in Fig. 2, for it by the same movement cuts the cord and compresses both cut ends, thereby supplying the place of scissors and ligatures. The clamp having been opened, the cord when it has ceased to pulsate is placed between the blades, resting on the
plain side; the knifed edge is then pressed firmly down and retained in position with the catch.” [1, p1373]

Megennis’ clamp looks something like a guillotine, but notice that his instruction was to wait until the cord has ceased to pulsate before performing the simultaneous operation of clamping and cutting.

Wechsler (1912) published a brief note in the American Journal of Obstetrics and Diseases of Children on use of an obstetric clamp, stating, "I desire to present to the profession a little device for use on the cord instead of the usual ligature." [2, p85].

Wechsler reported that on a recent visit to Vienna, he had witnessed the method of clamping and dressing without ligature in the Schauta Clinic. The clamp is pictured and noted to be smaller than the "ordinary Hemostat" used in Vienna. The rationale for use of a clamp was that it lessens the danger of infection. Its use was described as follows:

"Clamping the cord is accomplished in the following way:
1. Wait until pulsation has ceased;
2. Clamp cord about one inch from umbilicus;
3. Cut cord even with clamp.
The infant is then removed by the nurses and the clamp allowed to remain on stump of cord for fifteen minutes, or about the time the placenta has been expelled then the clamp is ready to taken off." [2, p86]

References

4 – The clamp a decade later
Zeigler (1922) published an article on instruments used in obstetrics, and commented on use of a clamp as follows:

"The primary object of ligating or clamping the cord is, of course, to prevent hemorrhage; and while it is true that hemorrhage would rarely occur even were the cord not compressed, especially after the establishment of respiration, the fact is that hemorrhages have occurred and even with fatal termination. In fifteen years I have had two cases of secondary hemorrhage from the cord which were all but fatal. It is likely, therefore, that some form of compression will always be regarded as necessary." [1]

Note Ziegler's remark that hemorrhage would rarely occur even were the cord not compressed, especially after the establishment of respiration. This corroborates the observation of Gunther
(1957) that cessation of placental transfusion was often apparent after a main reservoir had been filled [2]. This reservoir would appear to be the capillary system surrounding the alveoli of the lungs, as described by Jäykkä (1958) and Mercer & Skovgaard (2002) [3, 4].

Placental blood is respiratory blood. Later research by Redmond et al. (1965) provided dramatic evidence that the infant’s first breath occurs with redirection of blood from the placenta to the lungs [5].

Ziegler’s paper described several new devices for use in obstetrics, of which the clamp was one, a replacement for the earlier technique of tying the cord. That not all obstetricians clamped or tied the cord at that time can be inferred from his next statement:

"To those members of the profession whose custom it is to clamp the cord, this clamp will make its strongest appeal."

References
1. Ziegler CE (1922) Additions to our obstetric armamentarium.
2. Gunther (1957) The transfer of blood between baby and placenta in the minutes after birth
3. Jäykkä (1958) Capillary erection and the structural appearance of fetal and neonatal lungs
5. Redmond et al. (1969) Relation of onset of respiration to placental transfusion.

5 – The clamp as a complication of a simple procedure
In a presentation in April 1925 at the meeting of the New Orleans Gynecological and Obstetrical Society, Dicks (1925) promoted use of a clamp to prevent infection. He described his procedure as follows:

"After the cord and surrounding skin are painted with one-half strength tincure of iodine and pulsation has ceased, the Martinez clamp, which of course, has been sterilized, is placed on the cord as near the skin margin as possible in the long axis of the body. The jaws are closed slowly; if this is done too rapidly there is some danger of rupturing the cord below the clamp. The cord is then cut off close to the jaws of the clamp, and an alcohol spong applied for a few minutes to dehydrate it. A gauze roll is place about the body, including the clamp. Twenty-four hours later the instrument is removed and that portion of the cord which has been compressed and which is as thin as a piece of parchment can either be trimmed off at once or left to fall off, which it does within a few days." [1, p 708].

Among the discussants of this paper, WE Levy commented:
"I am rather inclined to disagree with those who advocate the use of a clamp. To me the ligation of the cord is one of the simplest processes in obstetrics, and why complicate what is inherently simple? I quite agree that the cord should be tied as close as possible to the skin margin, but a piece of tape does that just as well as an
instrument. The clamp crushes and macerates the tissues, and macerated tissue, as is well known, is prone to develop bacteria. This also holds true of the so-called milking of the cord, which frequently breaks down the outer surface and so favors the entrance of infection." [1, p740]

Of note is that during the early twentieth century, use of sterile techniques and antiseptic agents became increasingly important. However, waiting for pulsations of the umbilical cord to cease before ligating it in the traditional way, or by use of the newly introduced clamp, remained the standard of care. The comment by Levy above provides evidence that milking the cord to maximize transfer of blood to the baby was a technique used by some.

Reference
1. Dicks JF (1925) Treatment of the umbilical cord by short ligation and the use of a clamp.

6 – The clamp eight decades later
In November 2006 the recommended protocol for clamping the umbilical cord was published in the journal Obstetrics & Gynecology [1]. The clamp introduced as a hygiene measure in 1912 has now become adopted for routine use in childbirth:

“Immediately after the delivery of the neonate, a segment of umbilical cord should be double-clamped, divided, and placed on the delivery table pending assignment of the 5-minute Apgar score. Values from the umbilical cord artery provide the most accurate information regarding fetal and newborn acid-base status. A clamped segment of cord is stable for pH and blood gas assessment for at least 60 minutes, and a cord blood sample in a syringe flushed with heparin is stable for up to 60 minutes (13, 14). If the 5-minute Apgar score is satisfactory and the infant appears stable and vigorous, the segment of umbilical cord can be discarded.” [1, p1321]

Citations 13 and 14 from the article excerpt above:

Not just one clamp, but two are applied, and the purpose is to look for signs of abnormal respiratory function immediately after birth – abnormal respiratory function from the placenta, because the newborn infant may not have taken its first breath yet.

Wiberg et al. (2008) have pointed out that interpretation of cord blood pH and ratios of oxygen and carbon dioxide requires understanding of the process of transition from fetal to postnatal respiration [2]:
“The first several breaths are ineffective for oxygenation due to dead space ventilation with the alveoli remaining unexpanded, but after approximately the fifth breath the pulmonary ventilation is established, i.e. within the first 30 seconds of life. [2, pp701-702]

An infant born alive is alive because of oxygen delivery from the placenta. Circulation from the placenta does not stop until the lungs are fully functional – unless this postnatal circulation is prevented by use of a clamp.

During fetal life the lungs receive only eight percent of the cardiac output, just enough for development and growth. After birth the capillaries around the alveoli must be filled with blood to become functional. Exchange of carbon dioxide for oxygen in the placenta or the lungs is a function of the hemoglobin molecule. Release of carbon dioxide from newly filled capillaries into the alveoli may be what inflates the alveoli, and the first exhalation may precede the first breath.

Clamping the cord prevents ongoing postnatal circulation from the placenta. This is certainly a stressor for any infant, no matter how soon after birth breathing is established. Respiratory depression occurs in 5 to 6 per 1000 newborn infants [3, 4]. Because autism is associated with complications at birth, the statistic for respiratory depression at birth should be compared to that for autism prevalence, 2 to 6 per 1000, or 1 in 500 to 1 in 166, and perhaps still increasing as more and more (especially younger) obstetricians perform immediate clamping of the umbilical cord at birth [5, 6].

Use of the obstetric clamp has gone far beyond what it was originally intended for. Its use disrupts a normal physiological function, which may seem harmless for most newborn infants, but should be examined as a possible cause of 5 to 6 permanently disabled children who will be in need or life-long assisted living. Use of a clamp on a pulsating umbilical cord should be viewed as a serious medical error.

References
2. Wiberg N et al. (2008) Delayed umbilical cord clamping at birth has effects on arterial and venous blood gases and lactate concentrations.
5. Williams K et al. (2008) The prevalence of autism in Australia. Can it be established from existing data?
7 – What’s so terrible?
Oxygen is the most essential ongoing need for all species dependent upon aerobic metabolism. This is so taken for granted, that it often goes without saying, but surpasses in urgency the requirements of warmth, food, shelter etc. that make up the hierarchy of human or animal needs [1]. Use of oxygen masks is demonstrated by airline crews before every flight, with a reminder to adults to activate their own before placing a mask on a child. One of the most disturbing images from the 9/11 attacks is that of people jumping from the burning World Trade Center towers, which may indicate not only the confusion that occurs during suffocation, but the instinct to do anything for one more breath of air.

The need is understood for immediate action to clear the airway, give rescue breaths, and chest compressions to maintain circulation in adult victims of choking or cardiac arrest [2]. That the newborn infant can withstand a few minutes of oxygen insufficiency is a common misunderstanding. The newborn can survive without oxygen longer than older children or adults, but the brain will suffer impairment or frank damage in one of two clear-cut patterns of damage [3].

Total cutoff of oxygen or circulation results in damage of brainstem nuclei, thalamus, and basal ganglia [3]. The brainstem pattern of damage also occurs in adults who survive resuscitation from cardiac arrest [4, 5]. Hypoxia, or partial oxygen insufficiency, spares the brainstem centers, but results in damage of the cerebral cortex [3]. Damage of the cortex leads to cerebral palsy, and this was the outcome sought in experiments with monkeys [3, 6]. Asphyxia was (in early experiments) inflicted by delivering the infant head into a saline-filled bag, then clamping the umbilical cord. Some of the monkeys suffered respiratory distress following resuscitation leading to more extensive damage. Damage restricted to the brainstem was considered minimal [6]. The auditory system was most severely affected, but the effect on language development was unfortunately not considered, thus dismissal of brainstem damage as minimal.

Since the mid 1980s clamping the cord within the first minute of birth has become part of standard practice in obstetrics. Most infants begin breathing immediately at birth, which means the lungs normally take over the function of respiration quickly. If the baby has not begun breathing, resuscitation procedures are followed but, with disconnection from the placenta, a lapse in respiration has been allowed to happen. This cannot be viewed as innocuous. Impairment in some degree is likely to have affected the auditory pathway of the brainstem.

Auditory system impairment may be only the tip of the iceberg. Not only autism, ADHD, dyslexia, and other learning disorders are on the increase, but so are asthma, heart murmurs, intestinal disorders, obesity, and diabetes in childhood. Even if an infant begins breathing right away at birth, clamping the umbilical cord prevents completion of full placental transfusion.

Prospective parents are given a great deal of information and encouragement to bank their baby’s umbilical cord blood, and the earlier the cord is clamped the more blood can be
obtained for banking. The blood collected for banking is not extra blood, or blood left over. Before birth, placental blood is part of the infant’s total circulation. In the placenta carbon dioxide is exchanged for oxygen, a process that is transferred to the lungs during transition from placental to pulmonary respiration. By nature’s plan circulation to the placenta continues after birth until the capillaries surrounding the alveoli are completely filled with blood. Pulsations of the umbilical cord after birth are from the infant’s heart continuing to pump blood back to the placenta for oxygen. Pulsations of the cord cease naturally when oxygen content of the blood returning to the placenta is equivalent to what the placenta would provide before the lungs become functional [7, 8].

If the umbilical cord is clamped before full perfusion of the lungs has taken place, blood may be drained from other organs to fill the capillaries that supply the alveoli. Redistribution of blood to maintain brainstem centers that control heartbeat and breathing may also take place. Organs like the GI tract and pancreas may thus incur injury from hypoperfusion and set the stage for future problems. The brainstem centers that control peristalsis, eye movements, vestibular and other autonomic functions may also suffer degradation of function. What is or is not spared may be quite variable.

Deaths of young athletes who collapse during competition are frightening, as were reports of a professional football star who suffered a stroke [9]. Some strokes and migraine headaches appear to be due to a patent foramen ovale [10, 11]. The foramen ovale and ductus arteriosus are the shunts in the fetal heart that send blood to the placenta during gestation [12, 13]. At birth the shunts should close, and circulation is redirected to the lungs for oxygenation. Patent foramen ovale (PFO) has been reported as an anatomical variant with a prevalence of about 27 percent, but prevalence appears to be greater among younger patients [11, 14]. Termination of postnatal placental circulation should be considered a possible factor when the foramen ovale and ductus arteriosus fail to close at birth. Failure of these shunts to close represents failure of full transition from fetal to neonatal circulation.

Injury that can affect later-born children can also occur. Blood left in the placenta creates pressure and bursting of small capillaries in the placenta, thus allowing fetal blood to enter the maternal circulation [15, 16]. Maternal antibodies may be produced to fetal antigens. The most serious is maternal antibody produced by a mother with Rh-negative blood to the Rh factor of Rh-positive blood from her baby [17, 18]. The resulting “erythroblastosis fetalis” that occurred in second- and later-born infants of a mother with Rh-negative blood was treated in the 1950s by total replacement of the the baby’s blood [19, 20]. This was done to prevent kernicterus caused by bilirubin entering the brain. RhoGAM was developed in the 1960s and is now routinely given to Rh-negative mothers to prevent antibody formation [21]. Questions remain [22]. Kernicterus (brain damage from bilirubin) has not been eradicated, and may also be another disorder on the rise again [23].

5. Janzer RC, Friede R (1980) Hypotensive brain stem necrosis or cardiac arrest encephalopathy?
9. Bruschi T with Holley M (2007) Never give up: My stroke, my recovery, and my return to the NFL.
15. Dunn PM (1966) The placental venous pressure during and after the third stage of labour following early cord ligation.
18. Levine P et al. (1941) Isoimmunization in pregnancy: its possible bearing on the etiology of erythroblastosis fetalis.
22. Wickham S (2001) Anti-D in midwifery: panacea or paradox?
8 – Quotes from obstetric textbooks up to the time of the Apgar score

Frischkorn and Rucker (1939) noted that with use of anesthesia, pulsations of the umbilical cord continue longer than in infants born without use of anesthesia [1, 2]. In one case they observed pulsations to continue for 50 minutes after birth. Did prolongation of pulsations perhaps have had something to do with an increasing tendency to tie off the cord early? After introduction of the clamp, ligation of a taut pulsating cord would certainly be easier.

Following are quotes from obstetric textbooks up to the time of Virginia Apgar, an anesthesiologist at the Sloane Hospital (Columbia University) where, by the 1950s, clamping of the cord within one minute of birth was adopted for preservation of the “sterile field” around the birth canal. By this time, women were also often placed in a lithotomy position during the second stage of labor, with legs up in stirrups and the vaginal area shaved and swabbed with antiseptic.

Semmelweis was correct in pointing out the medical error in which doctors left the cadaver room to deliver a baby without even washing their hands [3-5], but throughout history how sterile has the outlet of the birth canal been?

The following quotes from textbooks following use of anesthesia in childbirth up to the mid 20th century show that the tradition continued of waiting at least for breathing to be established before ligation of the umbilical cord:

**Cazeaux (1871)**

“...the circulation existing between it [the child] and the placenta is observed to continue for some time... pulsations in the arteries gradually cease, commencing at their placental extremity; and some authors have advised this event to be waited for before cutting the cord...” [6, p406]

**Lusk (1882)**

"Infants which have had the benefit of late ligation of the cord are red, vigorous, and active, whereas those in which the cord is tied early are apt to be pale and apathetic."

"1. The cord should not be tied until the child has breathed vigorously a few times. When there is no occasion for haste, it is safer to wait until the pulsations of the cord have ceased altogether.

2. Late ligation is not dangerous to the child. The child receives into its system only the amount of blood required to supply the needs created by the opening up of the pulmonary circulation." [7, pp214-215]

**Jellett (1910)**

"As soon as the child is born, its eyes are wiped, any mucus in the air passages is removed, and it is placed in a convenient position between the
patient's legs. The cord is tied as soon as it has stopped pulsating, and the infant is then removed." [8, p350]

Williams (1917)
"Immediately after its birth the child usually makes an inspiratory movement and then begins to cry. In such circumstances it should be placed between the patient's legs in such a manner to have the cord lax, and thus avoid traction upon it."

"Normally the cord should not be ligated until it has ceased to pulsate..."

"I have always practiced late ligation of the cord and have seen no injurious effects following it, and therefore recommend its employment, unless some emergency arises which calls for earlier interference." [9, pp342-343]

vonReuss (1921)
"... A compromise is usually adopted, in that the cord is not tied immediately after birth, nor does one wait till the expression of the placenta, but only until the cessation of pulsation in the cord, an average of five to ten minutes." [10, p419]

Williams (1927)
"I have always practiced late ligation of the cord and have seen no injurious effects following it, and therefore recommend its employment, unless some emergency arises which calls for earlier interference..." [11, pxx]

DeLee (1930)
“Tying the cord. – After waiting until the pulsation in the exposed umbilical cord has perceptibly weakened or disappeared, the child is severed from its mother. Until the cord is severed the child is still part of its mother and has no legal existence... During the four or eight minutes while waiting to tie the cord the child obtains from 40 to 60 gm. Of the reserve blood of the placenta – a fact that was first shown by Budin. The blood is pressed into the child by the uttering contractions, and part is aspirated by the expanding chest. This extra blood the child needs in its first days of life, and observation has shown that such children lose less in weight and are less subject to disease...” [12, p330]

Baer (1933)
"In most clinics the cord is not tied until pulsation has ceased. This is based on the accepted fact that the delay provides the infant with an additional average of 60 to 90 cc of blood. With premature infants or twins, most of which are usually below the weights of average single infants, this additional blood is a distinct advantage. In full-term infants of normal size the advantage is more theoretical than real." [13, p828]

DeLee (1936)
"After waiting until the pulsation in the exposed umbilical cord has perceptibly weakened or disappeared, the child is severed from its mother."

"During the four or eight minutes while waiting to tie the cord the child obtains from 40 to 60 gm of the reserve blood of the placenta – a fact that was first shown by Budin. The blood is pressed into the child by the uterine contractions, and part is aspirated by the expanding chest. This extra blood the child needs in its first days of life, and observation has shown that such children lose less in weight and are less subject to disease. It is an error, on the other hand, to force the blood of the placenta into the child by stripping the cord toward the child. This overloads its blood vessels, causes icterus, melena, even apoplexy ..." [14, p334]

**Fitzgibbon (1937)**

"...If the infant has cried and has respired well for about five minutes, there is no advantage in leaving at attached any longer to the placenta. Its pulmonary circulation has been opened up and the pulmonary vessels filled with blood ..." [15, p128]

**Read (1944)**

"It is my custom to lift up the crying child, even before the cord is cut ..."

"Its first cry remains an indelible memory on the mind of a mother; it is the song which carried her upon its wings to an ecstasy mere man seems quite unable to comprehend." [16, p95]

**Eastman HJ (1950)**

"Whenever possible, clamping or ligating the umbilical cord should be deferred until its pulsations wane or, at least, for one or two minutes.

"There has been a tendency of late, for a number of reasons, to ignore this precept. In the first place the widespread use of analgesic drugs in labor has resulted in a number of infants whose respiratory efforts are sluggish at birth and whom the obstetrician wishes to turn over immediately to an assistant for aspiration of mucus, and if necessary, resuscitation. This readily leads to the habit of clamping all cords promptly." [17, pp397-398]

**References**

1. Frischkorn HB, Rucker MP (1939) The relationship of the time of ligation of the cord to the red blood count of the infant.
2. Rucker MP (1949) Late ligation of the umbilical cord.
9 – The Apgar score
Virginia Apgar introduced her system for scoring the condition of the newborn in 1953, noting that when mothers receive an excessive amount of depressant drugs during labor, it is common for an infant to breathe once, but then become apneic for many minutes. “A satisfactory cry is sometimes not established even when the infant leaves the delivery room”

We need to ask why the umbilical cord should ever be cut before a satisfactory cry is established. What was the justification for abandoning the traditional teaching that breathing must be clearly established before ligation of the cord?

In 1958, Apgar (and her colleagues) wrote that scoring at one minute was done because this represented the time of most severe depression:

"In the Sloane Hospital the cord has been cut by this time, and the infant is in the hands of an individual other than the obstetrician. In many hospitals, such is not the case. Those obstetricians who practice slow delivery and delayed clamping of the cord until pulsations of the umbilical artery cease still have the infant in the sterile field. However, if the obstetrician is reminded of the passage of time by another observer, he may assign a score even though the cord is still attached," [Apgar et al.1958, p 1987]

Thus the Apgar score devised over 50 years ago reflected the perceived need to remove the newborn from the "sterile field" for repair of the episiotomy, manage delivery of the placenta, and to give the infant to neonatal specialists, often for resuscitation.
Apgar et al. also wrote in the 1958 paper:

“All infants with a score of 8, 9, or 10 are vigorous and have breathed within seconds of delivery. In this group, scores of 8 or 9 reflect a lower score for color. The infants with a score of 4 or less are blue and limp and have failed to establish respiration by one minute.” p 1987

The Apgar score is all about how well a newborn establishes respiration. In contrast to the opinion expressed by White in 1773, Apgar and her colleagues expected that the transition from fetal to neonatal respiration should take place within seconds of delivery.

If failure to breathe persists for five minutes, the outcome is well recognized as ominous.

Apgar et al. (1958) pointed out that many obstetricians at that time still practiced "slow delivery," waiting for pulsations of the cord to cease, and they suggested that a score could still be assigned, obtaining the heart-rate of the infant by palpating the umbilical cord.


10 – Quotes from obstetric textbooks after 1950

Greenhill (1951)
"After waiting until the pulsation in the exposed umbilical cord has ceased, the child is severed from its mother."

"DeMarsh, Alt, Windle and Hillis showed that those infants whose cords were not clamped until the placenta had separated from the uterus had on average 0.556 million more erythrocytes per cubic millimeter and 2.6 gm more hemoglobin per 100cc during the first week than those whose cords were clamped immediately. These authors maintained that early clamping of the umbilical cord is equivalent to submitting the child to a hemorrhage at birth. Wilson, Windle and Alt found that infants whose umbilical cords were clamped immediately after birth had a lower mean corpuscular hemoglobin at eight and ten months of age than those whose cords were clamped after the placenta began to descend into the vagina. It was suggested then that early clamping of the cord may lead to an iron deficiency during the first year of life."

"McCausland, Holmes and Schumann advise stripping the cord and placental blood into the infant because it is harmless if done gently and because term
babies receive about 100cc of extra blood in this way. These authors claim that babies receiving this blood had higher erythrocyte counts, higher hemoglobin values, higher initial weights and less initial weight losses." [1, p.251]

**Greenhill (1955)**

"Immediately after the baby is delivered it should be held well below the level of the vulva for a few minutes or placed in a warm container the level of which is considerably below the mothers' buttocks (Fig 279). The purpose of keeping the baby at this level is to permit the blood in the placenta to get to the baby. Dieckmann and associates maintain that this procedure will add from 50 to 75 percent of the blood in the placenta and cord to the newborn child. If the placenta separates while waiting, expressing it from the uterus and holding it elevated for two or three minutes will accomplish the same purpose. The cord is cut after about three minutes or after it collapses. If the baby is in a special container, it is left in until after the cord is cut. As soon as possible after delivery any mucus in the air passages must be removed with a soft rubber bulb or a tracheal catheter.

Tying the Cord. After waiting until the pulsation in the exposed cord has ceased, using dull scissors, the child is severed from its mother. With a piece of linen bobbin, coarse silk, rubber band or any sterile strong string, the cord is ligated close to the cutaneous margin of the umbilicus, making sure that there is no umbilical hernia which might allow a loop of intestine to be caught in the grasp of the ligature. It is important to leave as little as possible of the cord to be cast off except when a baby has erythroblastosis…"

**Greenhill (1965)**

"After pulsation in the exposed cord has ceased, using dull scissors, the child is separated from its mother." [3, p376]

**Taylor (1966)**

"After delivering the child, the obstetrician suspends it by its feet … During this time the fluid within the tracheobronchial tree may be expelled by gravity. Most infants take their first extrauterine gasp at this time, and it is well to have the trachea clear."

"If the obstetrician waits until the cord stops pulsating, the child receives a considerable amount of blood (up to 100 ml). This procedure is harmless to the normal infant and may be beneficial. However, the extra blood volume from the placenta may be detrimental in some pathological conditions of the infant. The most notable of these are maternal-fetal blood group incompatibilities, anomalies of the infant cardiovascular system, or severe fetal asphyxia."

"In normal full-term deliveries, the cord is clamped with two hemostats as soon as the cord stops pulsating." [4, p202]
Fitzpatrick et al. (1966)
"…The infant usually cries immediately, and the lungs become expanded; about this time the pulsations in the umbilical cord begin to diminish. The physician usually will defer clamping the cord until this occurs, or for a minute or so if practicable, because of the marked benefit of the additional blood to the infant." [5, p268]

“Emergency delivery… There is no hurry to cut the cord, so this should be delayed until proper equipment is available. It is a good plan to clamp the cord after pulsations cease (but not imperative at the moment) and to wait for the physician to cut the cord after he arrives." [5, p288]

Bodyazhina (1983)
"The umbilical cord should be tied up after its vessels stop pulsating, which occurs in 2-3 min following the delivery of the infant. In the course of a few minutes that the umbilical cord pulsates, from 50 to 100 ml of the blood is delivered into the vascular system of the foetus from the placenta. As soon as the pulsation discontinues, the cord should be cut off and tied up in aseptic conditions." [6, p156]

Beischer & MacKay (1986)
"The optimum time of clamping is 30-60 seconds after birth: This will provide some 80 ml of extra blood to the baby. Excess blood volume in the baby can be a disadvantage, producing polycythemia and hyperviscosity, with such attendant problems as respiratory distress, heart failure, jaundice, convulsions and apathy." [7, p381]

"Apgar scores are recorded at 1 minute and again at 5 minutes, timing the observations accurately... Also the time to first breath and time to the establishment of regular respirations are recorded.

… Permanent cord clamps or ligatures (Figure 26.27) or special bands are applied to the umbilical cord as soon as possible after birth…" [7, p470]

"The optimal time for clamping (or tying) the cord is not known for certain. Late clamping of the cord results in an additional volume of blood reaching the infant. This may result in hyperviscosity, jaundice and cardiorespiratory, neurological and renal problems. The extra blood specifically aggravates jaundice in premature infants and in those with erythroblastosis, so early clamping of the cord is advised in such infants." [7, p546]

"Q: What is the significance of continued pulsation of the arteries in the umbilical cord at birth?

A: It means that respiration has not commenced. The physiological stimulus causing closure of umbilical arteries (and ductus arteriosus) is an increase in oxygen saturation of the blood which occurs when the lungs expand with air." [p710]

"Routine practices concerning the time for clamping the umbilical cord vary. If the child's condition is satisfactory cord clamping and severing can be delayed until pulsation has stopped and the infant is position at or below the level of the mother. The additional blood transfused from the placenta can
be as much as 100 ml. The benefits of this are not fully evaluated but the additional volume may be harmful in preterm infants. Early clamping facilitates prompt resuscitation, if required, and transfer to the mother's arms…" [7, pp734-5]

Kraybill (1987)
"…with present information it seems reasonable to avoid the extremes of immediate and of very late clamping. The first 30 to 60 seconds after delivery are well spent in suctioning the airway … The normal newborn invariably cries during this interval …" [8, p258]

Hibbard (1988)
"Apgar scores are recorded at 1 minute and again at 5 minutes, timing the observations accurately (see chapter 43, Table 43.1). Also the time to first breath and time to the establishment of regular respirations are recorded."
"Permanent cord clamps or ligatures (Figure 26.27) or special bands are applied to the umbilical cord as soon as possible after birth…" [9, p470]

McGregor Kelly (1994)
"…As soon as possible after suctioning, the cord is clamped…"
"…consequences of a significant shift [of blood volume] toward the infant include polycythemia, circulatory volume overload, and hyperbilirubinemia, and these generally outweigh any potential advantage of augmenting the infant's iron reserve…" [10, p301, citing Cunningham et al., Williams Obstetrics, 18th ed.]

Cunningham et al. (1997)
"Although the theoretical risk of circulatory overloading from gross hypervolemia is formidable, especially in preterm and growth-retarded infants, addition of placental blood to the otherwise normal infant's circulation ordinarily does not cause difficulty. Our policy is to clamp the cord after first thoroughly clearing the infant's airway, all of which usually takes about 30 seconds." [11, pp336-337]

Turrentine (2003)
(1) Doubly clamp cord segment (10-20 cm) immediately after birth in all deliveries, and place on table.
(2) pH and acid-base determinations indicated for:
  - prematurity
  - meconium
  - nuchal cord
  - low Apgar scores (< 7 at 5 minutes)
  - abnormal antepartum fetal heart tracing
  - any serious problem with delivery or neonate's condition
(3) If unable to obtain cord specimen, aspirate artery on chorionic surface of placenta
(4) Discard cord segment if 5 minute Apgar score satisfactory and newborn stable/vigorous [12]
"... Our policy is to clamp the cord after first thoroughly clearing the airway, all of which usually requires about 30 seconds." [13]


3. The obstetric clamp (upto mid-20th century)

1 – The clamp in the 1930s, and banking of umbilical cord blood
New devices for clamping the umbilical cord continued to be introduced during the 1930s [1-5]. These appear to have been used sooner after birth in many cases, without waiting for pulsations of the cord to cease, and residual blood in the placenta was beginning to be collected for blood banks [7-10].

The paper by Goodall et al (1938) begins with a viewpoint on childbirth teachings of the day:

"The teaching that, if the blood is left in the placenta, placental detachment from the uterine wall is hastened, has never had any scientific appeal to us. Consequently, it
became a problem to be proved or disproved. So at every birth, on our service, the clamp on the cut cord was released with the cord in a pendent position and the placenta was emptied."

Further observations made by Goodall et al are of interest with respect to the pressure of blood left in the placenta after clamping. They noted that during blood collection, the cord lay flaccid instead of quite turgid as was the case when waiting for delivery of the placenta with the clamp in place. Separation of the placenta was not appreciably changed either, in elapsed time or completeness. These authors commented on another discovery they made:

"The blood pressure in the cord was great, projecting the blood frequently 3 feet distant, and the flow kept up a surprisingly long time."

This was when they asked themselves, "Why waste all this valuable material?" So they set about finding means to preserve the lost blood. Many articles on how to collect, store, and use placental blood appeared within the next two years.

Now, 70 plus years later, a whole industry has arisen to provide umbilical cord blood banking, with widespread marketing aimed at prospective parents. Having the father clamp the cord has also been widely adopted as a way to involve the father in the childbirth process.

References
1. Ryder GH (1932) Presentation of instruments: (1) A uterine packer for cesarean sections; (2) An umbilical cord clamp.
2. Kane HF (1934) An umbilical cord clamp.
5. White MR. Umbilical cord clamp.
11. Halbrecht J (1939) Fresh and stored placental blood.

2 – Placental transfusion
Frischkorn and Rucker (1939) measured red blood cell counts in addition to weight in 400 infants [1]. The cord was not tied until pulsations ceased in 59 cases, Frischkorn and Rucker described use of sodium amytal scopolamine analgesia analgesia and ether
anesthesia in all cases. They noted with interest that the cord continued to pulsate longer than in Budin's cases, which (in 1875) pre-dated use of anesthesia [2]. In one of Frischkorn and Rucker's cases, pulsations continued for 50 minutes.

Blood counts were made within 24 to 36 hours of birth, with a range of 3.28 to 7.12 million red blood cells. The average red cell count in the 59 infants whose cords were not tied until after pulsations ceased was 5,783,400, as opposed to the average for 333 cases in which the cord was still pulsating when tied was 5,198,919; the difference was 584,481.

With the now nearly universal practice of immediate cord clamping, how many doctors trained in the last two decades have ever been in attendance at what Apgar would (within the next 20 years) refer to as a "slow birth," waiting for pulsations of the cord to cease. We therefore need to go back to historical accounts, as in the case of vanishing diseases like smallpox, neurosyphilis, tuberculosis, leprosy, or polio. A paper by Frischkorn and Rucker (1939) paper would be as useful to include in a Cochrane Review as any of the randomized-controlled trials of "delayed cord clamping" so highly valued today.

Frischkorn and Rucker provide a description of postnatal umbilical cord function that perhaps even in the 1930s was not waited for or witnessed by many obstetricians:

"If a cord be watched immediately after delivery the umbilical vessels can be seen to pulsate strongly throughout their entire length. In a varying length of time the pulsations cease in the more distal part and as this occurs the umbilical vessels collapse. This process of cessation of pulsation and collapse of the vessels proceeds toward the umbilicus until finally there is no pulsation even at the navel. The vessels are then entirely collapsed. If now the cord be tied and cut very little blood will escape from the placental end." [1, p 593]

References
1. Frischkorn HB, Rucker MP (1939) The relationship of the time of ligation of the cord to the red blood count of the infant.
2. Budin, P (1875) A quel moment doit-on pratiquer la ligature du cordon ombilical?

3 – Condemnation of the clamp
Windle (1940) presented a paper at a "Round Table Discussion on Anemias of Infancy" as part of the tenth annual American Academy of Pediatrics [1]. In his talk Windle began by summarizing research on development of red blood cells, which begins in the wall of the embryonic yolk sac. Blood vessels begin to form during the fifth week, and after sufficient
development of the liver, blood cell formation becomes one of the fetal liver's primary functions. With development of the fetal spleen and bone marrow, these take over as the major sites for blood cell formation.

How essential oxygen delivery is, that red cells, blood vessels, and circulation powered by the fetal heart (the earliest functioning organ) follow such an elegant maturational plan! This knowledge remains current [2-4]. Why is it not incorporated into the education of most obstetricians, in whom we place our trust for safe delivery of our children into this world?

Windle continued with a detailed description of how oxygen is transferred across the placenta, and how fetal hemoglobin is designed to readily take up oxygen at low partial pressures on the maternal side of the placenta, again emphasizing the importance of maintaining full aerobic activity. Placental blood is fully part of the fetal circulatory system, and found by many investigators to contain one-fifth to one-fourth of the total fetal blood at birth. Windle pointed out that this placental blood does not pass into the infant at birth until uterine contractions have a chance to compress the placenta, and he stated:

"... The rather common practice of promptly clamping the cord at birth should be condemned. Of course, this will make it impossible to salvage placental blood for 'blood banks.' However, the collection of usable quantities of placental blood robs the newborn infant of blood which belongs to him and which he retrieves under natural conditions... Immediate clamping of the cord is comparable to submitting the infant to a rather severe hemorrhage." [1, p546]

Windle with DeMarsh, Wilson, and Alt (1941, 1942, 1948), and like many before and since, did research with human infants, assigning them to groups for immediate or delayed clamping of the cord [5-8]. I am not sure I understand why any more "randomized controlled trials" need to be done. Clamping of the cord had been adopted by some obstetricians during the 1930s, as described above, for the purpose of banking placental blood. Thus immediate effects of cord clamping appeared to do no harm, but this illustrates the hardness of most newborn infants. It seems clear that newborn infants have the capacity to adapt to adverse situations, but this should not be confused with what provides the healthiest start in life.

In any case, Windle and his colleagues found increased erythropoiesis (more active blood formation) in infants when the cord was clamped early that when it was clamped late. Early clamping of the umbilical cord leaves the infant in an anemic state. The main reason immediate clamping of the cord has gained favor, is the thinking that fewer red cells leads to less likelihood of developing jaundice, with the aim of preventing bilirubin staining of nuclei in the subcortical motor system, or kernicterus [9, 10]. This goal has not been accomplished. Sadly, kernicterus is still prevalent [11].

Windle would during the 1950s begin doing research on the effects of asphyxia at birth in monkeys [12]. The goal was to produce a primate model of cerebral palsy. The finding of damage restricted to the brainstem was unexpected, but in fact the brainstem pattern of
damage they observed was similar to that found in patients with kernicterus. Ranck and Windle ended their paper with the following comment:

“The human neuropathologic entity most closely resembling the effects of asphyxia neonatorum in the monkey is kernicterus. There are similarities in the distribution and type of nerve cell changes in both conditions. Major differences between the findings in the monkey and those in human infants with kernicterus are absence in the former of the usual history of erythroblastosis fetalis, lack of clinical jaundice, lack of pigment in the lesions, frequent presence of neuroglia cell damage, and presence of marked astrocytic and phagocytic reactions.” [12, p153]

Kernicterus is a form of cerebral palsy in which the afflicted child displays involuntary movements (called athetosis) and has problems with eye movements, especially in upward gaze. Five years later Windle and his colleagues published results of a follow-up investigation on producing experimental kernicterus in monkeys [13]. High levels of bilirubin did not cause kernicterus, but kernicterus was produced by bilirubin following asphyxia at birth. The brainstem nuclei damaged by asphyxia were selectively stained by bilirubin.

References
1. Windle WF (1940) Round table discussion on anemias of infancy.
5. Wilson EE et al. (1941) Deprivation of placental blood as a cause of iron deficiency in infants.
6. DeMarsh QB et al. (1941) The effect of depriving the infant of its placental blood; on the blood picture during the first week of life.
8. DeMarsh QB et al. (1948) Factors influencing the blood picture of the newborn; studies on sinus blood on the first and third days.
13. Lucey JF et al. (1964) Kernicterus in asphyxiated newborn monkeys.

4 – Manipulations with the clamp
Given any novel instrument, it seems to be part of human nature to experiment with variations in its use. Fortier (1945) stated:
"Recent literature has emphasized the importance of delayed clamping of the cord [i, ii], one writer's work suggesting that there is even an increase in the infant's blood volume during the period of placental expulsion [ii].

During the past several months I have been attempting to improve on the above-mentioned method of delayed clamping of the cord by an immediate clamping of the umbilical arteries..."

"... In most cases the umbilical arteries are easy to define and clamp. In large cords a single blade of the hemostat is made to pierce the cord adjacent to the vein, and all tissues except the vein are clamped." [1, p305]

Fortier explained that this procedure disrupts the blood flow to the placenta, and results in exsanguination of the placenta into the body of the infant, via the umbilical vein. The explanation continues with the thought that this blood would otherwise remain in the placenta, or be spilled in the practice of bleeding the placenta to facilitate its separation and expulsion.

Fortier's article provides evidence that clamping the cord had already become standard procedure in obstetric practice, and that other manipulations had also been adopted to hurry the third stage of labor, and get the placenta delivered as quickly as possible.

Fortier, on the other hand, commented that he had frequently observed that in cases of asphyxia administration of oxygen to the mother improves the color of the infant, and that for this reason he never clamped the umbilical arteries until the newborn infant cries. He therefore followed what most people would consider to be common sense, unlike some academicians of today who describe experiments in which the cord is clamped before the first breath.


5 – Research on anatomy and physiology of the umbilical cord
Ligation of the umbilical cord came into use as a means to prevent bleeding. Spivack (1946) studied the structure and physiology of the umbilical cord, and its blood vessels; the infant's heart pumps blood through the umbilical arteries to the placenta, which delivers oxygen and nutrients to the baby via the umbilical vein. Spivack observed that the umbilical arteries close quickly after onset of respiration, and commented:

"Oxygenation of the newborn's blood after establishment of its pulmonary respiration is the main factor in bringing about closure of the umbilical arteries..."

"...Experience since long ago has taught some clinicians that ligation of the cord is not paramount in the care of the stump." [1, p398]
Spivack cited Engelmann (1883), who noted that the umbilical arteries have an intrinsic capacity to check their bleeding in unaided labor, and Rachmanow's (1914) series of several thousand cases in which the cords were not tied, and not a single newborn died of hemorrhage. Rachmanow warned however, that spontaneous cessation of pulsation of the cord and establishment of respiration are essential conditions before severance of the cord.


**6 - More on blood volume increase with delayed ligation of the umbilical cord**

Ballentine's 1947 paper reports investigation of the effects of delaying ligation of the cord on weight gain as a measure of placental transfusion.

Experimental groups were: 30 infants subjected to cord ligation after being placed onto scales at the time of delivery, 30 infants weighed at time of delivery and again after the cord had stopped pulsating, and 30 infants weighed at delivery and following transfusion from the placenta placed in a rack as high as the length of the cord would allow.

In the second group, pulsations in the cord continued for seven to thirty minutes (average 21.7 mins). In the group with delivered placenta above the infant, pulsations continued for 12 to 30 minutes (average 23.8 mins). Elevation of the placenta did not increase weight gain. This indicates that postnatal placental transfusion is controlled by the infant's need for continuing fetal circulation, until full transition to pulmonary respiration has been established.

Blood volume increased from 37 to 187 cc (average 96cc) in the second group, and from 53 to 125 cc (average 87cc) in the group with elevated placenta.

Ballentine also reported that 55 percent of the blood flowed into the infant from the placenta in the first minute and 84 percent in the first five minutes -- the two time points that Apgar would within the next five years chose for evaluating a newborn infant's condition.

Intravenous ergotrate was used to shorten the third stage of labor, which provided the group with elevated placenta.

Ballentine wrote that 135 cases were studied, with equal numbers of primi- and multiparous women, and only vertex presentations. Nembutal in small doses was used as premedication. Inhalation anesthesia was used at time of delivery. All mothers were given intravenous ergotrate with delivery of the anterior shoulder to shorten the third stage of labor, and which was noted to result in prompt delivery of the placenta. One infant was delivered by cesarean section, and episiotomies were performed in approximately 75 percent of cases.

Ballentine commented that transfusion as a means of combating shock may be accomplished by postponement of severance of the cord, and added:
"Such a measure is of desirable therapeutic value for infants manifesting vary degrees of shock as a result of birth trauma following difficult labor or delivery." [1, p726]

This paper was presented at a meeting of the Medical Society of the State of Pennsylvania, October 8, 1946. Comments of one discussant, Josiah R. Eisaman Jr, were included in the published article, who offered the opinion that among some obstetricians:

"There seems to be undue haste in severing the umbilical cord immediately after the second stage of labor...
...This practice involve many poorly understood changes in neonatal physiology, i.e., closure of the ductus arteriosus and ductus venosus...
...Not long ago placental blood was recommended for transfusions. The volume so obtained was 125 to 250cc, providing immediate ligation of the cord was performed." [1, p728].


7 – Effects of anesthesia and Ergotrate on postnatal placental transfusion
Rucker (1949) made a presentation at the annual meeting of the South Atlantic Association of Obstetricians and Gynecologists. He had, with Frischkorn 10 years earlier, described the appearance of umbilical cord pulsations as part of a study to determine the increase in blood volume gained during postnatal placental transfusion. He emphasized some interesting points:

"We found that whether or not the cord had ceased to pulsate was the significant factor and not the length of time that the exposed cord was allowed to pulsate."

Pulsations of the cord are from the infant's heart, and indicate continuing need of placental circulation. Clearly events in transition from placental to pulmonary respiration are still not well understood. Wouldn't it better then to go along with nature's time-table?

Rucker also noted:
"In our series, the cords continued to pulsate for a longer time than in Budin's (1875) cases, and we thought that this difference might have been due to the anesthesia that our patients received."

Use of the uterotonic drug Ergotrate, however, caused the cords to cease pulsating sooner.
Reference

8 – Mid-twentieth century survey of opinion
McCausland et al. (1949) sent a questionnaire to 1,900 diplomates of the American Board of Obstetrics and Gynecology to determine the usual practice at that time of handling the umbilical cord at birth. Replies from almost every state numbered 1,198 and revealed that 497 (41.5%) clamped the cord immediately after birth, 400 clamped the cord within five minutes after birth, and only 191 waited for pulsations to cease. However, 455 practiced stripping of the cord.

McCausland et al. recommended stripping of the cord, especially for premature infants, whom they described as not only underdeveloped, but often in varying degrees of hock. They began stripping the cord because they maintained that there are times when the condition of the mother or baby made it advisable to wait for the cord to stop pulsating, but they pointed out that giving a transfusion via hypodermic syringe to a baby in an incubator was difficult and traumatic. They stressed that the additional blood was of benefit for any infant born in any degree of shock following a long labor or difficult delivery, and helped fill the capillary bed of the expanding lungs.

McCausland et al. reviewed the research of the preceding 75 years, beginning with that of Budin (1876) and Schucking (1877), added some data of their own, provided a summary of attitudes just before the midpoint of the twentieth century, and voiced their own reasons in favor of stripping additional cord blood into the newborn infant:
"The fetal circulation is well known to all obstetricians up until the delivery of the child. What happens and what should be done between the second and third stages of labor has caused a great deal of confusion and there is wide variance in practice. The authors believe that as soon as the child is delivered there is an immediate reduction in the size of the placental site, the placenta begins to separate at once, and thus placental circulation is disrupted. Then the uterus contracting upon a blood-filled placenta forces blood through the umbilical vein into the baby...
... The umbilical vein remains dilated long after the umbilical arteries have ceased to pulsate. The cessation of pulsation of the cord is not the criterion as to the proper time for clamping the cord. Instead, when the contracting uterus no longer causes pressure in the umbilical vein, that would be much better time to sever the cord." [1, pp195-6]

What ensures full and healthy transition from placental to pulmonary respiration remains confusing still, nearly six decades later. McCausland et al. stressed the importance of the capillary bed of the expanding lungs.

Respiration, in the lungs, is an exchange of carbon dioxide for oxygen. Bohr et al. (1904) provided evidence that the hemoglobin molecule receives oxygen with the release of carbon dioxide [2, 3]. White (1773) pointed out that the shunts in the heart
cannot be expected to close at the instant of birth [4]. What triggers closure of the foramen ovale and ductus arteriosus is still not well understood [5, 6]. However, there should be no confusion that the capillary bed surrounding the alveoli must be filled with blood before the exchange of carbon dioxide for oxygen can begin in the lungs.

What initiates opening of the alveoli at birth? Could it be they first fill with carbon dioxide? Then exhalation would precede the first breath. This is where research efforts should be focused, not on more randomized-controlled trials of "delayed clamping" of the umbilical cord. On what evidence is the current practice of clamping the cord within seconds of birth justified? Doesn't this need to stop?

References

4. The obstetric clamp (post mid-20th century)

1 – Placental transfusion after cesarean delivery
Landau et al. (1950) described the respiratory distress that often afflicted infants born by cesarean section. They compared the symptoms with those of hematogenic shock, and they described how the delivery procedure might be the cause:
"Usually at the time of cesarean section as soon as the uterus is opened the operator delivers the infant as rapidly as is consistent with the infant's safety. The cord is clamped and cut immediately and the infant is handed to the waiting assistant..."

...This is in marked contrast to the procedure during normal or vaginal delivery. At this time the cord is not clamped and severed until pulsations have ceased."
Landau et al. (in Hannibal Missouri) thus practiced what Apgar and her colleagues referred to as "slow birth." Landau et al. further commented:

"The thought occurred to us that the immediate clamping and cutting of the cord might be the essential point of difference between the cesarean- and the normally delivered infant."

They proceeded to adopt a new procedure for cesarean deliveries:

"The assistant designated to care for the infant is scrubbed and stands to the left of the operator. After the infant is delivered from the uterus this assistant holds the infant by the legs with the head down. The pharynx is aspirated by means of a rubber bulb syringe. The cord is neither clamped nor severed. The placenta is separated from the uterus and wrapped in a large turkish towel...

...The placenta is suspended from a standard by means of a clamp attached to the towel...

...The cord is not cut until its blood vessels have collapsed. It is then clamped, cut, and tied in the usual manner. The placenta is usually drained and the cord collapsed in from six to ten minutes."

Landau et al. commented that in 87 sections done since instituting this technique, there were no instances of respiratory distress, and that for this reason they did not feel justified in running a control series. This seems far more ethical than the current academic standard requiring random assignment of subjects to groups to receive a treatment or to not receive the treatment.


2 – Childbirth in the 1950s
By the time Apgar was developing her newborn score, Colozzi (1954) remarked:

"It is difficult to assay the various methods of umbilical cord clamping. Every physician employs a different technic and usually establishes a pattern that he carries out routinely in his obstetric work. At times this pattern is influenced by the equipment, the nursing situation, hospital policy in care of the newborn and various emergencies arising in the mother or the infant...

... It has been observed that the cord is often clamped immediately, either as a routine procedure or so that the infant can be handed to a nurse for resuscitation and aspiration." [1, p629]

On the other hand some practitioners viewed so strongly in the need for full placental transfusion, that they would strip the cord three or four times to squeeze all residual blood into
the child [2]. A survey in 1949 of 1900 members of the American Board of Obstetrics and Gynecology found two thirds regarded placental transfusion as a matter of minor importance, but nearly one quarter (455) used the stripping procedure [3].

A year later, Landau et al. (1950) determined that immediate clamping of the cord after Cesarean section was leaving the newborn in a state of hypovolemic shock, which they were able to counteract by holding the placenta above the infant to obtain drainage through the still intact pulsating umbilical cord [4].

Colozzi (1954) investigated red cell and hemoglobin values in infants with immediate cord clamping, delayed cord clamping with infant above or below the level of the uterus during the period of postnatal transfusion, and stripping [1]. In the group subjected to immediate clamping, some of the red-cell and hemoglobin levels were thought to be alarmingly low. Postnatal transfusion with the infant held above the level of the uterus appeared comparable to that with the infant below the uterus, the reason apparently due to uterine contractions - though the infant heart may have a lot to do with regulating blood flow back to the placenta. Stripping the cord led to the highest red-cell and hemoglobin values.

Although stripping the cord is not totally natural, Colozzi's concluding comments may be worth keeping in mind:

"Too often, after a traumatic delivery or intrapartum bleeding episode, the physician is in great hast to clamp the cord and give a pale, listless infant to a nurse for aspiration and resuscitation. Usually, these infants are described as having asphyxia pallida, and their prognosis is grave. They respond poorly to oxygen administration, and worse to other heroic measures of resuscitation. Their main difficulty is shock and blood loss, which are inadequately corrected by oxygen and are not improved by rough handling. I have seen several infants with asphyxia pallida who were very pale and listless, with a rapid pulse and a very weak cry; with gentle, slow, methodical cord stripping, they were transformed within a few minutes to ruddy, lustily-crying infants." [1, p632]

Colozzi also provided advice on finding the cord around an infant's neck during delivery:

"Another situation commonly encountered is the infant with a loop or two of cord around its neck. Usually, the most expeditious measure is to clamp and cut the cord in situ. This actually amounts to immediate clamping in an already depressed baby. Every effort within reason should be made to slip the loops over the infant's head and allow it the benefit of its own blood." [1, p632]

Colozzi's (1954) research was among many that can be called "randomized controlled trials." These continue to the present day, for what reason it is hard to fathom. If only heed were paid to the non-invasive research data that awaits rediscovery in medical journals going back over 130 years ago. Even then, research was carried out assigning groups of infants to early and some to delayed cord clamping. The major difference from such
research today is the difference in what was considered early or delayed.

Hormann & Lemtis (1954), in the tradition of Schucking (1877 & 1879), Hofmeier (1878 & 1879), Ribemont (1879 -1881), vonEngel (1885), Kostlin (1898), Haselhorst (1929), and Allmeling (1930), measured weight-gain in newborn infants during the period of continuing umbilical cord pulsation. They collected data on 100 babies. They found that during the first minute after birth infants received on average 78 percent of the total transfusion, with loss and gain fluctuations in the succeeding minutes, diminishing up to 12 minutes after birth.


3 – Initial circulation to the alveoli

Jäykkä (1954) proposed a theory, contrary to prevailing opinion, that lung expansion at birth was not initiated by respiratory effort of the newborn, but by blood filling the capillaries around the alveoli [1]. He tested this theory using the un-inflated (atelectatic) lungs of fetuses who had died before birth. Injection of fluid (macrodex solution) into the pulmonary artery of one lung resulted in expansion of the alveoli of that lung. Expansion occurred first in the most distal alveoli, with expansion in three stages of the more proximal alveoli toward the center of the lung.

In a second experiment, Jäykkä placed un-inflated fetal lungs in a jar covered with a rubber membrane to simulate movement of the diaphragm. An air-inlet tube was connected with the trachea, and a tube for injection of fluid with the pulmonary artery of one lung. The lung injected with fluid filled with air following movement of the rubber diaphragm, and when removed from the jar was found to float in water. The other lung remained dense, and sank in water.

Under the microscope, the alveoli of the lung injected with fluid were fully opened, whereas only partial opening had occurred in the other lung.

Jäykkä concluded with an explanation for the existence of the foramen ovale and ductus arteriosus:
"They are indispensable in preventing the initiation of blood flow and the increase of blood pressure in the pulmonary circulation." [1, p408]

Jäykkä (1958) reported on the appearance of lungs of pre-term and full-term infants who died before or shortly after birth, and described two kinds of expansion: (1) that characteristic of inflation by air only, and (2) expansion by what he termed "erectile force." [3]

Inflation with air led to abnormal expansion in an irregular pattern with large areas of lung remaining uninflated while other areas appeared overinflated. India ink injections into the pulmonary artery revealed lack of circulation to areas that failed to inflate. India ink also revealed a bypass circuit, remnant of prenatal circulation. Infants with irregular lung expansion of this type also frequently had hyaline membranes and fit descriptions in the literature of "congenital alveolar dysplasia."

Expansion by erectile force was seen in infants who died during delivery, with premature expansion of the alveoli and aspirated matter in the air spaces. This appears similar to descriptions of meconium aspiration syndrome, which Matsuishi et al. (1999) described in infants who later developed autism [4]. Determining what might trigger prenatal alveolar expansion should have fundamental bearing on the factors involved in normal postnatal transition.

Jäykkä (1958) concluded this paper, based on case reports, with the comment:

"More attention should, in my opinion, be paid to the circulatory relationships and attempts should be made to devise resuscitation procedures that promote capillary expansion. Of course, ventilation is necessary if the infant is apneic, but forceful introduction of air into an atelectatic lung may cause an abnormal expansion of the inflation type."

Fifty years later, are the mechanisms for lung expansion or closure of the foramen ovale and ductus arteriosus any better understood? Until nature's plan is deciphered, is there any justification for circumventing it?


4 – Postnatal transfer of blood from the placenta
Apgar's newborn scoring system seems clearly associated with the vogue of early clamping of the umbilical cord -- done with the aim of transferring the infant to a specialist and maintaining a sterile field for prompt suturing of incisions made for episiotomy or cesarean delivery. Meanwhile, advocates of what Apgar referred to as "slow birth" continued a long tradition of measuring the amount of placental blood an infant got if the cord was left unclamped until pulsations in it ceased.

Pulsations continue as long as the valves in the infant's heart direct blood to the placenta through the umbilical arteries, and cease when pulmonary respiration is fully established with closure of the foramen ovale and ductus arteriosus in the heart (Dawes et al. 1953).

Changes in circulation through the heart and lungs were determined in research with newborn lambs. These experiments did involve "tying the cord," which might explain the finding of a pattern of "neonatal circulation" intermediate between that of the fetus and that of the adult. Born et al. (1954) found the ductus arteriosus begins to close within 5 to 15 minutes of pulmonary ventilation with continuing constriction for several minutes, but remained partially patent for 12 hours or more. The foramen ovale, on the other hand, closes within a minute following birth, forcing circulation to the lungs.

Gunther (1957) weighed infants for up to 20 minutes after birth, with the umbilical cord intact allowing ongoing placental circulation. Fluctuations in weight occurred in response to uterine contractions, elevation of the baby above or below the mother's uterus, and pulsations of the cord.

Most interesting of Gunther's findings were the annotations of the weight gain/loss tracings. In figure 5 above (pxx - Gunther’s figure 1) postnatal activity and weight profile are shown for a baby who started crying only 9 minutes after birth, and with pulsations of the cord continuing for 19 minutes after birth. What would have been the Apgar scores and fate of this child had the cord been cut within the first minute after birth?

Likewise, in figure 6 (Gunther’s figure 3), resuscitation was started within one minute on an infant described as "slow to cry." Crying began more than 6 minutes after birth following a uterine contraction and additional weight gain from placental blood. Pulsations of the cord continued throughout the 10 minute interval shown in the graph. This would surely have been another infant described as severely depressed by Apgar, and with an ominous outcome.
Gunther commented, "These records confirm once more that, if the cord is left untied, a baby will usually increase his blood volume by a significant amount." She compared her findings to those of Haselhorst (1929) and Allmeling (1930), noting that placental transfusion increased a newborn's weight by 0.8 to 4.7 percent, which (assuming blood volume is about 10 percent of an infant's weight) amounts to as much or more than 40 percent of the baby's blood volume.

At this point in time, "pulmonary syndrome," later referred to as hyaline membrane syndrome, was a major concern, and quite widely attributed to the new vogue of early umbilical cord clamping. Gunther commented that even while pulsations of the cord continued, cessation of placental transfusion was often apparent, "as if a main reservoir had been filled," and she cited the research of Jaykka (1957) who determined that inflation of the lungs occurred with increasing blood flow into the alveolar capillaries - the shift of blood volume from the placenta to the lungs.


5 – Human assisted delivery of thoroughbred foals
The Lancet published a letter from Mahaffey and Rossdale (1957) describing their observations on a convulsive syndrome affecting about 2 percent of thoroughbred foals delivered with human assistance. Their letter was in response to the article by Gunther (1957) on postnatal transfusion and an earlier paper by Bonham Carter et al. (1956) on pulmonary problems and "cerebral irritation" in human infants.

Mahaffey and Rossdale stated, "For a considerable time we have been greatly concerned with the possibility that the syndromes are associated with very early severance of the umbilical cord." They went on to suggest that this practice may deprive the newborn foal of up to 1500 ml of placental blood, which may be more than 25 percent of a normal foal's blood volume, and then commented:

"It seems more than a coincidence that, as far as we can verify, the syndromes do not occur in thoroughbred foals which are born unattended in open paddocks in Australia, but are well known in France and Italy, where the cord is always severed by attendants within seconds of birth. Further, in Europe the disease seems to be unknown in breeds of horses other than thoroughbreds and these generally foal without human 'interference.' Other domestic species which give birth to their young alone, and 'naturally,' are similarly unaffected."

Mahaffey and Rossdale (1959) described the pulmonary pathology associated with convulsive foal syndrome along with the neonatal behavioral disturbance. The condition was reported to follow an apparently easy delivery, but when attempting to get to his feet for the first time, the foal begins jerking his head up and down, becomes unsteady on its feet, and falls down. The animal may emit a barking noise associated with rapid respirations and increased heart rate, then go into violent convulsions. About half of the foals recover without any apparent residual effects, but may pass through a period of seeming blindness, wandering aimlessly about before learning to suck from their mother.

In foals that died, aeration of the lungs was found to be incomplete. Lung tissue was described as dark and dense, resembling fetal liver, as opposed to the pink feathery appearance throughout the lungs of foals that did not experience respiratory problems or convulsions in the newborn period. Abnormalities of lung tissue were noted to be comparable to that described in human infants dying of pulmonary syndrome. Mahaffey and Rossdale also noted that the ductus arteriosus was patent to a marked degree in the convulsive foals, an indication of incomplete transition to normal postnatal circulation. They attributed these abnormalities to the conduct of human assisted parturition:
"Variable degrees of traction are usually practised by attendants when the head and forelegs are emerging from the vulva. The amnion is prematurely ruptured by hand, the legs are grasped and a pull is exerted upon them... the umbilical cord is ruptured with such haste that the newborn foal (weighing 100-120 lb.) is deprived of an average of 1020 ml. of blood and often 1500 ml. -- probably about 30% of its potential blood-volume.

Under normal conditions a mare usually rests for period of up to half an hour after parturition, during which the foal also is inactive. The cord remains intact and is not broken until the mare (sometimes the foal) attempts to get to its feet. Meanwhile virtually all the blood in the placenta has passed back into the circulation of the foal, and it is difficult to collect even 50 ml. of blood when the cord ruptures at this stage."

Dunn (1972) acknowledged the importance of observations on the convulsive foal syndrome for understanding respiratory distress in human infants, which he described as a maladaptation to extraterine life, most frequently in preterm infants. He discussed deficiency of surfactant in preterm infants and frequent association with Caesarean section as etiological factors. The child delivered by Caesarean, "is often born in a state of blue asphyxia -- apnoeic and cyanosed, yet with vigorous cord pulsation... In most cases the pulsating umbilical cord is clamped at once to allow the obstetrician to complete the operation." Dunn commented further:

"In fact there is no reason why the cord should be clamped at all and since 1961 I have been advocating and practising delivery of the infant and placenta together as one unit, both being laid together at the same level and the cord only ligated after respiration has been established and all pulsation has ceased.

It is of interest that this practice was widely followed throughout most of the world until the recent spread of Western civilisation. Even today it is still adhered to in many isolated and primitive communities. It is of course practised by many animals.

In this context it was with tremendous interest that I read of Mahaffey and Rossdale's (1959) observation that "barkers" were never found among foals born in the open field but only among those delivered indoors with human supervision, including early ligature and division of the umbilical cord."

In 1976 Palmer and Rossdale reported neuropathological changes found in 18 foals that had exhibited signs of the "convulsive foal syndrome." A spectrum of changes in the brain were observed, including ischemic necrosis within the cerebral cortex in nine of the foals, with involvement of the diencephalon and brainstem in three of these. Hemorrhagic damage of the cerebrum, and sometimes the brainstem and cerebellum, was observed in the other nine foals.

Palmer and Rossdale compared their findings with the two patterns of damage described by
Myers in 1972 seen in monkeys subjected to hypoxia and or asphyxia shortly before or after birth. Myers subjected monkeys to partial hypoxia late in gestation, which resulted in damage of the cerebral cortex similar to that seen in human cases of cerebral palsy. On the other hand, when he inflicted catastrophic total asphyxia at birth for several minutes, damage was restricted to the brainstem. Palmer and Rossdale found brainstem damage in foals who suffered apnea at birth, including lesions of the inferior colliculi as had been the case in monkeys subjected to asphyxia.


6 – Pulsation of the umbilical cord stump and respiratory distress
Desmond et al. (1959) investigated stages of postnatal recovery in infants with a history of fetal distress. For their study they selected infants in the newborn nursery who displayed pulsation of the umbilical cord stump, because:

"More recent experience with distressed infants revealed that certain of these infants show disturbances in the closure of umbilical vessels after birth." [1, p131]

Landau et al. (1950), less than a decade earlier, had described the problem with cesarean delivery to be the immediate clamping and cutting of the cord, which they addressed by hanging the placenta in a towel above the infant, and waiting for pulsations in the cord to cease -- a procedure that involved six to ten minutes [2].
Desmond et al. in the introduction to their study continued:

"The umbilical arteries normally cease to pulsate within a short period after the infant has been delivered." [1, p131]

They cited 30 minutes reported by Haselhorst and Allmeling (1929) as the upper limit for pulsations of the cord to continue, and citing Windle (1941), Barclay et al. (1945) and Rachmanov (1914) [3-6] commented:

"While ligation of the umbilical cord immediately after birth is a tradition in modern obstetrics, the danger of hemorrhage from cords left unligated is not great" [1, p131]

Desmond et al. waited far longer than 30 minutes:

"Forty-one infants manifested prolonged pulsation of the cord after delivery. The mean duration of cord pulsation was 5 hours, with a range of from 40 minutes to 13 hours after birth." [1, p132]

Desmond et al. used Apgar's scoring system. Of the 41 infants followed, 21 (51%) had Apgar scores of 5 or less during the first one to two minutes after birth. Three of the infants appeared to recover, 8 had transient difficulties, and 30 had persistent problems. Five infants died during the first 11 hours of life. Two additional infants later succumbed to infections.

Persistent problems included cardiopulmonary difficulties in 17 infants, clearcut neurological problems in 6, and umbilical hemorrhage in 3.

Desmond et al. concluded that pulsation of the umbilical cord stump in the newborn period is associated with difficulty in transition from intrauterine to extrauterine life. They reported:

"Seventy-three per cent of the infants had either fetal distress prior to delivery or difficulty with the onset of respiration on delivery." [1, p145]

According to Desmond et al., the depression at birth resulted from a poor intrauterine environment, and:

"Upon delivery, the infant was separated from further adverse intrauterine influences and his immediate neonatal problem became one of recovery as well as of transition." [1, p141]

However, these infants were born alive. How poor could the intrauterine environment have been? Before separation from the mother at delivery, oxygen was being delivered from the placenta. The continuing pulsation of the umbilical stump, for hours after birth, indicates
persistence of fetal circulation, through shunts in the heart continuing to divert blood flow away from the lungs and attempting to signal the amputated placenta for ongoing support.

What is the signal, and where does it come from, that closes the foramen ovale and ductus arteriosus? Until this is understood, can we presume to be able to aid recovery of a newborn in respiratory distress? The signal may well be the volume of blood needed to fill the capillaries around the alveoli. Recovery in the newborn nursery often depends upon giving the distressed infant blood transfusions or blood volume expanders [7].

As recently as 1986, Beischer and MacKay, in their textbook of obstetrics, described the significance of continuing pulsation of the umbilical arteries. By then immediate clamping of the cord at birth was more common than in 1959:

"Q: What is the significance of continued pulsation of the arteries in the umbilical cord at birth?
A: It means that respiration has not commenced. The physiological stimulus causing closure of umbilical arteries (and ductus arteriosus) is an increase in oxygen saturation of the blood which occurs when the lungs expand with air." [8, p 710]

7 – The respiratory distress syndrome
James (1959) was co-author with Apgar in 1958 of the paper in which they explained that at the Sloane Hospital (at Columbia University) the umbilical cord was cut within the first minute after birth to preserve the "sterile field," and that all infants with Apgar scores of 8, 9, or 10 had breathed within seconds of delivery. In his paper on respiratory distress a year later, he cites delay in onset of respiration at birth as the primary etiologic factor:

"A review of the obstetrical histories in infants who show a rising respiratory rate has indicated that delayed respiration at birth, even for 2 minutes, seemed to affect markedly both the incidence of abnormal breathing and subsequent." [1, p1089]

Ersch et al. (2007) have documented an increasing incidence of respiratory distress in neonates over the past three decades [2]. They suggest that this increase can be correlated with the increase in deliveries via caesarean section.

In progress


8 – Cardiac murmer and patent ductus arteriosus
Experiments with sheep conducted by Dawes and co-workers during the 1950s are cited as providing evidence that the ductus arteriosus begins to constrict with spontaneous respiration or positive pressure ventilation of the lungs, but that it normally remains open for several hours following birth [1-6]. They described a "neonatal circulation" intermediate in type between that of the fetus and adult. The umbilical cord was tied in most of their experimental animals at varying times before or after ventilation. The tradition of "slow birth" and waiting for pulsations to cease before cutting the cord appears to have lost favor during the 1950s, while ligation became more and more the standard thing to do.

Burnard (1958, 1959) reported cardiac murmurs from blood flow through a persistent ductus arteriosus to be more common in infants with a delay of three minutes or more in establishing normal breathing after birth. [7, 8]. He also reported a finding of enlarged hearts in affected babies [9]. Burnard later worked with Apgar and James, and published a paper with James on enlargement of the heart in infants who suffered asphyxia [11]. In some of the infants in this study, placental transfusion was allowed or even promoted by stripping the cord. The conclusion was carefully couched in terms that would not negate the policy of clamping the umbilical cord within a minute after birth, the protocol used by Apgar and James for more than a decade.
Now more than 50 years after routine clamping of the umbilical cord at birth, remnants of fetal circulation are being visualized in MDCT (multidetector computed tomography) images [12].

References
13. Link to Children's Hospital Boston page on patent ductus arteriosus ......
5. **1960s error entrenched**

1 – **The Hesseltine clamp in use for 30 years**

Hidvegi and Hesseltine (1966) proudly celebrated use of the Hesseltine clamp for nearly three decades:

"In May, 1937, a report was given of a simple and safe umbilical cord clamp. Directions were advanced for its use and documentations of it reliability and safety were stated...

...It has been used routinely at this institution on some 90,000 newborns since July 1, 1937.

...Improvement has been made recently by the placement of serrations on the proximating surfaces of both arms. These imprints provide added resistance to slippage if the cord is unintentionally severed adjacent to the clamp.

...The device as designed will withstand pressure up to 200 mm mercury." [1, p567]

"The manufacturer (The American Coil Spring Company) reports the six millionth (6,000,000) clamp was produced on July 15 1965...

Obviously, then, a minimum of six million babies have been treated by the clamp... each clamp has been used an average of five times at a minimum. On this assumption, six million clamps represent a usage upon, at least, 30 million newborn infants.

...This one unit instrument is uncomplicated in application, reusable inumerable times and economical in service...

Another advantage is that if the instrument is unsatisfactorily located, it can be easily removed and confidently re-applied." [1, p568]

The American Coil Spring Company of Muskegon MI remains a thriving business, though umbilical clamps are not advertised on their website: [http://www.americancoil.com/](http://www.americancoil.com/)

Hesseltine (1937) introduced this clamp with the following remarks:

"Many types of instruments and appliances have been devised and used to replace ligation in the care of the umbilical cord of the newly born infant. Ligation is still the most commonly used but it popularity is obviously waning. Any successful method must provide complete asepsis, proper hemostasis, and normal wound healing." [2, p884]
Instructions on time of clamping were not given as they were by Wechsler (1912) or Dicks (1925), who both stated that the clamp should be applied after pulsations in the cord had ceased [3, 4].

It seems clear though that by the 1930s collection of umbilical cord blood to be stored for transfusions had become popular. Therefore, Hesseltine's remarks about the pressures the clamp should withstand make it apparent that this and other clamps were already applied before pulsations in the cord had ceased:

"Since Nov. 15, 1935, to the present time over 1,500 unselected babies have had their cords treated by this method. Since the systolic blood pressure of newly born infants probably does not exceed 100mm mercury and these clamps prevent vascular leaks with pressures in excess of 250 mm. mercury and do not slip, there should be no bleeding. This contention is verified by complete hemostasis in all applications." [2, p885]

References

2 – Introduction of more clamps
Payton (1960) introduced yet another clamp, a nylon disposable clamp with a snap to prevent its reopening once clamped shut:

"Ideally, the obstetrician and pediatrician have several aims in mind when severing and occluding an umbilical cord during the third stage of labor. The primary aim is complete hemostasis of any sized cord, preferably obtained without cutting into the jelly of Wharton." [5, p1024]

Thus permanent clamping during the third stage of labor was apparently common by the 1960s.

Mayer (1964) described a clamp combined with scissors, introducing it as follows:

"It is present obstetric practice at all deliveries, whether vaginal (with or without forceps) or caesarean section, to clamp the umbilical cord in two places and cut between them with a pair of scissors. The clamps usually used are pairs of Spencer Wells forceps or the new type disposable plastic clamps."
Such a series of actions is necessarily time consuming at the very moment when valuable seconds could be spent in infant resuscitation or maternal haemostasis." [6, p1692]

Thus what Apgar had referred to as "slow birth," waiting for pulsations of the cord to cease, seems to have been completely forgotten about by the mid 1960s.

References

3 – Controversy over umbilical cord clamping
Stembera et al. (1963) reported measurements of blood flow in infants immediately following birth [1]. They found that in the period up to 100 seconds after birth blood flow from the placenta continued at a rate of 75 ml per minute per kilogram, then decreased sharply. Their results are comparable to those of earlier researchers [2-4]. In addition to the continuing blood flow within the first two minutes after birth, the rates correlated with body weight, with higher rates of blood flow to heavier babies.

In earlier research (published in German and Czech journals) Stembera et al. found that the placenta begins to separate from the wall of the uterus at about 2 minutes after birth, and that the concentration of oxygen in the umbilical arteries begins to decline only 60 to 90 seconds after the first breath. They thus concluded:

"After inclusion of all of our previous data with those in the present communication, it would appear that the first 100 seconds after birth is a period during which the flow and metabolic conditions in the maternal-placental-fetal system continue essentially in a manner similar to that in utero" [1, p573]

The work of Stembera et al. confirms White's (1773) statement nearly 200 years earlier, that the changes that must take place in the transition from fetal to neonatal circulation cannot be expected to take place within an instant of time, and at the will of a bystander [5].

That most infants appear unharmed by immediate clamping off of ongoing postnatal placental support reflects the ability of the very young to recover and heal quickly.

References

4 – Concerns over cesarean deliveries
As in the 1940s and 1950s, concerns continued to be raised by some over the safety of clamping the cord. Recognition of increasing numbers of newborn infants developing respiratory distress syndrome, as possibly related to not waiting even for the first breath before clamping the cord, motivated more research to investigate consequences of early versus "late" clamping. Application of the clamp early was clearly so widespread by this time, that apparently no ethical problem was perceived in randomly assigning infants to early or late clamping groups for research, even when the question was whether early clamping might not be safe.

Two important articles appeared in the Lancet for June 9, 1962 along with an equally thoughtful editorial [1-3].

Bound et al. (1962) investigated pulmonary syndrome in two groups of infants. In the first group, born between January 1957 through May 1959, the cord was usually ligated immediately after birth, except in cases in which mucus first had to be aspirated from the pharynx. Delay in use of the clamp in these cases indicates instinctive good judgement was still exercised, based on individual circumstances. Infants born between June 1959 through June 1961 comprised the second group, when three to five minutes after delivery elapsed before applying the clamp. The number of cases of pulmonary syndrome was found to be significantly less in the second period, and the reduction was most significant in low birth-weight infants (1501-2000 g).

Bound et al attributed the improved outcome to the delayed ligation of the cord during the second period:
"The results of this investigation indicate, within the limitations of a consecutive trial, that receipt of an adequate amount of placental blood is an important factor in the prevention of the pulmonary syndrome in premature babies." [1, p1202]

Bound et al. suggested that delayed ligation of the cord should become a standard procedure at the delivery of all premature babies.

Secher and Karlberg (1962) reviewed understanding of mechanisms involved in transition from intrauterine to extra-uterine circulation and respiration [2]. Karlberg's (1960) investigations and ideas about transfer of respiration from placenta to lungs were extensive and remain relevant to this still poorly understood phenomenon [4].

Secher and Karlberg, like Landau et al. (1950), recognized that the usual technique for caesarean section was un-physiological, and when performed in an emergency situation often left the infant in a state of circulatory insufficiency and shock. They adopted a method similar to that of Landau et al. (1950) providing postnatal placental transfusion to infants born by emergency Cesarean section by removing the placenta with the baby without cutting the cord and placing the placenta in a funnel hung above the baby (see picture below). For comparison, they did the same with vaginally delivered babies, using a temporary clamp on the cord until the placenta was delivered.

Secher and Karlberg cited several earlier investigations of placental transfusion [6-11], and concurred with Landau et al. (1950) by commenting:

"Late clamping of the cord has been an accepted rule in normal deliveries, and its importance was pointed out by Erasmus Darwin as early as 1801." [2, p1203]

Thus, though use of a clamp on the umbilical cord was in widespread use by the early 1960s, there were still proponents of the traditional method of waiting for, and promoting, placental transfusion after birth.


5 – Transfer of blood from placenta to lungs
Redmond et al. (1965) measured residual placental blood as an estimate of placental transfusion before and after onset of respiration. In 55 infants, the cord was clamped before onset of respiration, and in 97 after the onset of respiration. The plot of residual blood to onset of respiration (right & below) from the paper by Redmond et al. shows a dramatic drop in residual blood in cases where the cord was clamped after onset of respiration. Their own explanation of the data cannot be improved upon:

"Our data, obtained from normal uncomplicated pregnancies, clearly demonstrated that a placental transfusion is an inevitable physiological consequence of initial pulmonary expansion, over which obstetricians and paediatricians have little, if any, control.

...In infants who breathed before cord clamping, the difference in residual placental volume between those whose cords were clamped one minute after delivery and those whose cords were clamped three minutes or more after delivery was small...

...Had we defined early clamping and late clamping simply in relation to time of delivery, a number of babies whose cords were clamped within one minute would have been described as 'clamped early' (and by implication to have been deprived of placental blood); whereas placental transfusion had in fact already occurred..."

"...In a survey (Redmond and Ingall 1964) of 100 random deliveries * performed by 32 obstetricians in a private maternity hospital, the following figures were of interest. The time from delivery of the chin to delivery of the entire body averaged thirty-three seconds, to clamping fifty-nine seconds, and to first gasp thirty-eight seconds. Almost two-thirds of these babies gasped during delivery of the body and could have received a placental transfusion. The other third had their cords ligated before the
first gasp and were probably deprived of their placental blood. More than 90% of these babies had their cords clamped within a minute of delivery of the body (usual definition of early clamping). Although objective evidence was not obtained, we suggest that most of the babies could have received their placental blood before clamping if breathing started before ligation of the cord. The tendency for some obstetricians to deliver the head, aspirate the nose and mouth, and slowly extract the remainder of the baby probably aids the transmission of placental blood to the infant." [1, p284]

"The present evidence shows a definite relation between onset of respiration and occurrence of a placental transfusion, but the mechanism is not clear." [1, p285]

Redmond et al. compared their findings to those observed by Dawes et al. (1953) in lambs, but pointed out that Dawes et al. removed placental circulation by clamping the cord in their experiments [2]. Redmond et al. did not cite the work of Jäykkä (1954) a year earlier showing that fluid filling the capillaries surrounding the alveoli would cause them to open [3].

Beyond mechanical filling of the capillaries, the biochemistry of hemoglobin needs to be considered. Filling of the capillaries with blood brings hemoglobin to the alveoli laden with carbon dioxide, which may need to be exhaled before oxygen is taken up. Stemberra et al. (1963) provided evidence that placental circulation continues during the first 2 minutes after birth, whether or not respiration via the lungs has begun [4]. Receipt of oxygen by newly opened alveoli must be a first step. Sending blood with progressively more oxygen back to the placenta may be a signal for the placenta to begin constriction of the umbilical arteries, as suggested by Spivack (1946) [5].

Placental respiration continues during the 2 minutes of continuing placental circulation after birth. As pointed out by White (1773) the changes in circulation that take place following birth cannot be brought about in one instant of time, and certainly not at the will of a bystander with a clamp.


6 – Prenatal transfer of blood from placenta to lungs
Philip et al. (1969) reported placental transfusion in infants who suffered distress during delivery [1]. Data for this paper are from the same Boston City Hospital Unit where Redmond et al. (1965) worked [2], and the authors described the background for their research as follows:

"During the course of our continuing studies on placental transfusions we accumulated data on 200 newborn infants whose cords were ligated within seconds of delivery of the chin and before the onset of respiration (thus qualifying them for anybody's definition of early clamping). Ten of these infants were noted on analysis to have residual placental volumes that were much lower than expected. The purpose of this communication is to report our observations on these infants and to contrast them with infants who were also "early clamped" but whose residual placental volumes fell in the expected range.

...The infants forming the basis of this report were delivered at the Boston City Hospital. In all instances the cord was clamped less than 60 seconds after delivery of the chin and more than 10 seconds before the first breath." [1, p12]

Measurement of residual placental blood was an ongoing part of research at this site, thus the comparison control group were 20 infants born just prior and just subsequent to the 10 infants with evidence of foetal distress based on changes in heart rate and/or meconium staining of the amniotic fluid. The infants with difficult births had lower 1-minute Apgar scores (mean 4.9) that the comparison group (mean 8.5), but their neonatal course was described as uneventful. The table of statistics gathered is reproduced below.

From their opening remarks, it can be inferred that Philip et al. regarded postnatal transfusion as potentially harmful:

"The resurgence of interest in the potential pathological effects of a postnatal placental transfusion has rekindled interest in the physiology of this phenomenon in man." [1, p11]

The contrast in opinion with that of most earlier researchers is striking. "Delayed clamping" was beginning to be viewed as perhaps a blunder to be avoided.


7 – Respiratory distress syndrome

Reports of respiratory distress syndrome appear to have increased with more and more widespread clamping of the umbilical cord sooner and sooner after birth, though some have credited the pulmonary problems of premature infants to increased survival.

Moss et al. (1963) investigated the effects of clamping the cord before the onset of respirations in 129 infants who were premature, delivered by cesarean section, or born of diabetic mothers [1]. Because the initial gasp of premature infants and those delivered by cesarean section is often not strong enough to produce significant expansion of the lungs, Moss et al. defined "early clamping" of the cord as that performed before the second breath, and "late clamping" as that performed after the second breath. They assigned infants alternately to groups for early or late clamping of the cord.

The condition of 33 of the 42 premature infants in the "early clamped" group was depressed (Apgar scores 0 to 6). Only 13 of the 52 infants in the "late clamped" group were depressed. Of infants delivered by cesarean section 4 of 10 in the "early clamped" group and only 1 of 20 in the "late clamped" group had Apgar scores in the 0 to 6 range. Two of the 10 c-section infants in the "early clamped" group developed respiratory distress.

There were 8 deaths among infants weighing less than 1500 gm, and 6 of these were in the "early clamped" group. Postmortem examination in the "early clamped" group revealed pathology of the lungs, but lung pathology was not found in the 2 infants in the "late clamped" group who died.

Moss et al. pointed out that pulsations in the cord become progressively weaker and finally cease after the transition from placental to pulmonary respiration is complete. This represents a gradual change-over with only minor alterations in systemic blood flow, but with sudden occlusion of the cord before expansion of the alveolar vascular bed, systemic pressure may cause rupture of capillaries in the lungs, brain, and other organs. They concluded their paper with the following comment:

"The carefree manner in which the newly born infant is 'disconnected' from his 'oxygenator' without any assurance that respirations will ever begin is in sharp contrast to the meticulous care with which the thoracic surgeon prepares his patient from the pump-oxygenator." [6, p50]

Moss and Monset-Couchard (1967) four years later published a review of literature comparing the effects of early and late clamping of the cord, and began with the comment:
"Iatrogenic interruption of the placental circulation at birth has, in most cases, become an automatic procedure with little or no regard for the physiologic alterations evoked or for their subsequent effect upon the fetus." [2, p109]

Emmanouilides and Moss (1971) carried out a second experiment to investigate whether respiratory distress might be associated with clamping of the umbilical cord before establishment of respiration [3]. The earlier report by Moss et al. (1963) appeared to provide evidence of this [2], but drew criticism for errors in randomization [5, 6].

Randomization in the second study was done by clamping the cord "early" or "late" on alternate days. As in the first study, "early clamping" was defined as that performed before the second breath and "late clamping" as that after the second breath. The average time of clamping was 15 seconds after birth in all but 2 instances for the "early clamped" group, and 46 seconds for the for the "late clamped" group.

Each group was divided into subgroups because strict adherence to the protocol could not always be followed due to individual circumstances. Thus four groups were defined, I (n=55) and IV (n=15) for early clamping, and II (n=16) and III (n=61) for late clamping.

Infants in group II breathed so quickly after birth that full lung expansion (the second breath) took place before clamping. Infants in group IV had the cord clamped before the second breath in 7 cases because it was deemed hazardous to delay clamping. In 8 cases the cord was allowed to pulsate for 1 minute or more but finally clamped before the second breath because of concern over the delay in onset of respiration. That the cord was pulsating should indicate that oxygen was being supplied by the placenta.

Of the 55 infants in group I (with early clamping per protocol) 11 were described as "depressed." Of the 61 infants in group III (with late clamping per protocol) only 2 were depressed.

Respiratory distress developed in 40% of the 55 infants with early cord clamping (13 of 22 with vaginal delivery, 9 of 22 delivered by c-section). Respiratory distress developed in 11% of the 61 infants with late cord clamping (6 of 47 with vaginal delivery, 1 of 7 delivered by c-section). The difference was noted to be statistically significant (p=0.005).

In 10 of the early-clamped infants, distress persisted for more than 24 hours and 3 infants died and were found to have hyaline membrane disease.

Despite the clear findings reported, Emmanouilides and Moss did not express the strong opinions voiced in the papers by Moss et al. (1963) and Moss and Monset-Couchard (1967). They noted that their findings were at variance with those of Yao et al. (1969), who reported higher mortality in late-clamped infants [7].
The paper by Emmanouilides and Moss ends with a statement, now common in such research, the further well-controlled observations are needed, with larger numbers of preterm infants and enforced randomization. What is this religion of randomization? A different approach need to be found, perhaps with experimental animals instead of human infants, to come to a better understanding of the process by which an infant's lungs take over the function of respiration.

References

8 – Respiratory status
Taylor et al. (1963) questioned the safety of allowing a placental transfusion. [1] They cautioned that a rapid and large transfusion might overload the circulation of a newborn. They claimed that theirs was a "minority opinion" favoring early clamping, although by the early 1960s clamping and assigning Apgar scores was already common practice.

Taylor et al. observed respiratory status in 182 full-term and 340 premature infants assigned to groups for early or delayed cord clamping. The cord was clamped within one minute in the early-clamped group, and to minimize placental transfusion the infant was held above the perineum after delivery. In the late-clamped group the cord was clamped between 1 and 3 minutes and to maximize placental transfusion the infant was held below the perineum. A full 3 minutes was allowed to elapse before clamping for most of the late-clamped group.

Selection of patients for their groups is disturbing (if not despicable):

"The original plan was to study only infants born of ward mothers. Ward patients were assigned in rotation to Service I or II when first seen at the hospital...
...It became necessary to include private patients in the premature group to increase enrollment; the planned randomization of these infants as to time of cord clamping failed." [1, pp893-4]
In the 1960s health insurance was not provided by employers, and obstetric care was not normally covered in any insurance policies. I was a ward patient. My husband was a graduate student, and income from my work was our primary support with much disapproval and reprimand from everyone, including the obstetric residents in the clinic. In the 1960s women with young children or more than four to six months pregnant were not supposed to work [2]. This attitude was very detrimental to the care received by many of us who could not afford the fees of private and more experienced doctors.

Taylor et al. stated that their interest was in the effect of early versus delayed cord-clamping on the "clinical condition" of the newborn. Their measures of clinical condition were respiratory rate and presence or absence of retractions. They concluded from these observations, "that the time of cord clamping had little effect on neonatal survival."

No deaths occurred among full-term infants in the study by Taylor et al. However, in contrast to the research cited of von Engel (1885) and Bound et al. (1962) [3, 4], more deaths of premature infants occurred among those with delayed clamping of the umbilical cord. On the other hand, at autopsy atelectasis and hyaline membrane disease of the lungs was found more often in premature infants with early clamping of the cord.

Taylor et al. commented that the disagreement between their findings and those of von Engel and Bound et al. was unexplained, but they proceeded to criticise the experimental design of these two earlier studies. They also noted again that they had been unable to enforce randomization of premature infants selected for early or delayed clamping of the cord.

Randomized controlled trials continue to be held in highest esteem, but this needs to be questioned. Understanding of the physiology of fetal to neonatal transition should guide obstetric practice, not "evidence" obtained from random treatment of our children according to one protocol or another.

Taylor et al. cited the editorial in the Lancet [5] that accompanied the papers by Bound et al. (1962) and Secher and Karlberg (1962) [4, 6], and noted that the editorial provided a review of research on placental transfusion. The editorial cited a review by Köstlin (1898) of nearly sixty publications in the nineteenth century or earlier, plus papers by Budin (1875), von Engel (1885), Jäkkä (1954), Gunther (1957), Mahaffey and Rossdale (1959), and an unpublished version of the paper by Taylor et al. (1963) [7-11].

Taylor et al. also cited McCausland (1949), who had surveyed mid-twentieth century obstetric practice and found that 59 percent of obstetricians still practiced delayed clamping of the cord and 38 percent stripped blood from the cord into the infant [12]. Taylor et al. offered the following opinion:
"Proponents of delayed clamping of the cord suggest that the placental transfusion (which may exceed 30 percent of the infant's estimated blood volume) benefits the infant by filling his expanding pulmonary vascular bed, by initiating or aiding initial lung expansion, by prevention of 'hematogenic shock,' and by increasing hemoglobin concentration and supply of body iron." [1, p893]

Their view, on the contrary, was that allowing placental transfusion led to temporary hypertension in contrast to early-clamped infants for whom no significant elevation of blood pressure occurred. This reflects a belief that placental blood is not part of the total volume of fetal blood.

The placenta provides oxygen to the fetal circulatory system. Pulmonary blood volume is minimal during fetal life, but after birth no one would suggest that pulmonary blood is separate from that circulating through other organs of the infant. If placental blood is not transferred to the infant at birth, what will be the source of blood going to the newly inflated lungs? It will have to be drawn from other organs including the brain.

Is any more experimentation with human subjects really warranted?

References

9 – A parting gift
An editorial in the Lancet for January 28, 1967 introduced a paper by Kjeldsen and Pedersen (1967) on the respiratory-distress syndrome [1, 2], and opened with the following comments and questions:

"In the age of astronauts it is odd that we are still undecided about so small but fundamental a detail as when-or, for that matter, how-best to ligate the umbilical cord. The difficulty stems from the fact that a relatively large volume of blood can be transferred to the infant within a few seconds of birth and that, rarely, such plethora may embarrass cerebral blood-flow and lead to convulsions and unconsciousness. [3]. The normal baby at term receives a placental transfusion of as much as 60% of his blood-volume when clamping of the cord is delayed for five minutes [4]. Is this a physiological necessity, and, if so, what are the consequences when the infant is deprived of it? Does this large volume of blood rightfully belong to the infant or to his placenta? And how is this massive transfusion related to the onset of respiration and circulatory adaptation at birth?"
[1, p201]

The second question is odd. Blood in the placenta should be compared to blood circulating in the lungs after a baby begins breathing. The placenta is the prenatal organ of respiration. The blood rightfully belongs to the infant, of course. There is no need for blood in the placenta once respiratory function has been taken over by the lungs.

Continuing pulsations in the umbilical cord after birth are from the infant’s heart continuing to pump blood to the placenta as the lungs begin to expand with the first few breaths. When pulsations cease, little blood remains in the placenta. Unless interrupted by premature clamping of the cord, placental blood continues to deliver oxygen to the baby as it is transferred to the expanding circulatory system of the lungs [5, 6]

The editorial writers summarized and compared the research of Usher et al. (1963) and Redmond et al. Usher et al. used a radioactive tracer to measure the blood volume of newborn infants [4]. Redmond measured residual blood in the placenta [5].

"USHER et al. [4], using [131]I-albumin, studied the blood volume changes of normal-term babies. A 3500 g. infant had an average blood-volume of 275 ml., which was augmented by a transfusion of 160 ml. from the placenta if the cord was
not occluded for five minutes. Of this, a quarter was transferred in fifteen seconds and half in the first minute; and most of the transfused blood had left the circulation after four hours as a result of plasma shifts. By the third day, when the blood-volume had become stable, the average value for infants who had received no transfusion was 82 ml. per kg. (venous haematocrit 44%) as against 93 ml. per kg. (haematocrit 60%) in those who had.

REDMOND et al.[5] measured the residual placental blood-volumes at 191 uncomplicated vertex deliveries by the simple expedient of allowing the placenta to drain into a graduated cylinder from a height of 18 inches for twenty minutes. The residual placental volume was assumed to be indirectly proportional to the volume transfused, and was shown to depend not so much on the time of clamping of the cord as on whether it was clamped before or after the onset of respiration. The volume of blood left in the placenta averaged 40 ml. when the cord was clamped after the onset of respiration and 85 ml. when it was clamped before. Thus, it seems that a transfusion of blood normally takes place within seconds of birth and that approximately 45 ml. of this volume may be accommodated in the pulmonary circulation." [1, p201]

The work of Kjeldsen and Pedersen [2] was then introduced and discussed. Kjeldsen and Pedersen used the method of Redmond et al. [5] to measure residual placental volume in infants of diabetic mothers, low birth weight infants, and normal-term infants. Residual volume for infants of diabetic mothers was found to be almost double that of the normal-term infants. Infants of diabetic mothers were also slower to begin breathing.

The larger residual placental blood appears to be related to greater fetal blood volume in diabetic pregnancies. Further research on maternal diabetes has revealed that enlargement of the fetal heart and differences in fetal-placental blood flow during pregnancy are common. Up to 8 percent of children of diabetic mothers have persistent heart defects [7].

In addition to finding greater residual placental blood in maternal diabetes, Kjeldsen and Pedersen confirmed the finding of Redmond et al.:

"We have confirmed the correlation of the residual placental blood-volume with the onset of respiration, before and after cord clamping, demonstrated by Redmond et al. (1965). In DM and LBW infants the residual volume was smaller when the infant breathed before the cord was tied." [2, p183]

This study included 26 infants of diabetic mothers and 10 normal full-term infants. Although large for gestational age, the infants of diabetic mothers were delivered after induction of labor about 3 weeks before term. Thus 23 low birth-weight infants with almost the same degree of prematurity were included in this study.

Of the 23 low birth-weight infants, 13 developed the respiratory distress syndrome (RDS) and 3
of these died. Near-total pulmonary atelectasis was found at necropsy in all 3 infants who died with RDS. The average residual blood volume was larger in the low birth-weight infants who developed RDS. Seven of the 26 infants of diabetic mothers developed RDS, which was not correlated with residual placental blood, and all survived. In both groups incidence of RDS was higher in infants who had not breathed before the cord was clamped.

One of the infants of a diabetic mother died unexpectedly at 4 days of age, and was found to have congenital heart problem (coarctation of the aorta).

The routine methods of delivery of the infants in this research study are of interest:

"The routine methods of the department were observed. At the moment of delivery of the anterior shoulder methylergometrine maleate 0-2 mg. was given intramuscularly to all mothers. If the infant had been delivered by the vaginal route he was placed in the delivery bed below the vulva. Furthermore, if delivery was by caesarean section oxytocin 10 I.U. was injected into the uterine muscle at the moment of delivery, and the infant was held by his feet with his head down, lower than placenta if possible.

Clamping of the cord 60 seconds or more after delivery was our standard procedure, but the cord was not stripped. Early clamping was applied routinely whenever urgent resuscitation was found necessary.

By caesarean section, delivery was intentionally slow in head presentations to mimic the squeezing of thorax seen in normal vaginal delivery (Karlberg 1960, Karlberg et al. 1962). We have no standard routine for timing of clamping in delivery by section." [2, p181]

Thus in the mid 1960s in Denmark clamping of the cord occurred one minute or more after birth, except in cases when resuscitation was needed. Residual placental blood volume could therefore be reported along with time to onset of respiration (and maximal placental transfusion) before clamping of the cord. See table III from Kjeldsen and Pedersen below.

The findings of Kjeldsen and Pedersen and Redmond et al. would seem to suggest that allowing placental transfusion following birth is more than a parting gift. It should be viewed as a birth right.

References

10 – Postnatal placental respiration

Dunn (1966) wrote:

"The transfer of respiratory function from the placenta to the lungs at birth stands out as the most dramatic, complex and important event in our lives. How does this transfer take place? We know that there is often a delay after delivery before breathing commences and that a further interval must pass before pulmonary respiration meets the requirements of the newborn infant [2]. What of the placenta during this time? Does its respiratory function cease at the moment of delivery, or is it maintained until the lungs have assumed their new responsibility?"

[1, p607]

Much of the information in the Czech language reference cited by Dunn [2] may be found in Štembera et al. (1965) [3]. Štembera et al. showed that umbilical blood flow during the first two minutes after birth continues at the prenatal rate. Dunn cited other research indicating that oxygen delivery continues for 2 to 4 minutes after birth, and that even if a baby breathed within 30 seconds of birth, 5 minutes might pass before oxygen levels in the infant's major arteries rose to levels at or above those continuing to be received via the umbilical cord [4].

Dunn pointed out that ideas at that time about respiratory adaptation at birth were based on research that involved ligation of the umbilical cord [5-7]. That an infant, if assisted by ventilation with air or oxygen, can begin breathing after the cord is cut remains an ongoing fault of more recent research. Thus factors continue to be sought to determine why some infants lapse into "respiratory depression" at birth [8, 9].

Dunn was one of a dwindling few by the 1960s who seemed to understand the obvious, that oxygen transport from the placenta following delivery continues and remains sufficient to meet the infant's respiratory needs:

"Postnatal placental respiration has most to offer to the infant that is slow to breathe at birth. Blood flowing down the umbilical vein is directed through the
foetal pathways to the coronary and cerebral circulations [10]. In addition, it seems likely that this arterialised blood is directed into the pulmonary circulation when respiration starts [11]. If so, it may perform a most important service in helping to overcome the intense pulmonary vasoconstriction that accompanies asphyxial changes in the blood [12] and hence, by improving pulmonary perfusion, enhances the effectiveness of ventilation.

It is not possible fully to appreciate the significance of postnatal placental respiration without also taking into account the unique and fascinating characteristics of the umbilical circulation during the second and third stages of labour [13, 14, 15]. Immediately after delivery the placenta seems capable of both combating acidosis in the infant and providing it with oxygen, glucose [3] and a blood transfusion. Recent recommendations for neonatal resuscitation [16, 17] hardly ask for more. Perhaps CHARLES WHITE of Manchester [18] was justified after all when he wrote in 1773:

'The common method of tying and cutting the navel string in the instant the child is born, is likewise one of those errors in practice that has nothing to plead in its favour but custom.' [1, pp607-8]

Some of the citations in this brief and lucid annotation are disturbing to read. The paper by James et al. (1958) of which Apgar was a co-author, discusses the umbilical artery (singular) as the vessel that transports blood from the placenta to the fetus.

"The recent work of Dawes and associates [19], on the fetal circulation, indicates that the umbilical artery blood represents the blood going to the fetal tissues and not fetal venous blood." [5, p380]

In fact the paper by Dawes et al. clearly shows the umbilical vein as the conduit of blood from the placenta, 80 percent saturated with oxygen [19, p565, and pp574-5],

The tables in the paper by James et al. comparing pH, oxygen, and carbon dioxide in the umbilical artery and vein are difficult to interpret, and not clarified by the explanation:

"Blood samples were obtained from the artery and vein in a clamped segment of the umbilical cord at the moment of delivery." [5, p379]

None of the infants in this study were allowed the benefit of postnatal placental respiration.

"To determine the biochemical status of the depressed group, samples from either the umbilical artery, the portal vein area in the liver, or from the right or left atria have been used. This has been considered justifiable for several reasons. In many of these infants the heart rate is slow and the pulse feeble." [5, p381]
Can we trust they knew from where they were actually getting their samples? Then in describing oxygen levels in umbilical artery and vein blood:

"There is a wide range in the oxygen levels in both the umbilical artery and vein blood and in the A-V difference. All the infants exhibited some degree of asphyxia with a low oxygen saturation and a high CO2 tension. Of the 63 umbilical artery samples, 26 had an oxygen saturation below 10 per cent and 7 had no measurable oxygen. Fourteen of these severely anoxic infants were not depressed (score 8 and 9) and cried spontaneously within seconds of delivery" [5, p381]

In conclusion, the suggestion is made that asphyxia occurs during all births:

"These studies have revealed the varying degrees of asphyxia which occur during all forms of delivery. Contrary to earlier reports, ~, 4, ~ an infant may make the initial respiratory gasps with no measurable oxygen in his arterial blood. In this sense, anoxia, as measured by the oxygen saturation of the umbilical artery's blood, correlates poorly with postnatal vigor." [5, p385]

Respiratory depression was noted to occur in babies born alive in apparently very good condition (with placental function completely intact up to the time of birth):

"These are the infants who appear vigorous, with good tone and heart rate, yet fail to breathe immediately." [5, p391]

James et al. blamed anesthesia, and suggested regional anesthesia as preferable:

"Since inhalation anesthesia administered to the mother will always augment the metabolic depression, regional anesthesia would seem more desirable for delivery of an infant with fetal distress." [5, p392]

Why are the research data of Ranck and Windle (1959) and Faro and Windle (1969) neglected and forgotten [20, 21], while clamping the umbilical cord at birth, and assigning an Apgar score remain current? Placental respiration continues after birth, and every newborn child deserves to have this important continuing support from the mother protected.

(in progress)

2. Štembera ZK, Hodr J. Hladiny kyslíku v cévách pupecníkových po prvním vdechu plodu po porodu. Čs Fysiol 1962; 11:482.


6. 1970s focus on bilirubin

1 – Is placental transfusion unsafe?
By the 1970s the practice of clamping the cord was so widespread, at least in obstetric practice associated with academic institutions, that whether a placental transfusion should be allowed became a major topic for research. Thus the opening comment of the highly influential report of Saigal et al. (1972) states:

"In full-term infants placental transfusion increases the blood volume of the newborn by 40% to 60% within 5 minutes of birth. Most of the excess blood volume is eliminated within 4 hours by an extravasation of plasma from the circulation. For the remainder of the neonatal period, such infants retain a 50% larger red cell volume dispersed through a slightly enlarged blood volume, with higher hematocrit values than are found in infants whose umbilical cords are clamped immediately at birth." [1, p406]

Saigal et al. proceeded to note that the placenta is proportionately larger than fetal weight of a child born prematurely. They question how the circulation of a premature infant responds to the "volume overload" if a placental transfusion is allowed, and whether the immature liver is prepared to handle the greater amount of bilirubin produced by breakdown of red blood cells.

Saigal et al. note that research to date had dealt with the question of immediate versus delayed cord clamping, but not "intermediate" cord clamping. They thus designed the study reported to look at the effects of clamping immediately and at 1 and 5 minutes after birth. A randomizing protocol was used to assign infants to clamping of the cord at each of the time points. Blood volume was measured in 125 premature and 45 full-term infants using radioactive iodine.

Bilirubin levels greater than 15mg/100ml were viewed as dangerous, and exchange transfusions were therefore required for 7 premature infants, 5 of whom had cord clamping at 5 minutes after birth. Exchange transfusions were thought necessary for 2
infants with immediate clamping of the cord. None of the full-term infants had bilirubin levels greater than 14mg/100ml, but small increases were documented for infants with cord clamping at 1 and 5 minutes.

Respiratory distress occurred in 22 of the premature infants, 8 in the immediate clamping group, and 7 each in the 1- and 5-minute clamping groups. Presence or absence of respiratory problems was not associated with increased bilirubin levels, but Saigal et al. concluded their discussion with the statement:

"If delayed cord clamping is adopted as a means to reduce the incidence of respiratory distress syndrome in premature births, there will be accompanying augmentation of hyperbilirubinemia to deal with." [1, p 418]

This paper, with its single focus of bilirubin danger, has been one of the most influential in adopting immediate clamping of the umbilical cord at birth as a standard protocol.

Five years later Saigal and Usher (1977) described "symptomatic neonatal plethora" in 8 premature and 3 full-term infants with the suggestion that these conditions were caused by "large placental transfusions associated with delayed clamping of the umbilical cord" [2, p62]. These infants were noticed during an investigation of the effect of placental transfusion on respiratory distress syndrome. Again radioactive iodine was used to measure blood volume, with acknowledgement by Saigal and Usher that this was controversial.

The 8 premature children who exhibited symptoms of "plethoric" skin color, rapid respirations, and neurologic depression were hypervolemic, the 3 full-term infants with these symptoms had elevated hematocrits. Saigal and Usher stated implications of their findings as follows.

"After many years of controversy, the question of when to clamp the umbilical cord seems to be resolving towards a middle course. Excessive delay (more than 2 min) in cord clamping produces hyperbilirubinemia and sometimes symptomatic hypervolemia or polycythemia. Immediate cord clamping in premature infants tends to increase mortality from respiratory distress syndrome. It seems advisable, therefore, to delay cord clamping for 1 to 1 1/2 min in premature infants, with less delay in full-term infants." [2, p70]

Thus clamping the cord soon after delivery had become the norm. There seemed to be no memory of the traditional teaching of textbooks, or research like that of Gunther (1957) only 20 years earlier [3]. Treatment of mothers in premature labor with betamethasone began in the 1970s to prevent respiratory distress syndrome and hyaline membrane disease of the lungs [4-6]. The association of lung pathology with clamping of the umbilical cord had become irrelevant, but placental transfusion was now regarded as a potential hazard.
References
1. Saigal S et al. (1972) Placental transfusion and hyperbilirubinemia in the premature.

2 – Placental transfusion and onset of respiration
Philip (1973) reported measurements of residual placental blood volume correlated with neonatal blood volume and onset of respiration. As for safety or need for placental transfusion, Philip cites Botha (1968) on handling of the umbilical cord by people not yet influenced by academic medical advice:

"Human studies in a primitive community serve to reemphasize that nature (instinct) seems to allow a placental transfusion to occur before the cord is clamped." [1, p334]

Philip's research involved 57 infants, 28 had the cord clamped between 5 and 15 seconds after birth, and 29 had the cord clamped after the baby was judged to be breathing well. Philip reported that all infants had Apgar scores of 8 or greater at 5 minutes after birth.

Hematocrit (rather than invasive use of tracers) was used to judge blood volume. A striking fall in hematocrit on the fifth day of life was seen in the early-clamped group, as opposed to a significant elevation in the delayed group. This correlated with increased residual placental blood in the early-clamped group.

The results confirmed the finding of Redmond et al. (1965) that placental transfusion takes place with onset of respiration [3]. Philip found no differences in bilirubin between the two groups and commented:

"The fact that delayed clamping may contribute to hyperbilirubinemia is still used as an argument against this practice" [1, p341]

Philip however acknowledged the finding by Saigal et al. (1972) of increased bilirubin levels in premature infants allowed a placental transfusion [4].

Philip criticised the use of invasive injection of radioactive or other foreign materials to
measure blood volume. He concluded this paper, however, with a call for more research employing non-invasive measurement of residual placental blood volume and hematocrit:

"Further studies on infants of diabetic mothers, and low birth weight infants, using such methods, may yet allow the perinatal researcher to tell the obstetrician, with confidence, when to clamp the cord." [1, p342]

Perhaps with all of the evidence (data) in the research literature dating back to the 19th century, clamping the cord should be viewed as invasive. Philip and Saigal (2004) did come out with a recommendation to "wait a minute" [5].

References
1. Philip AG (1973) Further observations on placental transfusion.
2. Botha MC. The management of the umbilical cord in labour.
3. Redmond A et al. (1965) Relation of onset of respiration to placental transfusion.
5. Philip AGS, Saigal S (2004) When should we clamp the umbilical cord?
3 – Placental transfusion continuing after birth

Marquis and Ackerman (1973) measured oxygen, carbon dioxide, and pH in the umbilical arteries and vein in umbilical cord segments obtained from 1 to 37 seconds after birth, and they compared the values to the number of breaths taken before clamping of the cord. For 9 infants the cord was clamped 1 to 4 seconds after birth and before any breaths were taken. For 5 infants, the cord was clamped 30 to 37 seconds after delivery and after 3 to 6 breaths had been taken.

In every case, from 1 to 37 seconds after birth, oxygen, carbon dioxide, and pH were within the same range in the arteries and vein of the umbilical cord. The differences between arterial and venous blood were similar, regardless of time the cord was clamped. That oxygen in the umbilical arteries remained lower than in the umbilical vein returning to the infant provides evidence that oxygen continues to be delivered from the placenta, even in infants who had taken 3 to 6 breaths before cord clamping.

Marquis and Ackerman noted that as the lungs begin to function, oxygen levels in the umbilical arteries should begin to increase. The occurrence of 3 to 6 breaths did not result in increased oxygen in blood returning to the placenta within the 37 seconds before cord clamping in this study. Marquis and Ackerman cited the work of Stembera et al. (1965) who had shown that blood flow to the placenta continues for nearly 2 minutes after birth.

Marquis and Ackerman concluded:

"...if umbilical blood flow is not artificially interrupted, then placental gas exchange can make a substantial contribution to the infant's oxygen needs over the period of transition to pulmonary respiration.

...the first 5 breaths appear not to be effective ventilations, it may be beneficial to delay the clamping of the umbilical cord until the pulmonary respiration becomes effective." [1, p 363]

Of course, like so many researchers before, and continue to do, Marquis and Ackerman clamped the umbilical cords of 30 infants for the greater good of science. Isn’t it time to revisit the evidence gathered during the past century, and stop inflicting potential injury on human infants?

It may be time to begin looking at life-long development of individuals who exhibited respiratory depression following immediate clamping of the cord at birth. Retrospective research is frowned upon, and some data are always inaccurately recorded, but among the victims of the autism epidemic, sufficient information should be available.

Furthermore, impairments of the brainstem auditory system and its targets for growth and
development in the cerebral cortex can now be looked for using techniques like functional MRI (fMRI) imaging [3, 4].

References
1. Marquis L, Ackerman BD (1973) Placental respiration in the immediate neonatal period.

4 – Experimental hypoxia in fetal lambs
Oh et al. (1975) conducted experiments with sheep to determine the effect of hypoxia on fetal-placental blood flow [1]. These experiments can be compared with those of Myers (1972) on intrauterine hypoxia and brain damage in monkeys [2].

Surgery was performed to implant catheters for blood sampling and infusions of radioactive iodine and indocyanine green dye. After a 5-day recovery period maternal hypoxia was induced by covering the ewe's head with a 5-liter plastic bag.

After 15 minutes of hypoxia, maternal blood oxygen fell from 82 to 47 mmHg and fetal oxygen fell from 20 to 11 mmHg. Carbon dioxide and pH were essentially unchanged during or after hypoxia.

Only a slight reduction in maternal blood flow to the placenta was recorded, but fetal blood volume was significantly increased, and remained high during the 30 to 60 minute recovery period. Placental blood volume decreased during hypoxia and remained lower during the recovery period. Thus the fetus received a placental transfusion during the period of maternal hypoxia.

Oh et al. stated at the beginning of this paper:

"numerous studies in the past have shown that delayed clamping of the umbilical cord during vaginal delivery could result in a sizable amount of placental vlood transfusion to the fetus.

...In preterm infants who developed respiratory distress syndrome, the increment in blood volume may increase the mortality rate, although some studies suggested that higher blood volume may favor the outcome of premature infants with this disease." [1, p316]

Thus delayed clamping of the cord appears to have been a deviation from protocol, and uncertainty about the safety of allowing a placental transfusion was expressed.
The experimental finding suggests that hypoxia-induced shift of blood from placenta to fetus might be protective for the fetus. Oh et al concluded this paper with the remark:

"The clinical implication is that in delivering a fetus who shows signs of intrauterine fetal asphyxia, postnatal placental transfusion (for example by milking the umbilical cord) should probably be discouraged since a marked increase in neonatal blood volume is in many respects nonbeneficial to the physiologic adaptation during the immediate neonatal life." [1, p321]

The fear of blood volume overload during this period appears related to the perceived danger of the blood breakdown product bilirubin, which was associated with the form of cerebral palsy known as kernicterus [3].

References
1. Oh W et al. (1975) Placenta to lamb fetus transfusion in utero during acute hypoxia.

5 – Delivery room management
Tooley and Phibbs (1975) describe measures taken immediately after birth:

"...when the newborn infant may have cardiac arrest and apnea.

... Although infants must make a number of crucial adjustments immediately after birth, none is of more immediate importance than lung expansion and a change in the circulation, so that the blood returning to the heart goes through the lung." [1, p111]

Fetal and neonatal circulation are described and illustrated. The illustration (fig 9-1) of fetal circulation shows the umbilical arteries and vein connected with the placenta. Figure 9-2 on the next page illustrates the prior arterial and venous connections tied off, and the placenta is gone.

Tooley and Phibbs describe the beginning of neonatal circulation as follows:

"With the first breath the lungs expand, the pulmonary vascular resistance decreases and, when the cord is clamped, the systemic vascular resistance increases and left atrial pressure rises." [1,p112]

They proceed to describe closure of the fetal shunts, the foramen ovale and ductus arteriosus in terms of perivascular pH and oxygen tension, and state that hypoxia causes the release of
vasoconstrictor substances that activates a mechanism by which vasoactive substances constrict the precapillary arterioles.

These statements do not clarify how any specific biochemical processes go into effect, and would better be replaced with a statement that no one has yet really been able to explain how the alveoli open and receive the first breath. Instead attempts are made to explain constriction of the ductus arteriosus in terms of bradykinin, serotonin, and acetylcholine. Then:

"However, even when newborn infants are well oxygenated, closure does not always occur. Persistent patency of the ductus arteriosus is particularly common in prematurely born infants." [1, p113]

The chapter proceeds to explain:

"If, in the minutes following delivery, the infant does not expand his lung and establish respiration...

...When right atrial pressure is greater than left atrial pressure, the foramen ovale opens and blood flows through it right-to-left. This return to a fetal-like circulation is diagrammed in figure 9-3. In this situation, even vigorous assisted ventilation may be inadequate to decrease the pulmonary vascular resistance and promote conversion of the fetal to an adult type circulation.

...a shock-like state develops. Unchecked, this will progress to severe acidosis and hypoxia and cause myocardial failure and brain damage." [1, p115]

At least these authors acknowledge that the brain can be damaged when transition from fetal to neonatal circulation fails to take place. Again, figure 9-3 shows the umbilical arteries and vein tied off. The placenta is not part of the picture.

Thus we get a taste of how specialists in the field manage, rather than provide care for, the newborn baby in the delivery room, and that the assumption is common that neonatal circulation will somehow become rearranged after clamping off of blood flow to and from placenta.

Reference

6 – Kernicterus and the blood-brain-barrier (BBB)
Lou et al. (1977) addressed what appeared to be the primary concern over "delayed" cord clamping allowing placental transfusion [1]. Citing the paper by Lucey et al. (1964) [2] they stated:
"Asphyxiated infants are especially susceptible to kernicterus, even if their plasma-bilirubin levels are low.' Furthermore, it is very difficult to produce clinical and pathological signs of kernicterus by injection of bilirubin intravenously in normal infant monkeys, while kernicterus was readily produced in previously asphyxiated monkeys." [1, p1062]

Mossakowski et al. (1968) used Evans blue dye to investigate the blood-brain barrier in newborn monkeys subjected to asphyxia by clamping the umbilical cord and obstructing the airway [3]. Lou et al. also used Evans blue dye in fetal lambs subjected to oxygen insufficiency for 1-2 hours:

"The fetuses were asphyxiated by partially inflating a cuff around the umbilical cord. Asphyxia developed over a period of 1-2 h (pH about 6.90)." [1, p1062]

The initial response of the fetal lambs was a slowing of heart rate and increased blood pressure during the first half- to one-hour period of umbilical cord blood flow restriction. After that the blood pressure declined and remained low. Twinning is frequent in lambs, and Lou et al. used the twin as a control for the fate of Evans blue dye, and reported:

"We have found, in experimental asphyxia lasting 1-2 h, a striking discoloration throughout cortex and basal ganglia after intravenous injection of 3 ml/kg of a 2% solution of Evans blue in eight non-exteriorised fetal lambs, in contrast to the uncoloured brain tissue in non-asphyxiated twins acting as controls." [1, p1062]

In conclusion they commented:

"We suggest that the breakdown of the fetal blood/brain barrier to albumin is due to a combination of the initial moderate hypertension and severe vasodilation during asphyxia.7 The permeability of the blood/brain barrier to albumin in asphyxiated babies would facilitate the transport of bilirubin from plasma to neurones and thus explain the increased susceptibility to kernicterus." [1, p1063]

If a baby does not breathe right away at birth, should the umbilical cord be clamped off right away? Respiratory depression in infants born alive is a current concern and topic for research [4, 5]. If an infant is born alive, it has been receiving oxygen through the umbilical cord up to the time of birth. Shouldn't that lifeline be left intact until the lungs become functional?

Breakdown of the blood brain barrier by asphyxia has been shown to allow bilirubin and other substances in the circulation to enter the brain. High levels of bilirubin won't affect the brain if the blood-brain barrier has not been breached. Immediate clamping has been too long defended as a means to avoid circulatory overload and hyperbilirubinemia.
Lou et al. (1979) reported results of more research on the vulnerability of the blood-brain barrier to circulatory insufficiency in fetal lambs [6].

References
1. Lou HC et al. (1977) Breakdown of blood/brain barrier in kernicterus.
2. Lucey JF et al. (1964) Kernicterus in asphyxiated newborn monkeys.

7. Kernicterus and its causes

1 – Bilirubin and the blood-brain barrier
Jaundice is common in the neonatal period, the result of bilirubin from breakdown of red blood cells. Bilirubin remains at high levels in the circulation until liver enzymes mature that can convert it to a form that can be eliminated. Bilirubin causes no harm unless capillary and interfacing tissue membranes become disrupted and allow large molecules like bilirubin to pass from the circulation into cells of body organs. For the brain intact capillary and tissue membranes are referred to as the blood-brain barrier (BBB). Levine et al. (1982) provided a nice explanation of this:

“The blood-brain barrier is a complex regulatory interface which strictly controls passage of substances from cerebral vessels into the brain itself. In particular, large molecules such as albumin are normally excluded from the brain by this barrier. The barrier opens in certain disease states or with experimental manipulation. Opening may be reversible, as with trauma, tumors, heavy metal poisoning, irradiation, or in some cases of anoxia.” [xx, p256]

The idea persists, however, that bilirubin levels should be kept low, and this point of view has been a major rationale for clamping the umbilical cord as soon as possible after birth – to prevent transfusion of blood from the placenta [2].

References
1. Levine RL et al. (1982) Entry of bilirubin into the brain due to opening of the blood-brain barrier.

1. Concerns over infection

1 – Toxicity of antibiotics
Errors in treatment of human afflictions have occurred throughout history. Most are eventually corrected, and then forgotten about. Errors like the over-vaccination of young infants are the result of earlier success stories. Antibiotic substances were also enthusiastically developed following the success of penicillin in treating terrible infections like syphilis, but antibiotics (like other pesticides) are also toxic and associated with brain damage in premature infants [1, 2].

Sulfisoxazole (Gantrisin) was introduced in the early 1950s (the same time period that Apgar was developing her score for condition of infants at birth). Sulfisoxazole was adopted for use in combination with penicillin, and routinely administered to premature infants. Silverman et al. (1956) began investigating a new antibiotic, oxytetracycline (Terramycin). Excerpts from this paper provide the shocking details:

“One hundred ninety-three infants under the age of 120 hours were admitted to the premature nursery from December, 1954, to August, 1955. At the time of admission to the nursery, the infants were assigned to the study categories according to the decision contained in each (of a pre-arranged series of sealed envelopes. ... Ninety-seven infants were allotted to the oxytetracycline group and 95 to the penicillin/sulfisoxazole category. ... Twenty-seven infants who were enrolled in the oxytetracycline group died (before time age of 28 days), as contrasted with 60 deaths that occurred in the penicillin/sulfisoxazole category.” [1, pxx]

“One example of kernicterus was noted among 16 infants in the oxytetracycline group who died before the age of 120 hours and underwent necropsy. This incidence was in contrast to 12 instances of kernicterus that were noted among 33 necropsies on infants who received penicillin/sulfisoxazole and died during time trial period.” [1, pxx]

“After the conclusion of the present clinical trial there were many unanswered questions. However, because of time conspicuous difference in mortality rates in the two groups of infants, further extension of these observations in the nursery was contraindicated. Until further evidence from laboratory animals becomes available, no reasonable explanations for the observed differences in mortality rates and incidence of kernicterus can be offered.” [1, pxx]

2 – Developmental outcomes
Silverman (1959) followed the developmental progress of the surviving infants treated with sulfisoxazole or oxytetracycline.

“The neonatal experience of the original group of 192 premature infants in this study was startling. In the course of an evaluation of the effectiveness of two antibacterial drug regimens, we came upon an unexpected association between penicillin/sulfisoxazole treatment and high mortality. The high incidence of kernicterus observed at autopsy among the infants who received this treatment was equally disturbing and provocative.” [2, p744]

Silverman compared outcomes of premature infants treated with antibiotics to survivors of kernicterus caused by synthetic vitamin K and Rh factor incompatibility.

“A disturbingly high proportion (approximately one quarter) of these survivors of premature birth exhibited signs of neurologic deficit and mental retardation at the age of 2 years. This finding strongly suggests that the problem of brain damage among premature infants is one which requires at least equal consideration with the problem of reducing the mortality rate among these newborn infants.” [2, p746]

1. Silverman WA et al. (1956) A difference in mortality rate and incidence of kernicterus among premature infants allotted to two prophylactic antibacterial regimens.

2. The Apgar score

3. Oxygen intoxication or oxygen insufficiency?

   described some of the problems that arose in the search for ways to minimize infections in premature infants [1-3].
Robertson (2003) discussed many examples that illustrate how advances in understanding have been too quickly adopted for treatment without consideration of what might remain yet unknown [1-3].

   “In any rapidly changing medical field, treatments and procedures may be instituted without controlled outcome measurement that might reveal untoward effects. This lack of controlled measurements has certainly been true in neonatology. A classic example is using high oxygen concentrations in caring for premature infants, resulting in retrolental fibroplasia (RLF).” [1, p48]
But causes of retrolental fibroplasia (or retinopathy of prematurity) may also still not be fully understood [4-8]. Oxygen administration was adopted for infants in respiratory distress, and the underlying anoxia may in fact have caused damage to the retina, which like brainstem nuclei is neurologic tissue of high blood flow and high metabolic rate, thus susceptible to impairment by oxygen insufficiency [4-6].


4. Blood group incompatibilities

5. Vitamin K for hemorrhagic disease of the newborn

Ergotrate, oxytocin
Synthetic vitamin K
Hyaline membrane – surfactant – indomethacin – betamethasone
Patent ductus arteriosus – capillary bypass

In progress