The Argument For
the Role of Plasma Exchange in Severe
Sepsis with Multiple Organ Failure

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Disclosures

• Terumo BCT: Medical Advisor
• Alexion: Medical Advisor

Microbial Invasion

ACCP/SCCM 1992
### SEPSIS

**10-80% mortality**

Avg. 17%

11% for kids <1 year – teens

40% for ages >85 years

Women have lower age-specific incidence and mortality

70% in patients with ≥ 3 failing organs (NEJM 2003)

+ Thrombocytopenia 80% mortality

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#### Table 1. Characteristics of Patients with Sepsis, According to Subperiod.*

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Demographic characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age — yr</td>
<td>57.4±28.9</td>
<td>59.3±22.9</td>
<td>60.8±16.2</td>
<td>60.8±13.7</td>
</tr>
<tr>
<td>Male sex — %</td>
<td>49.6</td>
<td>48.9</td>
<td>46.8</td>
<td>48.0</td>
</tr>
<tr>
<td>Race — no./100,000 population (% of patients)†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>92.1 (81.2)</td>
<td>166.4 (80.3)</td>
<td>167.8 (78.5)</td>
<td>186.3 (76.3)</td>
</tr>
<tr>
<td>Black</td>
<td>163.0 (15.2)</td>
<td>301.7 (16.0)</td>
<td>322.8 (17.2)</td>
<td>378.2 (17.7)</td>
</tr>
<tr>
<td>Other</td>
<td>187.3 (3.6)</td>
<td>298.0 (3.7)</td>
<td>300.6 (4.3)</td>
<td>370.5 (6.0)</td>
</tr>
<tr>
<td>Length of hospital stay — days</td>
<td>17.0±8.5</td>
<td>15.6±6.0</td>
<td>15.3±4.0</td>
<td>11.8±2.6</td>
</tr>
<tr>
<td>Coexisting conditions — % of patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>5.7</td>
<td>7.3</td>
<td>9.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>8.6</td>
<td>9.9</td>
<td>11.6</td>
<td>15.2</td>
</tr>
<tr>
<td>Cancer</td>
<td>17.1</td>
<td>17.9</td>
<td>18.0</td>
<td>14.5</td>
</tr>
<tr>
<td>HIV infection‡</td>
<td>—</td>
<td>1.0</td>
<td>2.1</td>
<td>2.0</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>2.4</td>
<td>2.5</td>
<td>2.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12.2</td>
<td>14.5</td>
<td>16.9</td>
<td>18.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7.0</td>
<td>9.2</td>
<td>11.6</td>
<td>18.6</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>0.6</td>
<td>0.5</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>No. of organs with failure — % of patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>83.2</td>
<td>78.1</td>
<td>74.0</td>
<td>66.4</td>
</tr>
<tr>
<td>1</td>
<td>13.6</td>
<td>17.9</td>
<td>20.1</td>
<td>24.6</td>
</tr>
<tr>
<td>2</td>
<td>2.7</td>
<td>3.5</td>
<td>4.8</td>
<td>7.1</td>
</tr>
<tr>
<td>≥3</td>
<td>0.5</td>
<td>0.5</td>
<td>1.1</td>
<td>1.9</td>
</tr>
</tbody>
</table>

*NEJM 2003*
Thrombocytopenia-associated MSOF

ICU Patient
Severe Sepsis is associated with an Intense Endotheliopathy

- Increased cytokines & inflammatory mediators
- Endothelial activation & apoptosis, loss of vascular integrity
- Enhanced pro-thrombotic milieu
  - Tissue factor expression; release of PAI-1 (decreased fibrinolysis); decreased thrombomodulin; decreased ADAMTS13, increased vWF (ULvWF)
- Microvascular thrombosis, impaired tissue perfusion, organ failure
3 year old boy, Gram negative sepsis
Persistent MODS and Death

ADAMTS13 activity remained low
Presence of Ultra large vWF multimers
Elevated vWF Antigen, INR, and PAI-1 activity

<table>
<thead>
<tr>
<th>Day in MOF</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>%ADAMTS13 Activity</td>
<td>23</td>
<td>12</td>
<td>21</td>
<td>100</td>
</tr>
<tr>
<td>%vWF Antigen</td>
<td>238</td>
<td>338</td>
<td>320</td>
<td>100</td>
</tr>
<tr>
<td>Platelet Ct</td>
<td>52</td>
<td>29</td>
<td>37</td>
<td></td>
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<tr>
<td>INR</td>
<td>1.4</td>
<td>3.5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>PAI-1 activity</td>
<td>12.7</td>
<td>105</td>
<td>105</td>
<td>&lt;23</td>
</tr>
</tbody>
</table>

Nguyen TC. Crit Care Med 2008 Vol. 36, No. 10
Biomarkers of endothelial activation/dysfunction in infectious diseases

Table 1. Summary of biomarkers and cited references, by disease

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiopoietin-1</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>22 and 23</td>
</tr>
<tr>
<td>HUS</td>
<td>26</td>
</tr>
<tr>
<td>Malaria</td>
<td>28–33</td>
</tr>
<tr>
<td>Dengue</td>
<td>34</td>
</tr>
<tr>
<td>Angiopoietin-2</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>7–16, 18–21, and 25</td>
</tr>
<tr>
<td>HUS</td>
<td>26</td>
</tr>
<tr>
<td>Malaria</td>
<td>27–33</td>
</tr>
<tr>
<td>Dengue</td>
<td>34</td>
</tr>
<tr>
<td>Components of the coagulation pathway</td>
<td></td>
</tr>
<tr>
<td>von Willebrand factor</td>
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</tr>
<tr>
<td>Sepsis</td>
<td>10 and 17–39</td>
</tr>
<tr>
<td>HUS</td>
<td>N/A</td>
</tr>
<tr>
<td>Malaria</td>
<td>30, 40, and 41</td>
</tr>
<tr>
<td>Dengue</td>
<td>42</td>
</tr>
<tr>
<td>ADAMTS13</td>
<td></td>
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<tr>
<td>Sepsis</td>
<td>37, 39, 46, and 47</td>
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<tr>
<td>HUS</td>
<td>N/A</td>
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<tr>
<td>Malaria</td>
<td>48 and 49</td>
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<tr>
<td>Dengue</td>
<td>42</td>
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<tr>
<td>Thrombospondin</td>
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<tr>
<td>Sepsis</td>
<td>51–54</td>
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<td>HUS</td>
<td>N/A</td>
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<td>Malaria</td>
<td>55–57</td>
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<tr>
<td>Dengue</td>
<td>58 and 59</td>
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<tr>
<td>Soluble cell-surface adhesion molecules</td>
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<tr>
<td>sICAM-1, sVCAM-1</td>
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<tr>
<td>Sepsis</td>
<td>61–70</td>
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<td>HUS</td>
<td>80 and 81</td>
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<tr>
<td>Malaria</td>
<td>30, 41, and 82–85</td>
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<tr>
<td>Dengue</td>
<td>86 and 87</td>
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<tr>
<td>Mediators of vasomotor tone and permeability</td>
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<tr>
<td>VEGF</td>
<td>8, 22, and 89–93</td>
</tr>
<tr>
<td>Sepsis</td>
<td>96</td>
</tr>
<tr>
<td>HUS</td>
<td>99</td>
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<tr>
<td>Malaria</td>
<td>27 and 96</td>
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<tr>
<td>Dengue</td>
<td>97–100</td>
</tr>
<tr>
<td>sP3</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>90, 91, and 94</td>
</tr>
<tr>
<td>HUS</td>
<td>N/A</td>
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<tr>
<td>Malaria</td>
<td>41 and 96</td>
</tr>
<tr>
<td>Dengue</td>
<td>97</td>
</tr>
</tbody>
</table>

“...the exact targets for blood purification in sepsis are unknown.”

F. Zhou & J. Kellum

Crit Care Med 2013; 41:2209–2220
Hypothesis: How Might Plasma Exchange Therapy Work in Sepsis-Multiple System Organ Failure (MSOF)?

- Plasma exchange removes
  - Inflammatory mediators (endotoxin, cytokines)
  - Fibrinolytic pathway inhibitors (PAI-1)
  - Thrombogenic high molecular weight vWF

- Plasma exchange replenishes
  - ADAMTS 13
  - Physiologic anticoagulants (Protein C, ATIII, TFPI, etc.)

These changes restore vascular homeostasis (anticoagulant/profibrinolytic), abrogate microvascular thrombosis, improve tissue perfusion and reverse organ failure in “ischemic microangiopathy”, thereby improving survival
OLD OUT
NEW IN
PLASMA EXCHANGE MAN
J. Carcillo MD
Cytokines and Plasma Exchange in Primary Septic Shock

Gardlund B, et al. 1995

- **Design:** Observational study of 13 patients (10 meningococcal, 3 pneumococcal sepsis)
  - Septic shock < 24 hrs, no underlying disease
  - “Plasmapheresis” performed in 11

- **Results:**
  - Strong correlation between cytokine/mediator levels and severity of illness (APACHE II) [Endotoxin, TNF-a, IL-1b, IL-6, IL-1ra, PAI-1]
  - Survival 11/13 (10/11 TPE, 1/2 non-TPE)
  - TPE increased plasma clearance of TNF-a
    (t ½ 20.1 hrs → 2.3 hrs)
Plasma Concentrations of Mediators in Response to TPE

Hypothesis: How Might Plasma Exchange Therapy Work in Sepsis-Multiple System Organ Failure (MSOF)?

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  - Inflammatory mediators (endotoxin, cytokines)
  - Fibrinolytic pathway inhibitors (PAI-1)
  - Thrombogenic high molecular weight vWF

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  - ADAMTS 13
  - Physiologic anticoagulants (Protein C, ATIII, TFPI, etc.)

These changes restore vascular homeostasis (anticoagulant/profibrinolytic), abrogate microvascular thrombosis, improve tissue perfusion and reverse organ failure in “ischemic microangiopathy”, thereby improving survival
ADAMTS13 Activity is Decreased in Sepsis/Inflammation


Also reported in:
Bianchi V. Blood 2002;100:710
Nguyen T. Haematologica 2007;92:121
Ono T. Blood, 15 January 2006;107:528
Nguyen T.  
*Haematologica* 2007;92:121
Secondary Deficiency of ADAMTS13 May Play a Role in Renal Injury in Sepsis
### Table 3. Correlation between ADAMTS13 levels and organ injury in patients with sepsis-induced DIC

<table>
<thead>
<tr>
<th></th>
<th>ADAMTS13 activity less than 20%, n = 51</th>
<th>ADAMTS13 activity greater than 20%, n = 52</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.81 ± 1.70</td>
<td>0.96 ± 0.76</td>
<td>&lt; .01*</td>
</tr>
<tr>
<td>AST, IU/L</td>
<td>106 ± 128</td>
<td>182 ± 290</td>
<td>NS</td>
</tr>
<tr>
<td>ALT, IU/L</td>
<td>72 ± 109</td>
<td>122 ± 160</td>
<td>NS</td>
</tr>
<tr>
<td>Bilirubin, mg/dL</td>
<td>2.70 ± 3.13</td>
<td>2.20 ± 2.53</td>
<td>NS</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>2.3 ± 0.4</td>
<td>2.9 ± 0.7</td>
<td>&lt; .05*</td>
</tr>
<tr>
<td>CRP, mg/dL</td>
<td>13.50 ± 10.51</td>
<td>6.90 ± 8.61</td>
<td>&lt; .01*</td>
</tr>
</tbody>
</table>

**Organ injury, no. (%)**

<p>| | | | |</p>
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<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Renal injury</td>
<td>21 (41.2)</td>
<td>8 (15.4)</td>
<td>&lt; .05†</td>
</tr>
<tr>
<td>Liver injury</td>
<td>40 (78.4)</td>
<td>38 (73.1)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Table 4. Correlation between presence of unusually large multimers of VWF and serum creatinine levels of patients with sepsis-induced DIC and ADAMTS13 activity levels lower than 20%

<table>
<thead>
<tr>
<th></th>
<th>Presence, n = 26</th>
<th>Absence, n = 25</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, mg/dL</td>
<td>2.39 ± 2.24</td>
<td>1.34 ± 1.35</td>
<td>&lt; .05+</td>
</tr>
<tr>
<td>ADAMTS13 activity, %</td>
<td>6.6 ± 6.8</td>
<td>8.9 ± 6.0</td>
<td>NS</td>
</tr>
</tbody>
</table>
### Plasma Exchange or Filtration in Sepsis/MODS (I/II)

<table>
<thead>
<tr>
<th>STUDY</th>
<th>N</th>
<th>TRIAL DESIGN</th>
<th>PEX TECHNIQUE</th>
<th>PLASMA PROCESSED</th>
<th>PEX DURATION</th>
<th>SURVIVAL (PEX or PF v Control)</th>
<th>COMMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barzilay, 1989</td>
<td>31</td>
<td>Case series, comparison of 4 groups</td>
<td>CAVHP/D (n=11) v CAVH/D (n=6) v CAVH (n=14) v Control</td>
<td>4580 ml/day</td>
<td>NA</td>
<td>CAVHP/D 64% CAVH/D 50% CAVH 29% Control 13%</td>
<td>Waited 24 hrs and no improvement before ECT; Improved survival w/ ECT</td>
</tr>
<tr>
<td>Churchwell, 1995</td>
<td>8</td>
<td>Case series</td>
<td>PEX (6) or WBE (2)</td>
<td>1 – 1.5 PV or 2 WBV</td>
<td>1 d</td>
<td>7/8 (87.5%)</td>
<td>Pediatric meningococcal primary sepsis/DIC</td>
</tr>
<tr>
<td>Gardlund, 1995</td>
<td>13</td>
<td>Case series</td>
<td>PEX in 11</td>
<td>NA</td>
<td>NA</td>
<td>10/11 PEX v.1/2 Control</td>
<td>10 meningococcal, 3 pneumococcal primary sepsis</td>
</tr>
<tr>
<td>Stegmayer, 1995</td>
<td>27</td>
<td>Case series</td>
<td>Centrifugal PEX</td>
<td>3 L</td>
<td>1-10 (&quot;until DIC reversed&quot;)</td>
<td>22/27 (81%) v.20% expected</td>
<td>MSOF/Primary &amp; secondary sepsis; 5 deaths - 3 due to undrained abscess</td>
</tr>
</tbody>
</table>
# Plasma Exchange or Filtration in Sepsis/MODS (II/II)

<table>
<thead>
<tr>
<th>STUDY</th>
<th>N</th>
<th>TRIAL DESIGN</th>
<th>PEX TECHNIQUE</th>
<th>PLASMA PROCESSED</th>
<th>PEX DURATION</th>
<th>SURVIVAL (PEX or PF v Control)</th>
<th>COMMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reeves, 1999</td>
<td>30</td>
<td>RCT</td>
<td>Continuous Plasmafiltration</td>
<td>5 PV</td>
<td>34 hrs</td>
<td>57% v 50% P=NS</td>
<td></td>
</tr>
<tr>
<td>Schmidt, 2000</td>
<td>43</td>
<td>Historical Control</td>
<td>Plasmafiltration + CVVH</td>
<td>2 U FFP/10 Kg</td>
<td>6.4 d</td>
<td>45.8% v 42% P=NS</td>
<td>Sig. Improved survival in 1 &amp; 2 organ failure subsets</td>
</tr>
<tr>
<td>Hjorth, 2000</td>
<td>17</td>
<td>Case series, survival compared to expected mortality based on APACHE II score</td>
<td>Intermittent ultracentrifugation</td>
<td>Albumin stored plasma; 1-1.5 PV</td>
<td>Variable: 1 - 2 d</td>
<td>14/17 (82%) v 38% expected</td>
<td>Early inception of Plasma Rx</td>
</tr>
<tr>
<td>Busund, 2002</td>
<td>106</td>
<td>RCT</td>
<td>Continuous plasmapheresis</td>
<td>Albumin/FFP (1/1), 30-40 ml/kg</td>
<td>1-2 d depending on response</td>
<td>36/54 (66.7%) v 24/52 (46.2%)</td>
<td>PF initiated w/i 6 hrs; mean APACHE scores high – 56.4 &amp; 53.5</td>
</tr>
<tr>
<td>Stegmayer, 2003</td>
<td>76</td>
<td>Retrospective case series</td>
<td>Centrifugation</td>
<td>3 L</td>
<td>Median 2 (1-14)</td>
<td>82% v. 20% expected</td>
<td>Avg &gt; 4 failed organs</td>
</tr>
<tr>
<td>Darmon, 2006</td>
<td>36</td>
<td>Prospective non-randomized cohort; PI crossover to PE</td>
<td>Intensive PI 22 Centrifugation PE 15</td>
<td>PI:25 ml/kg daily; PE 60 ml/kg</td>
<td>Daily until CR or death</td>
<td>80.6% (all deaths in PI group)</td>
<td>Faster organ failure recovery with PE</td>
</tr>
</tbody>
</table>

Collectively, 8 of the 10 studies noted improved survival.
Brief Review Results of 3 RCTs Performed in Adults and Children
Continuous plasma filtration with **partial** plasma exchange was not effective

- Intensive short-term (36 h) plasmafiltration designed to remove inflammatory/cytokine biomarkers
- Partial FFP replacement (1 to 4 plasma/protein-electrolyte solution)
- Outcome 14 day mortality

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**Table:**

<table>
<thead>
<tr>
<th></th>
<th>Control Patients</th>
<th>Plasmafiltration Patients</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>16</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Male/female</td>
<td>8/8</td>
<td>10/4</td>
<td>NS</td>
</tr>
<tr>
<td>Adult/child</td>
<td>13/3</td>
<td>9/5</td>
<td>NS</td>
</tr>
<tr>
<td>Age (yrs), median (range)</td>
<td>67 (1.5–78)</td>
<td>36.5 (1.3–79)</td>
<td>.08</td>
</tr>
<tr>
<td>Weight (kg), median (range)</td>
<td>72.5 (10.7–120)</td>
<td>72.5 (10–90)</td>
<td>NS</td>
</tr>
<tr>
<td>Septic shock, n (%)</td>
<td>11 (69)</td>
<td>13 (93)</td>
<td>NS</td>
</tr>
<tr>
<td>Refractory shock, n (%)</td>
<td>6 (38)</td>
<td>3 (21)</td>
<td>NS</td>
</tr>
<tr>
<td>Bacteremia, n (%)</td>
<td>5 (31)</td>
<td>6 (43)</td>
<td>NS</td>
</tr>
<tr>
<td>Immunocompromise, n (%)</td>
<td>2 (13)</td>
<td>4 (29)</td>
<td>NS</td>
</tr>
<tr>
<td>APACHE II score (adults), mean (SD)</td>
<td>26.2 (8.9)</td>
<td>24.2 (6.1)</td>
<td>NS</td>
</tr>
<tr>
<td>PRISM score (children), mean (SD)</td>
<td>26.3 (10.1)</td>
<td>26.8 (6.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Calculated risk of death</td>
<td>68%</td>
<td>64%</td>
<td>NS</td>
</tr>
<tr>
<td>Organ failures per patient, mean (SD)</td>
<td>2.94 (0.55)</td>
<td>2.57 (0.94)</td>
<td>.37</td>
</tr>
<tr>
<td>14-day survival, n (%)</td>
<td>8 of 16 (50)</td>
<td>8 of 14 (57)</td>
<td>.73</td>
</tr>
</tbody>
</table>

**Footnote:** APACHE, Acute Physiology and Chronic Health Evaluation; PRISM, Pediatric Risk of Mortality; NS, not significant.

**Reference:** Reeves CCM 1999 24:2096-2104
Plasmapheresis in Severe Sepsis & Septic Shock: A Prospective, Randomized, Controlled Trial

*Busund R, et al 2002*

**Design:**
- Single center RCT, 106 pts, plasmaphaser (1800 ml, 1 or 2 days) vs. standard care (Heparin AC used)
- Sepsis: Abd>Lung>GU     Surg procedures: 65-70%
- Imbalance in Treatment grps: Younger age in PF (41 v 48 yrs; More abd sepsis in PF (33 v 16 pts)

**Results:**
- APACHE score at 24 hr decreased by 20% in PF grp.
- Survival at 28 days: 36/54 (66.7%) PF v 18/52 (46.2%) Control (p=0.05), p= 0.07 after correction for baseline imbalances
- Subgrp analysis showed survival benefit only in abd sepsis
  - Abd 11/33 (33.3%) v 11/16 (68.5%) p 0.03
  - Other 7/21 (33.3%) v 17/36 (47.2%) p 0.40
Plasmapheresis in Severe Sepsis & Septic Shock: A Prospective, Randomized, Controlled Trial

Busund R, et al 2002

- RCT 106 consecutive ICU patients
- 28-day mortality

<table>
<thead>
<tr>
<th></th>
<th>PEX (n=54)</th>
<th>Control (n=52)</th>
<th>p</th>
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<tbody>
<tr>
<td></td>
<td>18 (33.3%)</td>
<td>28 (53.8%)</td>
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<tr>
<td>ARDS</td>
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<tr>
<td>Bleeding</td>
<td>2</td>
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RCT of Plasma Exchange in Pediatric Patients with Thrombocytopenia Associated MOF

- Design: single center RCT in a pediatric ICU

- Inclusion criteria: children with platelet count < 100K and ≥ 3 failed organs for 24 h (a condition associated with 80% mortality in CHP PICU regardless of diagnostic category)

- Protocol: treatment within 30h of meeting criteria with plasma exchange for two 7-day cycles of 1.5 volume x 1 d followed by 1 volume x 6d, or until the resolution to < 3 organ failure for 48h

Nguyen TC. Crit Care Med 2008 Vol. 36, No. 10
Pediatric Logistic Organ Dysfunction Score

PELOD decreased from 25.0 ± 2.0 to 0.8 ± 0.6 with plasma exchange at 28 d

PELOD increased from 25.4 ± 2.3 to 73.6 ± 18.4 without plasma exchange at 28 d

\( p < 0.05 \)

Figure 3. Pediatric Logistic Organ Dysfunction Score, Mean with standard error for patients who received plasma exchange therapy (N = 5) and who did not receive plasma exchange therapy (N = 5) for each day x 28 days.
28-Day Survival

- Plasma exchange: 5/5 patients survived
- No plasma exchange: 1/5 patients survived

\( p < 0.05, \text{ Fisher exact test} \)
Plasma Exchange Replenishes ADAMTS13 Activity

ADAMTS13 Activity and PEx vs No PEx

Plasma Exchange
n = 4

No Plasma Exchange
n = 4

2F ANOVA  p<0.05
Outcomes of Previously Healthy Pediatric Patients With Fulminant Sepsis-Induced Multisystem Organ Failure Receiving Therapeutic Plasma Exchange

Fig. 1. Changes in organ failure index with therapeutic plasma exchange. All 11 patients had three or more organ dysfunctions (organ failure index >3) at the initial TPE. Ten of the 11 patients improved with TPE indicated by reduced organ failure index over time. One patient died on the day of his first TPE due to his underlying disease, indicated by the filled square at day one with six organ failed (organ failure index = 6).

Qu et al
Conclusions

• The pathophysiologic features of sepsis induced-MSOF provide a rational basis for consideration of plasma exchange therapy

• Uncontrolled and controlled clinical trials suggest that plasma exchange improves organ failure & outcome
  – “We found that hemoperfusion (RR, 0.63 [95% CI, .50-0.80]; p<0.001; 10 trials, n=557; or plasma exchange (RR, 0.63 [95%CI, 0.42-0.96]; p=0.03, 2 trials, n=128, decreased mortality in sepsis.” *

• A well-designed RCT is needed!

*F. Zhou & J. Kellum
Crit Care Med 2013; 41:2209–2220
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