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

**Worksheet author(s)**

<table>
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<th>Jay F. Goldsmith</th>
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**Date Submitted for review:** December 7, 2009 (Revised 2/15/10)

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**Clinical question.**

In term neonates without a detectable heart rate at birth and no other signs of life (P) is ten minutes (I) as opposed to 15 minutes or longer (C) of effective resuscitation a reliable measure of outcome (abnormal neurologic examination and/or death) (O)?

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

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

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**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 (including electronic databases searched).**

AHA Endnote, Medline, Embase, Cochrane and Pubmed databases; hand searches of journal references, review articles, articles on neonatal ethics; forward searches on most recent articles

- Key words “Zero Apgar score”, “Apgar score zero”, or Low Apgar score LIMITED by age group (newborn infant) (17 items); “apparently stillborn” (4 items)
- MESH term Resuscitation AND words “10 minutes” LIMITED by age group (newborn infant) (39 items)
- MESH term Cardiopulmonary Resuscitation AND words "10 minutes" LIMITED by age group (newborn infant) (8 items)
- MESH term Apparent Stillborn or Stillborn and Resuscitation LIMITED by age group (newborn infant): 23 items
- Eligible articles in reference lists of all articles that met inclusion criteria

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**State inclusion and exclusion criteria**

**Inclusion criteria:** All human papers published in full; case series, prospective or retrospective cohorts of newborns with severe asphyxia at birth who had reported outcomes either to discharge or longer term disabilities

**Exclusion criteria:** Animal studies, resuscitation beyond the first month of life; ethical discussions

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**Number of articles/sources meeting criteria for further review:**

- 10 (5 included in 2005 worksheet); 6 with LOE=P4, 4 with LOE=P5
# Summary of evidence

## Evidence Supporting Clinical Question:

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Evidence Supporting Clinical Question</th>
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<tbody>
<tr>
<td><strong>Good</strong></td>
<td>Jain et al. 1991-B,C,D</td>
</tr>
<tr>
<td></td>
<td>Casalaz et al. 1998-B,C,D</td>
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<tr>
<td></td>
<td>Haddad et al. 2000-B,C</td>
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<td></td>
<td>Patel and Beeby 2004-B,C,D</td>
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<tr>
<td></td>
<td>Harrington et al. 2007-B,C,D</td>
</tr>
<tr>
<td><strong>Fair</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Poor</strong></td>
<td>Koppe and Kleiverda 1984-B</td>
</tr>
<tr>
<td></td>
<td>Socol et al. 1994-B</td>
</tr>
<tr>
<td></td>
<td>Yeo and Tudehope – B,C,D</td>
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<tr>
<td></td>
<td>Berglund et al. 2008-B,C,E</td>
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</tbody>
</table>

**Level of Evidence**

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

*Italics = Animal studies*

## Evidence Neutral to Clinical question: None

<table>
<thead>
<tr>
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<tr>
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- A = Return of spontaneous circulation
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## Evidence Opposing Clinical Question:

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</thead>
<tbody>
<tr>
<td><strong>Good</strong></td>
<td>Laptook, et al 2009-C,D</td>
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<tr>
<td><strong>Fair</strong></td>
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<tr>
<td><strong>Poor</strong></td>
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**Level of Evidence**

- A = Return of spontaneous circulation
- C = Survival to hospital discharge
- E = Other endpoint
Prior to December 2009 only 9 retrospective case series could be found which gave enough information to include in this review. The manuscripts were hampered by several limitations: all reviews were retrospective; there was no indication of what the cause of the asphyxia was in most cases; no indication was given of how long the babies were without heart rate before birth except to indicate they did not show signs of prolonged fetal death (maceration, dependent lividity); there was no indication of the skill of the resuscitators or the efficacy of the process; some reports included all gestational ages and others reported only infants at term and near-term; the definition of mild, moderate and severe disabilities varied among reports; the length of follow-up also varied and some series only reported to hospital discharge. The technique for evaluating heart rate at birth was not given in any report (auditory, palpation, electronic) and the propensity for selection bias based on any number of factors could certainly alter the analysis of these results. The review by Harrington et al (2007) is the most recent of the retrospective published series and consistent with the earlier studies, most of which described newborns born before the year 2000. Based on only a total of 119 babies, a compilation of the reviews indicates that infants who fail to have return of spontaneous circulation by 10 minutes of life have a grim prognosis and that death or severe disability is likely in the overwhelming majority of cases. Therefore, based on this data there appears to be no reason to prolong resuscitation beyond 10 minutes if it has been performed appropriately and no heart rate has been detected. It is important to note that none of the retrospective published series has included babies who have been subjected to hypothermia and other newer therapies for asphyxia. However, a recently published paper by Laptook et al which reviewed infants enrolled in the NICHD hypothermia trial showed very high disability or death (76%) in infants with Apgar 0 at 10 minutes, but the outcomes for the survivors were more heterogeneous than previous reports with 6 of the 13 survivors having either mild or no disability at the 18-22 month assessment. It should be noted that this population starts off with a distinct selection bias, since these are infants who are capable of being resuscitated and possibly transported to the hypothermia centers.
**Citation List**


**LOE P5 - Supporting (retrospective cohort but with significant selection bias)**

Comment: Not really oriented to the clinical question and because of objectives of study, subject to great selection bias. Out of the 8 infants with documented asystole for more than 15 minutes, 7 died and 1 has cerebral paralysis (type of impairment not stated). In this review, there was documentation of poor adherence to resuscitation guidelines.


**LOE P4 - Supporting (retrospective cohort).**

Comment: The authors reviewed 454 newborn infants with Apgar=0 at 1st minute among 94,511 deliveries in 2 institution in the UK between 1986-94. The rate of successful resuscitation (42 of 45 = 93%) is much higher than reported in other studies (for example, Jain reports that 31 of 93 died in the DR). Among the 45 (26 fullterm) infants, 93 % were anticipated and received full resuscitation by trained staff. Out of the 45, 4 infants (GA 36-42 weeks) were still asystolic at 10 minutes (Apgar = zero at 10 minutes): 3 of them died in the first week of life and 1 had documented CP (quadriplegic) at more than 18 months of life. Similar problems to other series although there is more confidence that with trained staff the resuscitation was performed adequately.


**LOE P4 - Supporting (retrospective cohort).**

Comment: The authors identified 103 newborn infants with Apgar=0 at 1st minute among 81,603 deliveries >22 weeks and >500g in the University of Tennessee Hospital over a 14 year period (1996-1999). Among the 101, 33 with Apgar=0 at 1 and 5 minutes successfully resuscitated. Out of the 33, 16 infants were still asystolic at 10 minutes (Apgar = zero at 10 minutes): 14 of them died and 2 had hypoxic ischemic encephalopathy at neonatal period and non-documented follow-up. Only 63 % of the survivors (7 of 11) were examined at follow-up. The significance of gestational age on survival is noteworthy here as none of the babies less than 26 weeks who had Apgar 0 at 1 and 5 minutes survived. Similar issues to all other series including poor follow up percentage.


**LOE P4 - Supporting (retrospective cohort).**
Comment: The authors combine their data with other published data for the most recent review on this subject in the literature. The series suffers from the same problems as most of the others: small numbers, no indication of the skill of the resuscitators or efficacy of the process; case reviews go back to 1991. Only 9 infants met criteria of 0 Apgar at 10 minutes and 8 of the 9 died or had severe disability.


Comment: The largest series in this group. Dr. Jain gets credit for the appellation of "apparently stillborn". No indication was given how the absence of heart rate was determined (by stethoscope, palpation or ECG). The authors note specifically that of the 58 infants who had Apgar 0 at 10 minutes of life, 57 died and one was severely neurologically impaired. Only 70% of the survivors were assessed at follow-up, but the one survivor with 10 minute Apgar of 0 was in this group.


Comment: The authors identified 54 infants with perinatal asphyxia (not defined) with birth weight >2500g and gestational age >37 weeks in the Netherlands (1965-1975). Among them 3 were still asystolic at 10 minutes (Apgar = zero at 10 minutes) and all of these infants died. Similar problems to other studies. The authors were actually looking at another prognostic sign (return of spontaneous respirations), but they add 3 more infants to the analysis. Similar problems to other studies mentioned above.


Comment: This was a retrospective secondary analysis of the NICHD hypothermia trial. With an Apgar of 0 at 10 minutes, death or disability was very high (76%) which is similar but not as overwhelming as other similar retrospective reports. Of the babies who met this criteria of 0 Apgar at 10 minutes, there were 13 survivors of whom 6 had mild or no disability at 18-22 month follow-up. Whether the application of hypothermia affected this outcome is not given. It would seem that Apgar 0 at 10 minutes predicts poor prognostic outcome, but the survivors are more heterogeneous than previously thought and other predictors (cord pH, peripartal history, etc.) should also be considered before ceasing resuscitation attempts.

Comment: The authors identified all newborn infants with Apgar=0 at 1st and 5th minutes in 10 Level 3 NICUs of New South Wales, Australia (1992-2002). Among the 60 identified neonates with gestational age >36 weeks, 29 were still asystolic at 10 minutes (Apgar = zero at 10 minutes): 20 of them died, 8 developed cerebral paralysis (not stated age and type of disability) and 1 had minor fine motor dysfunction. Of the 29 patients, 28 had an audible heart rate at 15 minutes (time to have HR: 11-40 minutes). These findings support the dismal outcome of resuscitation regardless of how it is performed. The search strategy would not identify infants not transferred to these units if they were successfully resuscitated (doubt there would be many). Similar problems with this case series: retrospective collection of data and selection bias (asystolic babies non-resuscitated at discretion of the staff) and developmental assessment is not clear.


LOE P5 - Supportive (retrospective cohort)

Comment: The authors identified 28 infants with Apgar score <4 at 5 minutes with birth weight >2000g and gestational age >33 weeks (1984-1994). Only one infant in this group was still asystolic at 10 minutes of age and developed hypoxic-ischemic encephalopathy; that infant is reported as alive with moderate disability in childhood. This study was not oriented to the clinical question and only one infant fits criteria of 0 Apgar at 10 minutes.


LOE P5: Supportive (retrospective cohort).

Comment: This study describes outcomes following a 1 minute Apgar score of 0, but does not specify those with 0 at 10 minutes. However the authors reported that all 8 babies with a 5 minute Apgar score of 0 either died or were significantly handicapped. The authors recommended withdrawal of resuscitation if the Apgar score remains 0 after 5 minutes of resuscitation.