CRITICAL PATIENT ENCOUNTERS: USING $ETCO_2$ TO RECOGNIZE SEVERE SEPSIS IN THE PREHOSPITAL SETTING

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Conflict of interest Disclosure

- Authors Conflicts of Interest:
  - C. Hunter, No Conflict of interest

Topics

- Sepsis and acid/base physiology
- Prehospital sepsis care
- $ETCO_2$ as a diagnostic tool in sepsis
- Orange County EMS System Sepsis Alert Protocol
- Preliminary Findings

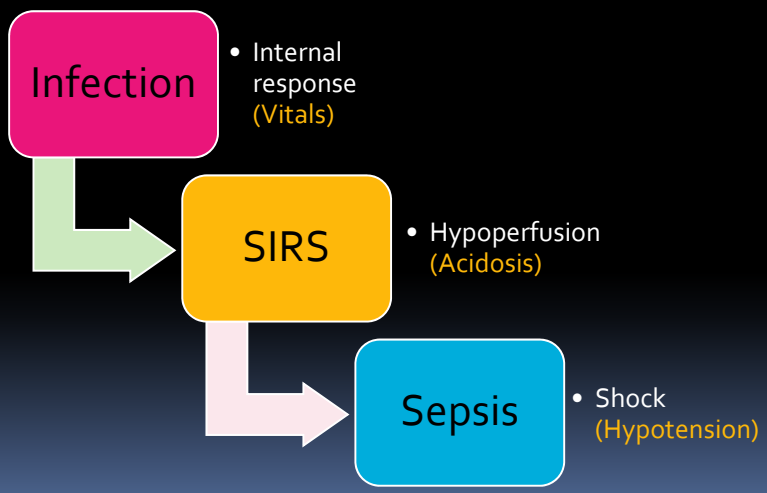
Sepsis

- End result of an overwhelming infection
- Hypoperfusion leads to end-organ damage and lactic acidosis
  - The severity of lactic acidosis predicts outcomes
- Early Goal Directed Therapy – early identification and aggressive therapy has been shown to improve outcomes
- Surviving Sepsis Campaign – guidelines for best practice

Prehospital Sepsis Care

- Frequent, high-mortality encounters
  - Seymour et al (2012) identified EMS transported more patients diagnosed with sepsis than STEMIs or CVSs, and there was a 19.7% mortality rate
- Prehospital interventions can make a difference
  - EMS transport decreased time to antibiotics and initiation of EGDT Studnek et al., 2012
  - Prehospital IV access and fluid administration improved survival Seymour et al., 2014
  - Prehospital sepsis protocol decreased mortality Guerra et al., 2013
- **Early recognition and fluid resuscitation may be most important**

Development of Sepsis



Respiratory Cycle

Oxygen -> lungs -> alveoli -> blood

Oxygen

breath

CO_2

lungs

CO_2

blood

muscles + organs

Oxygen

cells

energy

Oxygen + Glucose

CO_2

Oxygenation and Ventilation

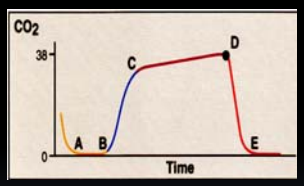
Oxygen -> lungs -> alveoli -> blood

Oxygen

breath

CO_2

lungs



muscles + organs

Oxygen

CO_2

blood

energy

cells

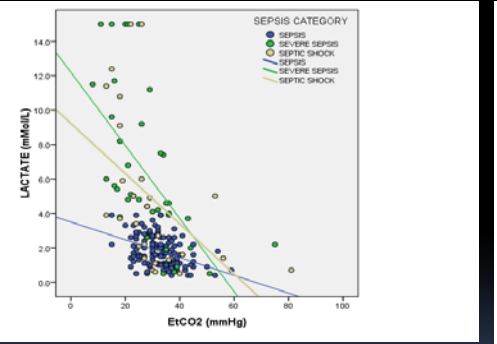
Oxygen + Glucose

CO_2

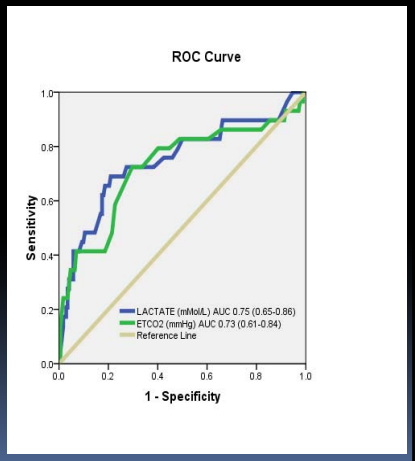
ETCO2 provides a non-invasive mechanism to detect metabolic acidosis

- $ETCO_2$ correlates with serum bicarbonate and PH levels in children and adults with Diabetic Ketoacidosis Fearon et al., 2002, Soleimanpour et al., 2013
- $ETCO_2$ correlates with serum bicarbonate in children with gastroenteritis Nagler et al., 2006
- $ETCO_2$ correlates with serum bicarbonate and lactate levels in patient with undifferentiated shock and metabolic disorders Kehng and Rahman 2012, Kartel et al., 2006
- $ETCO_2$ correlates with lactic acidosis and poor outcomes in patient with severe trauma Deacon 2004, Caputo et al., 2012

ETCO2 predicts mortality in Emergency Room patients with suspected sepsis



	Correlation Coefficient ETCO2-Lactate	P-Value
Sepsis	-0.421	<0.001
Severe Sepsis	-0.597	<0.001
Septic Shock	-0.482	0.011



ETCO2 predicts mortality in Emergency Room patients with suspected sepsis

ROC Curve performance of ETCO2 and Lactate in predicting mortality

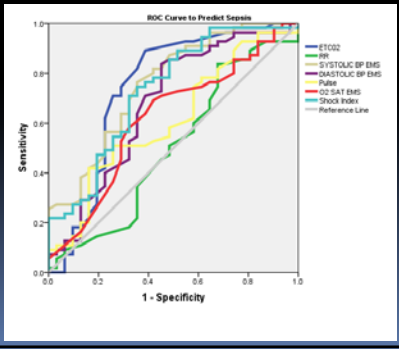
	ETCO2 AUC (95%CI)	Lactate AUC (95%CI)
Sepsis Categories		
Suspected Sepsis	0.60 (0.37-0.83)	0.61 (0.36-0.87)
Severe Sepsis	0.67 (0.46-0.88)	0.69 (0.48-0.89)
Septic Shock	0.78 (0.59-0.96)	0.74 (0.55-0.93)
Intubation		
Intubated	0.77 (0.60-0.94)	0.82 (0.68-0.96)
Not Intubated	0.72 (0.56-0.88)	0.64 (0.46-0.82)

The role of ETCO2 in sepsis

- $ETCO_2$ is a non-invasive outcome predictor in suspected sepsis
- $ETCO_2$ performs as well as serum lactate predicting mortality in septic patients
- $ETCO_2$ may provide a method for earlier identification and intervention in patients with suspected sepsis

A role for ETCO2 in the out of hospital diagnosis of sepsis

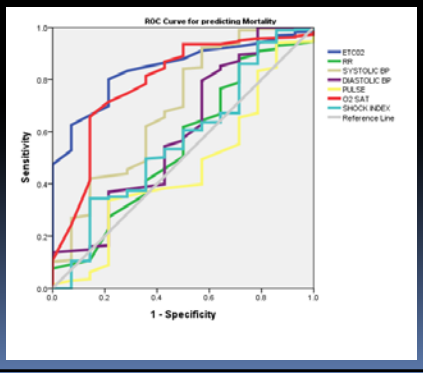
	Infection without Sepsis N=55 (95%CI)	Infection with Sepsis N=31 (95%CI)	Total N=86 (95%CI)	P-Value
ETCO2	**35 (33-37)**	**28 (22-33)**	**32 (30-35)**	**0.013**
Respiratory Rate	28 (25-31)	29 (25-32)	28 (26-30)	0.763
Systolic BP	143 (136-151)	73 (66-81)	81 (77-85)	<0.001
Diastolic BP	85 (80-90)	74 (56-91)	86 (84-88)	0.006
Pulse	101 (93-109)	111 (101-121)	104 (98-110)	0.123
Oxygen Saturation	92 (90-94)	88 (83-92)	91 (88-94)	0.072
Shock Index	0.74 (0.66-0.82)	1.02 (0.88-1.15)	0.84 (0.76-0.91)	<0.001



	AUC (95% CI)	P-Value
ETCO2	**0.74 (0.62-0.87)**	**<0.001**
Respiratory Rate	0.50 (0.37-0.64)	0.982
Systolic BP	0.76 (0.65-0.86)	<0.001
Diastolic BP	0.68 (0.55-0.80)	0.007
Pulse	0.61 (0.49-0.74)	0.090
Oxygen Saturation	0.62 (0.49-0.74)	0.069
Shock Index	0.73 (0.62-0.85)	<0.001

Prehospital ETCO2 predicts mortality in patients with SIRS

	Survivors N=371 (95% CI)	Non-Survivors N=14 (95% CI)	Total N=385 (95% CI)	P-Value
ETCO2	**34 (33-35)**	**23 (19-26)**	**33 (32-34)**	**<0.001**
Respiratory Rate	29 (28-30)	31 (26-36)	29 (28-30)	0.519
Systolic BP	142 (139-145)	113 (88-138)	141 (138-144)	0.001
Diastolic BP	86 (84-88)	74 (56-91)	86 (84-88)	0.131
Pulse	114 (112-117)	111 (100-123)	114 (112-117)	0.617
Oxygen Saturation	94 (93-95)	85 (79-90)	93 (93-94)	<0.001

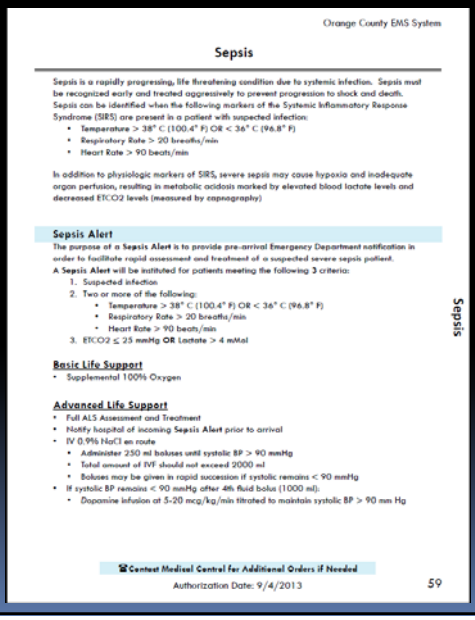


	AUC (95% CI)	P-Value
ETCO2	**0.84 (0.77-0.92)**	**<0.001**
Respiratory Rate	0.55 (0.38-0.71)	0.563
Systolic BP	0.69 (0.54-0.85)	0.014
Diastolic BP	0.60 (0.43-0.77)	0.226
Pulse	0.46 (0.30-0.62)	0.604
Oxygen Saturation	0.79 (0.66-0.92)	<0.001
Shock Index	0.57 (0.40-0.73)	0.411

ETCO2 in Emergency Department Sepsis Protocol

- ORMC ED began an internal sepsis screening protocol for those with suspected infection and ≥ 2 SIRS criteria (hold ICU beds, contact pharmacy)
- $ETCO_2$ and serum lactate levels were collected in triage
- Of 54 activations 87% were diagnosed with sepsis
- Mean lactate levels were 3.4 (95%CI 2.6-4.2) vs 2.1 (95%CI 0.5-3.7; p=0.169
- Mean $ETCO_2$ levels were 31 (95%CI 27-34) vs 47 (95%CI 33-66; p=0.001)
- The AUC for $ETCO_2$ predicting sepsis was 0.87 (95%CI 0.75-0.98) and for lactate was 0.68 (95%CI 0.42-0.93)
- **Low $ETCO_2$ predicted sepsis in a triage screening tool**

Orange County EMS System Sepsis Protocol



Orange County EMS System

Sepsis

Sepsis is a rapidly progressing, life threatening condition due to systemic infection. Sepsis must be recognized early and treated aggressively to prevent progression to shock and death. Sepsis can be identified when the following markers of the Systemic Inflammatory Response Syndrome (SIRS) are present in a patient with suspected infection:

- Temperature > 38° C (100.4° F) OR < 36° C (96.8° F)
- Respiratory Rate > 20 breaths/min
- Heart Rate > 90 beats/min

In addition to physiologic markers of SIRS, severe sepsis may cause hypoxia and inadequate organ perfusion, resulting in metabolic acidosis marked by elevated blood lactate levels and decreased ETCO2 levels (measured by capnography)

Sepsis Alert

The purpose of a **Sepsis Alert** is to provide pre-arrival Emergency Department notification in order to facilitate rapid assessment and treatment of a suspected severe sepsis patient. A **Sepsis Alert** will be instituted for patients meeting the following 3 criteria:

1. Suspected infection
2. Two or more of the following:
   - Temperature > 38° C (100.4° F) OR < 36° C (96.8° F)
   - Respiratory Rate > 20 breaths/min
   - Heart Rate > 90 beats/min
3. ETCO2 ≤ 25 mmHg **OR** Lactate > 4 mMol

Basic Life Support

- Supplemental 100% Oxygen

Advanced Life Support

- Full ALS Assessment and Treatment
- Notify hospital of incoming **Sepsis Alert** prior to arrival
- IV 0.9% NaCl en route
  - Administer 250 ml boluses until systolic BP > 90 mmHg
  - Total amount of IVF should not exceed 2000 ml
  - Boluses may be given in rapid succession if systolic remains < 90 mmHg
- If systolic BP remains < 90 mmHg after 4th fluid bolus (1000 ml):
  - Dopamine infusion at 5-20 mcg/kg/min titrated to maintain systolic BP > 90 mm Hg

☎ Contact Medical Control for Additional Orders if Needed

Authorization Date: 9/4/2013

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Sepsis

Accuracy of a prehospital sepsis alert protocol utilizing ETCO2

- Preliminary pilot study to determine the accuracy of the protocol
- Poor protocol compliance created a study group
- 38 sepsis alert called by single agency to single ED
- 14 (37% appropriately called based on $ETCO_2 \leq 25mmHg$, 24 (63%) had ≥ 2 SIRS criteria but $ETCO_2 > 25mmHg$
- Mean $ETCO_2$ in appropriate alerts was 18 (95%CI 15-20) vs 32 ((95%CI 29-35; p=0.001). Mean lactate levels in the ED were 5.3 (95%CI 2.5-8.2) vs 2.1 (95%CI 1.7-2.6; p=0.003)
- The correlation between $ETCO_2$ and lactate was -0.50, p=0.008
- The AUC for $ETCO_2$ predicting appropriate activation of sepsis alert was 0.97 (95%CI 0.91-1.0)
- Using the $ETCO_2 \leq 25mmHg$ cut off yielded a sensitivity of 100% and a specificity of 95%
- **When appropriately used, the Orange County EMS System sepsis alert was highly sensitive and specific**

Effectiveness of a prehospital sepsis alert protocol utilizing ETCO2

- Prospective pilot pre/post intervention study to assess impact of patient care in single ED
- 137 cases (110 pre, 27 post)
- Initiation of prehospital sepsis alert decreased:
  - Time to blood culture 27 (95%CI 18-36) vs 14 (95%CI 9-19)
  - Time to antibiotics 56 (95%CI 39-74) vs 40 (95%CI 24-55)
  - Time to fluids 34 (95%CI 17-52) vs 10 (95%CI 4-16)
  - Length of Stay 13 (95%CI 11-16) vs 9 (95%CI 6-12)
  - ICU Admission 53% (95%CI 43-62%) vs 33% (95%CI 14-52%)
  - Mortality 14% (95%CI 7-20%) vs 7% (95%CI 0-18%)
- **Preliminary data, but…**

Take Home Points

- Early identification and resuscitation by prehospital providers may improve outcomes for patients with sepsis
- Low $ETCO_2$ is correlated with an acidotic state, and in the setting of suspected sepsis it serves as a similar outcome predictor to serum lactate levels
- $ETCO_2$ may be used as a non-invasive, real time adjunct screening tool to create protocols for prehospital sepsis identification

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