Table of contents

SEPSIS
First successful combination of ECMO with cytokine removal therapy in cardiogenic septic shock: A case report 04 - 05
Use of a novel hemoadsorption device for cytokine removal as adjuvant therapy in a patient with septic shock with multi-organ dysfunction: A case study 06 - 07
Septic shock secondary to β-hemolytic streptococcus-induced necrotizing fasciitis treated with a novel cytokine adsorption therapy 08 - 09
Effects of a novel cytokine haemoadsorption system on inflammatory response in septic shock after cephalic pancreatectomy – a case report 10 - 11
Pattern of cytokine removal using an adsorption column CytoSorb during severe Candida albicans induced septic shock 12 - 13
Improvement of hemodynamic and inflammatory parameters by combined hemoadsorption and hemodiafiltration in septic shock: a case report 14 - 15
Hemoadsorption using CytoSorb beads (CytoSorbents) in a cirrhotic patient with septic multiorgan failure 16 - 17
Can cytokine adsorber treatment affect antibiotic concentrations? – A case report 18 - 19

CARDIAC SURGERY
Systemic Inflammatory Response Syndrome in der Herzchirurgie: Neue Therapiemöglichkeiten durch den Einsatz eines Cytokin-Adsorbers während EKZ? [Systemic Inflammatory Response Syndrome in Cardiac Surgery: New possibilities for treatment through the use of a cytokine adsorber during ECC?] 20 - 21

LIVER
First description of SPAAD combined with cytokine adsorption in fulminant liver failure and hemophagocytic syndrome due to generalized HSV-1 infection. 22 - 23
First use of CytoSorb with pruritus – a case report 24 - 25

MYOGLOBINEMIA
CytoSorb™ in a patient with legionella-pneumonia associated rhabdomyolysis 26 - 27
First successful combination of ECMO with cytokine removal therapy in cardiogenic septic shock: A case report

Bruenger F, Kizner L, Weile J, Morshuis M, Gummert JF.
Clinic for Thoracic and Cardiovascular Surgery, Heart and Diabetes Center (HDZ) North Rhine-Westphalia, Bad Oeynhausen, Germany.
Int J Artif Organs. 2015 Feb 3;0(0):0

Summary
This case study reports on a 39-year-old patient presenting at a hospital with fulminant ARDS and cardiogenic septic shock. After implantation of a veno-arterial ECMO for circulatory support the patient developed acute renal failure making initiation of CVVH necessary. Due to a complete cardiac arrest in both ventricles, a left ventricular assist device (LVAD) in combination with right ECMO (rECMO) was implanted with manifest septic conditions. In the post-operative course his condition deteriorated drastically and a CytoSorb hemoadsorption device was therefore installed in the CVVH circuit resulting in a decrease of IL-6, procalcitonin, and C-reactive protein concomitant with significantly reduced vasopressor support. No adverse device-related side effects were documented during or after the treatment sessions. This is the first clinical case report of a highly septic patient treated with the combined use of LVAD, rECMO, CVVH, and CytoSorb. The combination was practical, technically feasible, and beneficial for the patient and might represent a reasonable approach to improve survival in patients with multiple organ dysfunction necessitating several organ supportive techniques.

Case presentation
- A 39 year old male with a history of dilated idiopathic cardiomyopathy (LV-EF 20%) was scheduled for regular ambulatory check up in the hospital from 2006 to 2012.
- Medical history included secondary pulmonary hypertension, mitral valve insufficiency grade II - III, chronic renal failure, hypothyroidism and nicotine- and anabolic abuse.
- A dual-chamber implantable cardioverter-defibrillator (ICD) was implanted already in 2006 and the patient was planned for heart transplant as from January 2007.
- In early January 2013 the patient had been at the HDZ Bad Oeynhausen for a 3-day routine check and presented one week later at an external hospital with complaints of dyspnea.

Treatment
- CytoSorb was installed into the CVVH circuit (AK200®, Gambro)
- Sessions were run on the first day as well as on day 2 and 4 after the operation over periods of 18 to 21 h each
- Blood flow rates were between 155 ml/min and 240 ml/min
- Anticoagulation was achieved using heparin, targeting a partial thromboplastin time (PTT) of 60 to 80, monitored every 4 h

- After a short period of primary non-invasive ventilation the patient drastically deteriorated, was intubated and further ventilated mechanically
- Subsequent chest X-ray confirmed massive bilateral infiltrates
- Within several hours the patient developed a fulminant ARDS and cardiogenic septic shock
- Implantation of a veno-arterial ECMO on site and transport back to HDZ
- Patient developed an acute renal failure on top of his chronic renal insufficiency making CVVH necessary while the need for vasopressors increased drastically
- Due to a global cardiac akinesia and high risk of intracardial thrombosis, decision was made for implantation of a left ventricular assist device (LVAD) in combination with a right ECMO (rECMO) in exchange for the veno-ECMO
- Operation was carried out despite full-blown sepsis with poor post-operative clinical condition
- As last resort decision, a CytoSorb hemoadsorption device was installed into the CVVH circuit

Results
- With start of the CytoSorb therapy in combination with ECMO, inflammatory markers IL-6, procalcitonin, and CRP markedly decreased during treatment and continued to decrease further in the following days
- Also vasopressors could be reduced significantly and were stopped during (for norepinephrine and vasopressin) and shortly after (for epinephrine) the last treatment

Measurements
- Inflammatory markers (IL-6, CRP, PCT) as well as need for vasoactive substances (norepinephrine, epinephrine, vasopressin) were determined

Patient Follow-up
- The rECMO was explanted 19 days and ventilation stopped 27 days after the treatment.
- For regeneration of the kidney the patient received Linezolid, Meropenem, Moxifloxacin, Voriconazol and Acyclovir as boluses with no adaptation of dose at any time.
- The patient is still listed for transplantation.

CONCLUSIONS
- This is the first clinical case report in a patient treated with LVAD, rECMO, CVVH, and CytoSorb in a combined fashion.
- The combination was practical, technically feasible and highly beneficial for the patient.
- After commencement of CytoSorb treatment, the patient’s inflammatory status improved and vasopressor support could be reduced and tapered out.
- No adverse or any device-related side effects were documented during or after the treatment.
- Taken together, CytoSorb could be simply used in combination with ECMO, resulting in considerable benefits for the patient, thus representing a reasonable approach to improve survival in patients with several organ dysfunctions and the need for multiple organ supportive techniques.
Use of a novel hemoadsorption device for cytokine removal as adjuvant therapy in a patient with septic shock with multi-organ dysfunction: A case study

Basu R, Pathak S, Goyal J, Chaudhry R, Goel RB, Banwal A
Department of Critical Care and Artemis Health Institute, Gurgaon, Haryana, India
Indian J Crit Care Med 2014;18:822-4

Summary
This case study reports on a 36-year-old female diagnosed to have septic shock (urosepsis) with multi-organ dysfunction (ARDS, AKI, arterial hypotension) and a low perfusion state. SOFA score was 15, MODS score 10 and APACHE II score 30. CytoSorb was added along with CRRT and three consecutive treatments were run in the following three days. After initiation of therapy the patient improved hemodynamically. During the further course urine output increased with improvement in ventilator parameters. SOFA score at the end of treatment was 4, MODS score was 5 and APACHE II score was 7. No adverse events occurred and laboratory parameters before and after CytoSorb therapy were within a normal range. This case report suggests that CytoSorb therapy in septic shock patients with multi-organ failure might be an option as rescue therapy.

Case presentation
• 36-year-old female was admitted to hospital with complaints of general body ache for the last 3 days, malaise and breathing difficulty for the last 2 days before admission
• The patient had a history of diabetes mellitus type II, obstructive sleep apnea, hypertension, hypothyroidism and morbid obesity
• On examination, patient had tachycardia, tachypnea and leukocytosis
• Patient was suspected to have an urinary tract infection
• Immediate initiation of antibiotic, fluid resuscitation and mechanical ventilation
• Patient continued to deteriorate with decreasing urine output
• SOFA score was 15, MODS score 10 and APACHE II score 30
• Diagnosis of septic shock (urosepsis) and MODS (ARDS, AKI, arterial hypotension) with initiation of renal replacement therapy (CVVH) in combination with CytoSorb

Treatment
• Patient received 3 consecutive CVVH sessions with CytoSorb in the following 3 days
• Flow rate was maintained at 250 ml/min
• Patient was anticoagulated with heparin to a target aPPT of 30–40 s

Measurements
• Need for vaspressors
• Hemoglobin, Hematocrit, Leucocytes, Platelets, aPTT, INR, Lactate, Total protein, FBS/RBS
• Sodium, Potassium, Calcium
• Creatinine, Urea
• SGPT, SGOT

Results
• Quick improvement of hemodynamics during CytoSorb therapy
• SOFA, MODS and APACHE II scores decreased significantly
• Antibiotic therapy was conducted with Meropenem 3x500mg p.d., without dosing adaption during CytoSorb therapy

Vasopressor schedule before and after CytoSorb therapy

<table>
<thead>
<tr>
<th>Vasopressor</th>
<th>Dose before CytoSorb therapy</th>
<th>Dose after CytoSorb therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine (µg/kg/min)</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Norepinephrine (µg/kg/min)</td>
<td>0.1</td>
<td>1.0</td>
</tr>
<tr>
<td>Dopamine (µg/kg/min)</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Vasopressin (IU/min)</td>
<td>0.06</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Laboratory parameters before and after treatment with CytoSorb

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>9.8</td>
<td>8.1</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>31.9</td>
<td>25.7</td>
</tr>
<tr>
<td>Leucocytes (mm³)</td>
<td>52.1</td>
<td>9.6</td>
</tr>
<tr>
<td>Platelets (mm³)</td>
<td>359</td>
<td>100</td>
</tr>
<tr>
<td>aPTT (s)</td>
<td>29.3</td>
<td>32.3</td>
</tr>
<tr>
<td>INR</td>
<td>1.24</td>
<td>1.2</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>4.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>2.33</td>
<td>1.58</td>
</tr>
<tr>
<td>Urea (mg/dL)</td>
<td>19.1</td>
<td>21.2</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>128.5</td>
<td>139.9</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>4.5</td>
<td>3.9</td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>1.00</td>
<td>1.11</td>
</tr>
<tr>
<td>Total protein (g/dL)</td>
<td>8.4</td>
<td>5.5</td>
</tr>
<tr>
<td>FBS/RBS (mg/dL)</td>
<td>96</td>
<td>145</td>
</tr>
<tr>
<td>SGPT (IU/L)</td>
<td>849</td>
<td>420.1</td>
</tr>
<tr>
<td>SGOT (IU/L)</td>
<td>769.6</td>
<td>269.1</td>
</tr>
</tbody>
</table>

aPTT: Activated partial thromboplastin time; INR, International normalized ratio; FBS/RBS: Fasting blood sugar/Random blood sugar; SGPT: Serum glutamic pyruvic transaminase; SGOT: Serum glutamic oxaloacetic transaminase

CONCLUSIONS
• This study reports on a successful outcome in a case of septic shock and MOF where CytoSorb was used as an adjuvant therapy
• CytoSorb in combination with CVVH helped to quickly stabilize hemodynamics
• With a high predicted mortality (~70-80%) the treatment managed to reduce SOFA score, MODS score and APACHE II score significantly
• Therapy was well tolerated with no adverse effects
• CytoSorb therapy in septic shock patients with MOF might be an option as rescue therapy
Septic shock secondary to β-hemolytic streptococcus-induced necrotizing fasciitis treated with a novel cytokine adsorption therapy

Hetz H, Berger R, Recknagel P, Steltzer H. Department of Anesthesiology and Intensive Care Medicine, AUVA Meidling Emergency Hospital, Vienna, Austria. Int J Artif Organs. 2014 May;37(5):422-6

Summary
This case study reports on a 60-year-old female who was admitted to hospital due to a forearm fracture. After surgical wound care by osteosynthesis the patient developed surgical wound infection progressing to necrotizing fasciitis with additional proven infection from β-hemolytic streptococcus. The patient went into septic shock exhibiting a full picture of a MODS. Therefore, the patient was treated with CytoSorb therapy over a period of four days, resulting in a significant reduction of IL-6 and an overall improvement of the patient's condition. In this case, CytoSorb seems to be an interesting and safe extracorporeal therapy to stabilize and bridge septic patients to surgery or recovery.

Case presentation
• 60-year-old female with no pre-existing diseases except hypertension and hypothyroidism
• Initial indication: radius fracture of the right forearm after an accident
• Immediate wound care by application of a plaster splint
• Operative osteosynthesis on the same day
• Swelling of the forearm expanding to the upper arm
• Collapse of the patient
• Transfer to ICU with septic shock
• Initiation of antibiotics and fluid therapy
• Requirement for vasopressors
• Development of oliguric acute renal failure and ARDS
• Initiation of CVVH and mechanical ventilation
• APACHE II score of 19 and a SOFA of 8
• Proven infection with β-hemolytic streptococci

Treatment
• Initiation of three CytoSorb hemoperfusion sessions on the first day as well as on day 3 and 4 after ICU admission in combination with standard continuous hemodialysis-CVVHD
• Treatment time: 36 hours in the first and 17-18 hours in the two following procedures
• Blood flow rates: 100 ml/min
• Dialysate flow: 2000-2150 ml/h
• Anticoagulation: regional citrate within the external blood circuit

Measurements
• Leucocytes, platelets
• Need for vasopressors
• IL-6
• Creatinine, cumulative urine output

Results
• CytoSorb effectively and significantly reduced IL-6 levels
• After the first session, IL-6 plasma concentration decreased from 70000 to 39100 pg/ml (-44.3%). The final IL-6 level after the third session was 66 pg/ml
• CytoSorb treatment was paralleled by a significant decrease of vasopressor need
• Antibiotic therapy was conducted with Ampicillin and Fosfomycin, with no reported adaption of dosage during CytoSorb therapy
• The patient could be successfully stabilized until surgical control of the infectious source was achieved

Plasma concentrations of IL-6 and creatinine and the need of noradrenalin during the course of the three treatment sessions until discharge from the ICU

Markers of inflammation, organ dysfunction, and need for vasopressors

<table>
<thead>
<tr>
<th>Before first CytoSorb treatment</th>
<th>After first CytoSorb treatment</th>
<th>After last CytoSorb treatment</th>
<th>At discharge from ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucocytes (x10^3 µl)</td>
<td>1850</td>
<td>13810</td>
<td>29000</td>
</tr>
<tr>
<td>Platelets (x10^3 µl)</td>
<td>194000</td>
<td>74000</td>
<td>49000</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>70000</td>
<td>39100</td>
<td>66</td>
</tr>
<tr>
<td>Cumulative urine output (ml/day)</td>
<td>200</td>
<td>410</td>
<td>410</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>2.07</td>
<td>1.88</td>
<td>1.37</td>
</tr>
<tr>
<td>Need for Noradrenalin (µg/kg/min)</td>
<td>1.18</td>
<td>0.24</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Post-treatment period and Follow-up:
• After the third CytoSorb treatment, hemofiltration was continued without CytoSorb as the need for vasopressors was significantly decreased and IL-6 levels were back in a normal range
• Despite considerable reduction of IL-6 levels, enucleation (amputation) was inevitable
• The general condition improved and the patient could be extubated 4 days after the third CytoSorb treatment

CONCLUSIONS
• Treatment was safe and well-tolerated, without adverse events
• CytoSorb significantly reduced IL-6, a predictor of mortality in sepsis and surrogate for cytokine storm
• The patient could be successfully stabilized until surgical infectious source control was performed and infected
• CytoSorb in combination with CVVHD and regional citrate anticoagulation could be run continuously for up to 36 h
• Hemoadsoption using CytoSorb seems to represent a promising approach for an effective and safe treatment of severe sepsis and septic shock.
Effects of a novel cytokine haemoadsorption system on inflammatory response in septic shock after cephalic pancreatectomy – a case report

Tomescu D, Dima SO, Tănăsescu S, Tănase A, Popescu M
Department of Anaesthesiology and Critical Care III, Fundeni Clinical Institute, Bucharest, Romania
Romanian Journal of Anaesthesia and Intensive Care 2014;21(2):134-138

Summary
This case study reports on a 50-year-old man with postoperative septic shock after undergoing cephalic pancreatectomy for a pancreatic cystic tumor. In total, two consecutive CVVH sessions with CytoSorb were performed over a period of 64 hours. The clinical effects associated with CytoSorb resulted in a rebalancing of cytokine levels and translated into a more stable haemodynamic profile with a stable cardiac output and normalization of systemic vascular resistance index and decreased vasopressor requirements. The technology was simple to use and could be easily added to conventional CVVH machines. The therapy was well tolerated with no adverse effects. The timing of CytoSorb use, whether early (after onset of SIRS) or late (after onset of organ dysfunction), has still to be established.

Case presentation
- 50 year old man was admitted to the ICU on the 5th postoperative day with hypotension, neurologic dysfunction and lactic acidosis after undergoing cephalic pancreatectomy for a pancreatic cystic tumor
- Laboratory test results showed an elevated white blood count (WBC) 13560/μl, C-reactive protein (CRP) of 75.5 mg/l, procalcitonin (PCT) 0.529 ng/ml, elevated bilirubin level of 7.6 mg/dl and lactic acidosis (pH = 7.12, base excess – 8 mmol/L and lactate 3.5 mmol/l)
- Treatment was initiated with fluid resuscitation and broad spectrum antibiotics
- The clinical state gradually improved over the next four days except for the neurologic deficit
- On day 5 of ICU stay an acute inflammatory response was noted
- Deterioration of neurologic status and development of ARDS
- Microbiological examination of the peritoneal fluid sample showed infection with Candida albicans and Klebsiella pneumoniae

Results
- Improvement in hemodynamics comparing parameters before the 1st and after the 2nd session:
  - stable cardiac output (4.7 l/min/m²)
  - increase in systemic vascular resistance index from 890 to 1040 dyn/s/cm⁻⁵*m²
  - decrease in vasopressor dose from 890 to 1040 dyn/s/cm⁻⁵*m²
  - Decrease of inflammatory markers comparing levels before the 1st and after the 2nd session:
    - CRP from 400 mg/L to 283 mg/l,
    - PCT from 100 ng/mL to 46 ng/ml
    - WBC count decreased from 16630/μl to 10310/μl

Measurements
- Parameters were determined before and after each CytoSorb treatment
- Cytokines and chemokines, PCT, CRP, white blood count
- Hemodynamic parameters (SVRI, cardiac output)

Treatment
-CytoSorb was applied in combination with CVVH over a period of 64 hours (24 hours each)
- Anticoagulation was achieved using heparin
- Measurements
  - Reduction in WBC correlated with a marked reduction in (IFNγ)
  - Increase of anti-inflammatory cytokine levels, especially IL-10 and IL-8
  - Decrease in pro-inflammatory cytokines especially IL-1β and TNFα
  - marked reduction in MCP-1 and GM-CSF

Conclusions
- Rebalance in cytokine levels comparing levels before and after each session:
  - decrease in pro-inflammatory cytokines especially IL-1β and TNFα
  - increase of anti-inflammatory cytokine levels, especially IL-10 and IL-8
- marked reduction in IFNγ
- reduction in WBC correlated with a marked decrease in both MCP-1 and GM-CSF
- Antimicrobial therapy was conducted with Meropenem, Fluconazole and Colistin, with no reported adaption in dosage during CytoSorb therapy

Post-treatment period and Follow-up:
- Decision to control the septic source was made, but the patient died 24 hours after the second CytoSorb was dismounted due to cardiac arrhythmia (ventricular fibrillation) unresponsive to resuscitation manoeuvres

Cytokine values during the use of CytoSorb

<table>
<thead>
<tr>
<th>GM-CSF</th>
<th>IFNγ</th>
<th>IL-1β</th>
<th>IL-2</th>
<th>IL-4</th>
<th>IL-6</th>
<th>IL-10</th>
<th>MCP-1</th>
<th>TNFα</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
<td>T4</td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
<td>T4</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>0.00</td>
<td>200.00</td>
<td>400.00</td>
<td>600.00</td>
<td>800.00</td>
<td>1000.00</td>
<td>1200.00</td>
<td>1400.00</td>
</tr>
<tr>
<td>PCT (ng/ml)</td>
<td>0.00</td>
<td>200.00</td>
<td>400.00</td>
<td>600.00</td>
<td>800.00</td>
<td>1000.00</td>
<td>1200.00</td>
<td>1400.00</td>
</tr>
</tbody>
</table>

The use of CytoSorb was associated with a more stable haemodynamic profile with near normal values for systemic vascular resistance

Dynamics of sepsis markers C reactive protein (CRP) and procalcitonin (PCT)

- The use of CytoSorb in combination with CVVH managed to re-establish a balance between pro- and anti-inflammatory cytokines that lead to a stable hemodynamic profile
- The technology was simple to use and could be added to conventional CVVH machines
- Therapy was well tolerated with no adverse effects
Pattern of cytokine removal using an adsorption column CytoSorb during severe Candida albicans induced septic shock

Bracht H, Schneider EM, Wöff M, Hohmann H, Georgieff M, Barth E
Department of Anesthesiology, University Hospital Ulm, Germany
Infection (2013) 41 (Suppl 1):S1–S90; Abstract No. 133

Summary
This case study reports on a 46 old female with hypodynamic septic shock and documented candidemia infection. CRRT was started in combination with CytoSorb therapy. Within 24 h of hemoadsorption, vasopressor and inotropic support could be withdrawn. Several inflammatory mediators (e.g. IL-6, IL-8, TNFα) could be reduced significantly. Interestingly, the authors also found an almost perfect immunological reconstitution of a variety of immune parameters including HLA-DR. This is the first successful use of CytoSorb during candida sepsis.

Case presentation
• A 46 old female was admitted to ICU with hypodynamic septic shock and documented candidemia after infection of an i.v. port
• On admission the patient was highly vasopressor and inotrope dependent and developed multiple organ failure
• Hemodynamic situation was desperate with accompanying low output syndrome

Treatment
• CRRT was started and additional hemoadsorption with CytoSorb was initiated for 24 hours

Measurements
• Levels of IL-1β, IL-6, sCD25, TNFα, Plasma Ferritin and LBP were measured before and after filtration

Results
• After 24 hours of hemoadsorption, norepinephrine requirements decreased dramatically from 0.7 to 0.2 µg/kg/min and inotropic support with Levosimendan could be withdrawn
• The patient showed an improvement in hemodynamic parameters with a decreasing heart rate, stabilized MAP and improved cardiac output
• Serum lactate concentration decreased from 15 to 3.4 µmol/l.
• IL-18 concentrations remained unchanged, but all other proinflammatory cytokines as well as the acute phase proteins TNFα and Ferritin decreased dramatically
• Lipopolysaccharide binding protein (LBP) was not elevated before and after filtration
• Metabolic parameters improved by elevation in base excess
• Flow cytometric analysis revealed an almost perfect immunological reconstitution of a variety of immune parameters including HLA-DR

Hemodynamic, metabolic and gas exchange variables before and after hemoadsorption

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>After Hemoadsorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>133</td>
<td>100</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>62</td>
<td>81</td>
</tr>
<tr>
<td>Cardiac Index (L/min/m²)</td>
<td>1.9</td>
<td>2.9</td>
</tr>
<tr>
<td>Stroke volume variation (%)</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Core Body Temperature (°C)</td>
<td>36.2</td>
<td>36.3</td>
</tr>
<tr>
<td>Base Excess (mmol/l)</td>
<td>-14.5</td>
<td>6.0</td>
</tr>
<tr>
<td>paO₂ (mmHg)</td>
<td>125</td>
<td>128</td>
</tr>
<tr>
<td>paCO₂ (mmHg)</td>
<td>27.1</td>
<td>38.2</td>
</tr>
</tbody>
</table>

Levels of IL-18, IL-6, sCD25, TNFα, Plasma Ferritin and LBP before and after hemoadsorption.

CONCLUSIONS
• First successful demonstration of CytoSorb use during candida sepsis
• Whether the improvement in the hemodynamic situation was also influenced by simultaneously initiated inotropic support cannot be ruled out
• Accompanying gram-negative or -positive infection could also have contributed to the sustained effects
• Further studies need to elaborate indication criteria for hemoadsorption and the differences between bacterial- and fungal-induced severe sepsis and septic shock
Improvement of hemodynamic and inflammatory parameters by combined hemoadsorption and hemodiafiltration in septic shock: a case report.

Mitzner SR, Gloger M, Henschel J, Koball S
Department of Medicine, Division of Nephrology, University of Rostock, Rostock, Germany

Summary
This case study reports on an 80-year-old male diagnosed of having pneumogenic septic shock. The patient was in clinical need for renal replacement therapy and therefore started on citrate-anticoagulated CVVHD in combination with CytoSorb hemoperfusion for 24 hours.

In the further course, plasmatic IL-6 and other markers of inflammation as well as need for vasopressors could be reduced drastically while treatment was safe and well tolerated. This is the first clinical case report in a patient with acute-on-chronic kidney failure and septic shock.

Case presentation
• 80 year old male who was stable on chronic hemodialysis for more than 12 months
• Past history included coronary artery disease with a myocardial infarction 14 months ago, end-stage renal disease due to nephrosclerosis, arterial hypertension and diabetes mellitus type II
• Admission of patient to the emergency department after collapse at the end of a regular dialysis session
• On examination, patient had fever (39.2°C), moist bilateral rales, O₂-saturation 79%, BP 126/60 mmHg, HR 130 bpm, lactic acidosis with pH 7.1, APACHE II 33, SAPS II 48
• Later blood cultures remained negative, however, bronchoalveolar lavage was positive for staphylococcus aureus
• Upon further deterioration of the circulatory situation, patient was diagnosed of having pneumogenic septic shock
• Need for mechanical ventilation and admission to ICU, start of noradrenaline 0.2 µg/kg/min
• Interleukin 6 level was elevated to 665 pg/ml

Treatment
• Initiation of one CytoSorb hemoperfusion session for 24 hours in combination with standard citrate-anticoagulated CVVHD

Measurements
• IL-6, CRP, creatinine, procalcitonin and leukocytes
• Need for noradrenaline

Results
• Noradrenaline could be reduced from a maximum of 3.0 to 0.4 µg/kg/min while MAP remained stable
• Values of IL-6, CRP, creatinine, procalcitonin, and leukocytes decreased during treatment and continued to decrease in the following days
• Antibiotic therapy was conducted with Ceftriaxone and Clarithromycin, with no reported adaption of dosage during CytoSorb treatment

CONCLUSIONS
• First clinical case report in a patient with acute-on-chronic kidney failure and septic shock
• Hemoadsorption with CytoSorb in combination with CVVHD
• Treatment appeared safe and effective in this single treatment
Hemoadsorption using CytoSorb beads (CytoSorbents) in a cirrhotic patient with septic multiorgan failure

Gruber A, Firlinger F, Lenz K, Clodi M
Department of Internal and Intensive Care Medicine, Konventhospital Barmherzige Brüder, Linz, Austria
Infection (2013) 41 (Suppl 1):S1–S90; Abstract No. 056

Summary
In this case study a 37-year-old patient with alcoholic liver cirrhosis and septic shock with multiorgan failure due to bilateral pneumonia (staphylococcus aureus) was successfully treated with CytoSorb. The authors found an immediate improvement in organ function with stabilization of hemodynamics, as well as pulmonary and renal function. This is the first successful clinical case of a patient with sepsis and multi organ failure on the basis of alcoholic liver cirrhosis treated with standard of care plus CytoSorb.

Case presentation
• 37 year old patient with alcoholic liver cirrhosis
• Admission to ICU because of multiorgan failure due to bilateral pneumonia with staphylococcus aureus sepsis
• Despite antibiotic treatment, deterioration of the patient (cardiovascular instability, renal insufficiency, hepatic encephalopathy, and respiratory failure)
• Calculated CLIF SOFA Score of 18 and original SOFA score of 16 (estimated mortality >90%)
• Ventilation of the patient with pressure support
• Hemodynamic stabilization with noradrenaline, terlipressin and hydrocortisone
• Plasma IL-6 concentration 27.423 pg/ml
• Treatment of anuria with CVVHD

Treatment
• CytoSorb was applied in combination with standard CVVHD on Prismaflex® (Gambro)
• Three consecutive CytoSorb treatment sessions over a period of 54 hours
• Anticoagulation was achieved using citrate
• Blood flow of 140 ml/min

Measurements
• CRP, IL-6, PCT
• Bilirubin
• Need for vasopressors

Results
• IL-6 concentration dropped to 2266 pg/ml after the first, to 812 pg/ml after the second and to 151 pg/ml after the third CytoSorb treatment
• Patient improved hemodynamically within 6 hours after the first hemoperfusion and noradrenaline could be stopped after this time period
• Cardiac index increased from 4.3 l/m² to 6.6 l/m² but dropped again to 4.3 l/m² before starting the second Cytosorb treatment
• FiO₂ could be reduced to 0.55 and pressure support to 14 mmHg after the second CytoSorb treatment
• Urine output increased and CVVHD could be stopped after 3.5 days of CytoSorb treatment
• Levels of bilirubin, PCT and CRP could be reduced significantly during the three treatment sessions

Post-treatment period and Follow-up
• The patient survived and is still alive 4 months after this event
Can cytokine adsorber treatment affect antibiotic concentrations? – A case report

Zoller M, Döbbeler G, Maier B, Vogesser M, Frey L, Zander J  
Department of Anesthesiology and Institute of Laboratory Medicine, University Hospital of Munich Großhadern, Germany  

Summary
This case study reports on a male patient with septic shock and multiple organ failure who was admitted to the ICU. The patient’s condition was characterized by an excessive inflammatory response. Initial laparotomy revealed an ischemic bowel with peritonitis with jejunum and colon segmental resection and ileotransverse colostomy being performed. Immediate antibiotic treatment with meropenem was started and linezolid was added 5 hours after admission. Due to persisting excessive cytokine storm, adjuvant therapy with a CytoSorb adsorber was initiated with a total of 4 treatments in the further course. Over the following days, the patient’s condition substantially improved. The use of CytoSorb in this patient with severe septic shock proved to be effective (decay of IL-6) and safe (antibiotic levels well above the lower of therapeutic range). This is the first time an in vivo pharmacokinetic monitoring of Linezolid and Meropenem during treatment with CytoSorb is described. In case therapeutic drug monitoring is not available, high loading doses and shorter intervals between antibiotic administrations could be used to achieve adequate antibiotic levels.

Case presentation
• Male patient with septic shock and multiple organ failure was admitted to ICU at the University Hospital of Munich
• Initial laparotomy showed an ischemic bowel with peritonitis
• Immediate jejunum and colon segmental resection with an ileotransverse colostomy was performed
• The further course of the treatment was characterized by severe sepsis with multiple organ failure and an excessive inflammatory response
• Antibiotic treatment with Linezolid (4 x 600 mg on day 1 continuing with 2 x 600 mg) and Meropenem (4g/d) was started
• As the patient revealed a persisting excessive cytokine storm, a CytoSorb adsorber was applied

Treatment
• 4 sessions with CytoSorb were performed over a period of 96 hours (day 1 – 7h, day 2 – 10h, day 3 – 8h, day 4 – 5h)

Measurments
• Analysis of antibiotic serum concentrations (i.e. Linezolid and Meropenem) to detect potential elimination by CytoSorb
• IL-6 elimination

Results
• Substantial reduction of IL-6 over the course of 4 CytoSorb treatments from 563000 pg/ml on day 1 to 19400 pg/ml on day 4
• High intra-patient variability for Linezolid and Meropenem levels was observed, which might be caused by adsorption effects by CytoSorb but also by the effects of critical illness
• By using a higher loading dose for Linezolid and Meropenem in this patient, all the antibiotic concentrations measured were sufficient and did not approach the lower limit of therapeutic level

Post-treatment period and Follow-up
• After four weeks and seven re-laparotomies the patient died from multiple organ failure

CONCLUSIONS
• First time in vivo pharmacokinetic monitoring of Linezolid and Meropenem during treatment with CytoSorb
• Use of CytoSorb in this patient with severe septic shock proved to be sufficient (decay of IL-6) and safe (antibiotic levels well above the lower of therapeutic range)
• Using a high loading dose for Linezolid and Meropenem, antibiotic concentrations were always within the therapeutic range
• However, the results indicate that Linezolid and Meropenem serum concentrations might be reduced by use of CytoSorb
• In the absence of therapeutic drug monitoring, high loading doses and shorter intervals between antibiotic administrations could be used to achieve adequate antibiotic levels
• Further studies are necessary to understand the impact of CytoSorb on concentrations of different antimicrobials
Systemic Inflammatory Response Syndrome in Cardiac Surgery: New possibilities for treatment through the use of a cytokine adsorber during ECC?

Born F, Pichlmaier M, Peterl S, Khadj N, Hagl C
Department of Cardiac Surgery, Ludwig-Maximilians University, Munich, Germany
Kardiotechnik 2/2014

Summary
The occurrence of the systemic inflammatory response syndrome (SIRS) is one of the most significant complications after cardiac surgical operations with the application of a Cardio-Pulmonary-Bypass (CPB). In this retrospective observational case series in 40 patients undergoing a major cardiac surgical procedure using CPB the hypothesis was tested, whether the intraoperative treatment with CytoSorb could have a positive effect on the post-operative laboratory markers for SIRS. Results show, that CytoSorb contributes to a significant reduction of markers of post-operative SIRS in those patients. This case series emphasizes the reliability and safety of CytoSorb also in the setting of cardiac surgery.

Case series presentation
- 40 patients undergoing a major cardiac surgical procedure with the application of CPB
- n=20 with CPB, n=20 with CPB + additionally implemented CytoSorb
- Retrospective analysis

Treatment
- Cardiac surgery using standard CPB protocol
- Intraoperative application of CytoSorb in treatment group (CS) for the entire time of operation

Measurements
- Blood samples were drawn from the patients immediately after the operation and 1-3 days post-operatively
- Measured parameters were C-reactive protein, procalcitonin, leucocytes, fibrinogen, IL-6

Results
- Treatment with CytoSorb had a direct and positive effect on the laboratory markers of post-operative SIRS
- There were significant differences in the inflammation parameters between the two groups immediately following surgery
- Interleukin-6: During the post-operative period, IL-6 was moderately elevated in the CytoSorb group and reached normal levels again over the course of the following 3 days. In the control group, IL-6 levels were already elevated post-operatively, and showed a trend that continues to increase further.
- Fibrinogen: In the CytoSorb group, values for fibrinogen consistently remained within the normal range during the post-operative period and began to drop after the third post-operative day. In contrast, levels in the control group rose significantly above the upper threshold value of the normal laboratory range and continued to increase further after day 3.
- Leukocytes: Leukocytosis developed in both groups immediately after the operation was finished. In the further course, leukocyte counts decreased faster with CytoSorb and remained below the leukocyte count of the control group for the entire observation period.
- Procalcitonin: The increase in procalcitonin was significantly less pronounced using CytoSorb therapy compared to the control group and the difference was highly significant at all measurement time points. In addition, the PCT decreased more quickly in the CytoSorb group throughout the post-operative period when compared to control.

CONCLUSIONS
- The data demonstrate the reliability and safety of the new CytoSorb therapy in the area of cardiac surgery
- Intra-operative use of CytoSorb during open heart surgery with application of CPB has a positive effect on clinical and inflammatory parameters of post-operative SIRS
- If results can be confirmed in a prospective controlled trial, CytoSorb could be established as a routine application in cardiac surgery
Summary
This case study reports on a 50-year-old immunocompetent woman who was admitted to hospital for acute hepatitis with acute liver failure. After transfer to ICU the patient rapidly developed MOF and was listed for highly urgent liver transplantation. Since existing liver support techniques (MARS® treatment) for bridging while awaiting for liver transplantation had no effect, Single Pass Albumin Dialysis (SPAD) in combination with CytoSorb was applied resulting in a marked decrease of IL-6, bilirubin as well as a reduction of vasopressor need. Orthotopic liver transplantation (OLT) could be successfully performed on the 4th day on ICU. CytoSorb treatment was safe and well-tolerated, without any adverse events occurring. Therefore, CytoSorb seems to be promising and new approach for patients with liver failure.

Case series presentation
• 50-year-old immunocompetent woman was admitted to hospital for acute hepatitis with ALF
• Liver biopsy revealed acute liver cell necrosis due to herpes simplex virus type 1 (HSV-1)
• Despite antiviral therapy liver failure progressed and patient was transferred to ICU
• Rapid development of MOF with hepatic coma, severe coagulopathy, acute anuric renal failure, respiratory insufficiency and arterial hypotension
• Patient was listed for highly urgent liver transplantation
• Additional diagnosis of hemophagocytic lymphohistiocytosis (HLH), secondary to HSV-1-infection
• Hemodialysis and extracorporeal liver support were initiated using MARS®-therapy (6 hours 1st day, 19 hours 2nd day)
• Increasing need for NE and excessively elevated concentrations of inflammatory markers indicated ongoing severe SIRS
• Hence extracorporeal therapy was changed to CVVHD with SPAD (12 hours of treatment)

Treatment
• One session of CytoSorb treatment was performed with a treatment duration of 20 hours
• CytoSorb was integrated in a predialyzer position
• Regional anticoagulation was performed using sodium citrate

Measurements
• Need for vasopressors
• IL-6, bilirubin

Results
• IL-6 levels fell from 81059 pg/ml to 17177 pg/ml after 12 hours of treatment
• Noradrenaline dosage was reduced to 0.25 µg/kg/min
• No further clinical deterioration of the patient
• Antiinfective therapy was conducted with Acyclovir, with no reported adaption of dosage during CytoSorb treatment
• Reduction of the moderately elevated bilirubin with SPAD + CytoSorb

Post-treatment period and Follow-up
• Successful OLT on 4th day on ICU
• Further improvement after OLT

CONCLUSIONS
• First report of the combined use of CytoSorb with SPAD in a patient suffering from ALF and probable HLH with severe SIRS listed for liver transplantation
• Major results of the intervention were a marked decrease of IL-6, and bilirubin, as well as a reduction of vasopressor need
• Treatment was safe and well-tolerated, without any adverse events
• Existing liver support technique (MARS® treatment) had no effect on the reduction of bilirubin
• CytoSorb might be a useful tool for patients with acute liver failure and severe hyperinflammatory syndromes
First use of CytoSorb with pruritus – a case report

Summary
This case study reports on a 44 year old male patient with pruritus and severe sleep disturbances. Prior medical conditions included primary sclerosing cholangitis with subsequent LTX and reLTX one month later due to primary graft failure. Efforts to treat the pruritus using drugs were unsuccessful. Therefore two treatment attempts were made using CytoSorb. Application of the adsorber resulted in a significant decrease of bilirubin and bile acid plasma levels and a concomitant improvement of the patients’ complaints. This is the first case reporting on the use of CytoSorb in the setting of pruritus.

Case presentation
- 44 year old male patient
- Underlying disease: primary sclerosing cholangitis
- LTX in 04/12 and reLTX in 05/12 due to primary graft failure
- Currently new listing for LTX (graft dysfunction)
- Severe itching since 6/2012
- Visual analogue scale (VAS) of 10 with severe sleep disturbances
- Drug treatment attempts by a dermatologist unsuccessful
- Current medications: Prograf, Cellcept, Ursofalk, ASS
- Specific medication for the treatment of pruritus initially rejected
- Decision to use CytoSorb as adjunctive treatment

Treatment
- 2 curative attempts with CytoSorb using a Multifiltrate® dialysis machine (Fresenius)
  - 1st treatment attempt: 5 sessions à 16 hours treatment, heparin anticoagulation, blood flow 120-150 ml/min,
  - 2nd attempt: 3 sessions à 8 hours treatment, confirmed HIT, change to citrate anticoagulation

Measurements
- Bilirubin, Bile acids, IL-6, PCT
- Visual analogue scale (VAS)

Results
- After 1st treatment attempt (5 x 16h sessions): Visual analogue scale (VAS) decreased from 10 to 0 for the next 3 weeks
- Before 2nd treatment attempt: VAS of 6-7
- After 2nd treatment attempt (3 x 8h sessions): VAS of 0 for the next 3 weeks
- Decrease of bilirubin and bile acid plasma concentrations during both treatment attempts
- No change in IL-6 and PCT during the first treatment attempt

Post-treatment period and Follow-up
- After the last CytoSorb treatment change to Prometheus® System (Fresenius) with no further improvement

CONCLUSIONS
- First use of CytoSorb in the setting of pruritus
- Remarkable decrease of plasma bilirubin and bile acid concentrations
- Considerable patient benefit through both treatment attempts, as assessed by a decrease of VAS to 0
Cytosorb™ in a patient with legionella-pneumonia associated rhabdomyolysis

Wegele M, Krenn CG.
Clinical Division of Anesthesiology and General Intensive Care Medicine Department of Anesthesia, General Intensive Care and Pain Control, Medical University of Vienna, Austria
ASAIO J. 2015 Jan 29

Summary
This case study reports on a 44-year-old man presenting with ongoing fever and impaired general condition for more than 5 days. Respiratory insufficiency finally led to hospitalization and rapid admission to an intensive care unit with intubation and ventilatory support. Chest X-ray and computed tomography confirmed the clinical diagnosis of ARDS. Investigation of patient’s specimen further revealed infection with legionella pneumophila. Despite administration of antibiotics, liver enzymes and parameters of renal function deteriorated in parallel within the following days, indicating a trend toward multiple organ failure. Creatine kinase and myoglobin levels increased in combination with reduced urine excretion. Therefore Cytosorb treatment was started in hemoperfusion-mode (stand-alone application form) on day 6 after admission. Within 8 hours, myoglobin levels decreased from 18390 to 10020 ng/ml and in a second cycle again declined from 13400 to 8359 ng/ml. The patient’s condition improved subsequently. Renal function completely recovered and hemodialysis was not necessary at any time of hospitalization. No side effects of therapy have been observed in this patient. This is the first time that a decrease of myoglobin levels following application of Cytosorb cartridge can be demonstrated in vivo.

Case series presentation
• 44-year-old man presented with ongoing fever and impaired general condition for more than 5 days
• Admission to ICU after clinical diagnosis for acute respiratory distress syndrome (ARDS) with proven infection from legionella pneumophila
• Despite administration of antibiotics, liver enzymes and parameters of renal function deteriorated in parallel within the following days, indicating a trend towards multiple organ failure
• Despite adequate fluid administration right from the beginning, creatine kinase and myoglobin levels increased in combination with reduced urine excretion

Treatment
• 2 sessions were run on 2 consecutive days (day 6 and 7 after admission) for 5-6 hours each
• Cytosorb was run on a multiFilter® (Fresenius) in hemoperfusion-mode (stand-alone mode)
• Blood flow rates were 300ml/min
• Enoxaparin was administered subcutaneously to prevent thromboembolic events but no additional anticoagulant was added to the extracorporeal system

Measurements
• Myoglobin levels, Noradrenalin
• Markers for renal function – i.e. creatinine, blood urea nitrogen, urine output
• Markers for liver function (bilirubin, overall protein, albumin, ASAT, ALAT, γGT, LDH)

Results
• Decrease of myoglobin levels from 18390 ng/ml to 10020 ng/ml within 8 h
• Further decline from 13400 ng/ml to 8359 ng/ml during the second cycle on day 7
• Parameters of renal function and liver enzymes improved within hours and subsequently during the next days
• In parallel the patient’s urine output increased from < 0.5 ml/kg/h to >1 ml/kg/h
• No side effects of therapy have been observed

Post-treatment period and Follow-up
• The patient’s condition improved subsequently
• Renal function completely recovered and hemodialysis was not necessary at any time of hospitalization
• Finally the patient was transferred to a normal ward on day 22

CONCLUSIONS
• First time that a decrease of myoglobin levels following application of Cytosorb cartridge could be demonstrated in vivo
• After commencement of Cytosorb treatment, the patient’s condition improved subsequently and renal function completely recovered. Renal replacement therapy could be avoided.
• No adverse or any device-related side effects were documented during or after the treatment sessions
• Whether application of Cytosorb prevents acute renal failure necessitating hemodialysis in patients with rhabdomyolysis in any case remains to be investigated in randomized controlled trials

Myoglobin levels during hemoperfusion with CytoSorb (1st run: 0-6 hours, 2nd run: 9-14 hours)

Course of standard laboratory markers and myoglobin levels during intensive care unit stay

<table>
<thead>
<tr>
<th>Length of ICU stay</th>
<th>Cytosorb 1st application - Cytosorb 2nd application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days</td>
<td>Time (h)</td>
</tr>
<tr>
<td>1</td>
<td>20:39:59</td>
</tr>
<tr>
<td>5</td>
<td>04:37:53</td>
</tr>
<tr>
<td>6</td>
<td>07:07:13</td>
</tr>
<tr>
<td>7</td>
<td>12:44:11</td>
</tr>
<tr>
<td>8</td>
<td>21:10:11</td>
</tr>
<tr>
<td>9</td>
<td>0.15</td>
</tr>
<tr>
<td>10</td>
<td>0.10</td>
</tr>
<tr>
<td>11</td>
<td>0.34</td>
</tr>
<tr>
<td>12</td>
<td>0.65</td>
</tr>
<tr>
<td>13</td>
<td>0.94</td>
</tr>
</tbody>
</table>

Table: Course of standard laboratory markers and myoglobin levels during intensive care unit stay
SIRS and Sepsis

REGAIN CONTROL