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

**Worksheet author(s)**  
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**Date Submitted for review:**  
February 28, 2009 (worksheet v.1)  
October 26, 2009 (worksheet v.2)

## 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? Intervention/therapy

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

## 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).

Ovid Medline: exp ‘Blood Volume’[MeSH] AND exp Resuscitation [MeSH]; *Bradycardia [MeSH]/pc, th, bl, dt, pp AND exp Resuscitation; exp Shock [MeSH] or *Hypovolemia [MeSH] AND *’Fluid Therapy’ [MeSH]; *’Fluid Therapy’ AND exp Resuscitation; *’Fluid Therapy’ AND *Bradycardia/p, th, bl, pp – all limited to ‘newborn infant (birth to 1 month)’.


Cochrane Library of Systematic Reviews: blood volume AND infant,newborn

AHA ECC EndNote library: fluid therapy; blood volume AND resuscitation

Google Scholar yielded results from ‘volume resuscitation newborn’ and Find Similar and Cited By features were used in Ovid Medline. Extensive hand searches of manuscript references and database searches by author name yielded much of the older literature.

## State inclusion and exclusion criteria

Studies are limited to those published in the peer-reviewed literature (no abstract only studies). Animal studies, case series and cohort studies are included as well as clinical trials and controlled studies due to the scarcity of available literature. All studies identified are in English.

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

17 articles met the criteria for further review. One review came from the Cochrane Database of Systematic Reviews and a few articles from Medline and Embase searches; however, most articles were identified from bibliographies and personal files.
**Summary of evidence**

**Evidence Supporting Clinical Question**

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
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<tr>
<td><strong>Simma 1997</strong></td>
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<td><strong>Pladys 1997</strong></td>
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<td><strong>Phibbs 1976</strong></td>
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<td><strong>Dawes 1963</strong></td>
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<td><strong>De Luca 2008</strong></td>
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<td><strong>Kirkman 1959</strong></td>
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<td><strong>Koranyi 1969</strong></td>
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<td><strong>Pollanen 1967</strong></td>
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<td><strong>Smith 1968</strong></td>
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<td><strong>VanHaesebrouck 1987</strong></td>
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<td><strong>Wallgren 1964</strong></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

| Good | | | | | |
|------|------|------|------|------|
| Fair | Wyckoff 2005 | Chamnanvanakij 2000 |
| Poor | | Osborn 2004 |

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**Level of evidence**

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

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# Evidence Opposing Clinical Question

| Good | | | | | Wyckoff 2007 |
|------|------|------|------|---------------|
| Fair | | | | Goldberg 1980 |
| Poor | | | | Mayock 2004 |

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**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
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D = Intact neurological survival  
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*Italics = Animal studies*
REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

Scant literature addressed the question of interest. Where considerable data do exist, with respect to hemorrhagic hypovolemic shock in the newly born infant, the evidence exists exclusively as case reports and case series (De Luca 2008, Kirkman 1959, Koranyi 1969, Pollanen 1967, Smith 1968, VanHaesebrouck 1987, Wallgren 1964). In light of the overwhelming agreement on the efficacy of volume in this situation, however, randomized clinical trials are not indicated.

With respect to other causes of non-response to ventilation, chest compressions, and epinephrine, there is little direct evidence for the utility of volume expansion, and some suggestion of potential harm (Wyckoff 2007). In non-resuscitation situations, rapid volume expansion may result in alterations in cerebral blood flow dynamics, such as decreased cerebral oxygen delivery (Mayock 2004) or potentially, intracranial hemorrhage in prematures (Goldberg 1980).

In order to advance knowledge in this area, a randomized trial could be justified to examine the specific question of volume expansion in the infant refractory to ventilation, chest compression, and epinephrine without any suggestion of hemorrhagic shock.

Acknowledgements:

Citation List

LOE 4 (fair, neutral)
COMMENT: Infants had a median postnatal age of 20 days. The etiology of bradycardia was doubtless different in this group, with an overrepresentation of severe bronchospasm, chronic lung disease, shock associated with sepsis or necrotizing enterocolitis, pneumothorax or inadequate ventilation.

LOE 5 (animal model, fair, supporting)
COMMENT: Initial resuscitation was provided by fluid infusion, with ventilation provided after 10-12 minutes (15 minutes in monkeys). Untreated animals in some cases required cardiac massage in addition to ventilation for recovery.

LOE 5 (poor, supporting)
COMMENT: Volume administered before chest compressions and epinephrine were needed.

LOE 5 (fair, opposing)
COMMENT: Volume infusion given in first 8 hours and not in setting of chest compressions and epinephrine administration.

LOE 5 (poor, supporting)

COMMENT: This effectively represents a systematic review of case reports and case series of hemorrhagic shock in the newborn.

LOE 5 (poor, supporting)

COMMENT: Two cases illustrative of obvious placental/umbilical cord bleeding are offered to highlight the setting of hemorrhagic shock.

LOE 5 (poor, opposing)

COMMENT: This is an uncontrolled, unblinded animal case series, but the results are somewhat consistent in their message with Goldberg 1980.

LOE 5 (poor-not directly relevant to question, neutral)

COMMENT: Four studies with 940 preterm infants (<1500g, <32 weeks gestation) included one study of 776 infants who were randomized at <2 hours of age to fresh frozen plasma (15 mL/kg), a gelatin based plasma substitute 20 mL/kg over 15 minutes or no treatment. Two other studies compared plasma 10-15 ml/kg and one used 20% albumin 15 mL/kg with no difference in death, intraventricular hemorrhage or long term disability. This population is not representative of babies of all gestations who do not respond to assisted ventilation, cardiac massage and epinephrine in the delivery room.

LOE 4 (fair, supporting)

COMMENT: In this case series, resuscitation included, as clinically indicated, any combination of oxygen, assisted ventilation, paracentesis, infusion of alkali (0.9M sodium bicarbonate at a rate of 1 mEq/kg of body weight per minute), and small exchange transfusions with whole blood or packed red cells to correct anemia. For hypotension that persisted after relief of asphyxia, repeated small infusions of blood or salt-poor albumin were given until pressures returned to normal.

LOE 5 (good, supporting)

COMMENT: Infants are 1 week of age and received volume expansion for a variety of reasons. Inclusion criteria of protracted cutaneous refilling time (≥ 4.5 sec) and low CO without severe cardiac dysfunction do not mimic the conditions in the delivery room for infants requiring CPR and epinephrine.
LOE 5 (poor, supporting)

COMMENT: Infant had Apgars 6 at 1 min and 4 at 15 min. The infant responded to a 100 mL transfusion of O Rh-neg blood.

LOE 5 (good, supporting)

COMMENTS: The study documents positive changes in hypotensive, ventilated infants in the NICU. There are no controls.

LOE 5 (poor, supporting)

COMMENT: This infant responded to ventilation and chest compression, but continued with extreme pallor, which resolved with transfusion.

LOE 5 (poor, supporting)

COMMENT: Although the 2 cases described did not receive chest compressions or epinephrine, they did require intubation. Both infants presented with tachycardia.

LOE 5 (poor, supporting)

COMMENT: Experiments were performed in stable, non-anemic patients with erythroblastosis.

LOE 4 (fair, neutral)

COMMENT: Likely many hypovolemic infants received volume as an initial resuscitative measure or as an adjunct to positive-pressure ventilation, but before chest compressions were necessary. Thus, the role of volume administration in resuscitation from hypovolemia should not be underestimated. Among infants with asphyxia, there was little to suggest that volume administration resulted in benefit, although the absence of a control group for these observations is severely limiting. This case series was conducted in the setting of infants unresponsive to CPR in the delivery room.

LOE 5 (animal model, good, opposing)

COMMENT: Although a neonatal model, pigs were studied at a mean of 8 days. After 5 min of resuscitation, piglets were randomized with blinding to 10 mL/kg IV over 5 min of NS, albumin or sham. Two boluses were given to approximate the mean number of infusions observed in the database study. For all treatment groups, the majority of piglets responded to effective ventilation and oxygenation alone. Fifteen of 37 piglets became asystolic and only 10 responded to chest compressions (1) or epinephrine (9). Asystolic piglets did not receive volume.