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

**Worksheet author(s)**  
Steven A Ringer MD PhD

**Date Submitted for review:**  
10-13-09

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**Clinical question.**  
For non intubated bradycardic neonates (P) requiring positive pressure ventilation, is the CO2 monitoring device (I) more effective than chest rise, color (C) for assessing adequate ventilation (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

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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

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**Search strategy (including electronic databases searched).**

**OVID: Medline 1950-present:**  
End tidal carbon dioxide/physiologic monitoring, & Newborn & Artificial respiration/Positive Pressure ventilation; 195 papers, 26 merit further review.  
Resuscitation & End Tidal Carbon dioxide, monitoring physiologic, Newborn 84 papers 18 merit further review,  
Positive pressure/volume & CO2 monitoring & Carbon dioxide monitoring neonate 15 papers 15 papers merit further review, 9 unique  
Capnography & Resuscitation 73 papers 11 merit further review 4 unique  
Capnography & Respiration/spontaneous respiration & Newborn 11 papers 6 unique

**PubMed**  
Carbon dioxide monitoring, Resuscitation, Newborn 78 papers, 20 merit further review  
Clinical Monitoring, resuscitation, carbon dioxide monitoring 177 papers, Add Newborn : 26 papers, 4 merit further review  
Carbon dioxide monitoring, clinical monitoring, newborn 115 papers 5 merit further review  
Chest Rise, carbon dioxide monitoring, resuscitation 1 paper merits further review

**EMBASE**  
Capnography, Newborn, Resuscitation 11 references 6 new  
Carbon Dioxide, Newborn, Resuscitation 6 references  
Bag Valve mask and End Tidal Carbon Dioxide (key words) 7 references

**ECC Master Library**  
carbon dioxide, newborn, resuscitation 13 references  
Capnography, newborn, resuscitation 4 references

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**State inclusion and exclusion criteria**

**Inclusion**  
Newborns (unless already listed as search criterion. Birth to 23 months used as inclusion criteria in most searches, but left out of “Capnography & Resuscitation” search and “Clinical Monitoring & carbon dioxide monitoring & resuscitation search”

**No specific exclusion criteria**

Non English papers were not excluded, animal studies were not excluded. Papers in which adults were studied were included if the area of study was related to the primary question of the use of CO2 monitoring when giving positive pressure ventilation to non-intubated patients

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

46 papers merit further review from these searches. After initial screening and elimination of duplicate entries, along with additional searched, 57 papers merit further review for possible inclusion, and are included in the End Note Library attached. Not all of these papers deal specifically with the question, in fact only a few papers do so, and these are in patient populations that are primarily different from the group of interest
## 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>Evidence</strong></td>
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<td>Erny 1983E</td>
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### Level of evidence

1. A = Return of spontaneous circulation
2. B = Survival of event
3. C = Survival to hospital discharge
4. D = Intact neurological survival
5. E = Other endpoint

*Italics = Animal studies*
### Evidence Neutral to Clinical question

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<td>Fair</td>
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<td></td>
<td>Bhat 2008E</td>
<td>Chen 2001E</td>
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<td>Sivan 1992E</td>
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<td>Hand 1989E</td>
<td>Klimek 2006E</td>
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<td>Singh 2006E</td>
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#### Level of evidence

- **A** = Return of spontaneous circulation
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*Italic* = Animal studies

### Evidence Opposing Clinical Question

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<td>Fair</td>
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<td>Hughes 2007E</td>
<td>Muniz 2008E</td>
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<td>Poor</td>
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- **A** = Return of spontaneous circulation
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*Italic* = Animal studies
Both hyper- and hypocarbia can have untoward consequences for the newborn including acidosis, alterations in cerebral blood flow or as a marker of lung overdistention and injury. In animal model, even very brief periods of hypocarbia can worsen cardiac injury from asphyxia {Borke et al, 2004 LOE 5}. Of greater practical importance, the provision of adequate artificial ventilation with a bag and mask during resuscitation is based almost entirely on clinical assessment of chest rise. Many studies {e.g. Bhende et al 1992 LOE 5, Bhende and Thompson 1995, LOE 5, Bhende et al 2002 LOE5, Repetto et al 2001, LOE 5} support the use of qualitative measurement of Carbon Dioxide (CO2) in the confirmation of endotracheal tube position during resuscitation of newborns and older patients, { Aziz et al, 1999 LOE 5}, although false readings can occur { Hughes et al 2007, LOE 4}. In 2005, ILCOR recommended it as a secondary assessment tool for endotracheal tube position in the delivery room.

In non-intubated patients, qualitative CO2 detection has been successfully used to confirm gas exchange in older children and adults as a component of a bag/mask system or by placing a measuring catheter at the mouth or nostril of the patient. {Cong and Sun 2008 LOE 5, Cote et al, 2007 LOE 4, Thomas et al 1993 LOE 5}. In the neonate two observational trials have been done {Leone 2006, 118:e202, Finer 2009; 123:865, LOE 4}. These studies demonstrated that infants, including low birth weight infants, frequently have airway obstruction during bag and mask ventilation, although it might be clinically unapparent. The use of CO2 detectors enhanced detection of these events and thereby improved ventilation.

Quantitative non-invasive measurement of Carbon dioxide tension has been studied in newborns of different gestational ages and with different disease processes { Aliwalas et al 2005 LOE 5, Arsowa et al 1997, LOE 5, Meredith and Monaco 1990, LOE 5 }, primarily during mechanical ventilation. In these studies, the quantitative measurements have been done using both end-tidal and transcutaneous methodologies. Overall, these methodologies appear to have equal accuracy. In newborns, correlation with arterial pCO2 has been shown to be good in the absence of significant lung disease, and less accurate in the presence of poor lung expansion, or RDS{ Chen and Chen 2001, LOE 5, Hand et al 1989 LOE 5, Nangia et al1997, LOE 5, Wu et al, 2003 LOE 5}. These studies were done in the pre- or early surfactant era, but there is no newer evidence that reliable quantitative measurements can be used in managing patients.

Quantitative CO2 measurements have been found to be useful as guides of mechanical ventilation on transport {Jacob et al, 1986 LOE 5, O’Connor and Grueber 1998 LOE 5 } in moving from the delivery room or in the NICU {Erny et al 1983 LOE 4, Leidig et al 1986 LOE 4, Rozyczki et al 1998 LOE5} , permitting lower peak pressures to be used. In older patients, CO2 monitoring has allowed earlier identification of changes in respiratory status or pulmonary mechanics than does clinical assessment alone {Burton et al, 2006 LOE5, Hsieh et al 2001 LOE 5, Sivan et al 1992, LOE 5 } and in assessing and adjusting ventilation during resuscitation { Pokorna et al 2006, LOE 5 } Measurements in older patients can be done over a very short period {Miner et al 2003 LOE 5}, and in animals even single breath measurements have been shown to aid adjustment of ventilation { Stenz et al, 1998, LOE 5}. Measurement of carbon dioxide production during neonatal resuscitation has been shown to be similar to clinical assessment of ventilation (good Heart rate and improving oxygen saturation {Plame-Kilander and Tunell 1993 LOE 4}.

In the small studies noted above, the use of qualitative CO2 detection appears to be of use in detecting airway patency, better than the assessment of chest rise alone and might be superior to clinical assessment in the determination of adequate ventilation. There is minimal evidence that it can be used in a quantitative manner to avoid excessive ventilation during short periods, especially in the presence of lung disease. Further study of qualitative measurements and the development or adaptation of devices for the easy measurement of CO2 while using a bag and mask, might improve utility of this technology is the assessment of adequate ventilation. The utility of quantitative measurements in the control of ventilation would be enhanced if studies in surfactant treated infants with a high rate of antenatal corticosteroid exposure demonstrated better correlation with arterial pCO2

Acknowledgements:
Citation List


Comment: This statement is a reflection of the earlier consensus statement about the value of end tidal CO2 monitoring during resuscitation


Comment: This small study of very premature infants shows moderate agreement between non-invasive methods and arterial pCO2 in these babies in the first 24 hours of life. It is relevant to the question as it indicates technical feasibility of the method. The study method is good. LOE D5


Comment: Not relevant


Comment: In ventilated preterm and term newborns, capnography can reveal differences consistent with V/Q disturbances and allow for modification of ventilation. It correlated with transcutaneous pCO2 but wasn’t the same. This is weakly supportive evidence that a semi-quantitative measurement of pCO2 can be helpful. LOE 5


Comment: A study demonstrating value of qualitative use of disposable ET CO2 Shows value of this in resuscitation for verifying tube position, but no information about improving ventilation beyond that. LOE 5 supportive


Comment: Prospective study showing correlation of ET CO2 and PaCO2 in ventilated newborns. The ET values were lower than the pCO2 in the majority of cases, and the important result is that the correlation was really poor in babies with HMD and Meconium aspiration syndrome. The lack of utility in lung disease certainly limits the value of the technique, particularly since this would not known during the initial resuscitation. In infants without lung disease, such as term infants with depression, it could be a valuable adjunct. LOE 5 Fair or poor support


Comment: Study examining utility of disposable CO2 indicator that shows it to be useful in identifying tube position (initial confirmation) but of no value in ongoing evaluation of tube position. Relevance to question is limited, but if anything it is unsupportive LOE5.


Comment: Weakly supportive of question, study shows utility of qualitative measurement for ETT position in children. No information about use in evaluating or directing ventilation. LOE5, Poor support

**Comment:** Weakly supportive of question, study shows utility of qualitative measurement for ETT position in children. No information about use in evaluating or directing ventilation. LOE 5, Poor support.


**Comment:** Not relevant to question.


**Comment:** This study in piglets demonstrates that even a brief period of hypercarbia after birth can increase the amount of injury due to ischemia. It is relevant to the question as evidence that even brief periods of abnormal pCO2 can change outcome is supportive of the need to know the pCO2 at all times during resuscitation following injury. LOE 5 Poor support.


**Comment:** This study of Emergency Department patients who had received procedural sedation compared the utility of ET CO2 monitoring as compared to clinical monitoring alone. The results indicate that the non-invasive monitoring revealed respiratory events that were clinically inapparent. Fair support LOE 5.


**Comment:** Study of 20 premature infants that demonstrates that ET CO2 is not reliable compared to arterial values in RDS. LOE 5 Neutral or Opposing.


**Comment:** A study evaluating the use of a mask adapter for ventilation of adults during GI procedures. Demonstrates that endtidal CO2 can be measured during mask ventilation in this population, supportive of question, LOE 5.


**Comment:** A study in children undergoing catheterization, demonstrates that endtidal CO2 measurements can be reliably made in this population of non-intubated patients. Fair Support of the question LOE 4.


**Comment:** not relevant.


Comment: A study if 25 ventilated newborns that demonstrates the utility of transcutaneous CO2 in ventilatory management over the course of hospitalization. Addresses and supports the use of noninvasive monitoring to adjust artificial ventilation. LOE 4


LOE 4 Fair Support

Comment: A small observational study in which colorimetric CO2 detectors were used during resuscitation, facilitating the recognition of intermittent airway obstruction.


Comment: Not relevant to question


Comment: Review article that is supportive of the value of monitoring and adjusting ventilation and the need for different strategies for different disorders, primarily in preterm infants. Informative but not directly relevant.


Comment: Study demonstrating utility of transcutaneous CO2 monitoring, problems and advantages of now older technology.


Comment: Study in critically ill premature infants that demonstrates good correlation between transcutaneous measurements and arterial, but worse with end tidal measurements. Again confirms the lack of correlation in the presence of significant lung disease LOE 4 Neutral to Opposing.


Comment: Not relevant to question

Comment: Study in infants and children that evaluates a method of quantitative analysis of breaths using noninvasive CO2 monitoring. This allows comparison of breaths between ventilator and patients spontaneous breaths, and can be used to determine readiness for extubation. LOE 5 Supportive tangentially only, no direct utility in resuscitation.


Comment: Potential for false positives on qualitative CO2 detectors from epinephrine


Comment: Not relevant to this question


Comment: Study of transported newborns that demonstrate the value of transcutaneous CO2 measurements during transport in improving overall ventilation (as defined by the amount of time with a normal pCO2 value) LOE 5 Fair support for question


Comment: Review


Comment: Study of disposable CO2 detector in children LOE 5 At best, this is tangentially supportive


LOE 4 Fair Support

Comment: A small observational study which demonstrates the utility of colorimetric CO2 detectors during bag and mask ventilation to ascertain adequate ventilation


Comment: A small RCT that shows no utility to using a respiratory function monitor as an adjunct to ventilation management in infants. LOE 5 Neutral


Comment: Older case study of a device that continuously monitors several parameters, including CO2 release in newborns that demonstrates that the system works and gives useful information LOE4 Level of support: Poor.

**Comment:** Prospective observational study of transcutaneous CO2 monitoring in ventilated newborns that demonstrates value in guiding ventilation. LOE 5


**Comment:** Evaluation of in line capnometer in ventilated infants that demonstrates minimal impact on gas flow and good correlation with arterial values. LOE 5 supportive but weakly related.


**Comment:** Study of quantitative ET CO2 in older patients that supports the utility of this method in assessing and adjusting ventilation. LOE 5 Fair support.


**Comment:** Case Report of failed valve resulting in incorrect capnographic reading and subsequent over ventilation.


**Comment:** Stud in ventilated infants that again demonstrates the general utility of ET CO2 measurements but the lack of good correlation in infants with RDS. Good correlation in infants with "asphyxia" and apnea which supports potential utility in initial resuscitation. LOE 5 Neutral or Poor support


**Comment:** Older review


**Comment:** RCT of transcutaneous CO2 during neonatal transport that demonstrates value of monitoring in reducing ventilator pressures, with presumed benefit in reducing lung injury. LOE 5 Supportive Fair


**Comment:** Not relevant

Comment: Study in which CO2 production was quantitatively measured during resuscitation of term and preterm infants. Demonstrates technical feasibility of measurement while using face mask (majority of patients) and thus provides fair support to the question. LOE 4


Comment: Adult study that demonstrates that measured ET CO2 is useful in assessing ventilation and directing changes LOE 5 Fair support


Comment: Not relevant


Comment: Capnography is useful in assessing ETT placement. Neutral LOE 5


Comment: Study in ventilated infants that demonstrates that continuous CO2 monitoring can help identify over or under ventilation and permit adjustments. LOE5 Fair support


Comment: Retrospective study that demonstrates that ETCO2 correlates well enough with arterial values in mechanically ventilated ELBW infants to be useful in trending and improved recognition of abnormal ventilation. LOE 5 Neutral


Comment: Study in children demonstrating good correlation with arterial values. Unclear significance for newborns Neutral LOE 5.


Comment: Lamb study that employed the analysis of a single breath to identify hypo or hyper ventilation from expired CO2 and assessment of lung volume. Supportive in that such measurements might permit very rapid assessment of ventilation and permit adjustment quickly, such as during resuscitation. Far from clinical applicability and no subsequent (to 1998) papers found. LOE 5

Comment: Study in adults demonstrating that reliable ET CO2 values can be obtained during mask ventilation, so tangentially supportive of the question LOE 5.