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

<table>
<thead>
<tr>
<th>Worksheet author(s)</th>
<th>Date Submitted for review:</th>
<th>February 9, 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.D. McMillan</td>
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## Clinical question.

In neonates requiring resuscitation and unresponsive to chest compressions/epinephrine (P) does the administration of volume (I) versus no volume (C) improve outcome (O)?

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

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 (including electronic databases searched).

**PubMed (February 2009)**

("Resuscitation"[Mesh] OR "Cardiopulmonary Resuscitation"[Mesh]) Limits: Humans, Newborn: birth-1 month AND Search saline OR volume OR blood OR albumin Limits: Humans, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Newborn: birth-1 month (311 articles-0 selected)

"Resuscitation"[Mesh] OR "Cardiopulmonary Resuscitation"[Mesh] AND saline OR volume OR blood OR albumin AND "chest compressions" OR "cardiac massage" OR epinephrine Limits: Clinical Trial, Meta-Analysis, Randomized Controlled Trial (72-0 articles selected)

("Resuscitation"[Mesh] OR "Cardiopulmonary Resuscitation"[Mesh]) AND Saline OR Blood OR Volume or Albumin AND birth OR delivery room (673 articles-1 selected).


**Embase (February 2009)**

'resuscitation'/exp OR 'resuscitation') AND [1976-2009]/py AND 'saline'/exp OR 'saline') OR ('blood'/exp OR 'blood') OR ('albumin'/exp OR 'albumin') AND [1976-2009]/py AND 'cardiac massage'/exp OR 'cardiac massage') OR 'cardiac compression' OR ('epinephrine'/exp OR 'epinephrine') AND [1976-2009]/py AND 'birth'/exp OR 'birth') AND [1976-2009]/py (8 articles-0 selected)

'resuscitation'/exp OR 'resuscitation') AND [1976-2009]/py AND 'saline'/exp OR 'saline') OR ('blood'/exp OR 'blood') OR ('albumin'/exp OR 'albumin') AND [1976-2009]/py AND 'cardiac massage'/exp OR 'cardiac massage') OR 'cardiac compression' OR ('epinephrine'/exp OR 'epinephrine') AND [1976-2009]/py (316 articles-1 selected same article as in PubMed search)

('resuscitation'/exp OR 'resuscitation') AND ('birth'/exp OR 'birth') AND [1970-2009]/py AND ('saline'/exp OR 'saline') OR ('sodium'/exp OR 'sodium') AND ('chloride'/exp OR 'chloride') OR ('albumin'/exp OR 'albumin') AND [1970-2009]/py (22 articles-0 selected)
Cochrane

Keyword: Saline - 47 articles, 0 selected
Keyword: Albumin – 28 articles, 0 selected


• State inclusion and exclusion criteria

Inclusion: Use of saline, albumin, dextran or blood as a volume expander during resuscitation.
See search strategy

Exclusion: Saline as a placebo or compared to another treatment (eg. Sodium bicarbonate or glucose)
Treatment other than with resuscitation (eg hypotension/ presumed volume deficiency in NICU)

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

6 articles - See “Search Strategy” above
# Summary of evidence

## Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th>Good</th>
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<tbody>
<tr>
<td>Fair</td>
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<tr>
<td>Poor</td>
<td><strong>Fischer, 1996 B</strong></td>
<td><strong>De Luca, 2008</strong></td>
<td><strong>Van Haesbrouck, 1987</strong></td>
<td><strong>Roberton 1997</strong></td>
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**Level of evidence**

A = Return of spontaneous circulation  
B = Cerebral blood flow  
C = Mortality or severe neurologic damage  
D = Cardiopulmonary function

*Italicics = Animal studies*

## Evidence Neutral to Clinical question

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<tbody>
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<td>Fair</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Poor</td>
<td><strong>Wyckoff, 2005</strong></td>
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<td></td>
<td><strong>Jameson, 1993 A</strong></td>
<td><strong>Laptook, 1982 B</strong></td>
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**Level of evidence**

A = Return of spontaneous circulation  
B = Cerebral blood flow  
C = Mortality and/or severe neurologic damage  
D = Cardiopulmonary function

*Italicics = Animal studies*
## Evidence Opposing Clinical Question

| Good |  |  |  |  | **Wyckoff, 2007 D**
|      |  |  |  | **Mayock, 2004 B**
|      |  |  |  | **Ditchey, 1984 B**
| Fair |  |  |  |  |
| Poor |  |  |  |  |
|      |  |  |  |  |
| 1    | 2 | 3 | 4 | 5 |

**Level of evidence**

A = Return of spontaneous circulation  
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*Italics = Animal studies*
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<th>REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:</th>
</tr>
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<tbody>
<tr>
<td>There is a paucity of human data upon which to rely to determine if (or when) intravenous volume expansion should be utilized during resuscitation. Validity of animal models of hemorrhagic or induced ventricular fibrillation in determining relevance in the delivery room is open to speculation. However, these studies suggest that increasing intravascular volume may be associated with decreased cerebral blood flow, decreased cerebral oxygen delivery and adverse effects on the lungs. The one animal study which suggested improvement in cerebral blood flow used hypertonic volume expansion which is not presently part of clinical care for human neonates. The only evidence to support use of volume during resuscitation of babies comes from case reports. The infrequency of use makes randomized clinical trials in newborn babies unlikely. We will likely need to extrapolate from other studies to obtain further information.</td>
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Acknowledgements:


**Citation List**


**Comment:** This is a case report as a letter to the editor describing successful resuscitation of a term neonate with assisted ventilation intravenous saline and blood. Later calculation was that the baby lost 81% of circulating red cell volume due to fetal maternal hemorrhage.

Level of Evidence: 4  
Quality: Poor  
Evidence: Supporting


**Comment:** Dogs with induced ventricular fibrillation received closed cardiac massage and one liter of either 0.9% saline or 10% dextran solution plus 44.6 meq. Bicarbonate. This increased forward blood flow (including carotid blood flow) but coronary and cerebral perfusion significantly decreased. Investigators suggest that this may be due to associated vascular distension. In this model the relative effects of saline or dextran and the sodium bicarbonate which was administered with other volume cannot be determined.

Level of Evidence: 5  
Quality: Good  
Evidence: Opposing


**Comment:** 14 adult cats with 15 min induced ventricular fibrillation had standard resuscitation. For 6 this included 2 ml/kg/10 min 7.5% NaCl/6% hydroxyethyl starch [none-8]. They had less decrease in forebrain and flow area (15 +/- 6% vs 28 +/- 13%). There was no difference in hemodynamics or cerebral blood flow. Applicability to human newborns receiving resuscitation which may include normal saline is limited.

Level of Evidence: 5  
Quality: Fair  
Evidence: Supporting


**Comment:** Swine with ventricular fibrillation were given epinephrine or epinephrine with 4 mL/kg hypertonic saline-dextran with improved cardiovascular pressures including coronary perfusion pressure in saline-dextran group. No difference in return of spontaneous circulation or survival to 30 minutes in this small study.
Decreased pH and increased pCO2 suggested indicative of better tissue perfusion with mobilization of lactate and pCO2 from tissues but no independent measurements. Application to humans at birth is limited.

Level of Evidence: 5
Quality: Fair
Evidence: Neutral


**Comment:** Asphyxia was produced by adding respiratory dead space (removed during resuscitation) prior to bleeding to hypotension. Plasmanate restored blood pressure without significant changes in cerebral blood flow (Does this lack of correlation have implications to care of human newborns?) Relevance of the model to human neonates is uncertain.

Level of Evidence: 5
Quality: Fair
Evidence: Neutral


**Comment:** Blood volume of very preterm (92-98 day) fetal sheep was expanded with 20 mL/ kg (estimated weight) 6% dextran-70 twice with and without following hypoxia. Volume expansion causes a dilutional anemia without increasing cerebral blood flow which decreases cerebral oxygen delivery. With hypoxia cerebral blood flow and oxygen delivery increased to the degree expected (no controls without volume expansion) from previous studies. Volume expansion above normal decreases cerebral oxygen availability; this may be somewhat modified in the presence of hypoxia,

Level of Evidence: 5
Quality: Good
Evidence: Opposing


**Comment:** Personal series of 50 medical legal cases indicate drugs utilized but not saline or albumin. Comments that hypovolemia and hypotension are uncommon with intrapartum asphyxia based on undefined literature review. Potential harm (unreferenced) suggests dopamine better and that blood should be given only to hypotensive newborns with evidence of blood loss.

Level of Evidence: 4
Quality: Poor
Evidence: Opposing

**Van Haesebrouck P, Vanneste K, de Praeter C, van Trappen Y, Thiery M** *Tight nuchal cord and neonatal hypovolaemic shock* *Archives of Disease in Childhood,* 1987; 62:1276-1277
**Comment:** This is a case report of two term babies who required ventilatory support and were given blood and plasma with improvements in acidosis and ability to extubate successfully.

Level of Evidence: 4  
Quality: Poor  
Evidence: Supporting


**Comment:** 37 - 8 day old piglets with mechanical ventilation asphyxiated with 7.5% CO2 and 5.3% O2 until pH <7.0 (actually 6.7), pCO2 >100, MAP <20 mmHg and HR <100 bpm. Resuscitation with IPPV and, if HR <60 bpm at 30 sec, closed-chest cardiac massage (30 sec) and epinephrine 0.01mg kg I.V. at 5 min. Boluses 2 x 10 mL/kg over 5 min (2 min between). HR responded to >100 bpm with ventilation (22), CPR (1), epinephrine (10) or remained asystolic (4). 2 hours post resuscitation saline treated had lower MAP (29 mmHg) than albumin (43 mmHg) or SHAM (48 mmHg). Albumin and saline had lower dynamic compliance and more pulmonary edema than SHAM. If response to ventilation alone those with volume had lower MAP (33 mmHg) than SHAM (50 mmHg). Newborn animal model not at birth. Resuscitation as for human neonates.

Level of Evidence: 5  
Quality: Good  
Evidence: Opposing


**Comment:** Retrospective review of 37, 972 newborns ≥34 weeks gestation included 23 admitted to NICU after CPR (0.06%). 13 had 21 ± 14 mL/kg volume infusion (0.03%) for persistent bradycardia (10) or suspected hypovolemia (3). 5 died in delivery room (4 or 5 had volume replacement). Babies receiving volume were more acidotic (cord pH 6.83 ± 0.19 vs 7.10 ± 0.37), had lower BP on arrival in NICU (32 ± 13 vs 49 ± 12 mmHg) which persisted over next two hours, had lower admission hematocrit (41 ± 13 vs 54 ± 8%) and more likely had bicarbonate as part of resuscitation. Use of volume in this large series was reserved for the most asphyxiated newborns. There is no equivalent comparison group to help determine if volume helps or harms either short or longer term outcome.

Level of Evidence: 4  
Quality: Fair  
Evidence: Neutral