WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

**Worksheet Authors:**
Gary M. Weiner, MD

**Date Submitted for Review:**
10/20/2009

**Clinical Question:**

In neonates (P), does milking of the cord (I) versus standard management (C), improve outcome (O)?

*The intervention for this review is limited to “milking” of the cord and does not consider delayed cord clamping, see NRP 030A and NRP 030B.*

**Is this question addressing an intervention/therapy, prognosis or diagnosis?**

Intervention

**State if this is a proposed new topic or revision of existing worksheet:**

New Topic

**Conflict of Interest Specific to this Question:**

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet?

No.

**Search Strategy:**

**Databases searched:**
Medline (OVID and PubMed), Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Embase, AHA Endnote master library, review references from retrieved articles, forward search all included studies using OVID “cited by” and “find similar” function.

**Search Terms:**

OVID Medline and Cochrane CENTRAL (10/01/09)
1 milk.mp. (83927)
2 milking.mp. (2384)
3 squeeze.mp. (1777)
4 squeezing.mp. (1209)
5 strip.mp. (9264)
6 stripping.mp. (6159)
7 umbilical cord.mp. or exp Umbilical Cord/ (28786)
8 6 or 4 or 1 or 3 or 2 or 5 (102724)
9 8 and 7 (298)
10 limit 9 to "newborn infant (birth to 1 month)" (185)

PubMed (10/01/09):
("umbilical cord"[MeSH Terms] OR "umbilical"[All Fields] AND "cord"[All Fields]) OR "umbilical cord"[All Fields] AND milking[All Fields] (9)

Cochrane DSR (10/01/09):
umbilical cord.mp. (64)
Embase (10/01/09):
(umbilical/exp OR umbilical) AND cord AND milking AND [embase]/lim (7)
(umbilical/exp OR umbilical) AND cord AND stripping AND [embase]/lim (12)
(umbilical/exp OR umbilical) AND cord AND squeezing AND [embase]/lim (1)

AHA Endnote Master Library (10/01/09):
“umbilical cord” (78)

Inclusion and Exclusion Criteria:

Inclusion Criteria:
1. Controlled clinical studies (randomized, quasi-randomized, non-randomized) among human newborns describing umbilical cord milking or stripping before cord clamping compared with clamping without milking or stripping
2. Meta-analyses or systematic reviews including a minimum of 2 controlled clinical studies (randomized, quasi-randomized, non-randomized) describing umbilical cord milking or stripping among human newborns before cord clamping compared with clamping without milking or stripping

Exclusion Criteria:
1. Studies where other aspects of cord management (e.g. timing of cord clamping) differ between the intervention and control groups
2. Case reports and case series
3. Duplicate publications of the same subjects and outcomes (only most recent or most complete publication included)
4. Unpublished studies, studies published only in abstract form, data published only as a “Letter to the Editor”

Number of articles/sources meeting criteria for further review:

Titles and abstracts were scanned to identify potentially relevant references for secondary review. A total of 13 potentially relevant references were identified:
- OVID → 5 potentially relevant references
- PubMed → 2 additional references
- Embase → no additional references
- Cochrane DSR → 2 additional references
- Cochrane CENTRAL → no additional references
- AHA Endnote Library → no additional reference
- Reviewing references from included searches, forward search and “find similar” → 4 additional references. These 4 historical articles were published between 1954-1963 and were identified from the reference list of an article published in 1969 (Walsh) that ultimately was not included. Their indexing in Medline was very limited and none included an abstract.

The full text of each potentially relevant reference was reviewed for inclusion and exclusion criteria. In total, 8 references met inclusion criteria and 5 references were excluded.
### Summary of evidence

#### Evidence Supporting Clinical Question

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<th>Level of Evidence</th>
<th>Evidence Supporting Clinical Question</th>
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<tr>
<td>Good</td>
<td>Hosono 2008&lt;sup&gt;E&lt;/sup&gt;</td>
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<td>Fair</td>
<td>Hosono 2009&lt;sup&gt;E&lt;/sup&gt;</td>
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<td>Archilei 1960&lt;sup&gt;E&lt;/sup&gt;</td>
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<td>Colozzi 1954&lt;sup&gt;E&lt;/sup&gt;</td>
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<td>McCausland 1949&lt;sup&gt;E&lt;/sup&gt;</td>
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#### Level of evidence

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  

*Italics = Animal studies*
### Evidence Neutral to Clinical question

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<td>Siddal 1953&lt;sup&gt;E&lt;/sup&gt;</td>
<td>Whipple 1957&lt;sup&gt;E&lt;/sup&gt;</td>
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**Level of evidence**

A = Return of spontaneous circulation  
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### Evidence Opposing Clinical Question

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**Level of evidence**

A = Return of spontaneous circulation  
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*Italics* = Animal studies

### REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

After delivery, a large volume of blood remains in the placenta and umbilical cord that could be the source for an autologous “placental transfusion”. Descriptions of delayed cord clamping have appeared in the obstetric literature since the end of the 19<sup>th</sup> century and the timing of cord clamping remains an area of active research. Studies investigating the role of delayed umbilical cord clamping for the purpose of placental transfusion are considered in two recent Cochrane systematic reviews (Rabe 2009, McDonald 2008) and are the subject of separate ILCOR reviews (NRP 030A, NRP 030B). The possibility that neonatal resuscitation will be delayed while waiting for blood to passively flow toward the baby has led some to recommend squeezing or stripping the cord toward the newborn immediately after birth in an effort to “milk” blood toward the baby and decrease the time required to transfer the placental blood to the newborn. This review focuses on studies where the intervention involves actively squeezing or stripping the umbilical cord toward the newborn immediately after birth compared with immediate cord clamping.

The largest body of evidence describing umbilical cord milking comes from studies published in the middle of the 20<sup>th</sup> century (1940’s-1960’s) using methodology and reporting styles that do not meet
contemporary standards. These studies (Archilei 1960; Colozzi 1954; McCausland 1949; Siddal 1952; Siddal 1953; Whipple 1957) describe consecutive series of primarily full-term, healthy newborns assigned in a non-randomized or quasi-randomized method to immediate cord clamping or cord milking. None of the newborns described in these studies required delivery room resuscitation and high-risk newborns were generally excluded. All of these studies are limited by incomplete data reporting and limited follow-up. The consistent conclusion from these studies, however, was that milking the cord immediately after birth resulted in an increase in the newborn’s hematologic indices (hemoglobin, hematocrit, blood volume) and may result in a shorter time required to regain birth weight. Both McCausland (McCausland 1949) and Colozzi (Colozzi 1954) found that milking the cord appeared to be effective as delayed cord clamping for increasing a healthy, full term newborn’s hemoglobin during the first 5 days of life. Similarly, both Archilei (Archilei 1960) and McCausland (McCausland 1949) found that, among healthy full term newborns, milking the cord appeared to be as effective as delayed cord clamping for improving weight gain during the first 5 days of life. None of these published studies described any adverse effects from cord milking. These non-randomized studies provide data to generate hypotheses, however, they do not provide sufficient evidence to adequately assess the safety or efficacy of cord milking among either full term or preterm newborns.

The best available evidence to evaluate whether outcomes are improved by umbilical cord milking comes from a single, small randomized controlled trial that is the subject of two separate publications (Hosono 2008, Hosono 2009). In this study, premature newborns (24-28 weeks gestation) were randomly assigned to immediate umbilical cord clamping (n=20) or cord milking (2-3 times over ~ 6 seconds) before clamping (n=20). The primary outcome measure was the relative risk of receiving a blood transfusion during the hospital stay using well-defined criteria. The experimental group had a decreased likelihood of receiving a transfusion during the hospital stay (RR 0.5, RD 0.35, NNT 2.8), fewer transfusions (1.7 vs. 4.0, p=0.02) and favorable secondary outcome measures including: a higher hemoglobin at birth (16.5 gm/dl vs. 14.1 gm/dl, p < 0.01), a shorter duration of both mechanical ventilation and oxygen administration (21.9 days vs. 36.1 days, p=0.04; 23.4 days vs. 46.6 days, p <0.01), lower incidence of oxygen administration at 36 weeks GA (0/20 vs. 4/20, p=0.02), and shorter interval to regain birth weight (28.5 days vs. 34.6 days, p=0.04).

Although there was no difference in mortality or significant morbidity (polycythemia, RDS, PDA, IVH, intestinal perforation, PVL, or ROP), the study lacked sufficient power to adequately evaluate these risks. A secondary analysis, published one year later, further explores additional secondary outcomes related to hemodynamic stability (Hosono, 2009). The incidence of hypotension at admission was lower in the experimental group (RR 0.42, RD 0.35, NNT 2.8) and fewer infants received volume expanders (RR 0.25) or vasopressors > 5 mcg/kg/min during the first 120 hours (RR 0.25). During the first 12 hours of life, the mean systolic and diastolic pressures were higher in the experimental group (data presented only graphically). From 24-hours to 120-hours of life, there was no difference between the groups as the systolic pressure in the control group increased, the diastolic pressure in the control group increased, and the diastolic pressure in the experimental group slightly decreased. During the first 72 hours of life, the mean urine output was higher in the experimental group (data presented only graphically), presumably reflecting improved renal perfusion.

Although umbilical cord milking appears to be a simple and promising intervention to decrease blood transfusions and improve hemodynamic stability among premature newborns (24-28 weeks gestation), there are currently insufficient data to fully evaluate the safety and efficacy of this procedure. There are no data meeting current standards to evaluate the efficacy and safety of this practice among healthy full term newborns or those requiring resuscitation.

Acknowledgements:
Dr. Vincenzo Zanardo (Professor of Pediatrics, Padua University School of Medicine, Padua, Italy) graciously provided assistance translating the text of an included reference (Archilei, 1960) from Italian to English for this review.
Citation List:


LOE: 2
Quality: Poor
Outcome: E (other)
Direction of Evidence: Supportive

Comment: This is a non-randomized experimental study published in Italian (translated for this review by Dr. Vincenzo Zanardo, University of Padua) comparing the weight curve of newborns with immediate cord clamping (control) with newborns whose cords were "stripped" after delivery. It is not clear how long cord clamping was delayed in the experimental group or how many times the cord was stripped. The manuscript states that newborns were excluded if their mother had Rh incompatibility, preterm delivery, severe "gestosis", or diabetes mellitus. The study included 238 full term, healthy newborns who were assigned to have their umbilical cords stripped until the cord appeared bloodless or have their cord cut immediately. Thirty eight were ultimately excluded because they "did not receive an adequate quantity of maternal milk" and their outcomes were not described. The final report includes 100 newborns in each treatment group. There are no demographic details provided for either group. The method of assignment to the experimental and control group is not defined. The observations are limited to the eight-day period of hospitalization. The individual(s) assessing outcomes did not appear to be blinded to the treatment assignment. Newborns were weighed after delivery and then daily. Beginning of the 4th day, subjects were also weighed before and after breastfeeding to measure the amount of milk fed.

Results are divided into 4 groups by birth weight (range 2500-5000 grams). Data are presented graphically and as daily mean weights within each group. Statistical comparisons are not included and there are insufficient data provided to retrospectively make comparisons. In all four groups, the experimental group appeared to have less absolute weight loss and a more rapid increase in weight after birth. The magnitude of the weight difference appeared greatest in the smallest birth weight group (2500-3000 grams) where the experimental subjects (n=10) had an average weight gain of 13 grams on the 8th day of life compared with an average weight loss of 227 grams in the control group (n=12). The authors state that they did not notice any adverse effects or other differences between the groups. They note that 37 experimental subjects developed jaundice compared with 30 control subjects but comment that jaundice was mild and rapidly resolved. No blood counts or bilirubin measurements are included in the manuscript.


LOE: 2
Quality: Poor
Outcome: E (other)
Direction of Evidence: Supportive

Comment: This is a non-randomized experimental study comparing 4 different methods of cord clamping among 100 consecutive full term, vaginally delivered, healthy newborns. The newborn was placed on the mother's abdomen and the cord clamped after pulsations ceased (group 1), the cord was clamped immediately after delivery (group 2), the newborn was placed below the placenta and the cord stripped 4-8 times until it was no longer distended with blood and then clamped (group 3), or the newborn was placed below the placenta and the cord was clamped after pulsations ceased (group 4). Capillary blood samples were obtained at 24 and 72 hours after birth (heel stick) and analyzed by a pathologist that was blinded to treatment group assignment. Data are presented as averages for each group. No statistical comparisons were made and there are insufficient data provided to make these comparisons retrospectively. The infants with cord "stripping" appeared to have the highest hemoglobin at both 24 and 72 hours (18.62 gm/100ml and 18.96 gm/100 ml) and when averaged across both time intervals (mean 18.79 gm/100 ml) compared with either delayed clamping group (overall mean 17.19 gm/100 ml for group 1 and 17.15 gm/100 ml for group 4) or the immediate clamping group (14.78 gm/100 ml). The author states that "No particular differences in general well-being were noted," however, there are insufficient data presented to evaluate the possibility of adverse effects. Observations were limited to the "usual" 5-day hospitalization period.

LOE: 1
Quality: Good
Outcome: E (other)
Direction of Evidence: Supportive
Comment: This is a well designed randomized controlled trial comparing the relative risk of red blood cell transfusion for anemia among infants born at < 29 weeks gestation following umbilical cord "milking" versus routine (immediate) clamping. The randomization list was concealed with serially numbered opaque envelopes. All potentially eligible and enrolled patients were accounted for at the conclusion. The patients were analyzed using the intent to treat principle. The clinicians were not blinded to the treatment assignment and it does not appear that the individual(s) assessing outcomes were blinded to treatment assignment. Aside from the experimental treatment, the groups were treated equally with a written guideline for transfusion criteria. Groups appear to have been similar at the beginning of the trial (the experimental group had a slightly higher gestational age and slightly lower percentage of males, neither statistically significant). The investigators supported their sample size based on the primary outcome of risk of transfusion at any time during the hospital stay based on finding a 45% difference between groups (80% power, two-sided alpha 0.05) using data from an earlier trial of early versus delayed cord clamping. The statistical analysis was appropriate for the hypothesis and data collected. The experimental group had a decreased likelihood of requiring a transfusion during the hospital stay (RR 0.5, RD 0.35, NNT 2.8), fewer transfusions and several favorable secondary outcome measures including: a higher hemoglobin at birth, and shorter duration of both mechanical ventilation and oxygen administration, lower incidence of BPD (oxygen administration at 36 weeks GA), and shorter interval to regain birthweight. There was no difference in mortality or significant morbidity including polycythemia, RDS, PDA, IVH, intestinal perforation, PVL, or ROP. This small study, however, lacked power to adequately evaluate the risk of these adverse events. A secondary analysis was published one year later to evaluate clinical signs of hemodynamic stability in these infants (see Hosono, 2009).


LOE: 1
Quality: Fair
Outcome: E (other)
Direction of Evidence: Supportive
Comment: This is a secondary analysis describing additional hemodynamic outcome data from a previously reported randomized controlled trial (see Hosono, 2008) evaluating 40 premature infants (< 29 weeks gestation) randomized to umbilical cord "milking" or routine cord care after delivery. The randomization list was concealed with serially numbered opaque envelopes. All potentially eligible and enrolled patients were accounted for at the conclusion. The patients were analyzed using the intent to treat principle. The clinicians were not blinded to the treatment assignment and it does not appear that the individual(s) assessing outcomes were blinded to treatment assignment. It is not clear that the groups were treated equally with respect to blood pressure treatment as there was no standardized guideline for the management of blood pressure and the clinicians were not blinded to treatment assignment. Aside from the experimental treatment, the groups appear to have been treated equally with respect to blood pressure measurement, PDA prophylaxis (indocin), and surfactant treatment for RDS. Groups appear to have been similar at the beginning of the trial (the experimental group had a slightly higher gestational age and slightly lower percentage of males, neither statistically significant). The sample size was based on the primary outcome variable for the initial study (need for packed red blood cell transfusion). The statistical analysis is appropriate for the data collected. The incidence of hypotension at admission was lower in the experimental group (RR 0.42, RD 0.35, NNT 2.8). Fewer infants in the experimental group received volume expanders or vasopressors (> 5 mcg/kg/min) during the first 120 hours. During the first 12 hours of life, the mean systolic and diastolic pressures were higher in the experimental group. From 24-hours to 120-hours, there was no difference between the groups as the systolic pressure in the control group increased, the diastolic pressure in the control group increased,
and the diastolic pressure in the experimental group slightly decreased. The mean urine output was higher in the experimental group, presumably reflecting improved renal perfusion.


LOE: 2
Quality: Poor
Outcome: E (other)
Direction of Evidence: Supportive

Comment: This "classic" study reported in 1949 is a non-randomized experimental study comparing the blood count and weight of 127 full-term newborns who had their umbilical cords clamped immediately after birth (n=41), clamped after allowing the cord to pulsate for 5 minutes (n=36), and clamped after stripping the umbilical cord toward the baby (n=50). It is not clear how infants were recruited for the study or how assignments to the three groups were made. No demographic data describing the infants are provided. Outcome measurements were not blinded, however, they appear to have been made objectively. Blood counts were measured twice (2-hours and 5 days of life) and weights were measured serially (intervals not clearly stated) during the first 6 days of life. Averages were reported without standard deviations and no statistical comparisons were made.

Infants in the "stripping" group appear to have a higher erythrocyte count at both 2 hours and 5 days compared with immediate cord clamping and fewer infants in the "stripping" group appear to have experienced a decline in their erythrocyte count during this interval. Infants in the "stripping" group appear to have a higher birth weight and experience less weight loss during the first week of life. The manuscript includes survey responses from 1,198 obstetricians describing their management of the umbilical cord at the time of delivery providing historical perspective.


LOE: 2
Quality: Poor
Outcome: E (other)
Direction of Evidence: Neutral

Comment: This quasi-randomized study compares the hemoglobin of 50 babies delivered by cesarean section whose cords were clamped immediately with 50 babies whose cords were "milked" before clamping. The assignment to treatment group was based on gender. At one center, all boys had their cords clamped immediately and all girls had their cords milked. At another center, the assignment by gender was reversed. The method of quasi-randomization was not blinded. Two exclusion criteria were noted: (1) stillborn infants and (2) cases where the surgical incision extended into the placenta causing suspected feto-placental hemorrhage. It is not clear from the manuscript if all eligible, consecutive newborns entered the study or if all newborns that entered the study were analyzed. It is not stated if subjects were all analyzed in the groups to which they were assigned. It is not specifically stated if groups were treated equally aside from the experimental treatment. No data are presented to determine if groups were similar at the start of the trial. Blood was obtained for analysis between 2 and 12 hours of life. The site of sampling is not stated.

The data are presented in tabular form in groups and as averages without standard deviations. There are insufficient data to make statistical comparisons. The authors report that the average hemoglobin for the immediate clamping group was 15.9 gm compared with 17.2 gm in the milking group. Reviewing the hemoglobin distribution presented in a tabular format, indicates that more babies in the immediate clamping group had a hemoglobin < 15 gm (7 vs. 21). The median hemoglobin cannot be calculated from the data provided.

All five "prematures" (birth weight < 2270 grams or 5 pounds) and one term infant with "diarrhea" were excluded from the author's description of the hospital stay. Insufficient data are provided to make a statistical comparison, however, a table of values indicates that babies in the milking group had a trend toward less weight loss during the hospital stay (65 gm vs. 107 gm) with no difference in the average length of the hospital stay (7.8 vs 7.9 days). Potential adverse events were not addressed except for the statement, "There was no apparent ill effect from forcing
in blood by milking or stripping the umbilical cord." The only reported death was a "premature" newborn in the milking group whose hemoglobin was 19.9 gm.

This "classic" study provides some evidence that umbilical cord milking among term infants delivered by cesarean section may result in higher initial hemoglobin levels when assessed shortly after birth. There are insufficient data presented to make any further conclusions.


LOE: 2
Quality: Poor
Outcome: E (other)
Direction of Evidence: Neutral
Comment: This quasi-randomized study among 100 vaginally delivered babies is similar to the previously reported study investigating cord milking among babies delivered by cesarean section reported by the same author in 1952 (Siddal 1952). The hemoglobin of 50 babies whose cords were clamped immediately were compared with 50 babies whose cords were "milked" before clamping. The assignment to treatment group was based on gender. For the first 50 subjects enrolled, the boys had their cords clamped immediately and all girls had their cords milked. For the second 50 babies enrolled, the assignment by gender was reversed. The method of quasi-randomization was not blinded. No exclusion criteria were described. It is not clear from the manuscript if all eligible, consecutive newborns entered the study or if all newborns that entered the study were analyzed. It is not stated if subjects were all analyzed in the groups to which they were assigned. It is not specifically stated if groups were treated equally aside from the experimental treatment. No data are presented to determine if groups were similar at the start of the trial. Blood was obtained for analysis between 2 and 12 hours of life and again on the 3rd day. The site of sampling is not stated.

The data are presented in tabular form in groups and as averages without standard deviations. There are insufficient data to make statistical comparisons. The authors report that the average initial hemoglobin for the immediate clamping group was 15.8 gm compared with 17.2 gm in the milking group and 16.8 gm vs. 15.7 gm at three days. Reviewing the hemoglobin distribution presented in a tabular format, indicates that more babies in the immediate clamping group had a hemoglobin < 15 gm (10 vs. 39). The median hemoglobin cannot be calculated from the data provided.

All seven "prematures" (birth weight < 2270 grams or 5 pounds) were excluded from the author's description of the hospital stay and subsequent outcomes. Insufficient data are provided to make a statistical comparison, however, a table of values indicates that babies in the milking group had a trend toward less weight loss during the hospital stay (2.4 ounces vs. 3.5 ounces). Potential adverse events were not addressed except for the statement, "there was no evidence whatsoever that milking or stripping the umbilical cord 'overloads blood vessels, causes icterus, melena, even apoplexy', or any other difficulty." No deaths were recorded in either group.

This "classic" study provides some evidence that umbilical cord milking among term, vaginally delivered newborns may increase the infant's hemoglobin when assessed shortly after birth. There are insufficient data presented to make any further conclusions.


LOE: 2
Quality: Poor
Outcome: E (other)
Direction of Evidence: Neutral
Comment: Non-randomized, concurrent control experimental study enrolling 38 full-term newborns from "uncomplicated" deliveries. Babies were divided into four groups: (1) immediate cord clamping, (2) 3-minute delay in clamping cord with the baby held below the introitus, (3) 3-minute delay in clamping cord with the baby held on mother's abdomen, (4) baby placed in obstetrician's lap and the cord milked 5 times before clamping (n=9). No statistical comparisons were made and there are insufficient data presented to make comparisons. The group with
cord milking appeared to have the highest hemoglobin and red cell volume on the first day of life and at 4 days. No other clinical outcomes are described.

**Excluded Studies**


**Reason for Exclusion:** Experimental group had both delayed cord clamping (until placental separation) and cord milking compared with immediate clamping


**Reason for Exclusion:** This review only describes studies comparing early and late cord clamping, none with cord milking.


**Reason for Exclusion:** This review only describes studies comparing early and late cord clamping, none with cord milking.


**Reason for Exclusion:** Experimental group had both delayed cord clamping (5-minutes) and cord milking (each 30-seconds) compared with immediate clamping

**Comment:** A non-randomized controlled experiment among term, vaginally delivered infants where 9 had their cords clamped immediately, 11 had cord clamping delayed for 5 minutes, and 7 had their cords stripped vigorously every thirty seconds during the 5-minute delay. Infants in both the delay and delay+ stripping groups had higher blood volumes, red blood cell volumes, venous hematocrits, and plasma volumes over the first 72 hours of life when compared to those with a cord clamped immediately. There was no significant difference between those with delayed cord clamping and those with delayed cord clamping + stripping. Six of seven infants with stripping had at least one venous hematocrit with polycythemia (venous hematocrit >/= 65%).


**Reason for Exclusion:** Experimental group had both delayed cord clamping (5 minutes) and cord stripping/milking compared with immediate clamping

**Comment:** Six infants had both delayed cord clamping and the cord was "stripped" vigorously 10 times over 5 minutes. These infants were compared with 31 infants who had immediate cord clamping. Assignment was not randomized and the method of subject selection was not described. There were no differences in the heart rate, PR segment, or QRS interval during the first week of life. Infants in the "stripping" group had longer P duration, Macruz index, P-R, and Q-Tc intervals; higher P waves; lower R/S ratios in V1 and V; and delayed inversion of the T wave in V1. One growth restricted (BW 2340 gm, 39 wk EGA) twin became cyanotic during the procedure. The author hypothesizes that this may be evidence of acute volume overload.