

## WORKSHEET for PROPOSED Evidence-Based GUIDELINE RECOMMENDATIONS

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| <b>Worksheet Author:</b>                           | <b>Home Subcommittee:</b> Neonatal Resuscitation Program Committee        |
| <b>Author's Home Resuscitation Council:</b><br>AHA | <b>Date Submitted to Subcommittee:</b> July 14, 2004; revised Nov 3, 2004 |

**STEP 1: STATE THE PROPOSAL.** State if this is a proposed new guideline; revision to current guideline; or deletion of current guideline.

**Existing guideline, practice or training activity:**

Dry and place under radiant warmer

**Step 1A: Refine the question; state the question as a positive (or negative) hypothesis. State proposed guideline recommendation as a specific, positive hypothesis. Use single sentence if possible. Include type of patients; setting (in-/out-of-hospital); specific interventions (dose, route); specific outcomes (ROSC vs. hospital discharge).**

Thermal stresses should be reduced during the resuscitation of neonates to minimize energy expenditure. Special strategies may be needed for preterm neonates who are particularly vulnerable to hypothermia.

**Step 1B: Gather the Evidence; define your search strategy.** Describe search results; describe best sources for evidence. Words used in strategy included: infant, premature; infant neonate; hypothermia; hyperthermia; body temperature regulation, and resuscitation

List electronic databases searched (at least MEDLINE (<http://igm.nlm.nih.gov/>) and hand searches of journals, review articles, and books.

MeSH Headings (infant, premature OR infant , newborn) AND (hypothermia OR hyperthermia OR body temperature regulation) AND resuscitation

Medline (1966-2004) –147 Hits

Cochrane database for systematic reviews, --1 review

Embase. (1988-2004)—50 hits

Embase (1980-1987)—3 hits

(infant, premature OR infant, newborn) AND (water-filled mattress OR chemical warmer OR heating mattress)

Medline (1966-2004)—26 hits

(infant, premature OR infant, newborn) AND ( plastic wrap OR polyethylene wrap OR plastic bag OR transparent wrap)

Medline (1966-2004) – 42 hits

MDCConsult, search and hand searches of journal and review articles were also undertaken.

- State major criteria you used to limit your search; state inclusion or exclusion criteria (e.g., only human studies with control group? no animal studies? N subjects > minimal number? type of methodology? peer-reviewed manuscripts only? no abstract-only studies?)

Limited to human studies; No other exclusions

- Number of articles/sources meeting criteria for further review: Create a citation marker for each study (use the author initials and date or Arabic numeral, e.g., "Cummins-1"). If possible, please supply file of best references; End Note 4+ preferred as reference manager, though other reference databases acceptable.

There were only 4 studies worthy of inclusion

(Vohra 1999; Bjorklund and Hellstrom-Westas 2000; Lenclen, Mazraani et al. 2002; Lyon and Stenson 2004)

## STEP 2: ASSESS THE QUALITY OF EACH STUDY

**Step 2A: Determine the Level of Evidence.** For each article/source from step 1, assign a level of evidence—based on study design and methodology.

| <b>Level of Evidence</b> | <b>Definitions</b><br>(See manuscript for full details)  |
|--------------------------|--|
| <b>Level 1</b>           | Randomized clinical trials or meta-analyses of multiple clinical trials with substantial treatment effects |
| <b>Level 2</b>           | Randomized clinical trials with smaller or less significant treatment effects                              |
| <b>Level 3</b>           | <u>Prospective</u> , controlled, non-randomized, cohort studies  |
| <b>Level 4</b>           | <u>Historic</u> , non-randomized, cohort or case-control studies   |
| <b>Level 5</b>           | <u>Case series</u> : patients compiled in serial fashion, lacking a control group                          |
| <b>Level 6</b>           | Animal studies or mechanical model studies   |
| <b>Level 7</b>           | Extrapolations from existing data collected for other purposes, theoretical analyses                       |
| <b>Level 8</b>           | Rational conjecture (common sense); common practices accepted before evidence-based guidelines             |

**Step 2B: Critically assess each article/source in terms of research design and methods.**

Was the study well executed? Suggested criteria appear in the table below. Assess design and methods and provide an overall rating. Ratings apply within each Level; a Level 1 study can be excellent or poor as a clinical trial, just as a Level 6 study could be excellent or poor as an animal study. Where applicable, please use a superscripted code (shown below) to categorize the primary endpoint of each study. For more detailed explanations please see attached assessment form.

| <b>Component of Study and Rating</b> | <b>Excellent</b>   | <b>Good</b>   | <b>Fair</b>  | <b>Poor</b>   | <b>Unsatisfactory</b>   |
|--------------------------------------|--|---|--|---|---|
| <b>Design &amp; Methods</b>          | Highly appropriate sample or model, randomized, proper controls<br><b>AND</b><br>Outstanding accuracy, precision, and data collection in its class | Highly appropriate sample or model, randomized, proper controls<br><b>OR</b><br>Outstanding accuracy, precision, and data collection in its class | Adequate, design, but possibly biased<br><b>OR</b><br>Adequate under the circumstances | Small or clearly biased population or model<br>Weakly defensible in its class, limited data or measures | Anecdotal, no controls, off target end-points<br>Not defensible in its class, insufficient data or measures |

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint

B = Survival of event D = Intact neurological survival

**Step 2C: Determine the direction of the results and the statistics: supportive? neutral? opposed?**

| <b>DIRECTION of study by results &amp; statistics:</b> | <b>SUPPORT the proposal</b>  | <b>NEUTRAL</b>   | <b>OPPOSE the proposal</b>                        |
|--|--|--|---|
| <b>Results</b>   | Outcome of proposed guideline superior, to a clinically important degree, to | Outcome of proposed guideline no different from current approach | Outcome of proposed guideline inferior to current |

|  |                    |  |          |
|--|--------------------|--|----------|
|  | current approaches |  | approach |
|--|--------------------|--|----------|

**Step 2D: Cross-tabulate assessed studies by a) level, b) quality and c) direction** (ie, supporting or neutral/ opposing); **combine and summarize.** Exclude the *Poor* and *Unsatisfactory* studies. Sort the *Excellent*, *Good*, and *Fair* quality studies by both *Level and Quality of evidence*, and *Direction of support* in the summary grids below. Use citation marker (e.g. author/ date/source). In the *Neutral* or *Opposing* grid use bold font for *Opposing* studies to distinguish them from merely neutral studies. Where applicable, please use a superscripted code (shown below) to categorize the primary endpoint of each study.

### Supporting Evidence

Thermal stresses should be reduced during the resuscitation of neonates to minimize energy expenditure. Special strategies may be needed for preterm neonates who are particularly vulnerable to hypothermia.

|                            |                  |                           |          |          |  |                                    |          |          |          |
|----------------------------|------------------|---------------------------|----------|----------|--|------------------------------------|----------|----------|----------|
| <b>Quality of Evidence</b> | <b>Excellent</b> |                           |          |          |  |                                    |          |          |          |
|                            | <b>Good</b>      | (Vohra <sup>E</sup> 1999) |          |          | (Lenclen, Mazraani <sup>E</sup> et al. 2002)     |                                    |          |          |          |
|                            | <b>Fair</b>      |                           |          |          | (Bjorklund & Hellstrom-Westas <sup>E</sup> 2000) | (Lyon & Stenson <sup>E</sup> 2004) |          |          |          |
|                            |                  | <b>1</b>                  | <b>2</b> | <b>3</b> | <b>4</b>   | <b>5</b>                           | <b>6</b> | <b>7</b> | <b>8</b> |
|                            |                  | <b>Level of Evidence</b>  |          |          |  |                                    |          |          |          |

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

### Neutral or Opposing Evidence

Thermal stresses should be reduced during the resuscitation of neonates to minimize energy expenditure. Special strategies may be needed for preterm neonates who are particularly vulnerable to hypothermia.

|                            |                  |                          |          |          |          |          |          |          |          |
|----------------------------|------------------|--------------------------|----------|----------|----------|----------|----------|----------|----------|
| <b>Quality of Evidence</b> | <b>Excellent</b> |                          |          |          |          |          |          |          |          |
|                            | <b>Good</b>      |                          |          |          |          |          |          |          |          |
|                            | <b>Fair</b>      |                          |          |          |          |          |          |          |          |
|                            |                  | <b>1</b>                 | <b>2</b> | <b>3</b> | <b>4</b> | <b>5</b> | <b>6</b> | <b>7</b> | <b>8</b> |
|                            |                  | <b>Level of Evidence</b> |          |          |          |          |          |          |          |

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

**META-ANALYSES: to provide a basis for Step 3**

|   |
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| <p><b>Are there two or more Level 1 studies in Step 2D that support the proposal and are statistically significant at <math>p &lt; 0.05</math>? No</b></p> <p><b>Do these supportive studies constitute at least one quarter of Level 1 clinical trials? No</b><br/>         (If the answer to both questions is “yes”, the null hypothesis is very likely to be false.)</p> <p><b>Do you think there are sufficient data to perform a formal meta-analysis? No</b></p> <p><b>Summarize core numeric data.</b> <i>If you can provide a formal meta-analysis, attach the most critical tabulations, and cite the methodology used.</i></p> |
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**STEP 3. DETERMINE THE CLASS OF RECOMMENDATION. Select from these summary definitions.**

| <b>CLASS</b>  | <b>CLINICAL DEFINITION</b>  | <b>REQUIRED LEVEL OF EVIDENCE</b>  |
|---|---|--|
| <p><b>Class I</b><br/> <i>Definitely recommended.</i><br/>           Definitive,<br/> <b>excellent</b> evidence provides support.</p> | <ul style="list-style-type: none"> <li>• Always acceptable, safe</li> <li>• Definitely useful</li> <li>• Proven in both efficacy &amp; effectiveness</li> <li>• Must be used in the intended manner for proper clinical indications.</li> </ul> | <ul style="list-style-type: none"> <li>• One or more Level 1 studies are present (with rare exceptions)</li> <li>• Study results consistently positive and compelling</li> </ul> |

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| <b>Class II:</b><br><i>Acceptable and useful</i>  | <ul style="list-style-type: none"> <li>• Safe, acceptable</li> <li>• Clinically useful</li> <li>• Not yet confirmed definitively</li> </ul>                                    | <ul style="list-style-type: none"> <li>• Most evidence is positive</li> <li>• Level 1 studies are absent, or inconsistent, or lack power</li> <li>• No evidence of harm</li> </ul>                       |
| <ul style="list-style-type: none"> <li>• <i>Class IIa: Acceptable and useful</i></li> </ul> <b>Good</b> evidence provides support | <ul style="list-style-type: none"> <li>• Safe, acceptable</li> <li>• Clinically useful</li> <li>• Considered treatments of choice</li> </ul>                                   | <ul style="list-style-type: none"> <li>• Generally higher levels of evidence</li> <li>• Results are consistently positive</li> </ul>   |
| <ul style="list-style-type: none"> <li>• <i>Class IIb: Acceptable and useful</i></li> </ul> <b>Fair</b> evidence provides support | <ul style="list-style-type: none"> <li>• Safe, acceptable</li> <li>• Clinically useful</li> <li>• Considered optional or alternative treatments</li> </ul>                     | <ul style="list-style-type: none"> <li>• Generally lower or intermediate levels of evidence</li> <li>• Generally, but not consistently, positive results</li> </ul>                                      |
| <b>Class III:</b><br><i>Not acceptable, not useful, may be harmful</i>  | <ul style="list-style-type: none"> <li>• Unacceptable</li> <li>• Not useful clinically</li> <li>• May be harmful.</li> </ul>   | <ul style="list-style-type: none"> <li>• No positive high level data</li> <li>• Some studies suggest or confirm harm.</li> </ul>   |
| <b>Indeterminate</b>  | <ul style="list-style-type: none"> <li>• Research just getting started.</li> <li>• Continuing area of research</li> <li>• No recommendations until further research</li> </ul> | <ul style="list-style-type: none"> <li>• Minimal evidence is available</li> <li>• Higher studies in progress</li> <li>• Results inconsistent, contradictory</li> <li>• Results not compelling</li> </ul> |

**STEP 3: DETERMINE THE CLASS OF RECOMMENDATION.** State a **Class of Recommendation** for the Guideline Proposal. State either **a) the intervention**, and then the conditions under which the intervention is either Class I, Class IIA, IIB, etc.; or **b) the condition**, and then whether the intervention is Class I, Class IIA, IIB, etc.

### **Intervention**

**Final Class of recommendation: Class IIB-Acceptable & Useful; fair evidence**

**REVIEWER’S PERSPECTIVE AND POTENTIAL CONFLICTS OF INTEREST:** Briefly summarize your professional background, clinical specialty, research training, AHA experience, or other relevant personal background that define your perspective on the guideline proposal. List any potential conflicts of interest involving consulting, compensation, or equity positions related to drugs, devices, or entities impacted by the guideline proposal. Disclose any research funding from involved companies or interest groups. State any relevant philosophical, religious, or cultural beliefs or longstanding disagreements with an individual.

Neonatologist involved in teaching, clinical care, research and administration as a university medical faculty for over 25 years. No conflicts of interest commercially or ethically.

**REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:** Summarize your final evidence integration and the rationale for the class of recommendation. Describe any mismatches between the evidence and your final Class of Recommendation. “Mismatches” refer to selection of a class of recommendation that is heavily influenced by other factors than just the evidence. For example, the evidence is strong, but implementation is difficult or expensive; evidence weak, but future definitive evidence is unlikely to be obtained. Comment on contribution of animal or mechanical model studies to your final recommendation. Are results within animal studies homogeneous? Are animal results consistent with results from human studies? What is the frequency of adverse events? What is the possibility of harm? Describe any value or utility judgments you may have made, separate from the evidence. For example, you believe evidence-supported interventions should be limited to in-hospital use because you think proper use is too difficult for pre-hospital providers.

Thermal stresses are inherent in the birth process for every infant. Current guidelines in the neonatal resuscitation program call for rapid drying of the infant and removing the wet linen after placing the infant on a radiant warming unit in the initial steps. These recommendations have been effective in reducing the

incidence of hypothermia in term infants. (Ryan CA, Clark LM, Malone A, Ahmed S. The effect of a structured neonatal resuscitation program on delivery room practices Neonatal Network 1999;18(1):25-30) However, current evidence indicates that premature or low birth weight babies are still at significant risk of hypothermia even when standard procedures are followed. (Costeloe K, Hennessy F, Gibson AT, Marlow N, Wilkinson AR, the EPICure Study Outcomes to discharge from hospital for infants born at the threshold of viability. Pediatrics 2000;106:659-691)

Since hypothermia has been known to increase mortality in premature infants since the seminal work by Silverman nearly a half century ago (Silverman, WA, Fertig, JW, Berger A The influence of the thermal environment upon the survival of the newly born premature infant Pediatrics 1958: 22: 876-886), it is obvious that modifications in our approach to their resuscitation may improve outcome.

Any technique to reduce heat loss during resuscitation after birth should present no barrier to infant accessibility, should allow visualization for assessment, and should be easily implemented. Heat shields, incubators, and opaque coverings are not suitable for these reasons. However, polyethylene or polyurethane plastic sheets are attractive because they are transparent; impermeable to water passage thereby reducing evaporative heat loss; and permissive of radiant heat transfer. Several early studies showed effective use of these items in term babies. (Sheldon RE, The Bowel Bag; A sterile, transportable method for warming infants with skin defects, Pediatric 53(2); BeschNF, Perlstein, PH, Edwards NK, Keenan WJ, Sutherland JM, The transparent baby bag NEJM 1971284(3)121-124) and one study explored the use in preterms ( Knauth A, Gordin M, McNelis W, Baumgart S, Semipermeable polyurethane membrane as an artificial skin for the premature neonate Pediatrics 2000 106:659-671).

Recent studies--one randomized, controlled trial, (Vohra vide supra) and one historical series with case controls (Leclen vide supra)--show the effective use of a plastic bag to enclose the very preterm, small infant from the neck down immediately after delivery without drying the infant before placing on a radiant warmer, subsequently drying the head and then proceeding with resuscitation. The bag remained in place until the baby was stabilized and admitted to the NICU. Short reports of implementation of the technique have reported success in the reduction of hypothermia rates for the small and preterm.(Bjorkland and Lyon, vide supra) In neither the original trial nor in the short reports of implementation of the technique have adverse events occurred.

In conclusion, it appears that the preterm infant less than <32 weeks has a reduced risk of hypothermia if placed inside a plastic bag from toes to shoulders immediately upon delivery without drying for resuscitation on a radiant warmer. The head should be dried when the baby is placed on the warmer. No adverse effects have been reported. The method is cheap, effective, and appears to be easily implemented. One RCT and 3 other reports appear to be inadequate to make a recommendation for a change in the current standard but the evidence is strong enough to suggest the consideration of this technique pending further, more extensive studies

**Preliminary draft/outline/bullet points of Guidelines revision:** Include points you think are important for inclusion by the person assigned to write this section. Use extra pages if necessary.

Attachments:

Printed (paper) bibliography; and on diskette using a reference manager. It is recommended that the bibliography be printed in annotated format. This will include the article abstract and any notes you would like to make providing specific comments on the quality, methodology and/or conclusions of the study.

Key figures or tables from evidence-based analysis

Full hard copies of most critical cited papers

### *Citation List*

| <b>Citation<br/>Marker</b> | <b>Full Citation*</b> |
|----------------------------|-----------------------|
|----------------------------|-----------------------|

|                      |  |
|----------------------|--|
| {Bjorklund, 2000 #1} | Bjorklund, L. J. and L. Hellstrom-Westas (2000). "Reducing heat loss at birth in very preterm infants." <u>J Pediatr</u> <b>137</b> (5): 739-40.   |
| {Lenclen, 2002 #2}   | Lenclen, R., M. Mazraani, et al. (2002). "[Use of a polyethylene bag: a way to improve the thermal environment of the premature newborn at the delivery room]." <u>Arch Pediatr</u> <b>9</b> (3): 238-44.\   |
| {Lyon, 2004 #3}      | Lyon, A. J. and B. Stenson (2004). "Cold comfort for babies." <u>Arch Dis Child Fetal Neonatal Ed</u> <b>89</b> (1): F93-4.  |
| {Vohra, 1999 #4}     | Vohra, S., G. Frent, et al. (1999). "Effect of polyethylene occlusive skin wrapping on heat loss in very low birth weight infants at delivery: a randomized trial." <u>J Pediatr</u> <b>134</b> (5): 547-51. |

\*Type the citation marker in the first field and then paste the full citation into the second field. You can copy the full citation from EndNote by selecting the citation, then copying the FORMATTED citation using the short cut, Ctrl-K. After you copy the citation, go back to this document and position the cursor in the field, then paste the citation into the document (use Ctrl-V). For each new citation press Enter to move down to start a new paragraph.

Bjorklund, L. J. and L. Hellstrom-Westas (2000). "Reducing heat loss at birth in very preterm infants." J Pediatr **137**(5): 739-40.

Abstract: NONE

**Level of Evidence 4-Supportive**

*NOTE: Retrospective study of 80 patients <28 weeks gestation born between Jan 1996 and Mar 1998 comparing babies cared for in a traditional manner of drying and placing on a warmer and the new method introduced in 1997 of placing the baby in a plastic bag as recommended in Vohra. Body temperature in 73.5% of the 11 patients treated with plastic bags was >36.5 degrees C on admission compared to 23% of the traditionally treated group. None of the plastic bag treated patients became hyperthermic. Additionally the highest FiO2 was significantly less in the plastic bag treated group. This was a retrospective review of application of new approach which resulted in positive outcome.*

Lenclen, R., M. Mazraani, et al. (2002). "[Use of a polyethylene bag: a way to improve the thermal environment of the premature newborn at the delivery room]." Arch Pediatr **9**(3): 238-44.

**BACKGROUND:** Early interventions, such as occlusive wrapping of very low birth weight infants at delivery reduce postnatal temperature fall. This new intervention was implemented in our hospital on January 2000. The aim of this study was to investigate retrospectively the effect of polyethylene wrap, applied immediately at birth, on thermoregulation. **PATIENTS AND METHODS:** Matched pair analysis was conducted for 60 infants delivered inborn at less than 33 weeks' gestation and 60 premature infants who were born during the second half of 1999 fulfilling the same criteria. The only difference in the management (medical and environmental) was wrapping with a polyethylene bag in the delivery room. Rectal temperature and other vital parameters were taken, after removal of wraps, on admission to NICU. **RESULTS:** The perinatal characteristics of both groups were comparable. Use of wrapping resulted in a significantly higher admission rectal temperature (difference in means = 0.8 degree C, p < 0.0001), this difference was also significant in infants < 30 weeks. The incidence of hypothermia (< 35.5 degrees C) was less frequent in infants enclosed in plastic bags (8.3% vs 55%). No side effects (skin burns, infection or hyperthermia) were attributable to the intervention. The heart rate was higher in the

wrapping group (163 +/- 16 vs 150 +/- 17 b/min,  $p < 0.01$ ), as well as the capillary glycemia (62 +/- 26 vs 45 +/- 30 mg/dl,  $p < 0.01$ ). There was no significant difference on arterial pressure. CONCLUSION: Occlusive wrapping with a polyethylene bag at birth prevented low rectal temperature in premature infants in the immediate postnatal period. This method is easy, practical and effective, and does not interfere with current practice for resuscitation.

**Level of Evidence 4-Supportive**

*Note: 60 premature infants <33 weeks matched with historical controls were wrapped in polyethylene bag and placed on a warmer. Incidence of hypothermia <35.5 degrees C was less frequent in treated group (8.3% vs 55%) Good size study.*

Lyon, A. J. and B. Stenson (2004). "Cold comfort for babies." Arch Dis Child Fetal Neonatal Ed **89**(1): F93-4.

ABSTRACT: NONE

### **Level of Evidence 5-Supportive**

*Note: Report in Letter; Retrospective review and report of 310 newly born infants of 23-28 weeks gestation delivered from 1994-2002. With the introduction of placing infants in plastic bags at birth as described by Vohra the mean temperature of these infants was 37 degrees C (0.7 SD) on admission to the nursery, whereas the mean of the group in 1994-1999 before the introduction of the bag technique was <36 with a wide range of variability. Another fairly large historical review of the introduction of a practice change with measurable improvement in outcome.*

Vohra, S., G. Frent, et al. (1999). "Effect of polyethylene occlusive skin wrapping on heat loss in very low birth weight infants at delivery: a randomized trial." *J Pediatr* **134**(5): 547-51.

**OBJECTIVE:** Significant evaporative heat loss in the very low birth weight infant can occur in the delivery room. We investigated the effect of polyethylene wrap applied immediately at birth (without drying) on rectal temperature measured at nursery admission. **STUDY DESIGN:** Sixty-two consecutive infants delivered at <32 weeks' gestation were stratified by gestational age and randomly allocated to resuscitation with polyethylene wrap. All infants were resuscitated under radiant warmers. Wraps were removed on nursery admission. Rectal temperature was taken by digital electronic thermometer. **RESULTS:** Fifty-nine of 62 recruited infants completed the study. Maternal temperature, delivery room temperature, transfer-incubator temperature, and time to admission were recorded. Use of occlusive wrapping resulted in a significantly higher admission rectal temperature in infants <28 weeks' gestation (difference in means = 1.9 C, P <.001). No significant difference was seen in admission rectal temperature in infants of 28 to 31 weeks' gestation (difference in means = 0.17 C, P =.47). All 5 deaths were in the nonwrap group (vs wrap, P =.04); their mean temperature was 35.1 C versus 36.5 C in survivors (P =.001). **CONCLUSIONS:** Occlusive wrapping of very low birth weight infants at delivery reduces postnatal temperature fall. This may result in a decreased mortality rate.

### **Level of Evidence 1-Supportive**

*NOTE: good quality randomized controlled trial with adequate numbers and significant results.*