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

State if this is a proposed new topic or revision of existing worksheet: revision of existing worksheet (W208)

Conflict of interest specific to this question

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

Grant/Research Support

Our research has been supported by Saitama Medical University and Japanese Ministry of Health, Labour and Welfare but not any Company nor non-governmental organization.

Consultant

Nothing to disclose

Speakers Bureau

Nothing to disclose

Stock Shareholder

Nothing to disclose

Employee

Nothing to disclose

Other

Nothing to disclose

Search strategy (including electronic databases searched).

The first search was done on 21st/22nd March 2008 by the core strategy outlined below:

(explode "Infant-Newborn"/ all subheadings ) AND ((volume* near expan*) in ti,ab) AND ( "Resuscitation"/ all subheadings in mjme) OR (explode "Cardiopulmonary-Resuscitation"/ all subheadings in mjme) OR (explode "Blood-Volume"/ all subheadings in mjme) OR ( "Fluid-Therapy"/ all subheadings in mjme) OR (explode "Blood-Substitutes"/ all subheadings in mjme) OR (blood-supply in sh)

★ MEDLINE

No. Records Request
1 388813 explode "Infant-Newborn"/ all subheadings
2 7190 (volume* near expan*) in ti,ab
3 204 #2 and #1
4 17016 "Resuscitation"/ all subheadings
5 1076 (#4 in mjme) and #1
6 6710 explode "Cardiopulmonary-Resuscitation"/ all subheadings
7 247 (#6 in mjme) and #1
8 21480 explode "Blood-Volume"/ all subheadings
9 222 (#8 in mjme) and #1
10 10534 "Fluid-Therapy"/ all subheadings
11 426 (#10 in mjme) and #1
12 7490 explode "Blood-Substitutes"/ all subheadings
13 69 (#12 in mjme) and #1
14 235711 blood-supply in sh
15 292247 #4 or #6 or #8 or #10 or #12 or #14
16 80 #3 and #15
17 23618 #4 or #6
18 706 #9 or #11 or #13
19 13 #17 and #18
20 270368 #8 or #10 or #12 or #14
21 6050 #20 and #1
22 71 #21 and #17
23 143 #16 or #22
24 4128838 tg=animals
25 10012550 tg=humans
26 3112904 #24 not #25
27 143 #23 not #26
28 7 #27 and (pt= guideline-)
29 0 #27 and (pt=meta-analysis)
30 7 #27 and (pt=practice-guideline)
31 14 #27 and (pt=randomized-controlled-trial)
32 23 #28 or #29 or #30 or #31
* 33 120 #27 not #32

★ Cochrane

ID Search Hits
#1 MeSH descriptor Infant, Newborn explode all trees 9691
#2 (volume* NEAR expan*):ti,ab,kw 413
#3 (#1 AND #2) #6
#4 MeSH descriptor Resuscitation, this term only 259
#5 MeSH descriptor Cardiopulmonary Resuscitation explode all trees 297
#6 MeSH descriptor Blood Volume explode all trees 837
#7 MeSH descriptor Fluid Therapy explode all trees 819
#8 MeSH descriptor Blood Substitutes explode all trees 1065
#9 (#4 OR #5 OR #6 OR #7 OR #8) 2968
#10 (#3 AND #9) 18
#11 (#3 AND NOT #10) 8
#12 (#4 OR #5) 551
#13 (#6 OR #7 OR #8) 2478
#14 (#12 AND #13) 61
#15 (#14 AND #1) 0

★ EMBASE

Session Results

<table>
<thead>
<tr>
<th>No.</th>
<th>Query Results</th>
<th>Results</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>(volume*:ti AND expan*:ti) OR (volume*:ab AND expan*:ab) AND [newborn]/lim AND [embase]/lim</td>
<td>211</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#2</td>
<td>'resuscitation'/exp AND [newborn]/lim AND [embase]/lim</td>
<td>1,240</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#3</td>
<td>('blood volume'/exp OR 'plasma volume'/exp) AND [newborn]/lim AND [embase]/lim</td>
<td>250</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#4</td>
<td>'fluid resuscitation'/exp AND [newborn]/lim AND [embase]/lim</td>
<td>9</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#5</td>
<td>'fluid therapy'/de AND [newborn]/lim AND [embase]/lim</td>
<td>179</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#6</td>
<td>'plasma substitute'/exp AND [newborn]/lim AND [embase]/lim</td>
<td>412</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#7</td>
<td>#3 OR #4 OR #5 OR #6</td>
<td>828</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#8</td>
<td>#2 AND #7</td>
<td>49</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#9</td>
<td>#3 OR #6</td>
<td>650</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#10</td>
<td>#4 OR #5</td>
<td>187</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#11</td>
<td>#9 AND #10</td>
<td>9</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#12</td>
<td>#2 OR #3 OR #4 OR #5 OR #6</td>
<td>2,019</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#13</td>
<td>#1 AND #12</td>
<td>50</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#14</td>
<td>#8 OR #11 OR #13</td>
<td>102</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#15</td>
<td>#14 AND ([cochrane review]/lim OR [controlled clinical trial]/lim OR [meta analysis]/lim OR [randomized controlled trial]/lim OR [systematic review]/lim)</td>
<td>8</td>
<td>30 Mar 2008</td>
</tr>
<tr>
<td>#16</td>
<td>#14 NOT #15</td>
<td>94</td>
<td>30 Mar 2008</td>
</tr>
</tbody>
</table>

★ AHA

volume~expansion 13
expand~volume 6
expanding~volume 1
fluid resuscitation 5
fluid therapy 14
plasma substitute 9
33 references

★ RCTs
EMBASE 8+MEDLINE 23-duplicate 0
(+Cochrane CDSR 3+Cochrane CCTR 23)

★ non-RCTs 165 references
AHA 33+EMBASE 94+MEDLINE 120-duplicate 9

The above search was refined by using the below strategy:

#1 399044 explode "Infant-Newborn"/ all subheadings
#2 7438 (volume* near expan*) in ti,ab
#3 38919 "Infusions-Intravenous"/ all subheadings
#4 272111 fluid* in ti,ab,kw
#5 17599 "Resuscitation"/ all subheadings
#6 6753 "Cardiopulmonary-Resuscitation"/ all subheadings
#7 22369 explode "Blood-Volume"/ all subheadings
#8 10796 "Fluid-Therapy"/ all subheadings
#9 7714 explode "Blood-Substitutes"/ all subheadings
#10 56947 explode "Serum-Albumin"/ all subheadings
#11 41496 explode "Water-Electrolyte-Imbalance"/ all subheadings
#12 8244 "Osmotic-Pressure"/ all subheadings
#13 970 "Rehydration-Solutions"/ all subheadings
#14 245135 blood-supply in sh
#15 314685 #2 or #3 or #4
#16 24258 #5 or #6
#17 380948 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14
#18 403219 #16 or #17
#19 889 #1 or #15 or #18
#20 85 #1 and #16 and #17
#21 952 #19 or #20
#22 4224261 tg=animals
#23 10272525 tg=humans
#24 3174374 #22 not #23
#25 952 #21 not #24
#26 12 #25 and (pt=guideline-)
#27 2 #25 and (pt=meta-analysis)
#28 17 #25 and (pt=practice-guideline)
#29 72 #25 and (pt=randomized-controlled-trial)
#30 95 #26 or #27 or #28 or #29
#31 857 #25 not #30

• State inclusion and exclusion criteria

Studies comparing effectiveness/safety of volume expansion for neonates requiring resuscitation
Studies looking at route of administrating volume expanders are excluded
Consensus statement, theoretical model and reviews are excluded except systematic reviews and/or consensus statements by formal consensus methods
Studies already included in included systematic reviews are excluded to avoid repeated inclusion

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

<table>
<thead>
<tr>
<th>LOE</th>
<th>0</th>
<th>Wyckoff 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOE 1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>LOE 2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>LOE 3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>LOE 4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>LOE 5</td>
<td>2</td>
<td>Laptook 1982, Wyckoff 2007</td>
</tr>
</tbody>
</table>
### Summary of evidence

#### Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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 Opposing Clinical Question

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint
**REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:**

The available evidence is generally weak. There is little evidence examined in newborn infants on effectiveness of volume expansion during active resuscitation, and there is some evidence provided by studies using a newborn piglet model. The aim of volume expansion for the target population is to maintain appropriate circulation to deliver oxygen to major organs soon after asphyxia. After life-threatening events, body fluid can be moved to the third space, and adding volume may benefit in maintaining circulation transiently. On the other hand, overloading of volume harms already asphyxiated newborn heart, and this should be avoided.

**Acknowledgements:**

We thank Mr T Swa, Reference Librarian from Osaka University Life Sciences Library, for his contribution to the development of the search strategies and for his through technical advice.

---

**Citation List**


---

<table>
<thead>
<tr>
<th>Reference Data</th>
<th>LOE</th>
<th>Quality of the evidence</th>
<th>Direction of the evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Laptook, B. S. Stonestreet and W. Oh. The effects of different rates of plasmanate infusions upon brain blood flow after asphyxia and hypotension in newborn piglets. J Pediatr 1982; 100(5): 791-6</td>
<td>LOE 5</td>
<td>Fair</td>
<td>Neutral</td>
</tr>
</tbody>
</table>