Sepsis: Epidemiology, Diagnosis, and Management

Updated January 2015
Getting on the same page: Sepsis definitions

- SIRS (maybe sepsis, maybe not)
  - Temp (<36, >38.3)
  - HR ( > 90)
  - RR (> 20 – or PCO2 < 32)
  - WBC (< 4, or > 12, or 10% bands)

- Sepsis
  - SIRS + infection site

- Severe sepsis
  - Sepsis with organ dysfunction

- Septic Shock
  - Severe sepsis requiring vasopressors

- Sepsis syndrome follows a continuum

- A patient classified as “severe sepsis” may actually be in shock, as shock is not defined by vasopressor requirement

- These definitions are most useful when conducting and evaluating studies (who is included)
Severe sepsis: “Sepsis with organ dysfunction”

Note that these patients, while not requiring vasopressors (not “septic shock”), may still have shock physiology and should be treated aggressively.

**TABLE 2. Severe Sepsis**

<table>
<thead>
<tr>
<th>Severe sepsis definition = sepsis-induced tissue hypoperfusion or organ dysfunction (any of the following thought to be due to the infection)</th>
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</thead>
<tbody>
<tr>
<td>Sepsis-induced hypotension</td>
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<tr>
<td>Lactate above upper limits laboratory normal</td>
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<tr>
<td>Urine output &lt; 0.5mL/kg/hr for more than 2 hrs despite adequate fluid resuscitation</td>
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<tr>
<td>Acute lung injury with $\text{PaO}_2/\text{FiO}_2 &lt; 250$ in the absence of pneumonia as infection source</td>
</tr>
<tr>
<td>Acute lung injury with $\text{PaO}_2/\text{FiO}_2 &lt; 200$ in the presence of pneumonia as infection source</td>
</tr>
<tr>
<td>Creatinine &gt; 2.0 mg/dL (176.8 μmol/L)</td>
</tr>
<tr>
<td>Bilirubin &gt; 2 mg/dL (34.2 μmol/L)</td>
</tr>
<tr>
<td>Platelet count &lt; 100,000 μL</td>
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<tr>
<td>Coagulopathy (international normalized ratio &gt; 1.5)</td>
</tr>
</tbody>
</table>

Epi: Despite medical advances, sepsis syndrome mortality is still significant

In-hospital mortality for all sepsis diagnoses (including those without severe sepsis or shock) These data, from 2003, likely overestimate current trends.

Epi: Severe sepsis mortality declining over time but still high

With septic shock, mortality 22% overall and up to 50% in those with highest APACHE scores

Better to be younger: in this study, patients with severe sepsis < age 44 mortality 7.3% (5% without comorbs, 17.2% with)

Kaukonen K et al JAMA 2014

Hospital mortality for severe sepsis declining over time, ~ 20% in 2012 (NZ/Australia)
Epi: Severe sepsis/septic shock mortality: 30 days ≠ 1 year!

Keep in mind: compare large epidemiologic study on last slide (crude mortality: 18% severe sepsis/shock, 22% septic shock) at hospital discharge to:

Current-era high-intensity center RCT for septic shock (enrollment from 2008-2013) at 60 days (comparable), to:

Same RCT at 1 year: > 40%!!
Still a morbid/mortal condition, even in high-performing centers

Kaukonen K et al
JAMA 2014
PMID: 24638143

ProCESS Investigators,
NEJM 2014
PMID: 24635774
Sepsis: Management

Goals of management:

1. Identify sepsis
2. Eradicate infection
3. Prevent or reverse organ dysfunction and shock; restore oxygen delivery to respiring cells
Core Management Principles

- Early Recognition
- Antibiotics
- Source control
- Rapid fluid resuscitation
- Judicious use of vasopressors
- Steroids (?)
You can’t treat what you don’t think of: Early recognition is key to the management of sepsis

“. . . the physicians say it happens in hectic fever, that in the beginning of the malady it is easy to cure but difficult to detect, but in the course of time, not having been either detected or treated in the beginning, it becomes easy to detect but difficult to cure.”

~ Machiavelli N. Il principe. S.l. [nach Ebert vielleicht Genf]; 1550,

• Consider sepsis in the differential diagnosis of every patient presenting with SIRS criteria.

• Be alert for sepsis masquerading as: alcohol withdrawal, intoxication, dehydration, etc. . . .
Core Management Principles

• Early Recognition
• Antibiotics
• Source control
• Rapid fluid resuscitation
• Judicious use of vasopressors
• Steroids (?)
Antibiotic Administration Principles

• Treat likely source of infection based on history, physical, and initial diagnostic testing

• Base empiric abx choices on prior culture data, pre-hospital situation, and local resistance patterns
  – Include MRSA and pseudomonas coverage, if appropriate

• Better too broad than too narrow

• Obtain cultures prior to antibiotic initiation when possible (core measure) - but do not delay antibiotic administration to obtain cultures
Delay of Antimicrobial Therapy Increases Mortality in Septic Shock

- Retrospective multicenter study including > 2000 patients with septic shock; EVERY HOUR of delayed abx therapy associated with higher mortality

- Mortality associated with delay of effective antibiotics was INDEPENDENT of other interventions and of underlying characteristics

Kumar et al. CCM 2006: 1589
Confirmed in larger cohort also including severe sepsis

- Retrospective multicenter study including > 28000 patients

- In-hospital mortality increases in linear fashion with time from first antibiotics.

- Timely antibiotic administration equally important IN THE ER or ON THE FLOORS, including in patients who are not hypotensive

Ferrer et al. CCM 2014;42(8):1749-55
Order all ICU antibiotics “STAT x1stDose”

- Also, inform the RN you ordered STAT antibiotics
- These two interventions have significantly decreased time to administration in our medical ICU
Choose antibiotic coverage that is APPROPRIATELY BROAD

- Retrospective multicenter study of septic shock
- “Right” abx identified by organism sensitivities when culture data available and by standard recommendations for empiric coverage when not
- If antibiotics covering the organism not administered by hour 48 of shock, > fivefold reduction in survival

Early source control crucial for closed-space infections

- Assess for closed-space collections or more extensive infection associated with primary site
  - UTI: obstructing calculus, peri-nephric abscess
  - Cellulitis: nec fasc, soft tissue abscess
  - Pneumonia: empyema
  - Bacteremia: osteomyelitis, deep tissue abscess, endovascular infection
  - C.dif: pan-colitis, toxic megacolon

- **Eradication of the source imperative**
  - Immediate surgical/IR consultation
  - Delay of source control over 6 hours after recognition of organ dysfunction associated with increased mortality
Core Management Principles

• Early Recognition

• Antibiotics

• Source control

• Rapid fluid resuscitation

• Judicious use of vasopressors

• Steroids (?)
Severe sepsis and septic shock: Protocolized Resuscitation

- Resuscitation protocol concept first came to widespread attention in 2001: “Rivers Trial”

- Early (?)
- Goal Directed (?)
- Therapy (?)

Rivers E et al, NEJM 2001; 345(19):1368-77
EGDT Principles:

Goal of Resuscitation Algorithm

• **Restore delivery of oxygen** to vital organs

  – \( \text{DO2} = \text{CO} \times \text{[Hemoglobin]} \times \%\text{saturation} \)
    - \( \text{CO} = \text{HR} \times \text{stroke volume} \)
    - \( \text{SV} = \text{dependent on preload, afterload, contractility} \)

  – Algorithm aimed at addressing the components of oxygen delivery to restore DO2 to respiring organs
Specialized Protocol

- ED Protocol – nursing driven
- Specialized 9 bed unit in ED
  - One attending
  - Two residents
  - Three nurses
- 6 hour protocol (remained in ED for at least 6 hours)
- Continuous ScvO2, CVP, and art line
EGDT group

- Faster IVF rate early
  - 3.5 versus 5 L in first 6 hours
  - Equal at 72 hours (13 L)

- More PRBC (45 versus 68% at 72 hours)
  - substantially more that would be transfused with current practice

- Less pressor req't (52 versus 37% at 72 hours)
  - More dobutamine (9 versus 15%)

- In-hospital mortality benefit (30.5% v 46.5%), 60-day mortality benefit (44.3% v 56.9%; NNT 8)
ProCESS Trial: 2014

• Recruited from ER, targeted severe sepsis/septic shock
  – Refractory hypotension or serum lactate > 4.0

• Enrolled within 2 hours of confirmed sepsis

• Three arms:
  – Protocol-based EGDT (Rivers)
  – Protocol-based “standard therapy”
  – Usual care

Protocol-Based “Standard Therapy”

- No req’t for central access
- No ScvO2, no CVP
- No inotrope req’t
- Transfusion threshold set to 7.5, not 10

The ProCESS Investigators
ProCESS Outcomes


Table 3. Outcomes.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Protocol-based EGDT (N = 439)</th>
<th>Protocol-based Standard Therapy (N = 446)</th>
<th>Usual Care (N = 456)</th>
<th>P Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death — no./total no. (%)</td>
<td>92/439 (21.0)</td>
<td>81/446 (18.2)</td>
<td>86/456 (18.9)</td>
<td>0.83§</td>
</tr>
<tr>
<td>In-hospital death by 60 days; primary outcome</td>
<td>129/405 (31.9)</td>
<td>128/415 (30.8)</td>
<td>139/412 (33.7)</td>
<td>0.66</td>
</tr>
<tr>
<td>Death by 90 days</td>
<td>269/439 (61.3)</td>
<td>284/446 (63.7)</td>
<td>256/456 (56.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>New organ failure in the first week — no./total no. (%)</td>
<td>165/434 (38.0)</td>
<td>161/441 (36.5)</td>
<td>146/451 (32.4)</td>
<td>0.19</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>12/382 (3.1)</td>
<td>24/399 (6.0)</td>
<td>11/397 (2.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>Respiratory</td>
<td>2.6±1.6</td>
<td>2.4±1.5</td>
<td>2.5±1.6</td>
<td>0.52</td>
</tr>
<tr>
<td>Renal</td>
<td>6.4±8.4</td>
<td>7.7±10.4</td>
<td>6.9±8.2</td>
<td>0.41</td>
</tr>
<tr>
<td>Use of hospital resources</td>
<td>5.1±10.8</td>
<td>8.5±12.0</td>
<td>8.8±13.7</td>
<td>0.92</td>
</tr>
<tr>
<td>Admission to intensive care unit — no. (%)</td>
<td>401 (91.3)</td>
<td>381 (85.9)</td>
<td>393 (86.2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Stay in intensive care unit among admitted patients — days</td>
<td>5.1±6.3</td>
<td>5.1±7.1</td>
<td>4.7±5.8</td>
<td>0.63</td>
</tr>
<tr>
<td>Stay in hospital — days</td>
<td>11.3±10.0</td>
<td>12.3±12.1</td>
<td>11.3±10.9</td>
<td>0.25</td>
</tr>
<tr>
<td>Discharge status at 60 days — no. (%)</td>
<td>3 (0.7)</td>
<td>8 (1.8)</td>
<td>2 (0.4)</td>
<td>0.82</td>
</tr>
<tr>
<td>Not discharged</td>
<td>16 (3.6)</td>
<td>22 (4.9)</td>
<td>22 (4.8)</td>
<td>0.51</td>
</tr>
<tr>
<td>Discharged to another acute care hospital</td>
<td>8 (1.8)</td>
<td>2 (0.4)</td>
<td>5 (1.1)</td>
<td>0.25</td>
</tr>
<tr>
<td>Discharged to nursing home</td>
<td>71 (16.2)</td>
<td>93 (20.9)</td>
<td>88 (19.3)</td>
<td>0.50</td>
</tr>
<tr>
<td>Discharged home</td>
<td>236 (53.8)</td>
<td>227 (50.9)</td>
<td>235 (51.5)</td>
<td>0.50</td>
</tr>
<tr>
<td>Other or unknown</td>
<td>13 (3.0)</td>
<td>13 (2.9)</td>
<td>18 (3.9)</td>
<td>0.73</td>
</tr>
<tr>
<td>Serious adverse events — no. (%)¶</td>
<td>23 (5.2)</td>
<td>22 (4.9)</td>
<td>37 (8.1)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

* Plus–minus values are means ±SD.
† Unless stated otherwise, P values are for a three-group comparison, with the use of Fisher’s exact test for categorical measures and linear models for continuous and normally distributed measures. Skewed outcomes were analyzed with the use of nonparametric alternatives.
‡ The P value for the primary analysis was for a comparison between the two protocol-based groups combined and the usual-care group, with the use of Fisher’s exact test. The three-group comparison, with the use of Fisher’s exact test, was also nonsignificant (P = 0.55), as was each of the two-way comparisons (with P values ranging from 0.31 to 0.89).
§ Included in the analysis were patients in whom new organ failure developed in the first week after randomization.
¶ A detailed list of serious adverse events is provided in Table S5 in the Supplementary Appendix.
Protocolized Resuscitation: Interim Conclusions 2014

• **Not necessary** to trend ScvO2 and CVP; so some patients may avoid invasive procedure

• **Not necessary** to transfuse to an outdated Hgb threshold

• Lack of difference between “usual care” and the protocolized groups may be because:
  1. ‘Usual care’ has evolved since Rivers; standard practice in experienced centers now includes vigilant monitoring with aggressive early resuscitation
  2. Study took place in high-volume academic centers

• **STILL IMPERATIVE** to attend to the basics of sepsis management: EARLY and FREQUENT assessment of organ perfusion, rapid restoration of circulating volume, and correction of refractory hypotension
Core Management Principles

- Early Recognition
- Antibiotics
- Source control
- Rapid fluid resuscitation
- Judicious use of vasopressors
- Steroids (?)
# Resuscitation Fluids: Which one? How much?


Acquisition costs vary by institution & volume.

**NS:** < $1  
**LR:** ~ $1  
**Plasmalyte:** $2-6

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**Table 1. Types and Compositions of Resuscitation Fluids.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Human Plasma</th>
<th>Colloids</th>
<th>Crystalloids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Human donor</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Albumin</td>
<td>4% Albumin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Human donor</td>
<td>4% Albumin</td>
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</tr>
<tr>
<td></td>
<td>Potassium</td>
<td>4% Albumin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Calcium</td>
<td>4% Albumin</td>
<td></td>
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<tr>
<td></td>
<td>Magnesium</td>
<td>4% Albumin</td>
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<tr>
<td></td>
<td>Chloride</td>
<td>4% Albumin</td>
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<tr>
<td></td>
<td>Acetate</td>
<td>4% Albumin</td>
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<tr>
<td></td>
<td>Lactate</td>
<td>4% Albumin</td>
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<tr>
<td></td>
<td>Malate</td>
<td>4% Albumin</td>
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<tr>
<td></td>
<td>Gluconate</td>
<td>4% Albumin</td>
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<tr>
<td></td>
<td>Bicarbonate</td>
<td>4% Albumin</td>
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<tr>
<td></td>
<td>Octanoate</td>
<td>4% Albumin</td>
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</tbody>
</table>

* To convert the values for potassium to milligrams per deciliter, divide by 0.2558. To convert the values for calcium to milligrams per deciliter, divide by 0.250. To convert the values for magnesium to milligrams per deciliter, divide by 0.4114.

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**NS:** < $1  
**LR:** ~ $1  
**Plasmalyte:** $2-6
Why you may not have heard of Hextend…

Black Box Warnings now on starches licensed in US: not for use in critically ill patients. Can still order at PUH.


The NEW ENGLAND JOURNAL of MEDICINE
Crystalloid v Albumin

- SAFE trial (7000 patients, “intravascular fluid depletion” – 19% severe sepsis)
- Randomized, blinded; 4% albumin v NS
- No difference (except $): 250 mL of 5% albumin costs $35-50
- Subgroup analysis (underpowered) in severe sepsis generated hypothesis for possible benefit of albumin in this group

Crystalloid v Albumin: Revisited in Severe Sepsis (2014)

- ALBIOS trial: crystalloid alone versus crystalloid+albumin (20%) to target albumin 3.0 or greater after initial resuscitation of patients with severe sepsis (n = 1800)

No survival advantage overall.

Possible benefit in septic shock subgroup...

Still expensive.


Resuscitation Fluids: How much?

• Feature of every sepsis protocol is early fluid challenge of ~30mL/kg (1.5-3L) via bolus in initial resuscitation.

• Fluid challenges should continue if the patient remains hypoperfused, provided the patient remains volume responsive.
  – Lactate clearance, UOP, peripheral perfusion etc.
  – Newer methods: pulse pressure variability, IVC diameter and collapsibility via ultrasound.

All of the listed measures are surrogates. What is the physiologic variable we hope will “respond” to volume?

\[ \text{DO2} = \text{CO} \times \text{[Hemoglobin]} \times \%\text{saturation} \]
Core Management Principles

- Early Recognition
- Antibiotics
- Source control
- Rapid fluid resuscitation
- Judicious use of vasopressors
- Steroids (?)
Vasopressors in sepsis:

which one(s)?
how much?
## Vasopressor Pharmacology

<table>
<thead>
<tr>
<th></th>
<th>$\alpha_1$</th>
<th>$\beta_1$</th>
<th>$\beta_2$</th>
<th>DA</th>
<th>MAP</th>
<th>PCWP</th>
<th>CO</th>
<th>SVR</th>
<th>HR</th>
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</thead>
<tbody>
<tr>
<td><strong>Dopamine</strong></td>
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<tr>
<td>&gt;10 mcg/kg/min</td>
<td>+++</td>
<td>++++</td>
<td>+</td>
<td>0</td>
<td>↑↑↑</td>
<td>↑</td>
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<tr>
<td><strong>Norepinephrine</strong></td>
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<tr>
<td>0.01-1 mcg/kg/min</td>
<td>++++++</td>
<td>++</td>
<td>0</td>
<td>0</td>
<td>↑↑↑</td>
<td>↑↑</td>
<td>↑↓</td>
<td>↑↑↑</td>
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<td><strong>Phenylephrine</strong></td>
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<tr>
<td>0.5-1.5 mcg/kg/min</td>
<td>++++++</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>↑</td>
<td>↑</td>
<td>↑↓</td>
<td>↑</td>
<td>NA</td>
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<tr>
<td><strong>Vasopressin</strong></td>
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<tr>
<td>$\leq$0.04 U/min</td>
<td>V1 (vascular smooth muscle)</td>
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<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
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<tr>
<td>V2 (renal collecting duct)</td>
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<tr>
<td><strong>Epinephrine</strong></td>
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<tr>
<td>0.01-0.1 mcg/kg/min</td>
<td>++++++</td>
<td>+++</td>
<td>++</td>
<td>↑↑</td>
<td>↑↑↑</td>
<td>↑↑</td>
<td>↑↑</td>
<td>↑↑</td>
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</tr>
</tbody>
</table>

Overgaard CB. Circulation 2008;118;1047-1056

Surviving Sepsis 2012: Pressor recs

- Norepinephrine as first-choice vasopressor
- Vasopressin (fixed-dose) may be added to norepi to decrease requirement or raise MAP
- Epi may be added or substituted if norepi insufficient (weak recommendation)
- Phenylephrine as salvage

Consensus guidelines, all recommendations do not have strong evidence support

Dopamine has equivalent mortality to norepinephrine in shock and sepsis with worse adverse effect profile.

With more dysrhythmia ...

Current SSC guidelines recommend dopamine only in highly selected patients (e.g. bradycardia).

How much?: Pressure targets

- "Titrate to MAP of 65"
- Purpose of maintaining a mean arterial pressure (MAP) is to perfuse, in particular, brain and kidney within their ranges of autoregulation
How much?: Pressure targets

- Recent study compared mortality and renal outcomes in ‘high MAP (80)’ vs ‘low MAP (65)’ titration parameters in patients with septic shock


- No survival benefit in ‘high MAP’ group

- Suggestion in secondary outcomes of less renal injury in high MAP group in patients with chronic hypertension (altered autoregulation curve?), but further studies needed

<table>
<thead>
<tr>
<th>Secondary outcomes — no./total no. (%)</th>
<th>Low MAP (65)</th>
<th>High MAP (80)</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death at day 90†</td>
<td>164 (42.3)</td>
<td>170 (43.8)</td>
<td>0.74</td>
</tr>
<tr>
<td>Survival at day 28 without organ support‡</td>
<td>241 (62.1)</td>
<td>235 (60.6)</td>
<td>0.66</td>
</tr>
<tr>
<td>Doubling of plasma creatinine</td>
<td>161 (41.5)</td>
<td>150 (38.7)</td>
<td>0.42</td>
</tr>
<tr>
<td>No chronic hypertension</td>
<td>71/215 (33.0)</td>
<td>85/221 (38.5)</td>
<td>0.32</td>
</tr>
<tr>
<td>Chronic hypertension</td>
<td>90/173 (52.0)</td>
<td>65/167 (38.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>Renal-replacement therapy from day 1 to day 7</td>
<td>139 (35.8)</td>
<td>130 (33.5)</td>
<td>0.50</td>
</tr>
<tr>
<td>No chronic hypertension</td>
<td>66/215 (30.7)</td>
<td>77/221 (34.8)</td>
<td>0.36</td>
</tr>
<tr>
<td>Chronic hypertension</td>
<td>73/173 (42.2)</td>
<td>53/167 (31.7)</td>
<td>0.046</td>
</tr>
</tbody>
</table>
Core Management Principles

- Early Recognition
- Antibiotics
- Source control
- Rapid fluid resuscitation
- Judicious use of vasopressors
- Steroids (?)
Corticosteroids in Sepsis

Rationale:

1) Corticosteroids increase the vasomotor catechol response
2) Corticosteroids may ‘replace’ the relative adrenal insufficiency sometimes observed in severe sepsis
3) Dysregulation of inflammation is a feature of severe sepsis/septic shock; steroids are therefore attractive therapeutically d/t their anti-inflammatory properties.

- Currently INSUFFICIENT DATA to recommend for or against “low-dose” steroids in septic shock
- Investigated since the 1960s, prospective (n=172) and retrospective analyses (n=328) in 1976 provided first support for their use in septic shock [Schumer W, Ann Surg. 1976 Sep;184(3):333-41; http://www.ncbi.nlm.nih.gov/pubmed/786190]
- Follow-up studies equivocal or negative. By early 1990s, meta-analyses suggested increased mortality risk, but dosing regimens were variable in included studies [Cronin L, CCM 1995; 23:1430-1439; http://www.ncbi.nlm.nih.gov/pubmed/7634816]
- Renewed interest and new trials over the last decade
Corticosteroid Pivot (Pro): Annane 2002

- Prospective RCT, 300 patients randomized to low-dose hydrocort (50 mg Q6H) and florinef for 7D, versus placebo
- ~ 75% of enrolled participants were non-responsive to cosyntropin stim
- Reduction in mortality and time to shock reversal in steroid group (more pronounced in cosyntropin non-responders)
- No difference in adverse events

Corticosteroid Pivot (Con): CORTICUS 2008

- Multicenter, prospective RCT: 499 patients with septic shock randomized to hydrocort 50 mg Q6H (then additional 6D of taper), versus placebo
  - Annane is 2nd author on this study
- No difference in mortality in entire group, in cosyntropin responders, or in cosyntropin non-responders
- Of note, this group was less ill (lower SAPSII and markedly lower overall mortality – 32%[low] v 61% in placebo groups) than Annane 2002.

Corticosteroids: Systematic Review 2009 (Pro?)

- Pre-specified subgroup examining low-dose (≤ 300 mg/D) for longer period (≥ 5D), more consistent with current practice
- Included 18 studies conducted in patients with severe sepsis/septic shock
- No mortality benefit overall

Annane et.al. JAMA 2009; 301(22):2362-75
Low-dose Long v High-dose Short
Patients with severe sepsis/septic shock

Suggestion that low-dose steroids may confer mortality benefit

Shock reversal at 7D was higher in steroid groups

Annane et al. JAMA 2009; 301(22):2362-75
Corticosteroids: Observational Data (Con?)

- Observational database studies (current), including from Surviving Sepsis campaign, found higher adjusted mortality in patients with septic shock receiving low-dose steroids
  

- Still no clear guidance on steroid use; current, well-designed RCTs are lacking.

- General consensus - don’t use unless refractory shock, and don’t use high-dose.

- A good review is cited below:
  
  Patel GP, Balk RA AJRCCM 2012; 185(2):133-9
Sepsis: Take Home Points

• High vigilance required to identify sepsis early
• Initiate appropriate infectious workup, antibiotics, and source control
• Target initial resuscitation within 6 hours, with eye to improving surrogate markers of oxygen delivery (MAP, UOP, lactate).
• Bolus isotonic crystalloid while volume-responsive.
• Norepinephrine pressor of first choice; data inconclusive regarding second-line agents. Generally avoid dopamine.
• ‘Low dose’ corticosteroids may be of benefit in refractory septic shock but data are equivocal – more studies needed.