

tic concepts like strict glycemic control, early goal directed therapy, low-dose hydrocortisone and active protein C and show significant reduction in mortality in clinical trials the actual medical situation especially at the ICU remains a major problem (recent review: Rice TW, Bernard GR. *Annu Rev Med* 2005;56:225–248). Given the fact that the first defense response against a bacterial infection is mainly enforced by phagocytes in particular granulocytes, we tested the idea of using these cells in an extracorporeal treatment procedure to treat septic individuals. After having shown significant improvement of survival both in rats with *E. coli* Sepsis and pigs with *S. aureus* sepsis, recently a clinical trial with 10 Patients with septic shock had been initiated at the University of Rostock. For the pig experiments, human hematopoietic precursor cells have been expanded and stimulated to differentiate towards functional granulocytic cells. In an animal model of sepsis, similar to the one described by Lee PA et al. (*Crit Care Med* 1998; 26:730–737), 21 female immature landscape pigs (weight: 7.5–12 kg) were given 8×10^9 cfu/kg living *S. aureus* i.v. and for 168 h clinical parameters and survival time were monitored. After a 1 hour infusion of bacteria and a 1 hour waiting period, the pigs were treated for 4 h by an extracorporeal plasma perfusion system containing a membrane-based bioreactor with 6.2×10^9 cells. Mean survival time of the septic control group (SCG, no extracorporeal treatment) and the control group (CG, extracorporeal treatment without cells) were 70 h and 75.2 h, respectively, while 6 out 7 pigs of the treated group (TG, extracorporeal treatment with cells) survived the whole observation time of 168 h (mean: 167.57 h). Statistic significance (log rank test) was seen between CG and TG ($P = 0.019$) and between SCG and TG ($P = 0.0001$); but not between CG and SGG ($P = 0.43$). Significant differences were also seen for cytokine levels, number of bacteria in the blood and coagulation parameters. No adverse effects were observed that could be ascribed to the presence of human phagocytes. Therefore, the extracorporeal immune support by phagocytes may improve the outcome of sepsis.

Apheresis Technologies

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Cryofiltration Techniques and Clinical Indications

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Cryofiltration apheresis is a procedure to remove cryoprecipitates to treat cryoprecipitate-induced diseases. Cryoprecipitate diseases include: Cryoglobulinemia, cryofibrinogenemia, and cryo positive cold IgM agglutinin hemolytic anemia. It selectively removes cryoprecipitates and it is very specific method to treat cryoprecipitate-induced diseases. The technology involves separation of plasma and subject to cold (4°C). All cryoproteins will precipitate and will be removed by the Cryofilter. The cryoprotein-depleted plasma will pass through a blood warmer to body temperature then mixed with the cells and returned to the patient. In this procedure only a few grams of unwanted cryoprecipitate is removed and the patient's own plasma is returned and no replacement fluid such as albumin or FFP is required. In the past APO6M made by Asahi Medical, Tokyo, Japan, with a 0.2 μm pore size and 0.65 m² surface area made of cellulose diacetate (CDA) has been used in the United States and Japan to remove cryoglobulins. The major disadvantage was frequent filter plugging due to small pore

size and is no longer used in the United States. The AC1740 filter made by Asahi Medical with a 0.02 μm pore size, a 1.70 m² surface area made of CDA membrane and Evaflux-4A made by Kuraray Company, Osaka, Japan, with a 0.03 μm pore size, a 2 m² surface area made of ethylene vinyl alcohol membrane are used to remove cryogel which is an agglutination complex of fibrinogen, fibronectin, fibrin split products and cold insoluble proteins with a heparin core, at a temperature between 2° and 10°C. These three filters have been used to treat ABO-incompatible transplant candidates and rheumatoid arthritis in Japan. The cryogel which is normally a very small amount cannot be measured as cryocrit or even shown as cryo positive plasma. Therefore, the plasma concentration of cryogel and the removal cannot be quantitated. This cryogel removal is not used in the US. We have used plasma filter Evaflux-2A with pore size 0.01 to remove cryoglobulins without cooling the plasma in the past in patients with mixed cryoglobulinemia. This plasma filter removes macromolecules greater than 200 000. This is semi-selective, better than plasma exchange but not selective or specific as cryofiltration. We have performed more than 1300 cryofiltration apheresis procedures on 47 patients. The cryo-filter has a large 4.3 μm pore size; a 0.135 m² surface area and made of acrylic copolymer pleat membrane by Pall Medical, Ann Arbor, MI, USA. This high capacity cryofilter allows us to remove a large amount of cryoprecipitate from cold plasma. We also use a thermoregulator with a cryofilter pressure monitor and alarm system which can cool and warm the chamber allowing us to keep the temperature constant at 4°C. The cooling coils made of plastic tubing to allow time to cool plasma and cryoproteins to precipitate. The cryofilter is housed inside the thermoregulator unit to remove cryoprecipitates. We performed 105 dual cryofiltration procedures using two cryofilters in parallel in 6 patients who had very high cryocrit. The advantage is to remove a large quantity of cryoprecipitate by being able to double the plasma flow in the same period of time. We performed 30 tandem cryofiltration and hemodialysis (CF/HD) in 3 critically ill patients requiring HD. These patients tolerated the procedures well. The advantage of this procedure is to save time and convenience for the patient and nursing staff that do the procedures. We performed 8 cryofiltration procedures for 5 patients with cold IgM agglutinin hemolytic anemia. The procedure was successful only to two patients who had cryo positive and high antibody titer. Their IgM antibodies are very active in cold and are in minute amounts, therefore cannot be measured as cryocrit. Cryofiltration apheresis effectively removes plasma cryoprecipitates. It preserves more than 90% of plasma protein such as albumin, immunoglobulins and fibrinogen. There is no complement activation. It does not require replacement fluid such as albumin or FFP. It selectively removes cryoprecipitate and is specific for treatment of cryoprecipitate-induced diseases. Dual cryofiltration is able to remove very large amount of cryoprecipitate. Tandem CF/HD is safe for critically ill patients who require HD. It is convenient to the patient and saves time and is very cost effective.

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Prometheus: Evaluation of Albumin's Deligation During Procedure Using the Method of Fluorescence Dyes

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The device named Prometheus has been created and produced in Germany (Fresenius, Germany). It is used for effectively removing pathological hydrophobic metabolites from albumin during plas-