Japan Journal of Critical Care for Endotoxemia

(abstracts, 2001-2006)

2001

Plasma Cytokine and NOx Levels of a Patient with Septic Multiple Organ Failure Treated with Polymyxin-B Immobilized Fiber.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.30-35 (2001)
Figure&Table&Reference: FIG.6, REF.21
Abstract: A 61-year-old male with multiple trauma developed hyperendotoxemia (more than 400 pg/mL) complicated by septic multiple organ failure. He was treated with polymyxin-B immobilized fiber (PMX) twice. Plasma levels of endotoxin, various cytokines, and the final products of nitric oxide metabolism (NOx) were measured. The plasma endotoxin levels were decreased by PMX, and the changes in NOx levels were similar to the changes in endotoxin levels. The TNF-.ALPHA., IL-6, and IL-8 levels, however, were hardly affected by PMX treatment. PMX decreased the patient's blood endotoxin levels, but did not decrease his blood cytokine levels. In view of the parallel lerels of blood endotoxin and NOx, blood endotoxin appears to be involved in the production of NO.

Study of Direct Hemoperfusion with Polymyxin-B Immobilized Fiber in Patients with Acute Lung Injury and Acute Respiratory Distress Syndrome.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.37-42 (2001)
Figure&Table&Reference: FIG.3, TBL.3, REF.6
Abstract: Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are characterized by severe acute hypoxemia and a high mortality rate. There are no effective drugs against ALI or ARDS. We have reported that direct hemoperfusion using a polymyxin-B immobilized fiber column (PMX) has been effective for ALI due to endotox in on test sheep. Fourteen men and six women (mean age: 63.2 years) were enrolledin the study. They were divided into two groups (respiratory and other) on the basis of their underlying diseases. Two ALI and eighteen ARDS patients were evaluated. We performed PMX after making diagnose of ALI and ARDS. PMX was carried out twice at a rate of 80-100 mL/minute for 2 hours, with a time interval of approximately 24 hours. We monitored systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and PaO2/FIO2 ratio (PF ratio) before and after PMX. Mortality was classified if patients were alive at day 30 after initiating PMX. The mortality rate of ALI and ARDS patients was approximately 20%. In the respiratory and other group, SBP increased significantly from 101.+-.23, 113.+-.15 mmHg to 130.+-.17, 142.+-.25 mmHg after PMX and to 121.+-.19, 131.+-.21 mmHg on the following day. After treatment the elevated SBP was further sustained. DBP increased significantly from 58.+-.19, 65.+-.10 mmHg to 77.+-.17, 80.+-.14 mmHg after PMX, and to 76.+-.17, 80.+-.14 mmHg on the following day. In the respiratory and other group, PF ratio increased significantly from 114.+-.52, 141.+-.58 Torr to 140.+-.67, 173.+-.82 Torr after PMX and to 149.+-.83, 185.+-.71 Torr on the following day. Twelve patients who had PMX induced within 48 hours after diagnosis revealed a low mortality rate of 17%. Cases in which PMX was induced within 48 hours showed a better outcome than those that were over 48 hours. CD 11 b positive neutrophils in peripheral blood decreased after PMX. In patients with ALI and ARDS, PMX improved circulatory disturbance and oxygenation in spite of underlying diseases.

Successful Treatment of Shock and ARDS with PMX after Pneumonectomy.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.44-48 (2001)
Figure&Table&Reference: FIG.7, REF.7
Abstract: A 79-year old man received a left pneumonectomy because of left primary lung cancer

that caused obstructive pneumonia. During surgery, there was no evidence of cardiopulmonary insufficiency. After 10 hours of surgery, progressive hypotension and severe hypoxia was detected. A chest roentgenogram revealed a decrease in opacity of the right lung field. We diagnosed the condition was caused by ARDS due to a second attack of septic shock caused by obstructive pneumonia. We introduced Polymyxin-B immobilized fiber (PMX) to control hypoxia due to ARDS. After 30 minutes of application of PMX, the patient's blood pressure and the tension of oxygen in the arterial blood increased immediately to a level much better than before. After 2 hours of PMX treatment, a chest roentgenogram suggested a remarkable reduction in ARDS. The patient was gradually able to be weaned from a mechanical ventilator 5 days after surgery.

Two Cases of Acute Leukemia Complicated by Septic Shock Successfully Treated with Endotoxin Adsorption Therapy.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.50-56 (2001)
Figure&Table&Reference: FIG.4, TBL.2, REF.6
Abstract: We report two cases of acute leukemia complicated by septic shock which was successfully treated by endotoxin adsorption therapy (PMX) during the chemotherapy. Case 1 developed septic shock subsequent to multiple organ failure (MOF) due to infection-induced hypercytokinemia. PMX, hemodiafiltration (HDF) and plasma exchange (PE) were simultaneously performed to eliminate endotoxin and cytokines. Case 1 recovered from septic shock and MOF. We suspect that the development of irreversible organ failure during a second attack was attenuated because of agranulocytosis. As soon as Case 2 lapsed into septic shock during treatment, PMX was performed. His shock state immediately improved. PMX was safely performed during bone marrow suppression using nafamostat mesilate as an anti-coagulation agent and platelet concentrates.

Effect of PMX-DHP According to Differences in Infection Site.
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Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.61-65 (2001)
Figure&Table&Reference: FIG.2, TBL.1, REF.4
Abstract: Patients with septic shock caused by intraperitoneal infections were classified as a group in which either septic shock was caused by biliary tract infections (n=8, Group C) or in which septic shock was caused by perforation of the lower digestive tract (n=19, Group P). Both groups were assessed for the clinical effect of PMX-DHP, inflammatory mediators and markers related to endothelial cell function. MOF score were obviously higher in Group C. The number of days from the onset of shock until PMX-DHP was performed was also greater for Group C (1.6.+-.0.8 days versus 0.9.+-.0.8 days). Although blood pressure elevating effects were observed in both groups, the magnitude for those effects was higher in Group P. The values of vascular endothelium markers (Thrombomodulin, PAI-1, ICAM-1, ELAM-1) before the start of PMX-DHP were higher in Group C. Vascular endothelial cell activation and its degree of impairment were considered to be greater in Group C than in Group P.

The Evaluation of Each Organ Dysfunction for the Colonic Perforation with Fecal Peritonitis Patient Who Carried Out PMX.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.67-73 (2001)
Figure&Table&Reference: FIG.6, TBL.2, REF.11
Abstract: The mortality of the colonic perforation with fecal peritonitis for the past 11 years from 1990 until 2000 in Fuji City General Hospital had improved significantly since applying PMX for medical treatment in 1997. Evaluating the organ dysfunction between survivors and non-survivors by Goris score and the SOFA score, the improvements of respiratory and liver function were found out. It is improving from an early stage especially about liver function. A possibility that the improvement of circulation that is the feature of PMX would lead to the improvement of liver function was guessed. Pulse dye densitometry using ICG made

it possible to measure cardiac output and hepatic blood flow simultaneously. Applying this method to the PMX patients, the increase of hepatic blood flow occupied to cardiac output would contribute to the improvement of liver function was suggested.

A Case of Liver Cirrhosis Complicated by Septic Multiple Organ Failure Two Years After Peritoneovenous Shunt. A Case of Survival with Direct Hemoperfusion Using Polymyxin-B Immobilized Fiber (PMX) Followed by Continuous Hemodiafiltration (CHDF).
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.98-103 (2001)
Figure&Table&Reference: FIG.4, TBL.1, REF.20
Abstract: A 70-year-old male with a peritoneovenous shunt (PVS) was hospitalized complaining of high fever and frequent watery diarrhea two years after the operation. Immediately after admission, systolic blood pressure dropped to 70 mmHg requiring a maximum dosage of noradrenalin. During the patient's first evening, lactic acidosis occurred and 200 mL of 7% NaHCO3 solution was administered. During the following morning, respiratory failure was apparent and artificial respiration was started. Considering the clinical course, septic multiple organ failure was suspected and PMX was performed followed by CHDF on the second day of hospitalization. During PMX, the patient's pressure rose and stabilized. Respiratory condition gradually improved and the patient was extubated on the 11th day of hospitalization. Both blood and ascites cultures showed E. coli growth; the blood endotoxin level measured 31.3 pg/mL at the time of admission and 10.9 pg/mL (cut-off level 5 pg/mL) after the PMX. On the 15th day of hospitalization, however, the patient became febrile (39.DEG.C.) and succumbed to shock. After the shunt was removed, the patient became afebrile and the clinical condition became stabilized.

A Case Report: Successful Treatment of Septic Shock and Acute Renal Failure Caused by Crescentic Glomerulonephritis.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.107-112 (2001)
Figure&Table&Reference: FIG.3, TBL.2, REF.6
Abstract: A young female with septic shock, including acute renal failure, and suffering from severe diarrhea and high-grade fever for several days, was treated with hemodiafiltration, but hypotension and cyanosis continued. The patients blood platelet count was also quickly depressed. Direct hemoperfusion using polymyxin-B immobilized fiber (PMX-DHP, Toraymyxin, Toray, Tokyo, Japan) was effective in improving her symptoms. Hemodialysis was stopped 7 days later. A kidney biopsy specimen revealed crescentic glomerulonephritis and severe acute interstitial nephritis. Oral corticosteroid was administered, in consideration of the kidney pathology findings. We postulate that PMX-DHP modified the pathogenesis of her nephritis because the patients made rapid recovery from acute renal failure without use of corticosteroid.

Two Cases Report: Remarkable Improvement of Hemodynamic State by Direct Hemoperfusion Using Polymyxin-B Immobilized Fiber on Gram-positive Bacterial Infection.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.114-117 (2001)
Figure&Table&Reference: FIG.2, REF.10
Abstract: Polymyxin-B immobilized fiber direct hemoperfusion (PMX-DHP) has wider acceptance as a treatment for endotoxemia. PMX binds endotoxin, increases systemic vascular resistance, and is effective in treating shock. We report two cases that improved the hemodynamic state after PMX-DHP, although there was no endotoxemia. Both cases was exhibited shock state at the time of ICU admission. There was no response to treatment, including fluid resuscitation, dopamine, or norepinephrine. After PMX-DHP, systemic vascular resistance and blood pressure increased remarkably, making it possible to reduce vasopressor. Recent reports indicate that Anandamide (ANA) is a common mediator of septic shock due to not only Gram-negative bacterial

infection but Gram-positive bacterial infection. It has also been noted that PMX-DHP adsorbed ANA, leading to the possibility that PMX-DHP is effective for Gram-positive bacterial infection.

A Case in Which Systemic Vascular Resistance is Reduced after PMX.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.119-124 (2001)
Figure&Table&Reference: FIG.5, TBL.2, REF.7
Abstract: It is said that PMX increases systemic vascular resistance (hereinafter called SVR). However, a case has arisen in which the first PMX reduced SVR and the second PMX performed 24 hours later raised SVR. The case relates to a 79-year-old male, who was diagnosed with colon sigmoideum perforative peritonitis and underwent surgery to construct an artificial anus. Because SVR tended to be reduced and cold extremity sense became greater during observation of the postoperative course in the ICU using a Swan-Ganz catheter, PMX was performed, but almost no rise of blood pressure and SVR was recognized. After completion of PMX of four hours, SVR was further reduced and blood circulation became further unstable. Pressor agent and fluid replacement were inceased and the second PMX performed 24 hours later recognized a remarkable rise of blood pressure and SVR, and 76 hours after entering the ICU, normal blood circulation was restored. The blood circulation status was different for the two PMX. However, two measurements of circulating blood volume indicated that the ICG mixing time was shortened, and similar effects were recognized for the distribution status of blood. IL-6 and TNF were reduced after PMX, but no great changes were recognized before and after PMX. Anandamide, which was kept at a low level throughout the course, failed to explain the changes in blood pressure. Isoprostan, which is regarded as an oxidative stress index, showed a high value immediately after operation, and was restored by a large amount of fluid replacement and a small amount of pressor agent, and the value had already reached a low level before the second PMX. A comparison of the effects of two PMX using blood circulation status, ICG distribution pattern, anandamide, and isoprostan resulted in different judgments for accommodation and validity....

Long-term Changes in Th1/Th2 and Cytokines Following PMX-DHP in Septic Shock.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.128-135 (2001)
Figure&Table&Reference: FIG.8, TBL.2, REF.7
Abstract: Abnormalities in the T helper 1 cell (Th 1) and T helper 2 cell (Th 2) (i. e., Th 1/Th 2 ratio below) have been reported in various diseases. Th 2 is predominant in septic shock. We previously reported a significant decrease in Th 2 immediately after endotoxin adsorption therapy (PMX-DHP). This study, investigated the long-term change in the Th 1/Th 2 ratio in the 7 cases of recovering septic shock. Th 1, Th 2, Th 1/Th 2 ratio, inflammatory cytokines (IL-6, IL-12), anti-inflammatory cytokines (IL-10, TGF-.BETA.), and HLA-DR were assayed. These assays were performed prior to PMX-DHP, immediately after, 24 hours after, 1 week, 2 weeks, 3 weeks, 4 weeks after, and results were compared. Th 1 increased in 6 subjects after PMX-DHP in conjunction with improved patient condition. Th 2 temporally decreased after 1 week. The Th 1/Th 2 ratio disclosed that Th 1 was predominant until 1 week after PMX-DHP (i, e. the Th 1/Th 2 ratio increased). IL-6 and IL-10 decreased in conjunction with improved patient condition. There was no correlation observed between IL-10 and Th 2. However, IL-12 increased with improved patient condition, and a correlation was not noted with Th 1. TGF-.BETA. showed no fixed trend, but HLA-DR increased with patient improvement.

Direct Hemoperfusion with Polymyxin-B Immobilized Fiber Induces Diuresis Via Elimination of Renotoxic Agent in Endotoxemic Patients.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.139-145 (2001)
Figure&Table&Reference: FIG.4, TBL.5, REF.8
Abstract: Factors related to the urination effect obtained by PMX-DHP treatment are examined in this study. Treatment was performed on seven patients who were diagnosed with perforative peritonitis and underwent abdominal surgery. PMX-DHP treatment

was performed fourteen times in total an all cases for two hours after surgery and on the following day, respectively. Urine retention was measured before treatment, during treatment, and two hours after treatment. Furthermore, blood was gathered and blood circulation was evaluated using a Swan-Ganz catheter before and after treatment. The volume of urine increased significantly during treatment and after treatment in comparison with that before treatment. It is assumed that improved systemic blood circulation contributed most significantly to the increase in the volume of urine after treatment. On the other hand, the increase in the volume of filtered thread bulb independent of systemic blood circulation is assumed to contribute most significantly to the increase in the volume of urine during treatment. Based on the aforementioned assumption, it is considered that the increase in the volume of urine in the early stage of PMX-DHP treatment resulted from the elimination of a factor that directly influences the filtration of thread bulb rather than improved systemic blood circulation. In addition, cases diagnosed as endotoxin-related renal insufficiency were demonstrated.

Analysis of Effect with PMX-DHP Regard as Blood Pressure.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.150-157 (2001)
Figure&Table&Reference: FIG.5, TBL.2, REF.16
Abstract: Recently, signal of peptideglycan that was common cell wall component of gram-positive and gram-negative bacteria induced anandamide. Moreover, it was shown that polymyxin B binds to anandamide and inhibits its cytotoxic effect. Those evidences were suggested that PMX-DHP could have effect of upreguration as blood pressure in cases of gram-positive bacterial infection. We evaluated efficacy of PMX-DHP in septic patient's different bacterial infection. It was shown that PMX-DHP has effect of upregulation as blood pressure during early state in group of each bacterial infection. It was suggested that PMX-DHP could remove common component of gram-positive and negative bacteria during early state. Moreover, we presented that septic patients of MRSA have decreased serum ANA levels after PMX-DHP. Those were suggested that PMX-DHP could have effect of therapy with septic patients of gram-positive bacterial infection.

Changes in Endotoxin and Cytokine by Blood Purification. Comparison between PMX-DHP for 24 Hours and PMMA-CHDF.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.159-162 (2001)
Figure&Table&Reference: FIG.2, TBL.1, REF.6
Abstract: We investigated changes in serum endotoxin and cytokine in 11 septic patients treated with PMX-DHP for 24 hours or PMMA-CHDF. Circulatory and respiratory parameters were improved more by PMX-DHP than by PMMA-CHDF. The endotoxin concentration significantly decreased after treatment with the two methods. But, PMMA-CHDF is more effective. The IL-6 concentration significantly decreased following treatment with the two methods. But, PMX-DHP is more effective. It is necessary to consider another mechanism for improving blood pressure using PMX therapy than removal of endotoxin in blood.

The Effect of Combined Use of Direct Hemoperfusion with Polymyxin-B Immobilized Fiber (PMX) and Continuous Hemodiafiltration (CHDF) in Patients with High APACHE-II Score Following Urgent Abdominal Surgery.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.5; NO.1; PAGE.164-167 (2001)
Figure&Table&Reference: TBL.4, REF.9
Abstract: The beneficial effect of postoperative use of PMX and/or CHDF was examined in severe septic MOF with high APACHE-II score (.GEQ.20). In the

CHDF alone (n=2), the reduction in the dose of vasopressor could not be done in all patients and the survival rate was 0%. In the PMX alone or in combined use with the CHDF group (n=20), the dose of vasopressor could be successfully reduced from 16.9 to 8.0 .MU.g/kg/min. Mean arterial pressure, however, was increased from 68.7 to 81.4 mmHg after two days of blood purification. Moreover, fourteen of the twenty patients (70%) survived septic shock after one month. In the severe postoperative MOF patients with high APACHE-II score, the survival rate in the PMX with or without CHDF was remarkably better than the results which has been reported previously in the literature. We concluded that aggressive prophylactic use of blood purification combined use of PMX was effective in recovery from hemodynamic instability and the outcome for severe postoperative MOF patients.

2002

Study on Two Patients Who Suffered Slight Perforative Peritionitis of the Lower Digestive Canal and Did Not Undergo PMX-DHP Application.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.56-62 (2002)
Figure&Table&Reference: FIG.12, TBL.1, REF.9
Abstract: To determine the need for PMX-DHP in a mild case, we examined blood circulation and measured various mediators of two patients suffering slight perforative peritonitis of the lower digestive canal to whom postoperative care had been given without the application of PMX-DHP, because the cases did not conform with the application criterion of this hospital. (Case 1)The case of a female patient, eighty-years old, for whom irrigation of abdominal cavity and provision of an artificial anus were performed under spinal anesthesia for paroxysmal perforation of S-shaped colic region. Eight hours elapsed from outbreak to operation. APACHE-II score before the operation was 11. (Case 2)The case of a female patient, sixty-nine years old, for whom irrigation of abdominal cavity, surgical removal of colic region, and provision of an artificial anus were performed under epidural anesthesia and general anesthesia for perforation of S-shaped colon diverticulum. Thirty-six hours elapsed from outbreak to operation. APACHE-II score before the operation was 14. In Case 1, IL-6 rose to 74,130pg/mL when the patient entered ICU, and continued to remain at 863pg/mL for 48 hours after it gradually decreased upon entering ICU. In Case 2, IL-6 was as low as 129pg/mL, the highest level after the operation, but it decreased to below the lowest limit detection value 12 hours later. TNF-.ALPHA., IL-10 showed the same trend as that for IL-6. Differing from the aforementioned three cases, anandamide repeatedly changed sharply during the process. It indicated the highest value 48 hours later in Case 1, and 6 hours and 96 hours later in Case 2. [Consideration] In the two cases, the period when anandamide reached a high value was observed. Although the necessity for the absorption of anandamide at such a level is not identified, application of PMX-DHP is considered to be effective for the two cases to absorb anandamide....

PMX-DHP for the Septic Shock Caused by Bowel Perforation and the Other Infectious Origin.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.63-68 (2002)
Figure&Table&Reference: FIG.3, TBL.4, REF.3
Abstract: [Introduction] We studied the effects of direct hemoperfusion with polymyxin-B immobilized fiber (PMX-DHP) on septic shock due to bowel perforation and compared the effects for infectious SIRS due to other causes. PMX-DHP was done in 30 cases for 3 years, and the 30 cases were divided into the three groups; the perforative group (P group; n=8), the other abdominal causes group (A group; n=10), and the sepsis due to extra abdominal origin group (E group; n=12). [Results] All cases of the P group survived and were discharged from ICU. The APACHE-II score and the SOFA score of the P group at admission to the ICU were lower than the scores of the other groups. Five of ten cases of the A group and 4/12 cases of the E group died in ICU. In the P group, PMX-DHP is effective for septic shock and a radical operation for the infectious origin was perfomed....

The Present Status of Direct Hemoperfusion with Polymyxin-B Immobilized Fiber (PMX-DHP) for Colorectal Perforation: A single Center Experience.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.69-72 (2002)
Figure&Table&Reference: TBL.3, REF.5
Abstract: The effects of PMX-DHP were examined on colorectal perforation with septic shock in our center. Twenty-four patients with postoperative colorectal perforation were treated with PMX-DHP to manage severe septic shock. Of which, sixteen patients received combined use with CHDF as a treatment for renal failure. Mean age was 64.8 and the number of failed organs was 3.0. Mean APACHE-II score was 26.3. Mean arterial pressure was 73.2mmHg with 17.5.MU.g/kg/min of vasopressor. Overall survival rate was 75.0%, or 18 cases. The dose of vasopressor could be successfully reduced within 48 hours from 22.6 to 8.4 in survival and 15.7 to 12.2 in non-survival cases. In conclusion, aggressive prophylactic use of PMX-DHP was effective in recovering from hemodynamic instability, and mortality particularly, in the case of combined use of CHDF for the patients complicated with renal failure.

Clinical Efficacy of APACHE-II Score and SOFA Score for Evaluating Severity in Patients with Lower Gastrointestinal Perforation and Efficacy of PMX-DHP for Their Treatment.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.73-77 (2002)
Figure&Table&Reference: FIG.7, TBL.1, REF.9
Abstract: We investigated the utility of APACHE-II score and SOFA score for evaluating severity in patients with endotoxin shock. In addition, we studied the efficacy of PMX-DHP (hemoperfusion with polymyxin-B immobilized fiber) and its indication for these patients using APACHE-II score and SOFA score. Thirty-three patients were divided into 2 groups (survivors and fatalities). Both scores were significantly higher for the fatalities. The death rate was statistically higher in patients with an APACHE-II score of over 19 and a SOFA score of over 6. Among patients receiving PMX-DHP, both scores decreased significantly, but were not reduced for the fatalities. PMX-DHP was effective in patients with an APACHE-II score of less than 21 and a SOFA score of less than 10. Continuous evaluation with both scores after surgery will be necessary, because both scores increased in some patients after surgery. In patients with an APACHE-II score of over 22 and a SOFA score of over 11, the second PMX-DHP or CHDF must be used for the rescue.

Indication of Endotoxin Adsorption Therapy for Intra-abdominal Sepsis.
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Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.78-83 (2002)
Figure&Table&Reference: FIG.6, TBL.4, REF.13
Abstract: Because of the role of endotoxin and gram-negative bacteria in the evolution of septic shock and multiple organ dysfunction syndrome (MODS) in intra-abdominal infection, endotoxin adsorption therapy has been studied as a potential therapeutic device. However, the indication of the endotoxin adsorption therapy is not clear yet. We evaluated usefulness of SOFA score as the indication for endotoxin adsorption therapy. Patients and Methods: Forty-one patients who fell into septic shock or MODS due to intra-abdominal infection enrolled in this study. Following our clinical indication, all patients were given endotoxin adsorption therapy for intra-abdominal sepsis, and were divided between survivors and non-survivor on day 28 of the observation period. Before the endotoxin adsorption therapy, SOFA score, lactate, and endotoxin were measured in the two groups. Results and Discussion: The survivors had significantly lower points in the SOFA score, especially for coagulation point and liver point of SOFA score before endotoxin adsorption therapy. In the same way, lactate in the survivors was lower than in non-survivors before endotoxin adsorption therapy. We conclude that SOFA score is useful as a clinical indication of endotoxin adsorption therapy. However, the positive rate of endotoxin before endotoxin adsorption therapy was under 20% in the two groups. Currently, it is unknown what is absorbed into the endotoxin adsorption column. In the exact standard, it is necessary to detect mediators absorbed in the endotoxin adsorption column.

Mechanism of Vasopressor by DHP with Polymyxin-B immobilized in MRSA Septic Patients: Absorption of Anandamide.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.101-107 (2002)
Figure&Table&Reference: FIG.5, TBL.2, REF.20
Abstract: Recent advances in septic shock research have led to rapid progress. Anandamide (ANA), one of the endogenous cannabinoids, has recently been reported to be produced via macrophages by the stimulation of lipopolysaccharide of Gram negative bacteria and, peptidoglycan and lipoteichoic acid of Gram positive bacteria, and to induce hypotension and tachycardia in rats. Polymyxin B immobilized fiber (PMX-F) was developed in Japan as a biomaterial for selectively detoxifying endotoxin. However, Maruyama et al reported that this substance also absorbs ANA. We investigated the serum levels of ANA after Direct hemoperfusion (DHP) therapy with PMX-F in MRSA septic patients. The serum levels of ANA were measured by HPLC analysis. There was a significant increase in blood pressure and a significant decrease in the catecholamine index after PMX-DHP therapy. There were significant decreases in the serum levels of ANA at the outlet of the column 30 minutes after initiation of PMX-DHP therapy and after PMX-DHP therapy in septic patients. In septic shock including severe MRSA infection, DHP with PMX-F was concluded to be effective. The effective mechanism might be due to removal of ANA.

Efficacy of PMX-DHP in Four Cases of Septic ARDS.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.112-120 (2002)
Figure&Table&Reference: FIG.10, TBL.1, REF.6
Abstract: Pulmonary oxygenation was significantly improved after PMX-DHP was performed in 4 cases of septic ARDS complicated with multiple organ failure. Case 1: An 86-year-old man had panperitonitis from a posterior peritoneal abscess caused by fish bone perforation. He suffered respiratory insufficiency on hospitalization and showed a decrease in blood pressure during surgery. As no improvement was observed in pulmonary oxygenation with maintenance therapy, PMX-DHP was performed on, the following day. Case 2: A 54-year-old woman had panperitonitis from idiopathic colosigmoid perforation. A decrease in blood pressure was observed before surgery and a decrease in pulmonary oxygenation was observed during surgery. She was admitted to the ICU and PMX-DHP was begun 4 hours later. Case 3: A 77-year-old woman suffered small intestinal strangulated ileus. During surgery, decreases in blood pressure and pulmonary oxygenation, anuria, and hepatic dysfunction were observed. PMX-DHP and CHDF were started immediately after admission to the ICU. Case 4: A 41-year-old woman developed ARDS following live kidney transplantation, which was complicated by hepatorenal syndrome due to fulminant hepatitis. She developed ARDS after the 2nd plasmapheresis and was admitted to the ICU. PMX-DHP and CHDF were performed as there was no improvement with maintenance therapy. While only CHDF was continued, ARDS occurred again after FFP transfusion 3 days later and 2nd PMX-DHP was performed. The P/F ratio (PaO2/FIO2) was significantly improved by PMX-DHP in all 4 cases and blood pressure increased in cases of shock. However, no correlation was observed between the two parameters. These results suggest that PMX-DHP contributed to suppressing the increased pulmonary permeability.

Study of Direct Hemoperfusion with Polymyxin-B Immobilized Fiber Effects on Pulmonary Oxygenation.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.123-127 (2002)
Figure&Table&Reference: FIG.4, REF.5
Abstract: Septic shock causes acute lung injury (ALI) in a portion with multiple organ dysfunction. In Japan, we apply direct hemoperfusion using a polymyxin-B immobilized fiber column (PMX-DHP) for septic shock, and it is suspected effective for septic shock. We evaluated the oxygenation improvement effect of PMX-DHP on ALI, which was based on septic shock.

We extracted 17 cases from January 2000 to August 2001, to whom PMX-DHP had been administered to patients with septic shock, and investigated A-aDO2, PaO2/FIO2 (P/F) ratio, Lung Injury Score (LIS) at the points of pre-PMX-DHP, the end of PMX-DHP, on the next morning. PMX-DHP was significantly effective for A-aDO2, P/F ratio, but LIS did not change significantly. In the investigation of prognosis, changes in their parameters were not significant between survivors and non-survivors. In patients with ALI, PMX-DHP improved oxygenation in spite of the prognosis.

Is It True That PMX-DHP Can Improve Lung Oxygenation?
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.129-134 (2002)
Figure&Table&Reference: FIG.7, REF.4
Abstract: In 119 cases (62+/- 16 years old, 82 men and 37 women) treated with PMX-DHP, changes in pulmonary oxygenation before and after PMX-DHP were examined, using PaO2/FIO2 as an indicator, separately according to the outcome (80 survivors and 39 who died). Improvement of PaO2/FIO2 was identified in 64% of all cases. In the survival group, there appeared to be a trend for PaO2/FIO2 improvement as blood pressure increased. In the non-Survival group, however, no improvement of PaO2/FIO2 was obtained, regardless of increase of blood pressure. There was no significant correlation between PaO2/FIO2 and the rate of change in endotoxin levels, TNF-alfa, and IL-6. Granulocyte elastase increased significantly after PMX-DHP treatment in both groups. In the survival group, PaO2/FIO2 appeared to increase as MIP-1-alfa decreases, suggesting the possibility that changes in MIP-1-alfa influenced PaO2/FIO2. As the mechanism for the improvement of pulmonary oxygenation by PMX-DHP has not been shown clearly, it remains to be examined further.

Study on Direct Hemoperfusion with Polymyxin-B Immobilized Fiber in Patients with Acute Respiratory Distress Syndrome and Hydrochloric Acid Induced Lung Injury in a Rat Model.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.137-142 (2002)
Figure&Table&Reference: FIG.4, TBL.2, REF.5
Abstract: Direct hemoperfusion using a polymyxin-B immobilized fiber (PMX-DHP) column was found to be effective for endotoxin-induced acute lung injury in a sheep model. On the basis of this report, we concluded that PMX-DHP was effective for improving blood pressure and PaO2/FIO2 (P/F) ratio of 20 patients with acute respiratory distress syndrome (ARDS). Next, we examined the effectiveness of PMX-DHP for septic ARDS patients with a respiratory disease as the underlying disease. We also determined why PMX-DHP was effective for lung injury using hydrochloric acid-induced lung injury in a rat model. As a result of PMX-DHP therapy for septic ARDS patients, all of the patients' blood pressure rose, and six of the eight patients showed an increase in P/F ratio. The P/F ratio of the two patients who died had worsened on the day after treatment with PMX-DHP. In the rat model with hydrochloric acid-induced lung injury, groups with PMX-DHP showed significant improvement in their P/F ratio, an increase in blood pressure and a decrease in the numbers of neutrophils in alveolar lavage fluid compared to groups without PMX-DHP. The development of ARDS enhances inflammatory cytokines, which are mainly produced by monocytes and neutrophils. Although we did not measure inflammatory cytokines in this study, we suspect that PMX-DHP had an effect on the circulating inflammatory cells, especially neutrophils.

Efficacy of Polymyxin-B immobilized Fiber with Direct Hemoperfusion (PMX-DHP) in Patients with Severe Biliary Tract Infections.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.161-165 (2002)
Figure&Table&Reference: FIG.3, TBL.3, REF.6
Abstract: Patients with septic shock caused by biliary tract infections derived from endotoxin occasionally

become severe shock and the mortality rate is high. We report beneficial effects of PMX-DHP on severe septic shock caused by liver and biliary tract infections. We experienced with 7 cases of severe biliary tract infections with shock using PMX-DHP from July 1995 to August 2001 in our institute. Percutaneous drainage was done for liver abscess in one patient and biliary tract infections in six patients. The mean ages of all patients was 66.57 years old. Combined use of continuous hemodiafiltration (CHDF) with PMX-DHP was selected because of renal failure in all patients. The vasopressor could be reduced in 4 cases within 2 days. Four patients (57.1%) survived for more than 28 days. Clinical features observed in this study were that septic shock caused by biliary tract infections tended to become severe, particularly at postdrainage, which might be related to the spill-over of endotoxin. PMX-DHP contributed to the improvement of recovery of patient hemodynamics and survival in a patient with severe biliary tract infection.

Treatment with Polymyxin-B Immobilized Fiber for Acute Pancreatitis.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.168-174 (2002)
Figure&Table&Reference: FIG.4, TBL.2, REF.14
Abstract: We examined the effects of polymyxin-B immobilized fiber therapy (PMX-DHP) for acute pancreatitis. Seven patients with septic shock among 35 severe acute pancreatitis patients ('92 to '01) underwent PMX-DHP. Septic shock associated with severe acute pancreatitis was considered for its indication. The severity score of acute pancreatitis of Japan's Ministry of Health. Labour and Welfare was 15.2.+-.3.5 for patients with PMX-DHP, whereas it was 10.6.+-.5.1 for these without PMX-DHP; i.e., PMX-DHP were performed for the severer acute pancreatitis patients. After PMX-DHP, parameters such as blood pressure improved in 5 of 7 patients, and 3 patients survived. Surgical treatments were performed on 5 out of 7 patients. One patient who underwent PMX-DHP before surgery, and one of 3 patients who underwent PMX-DHP after surgery, survived. Another patient who underwent PMX-DHP both before and after surgery died of sepsis. Two patients underwent PMX-DHP without surgery. One died of portal vein thrombosis and the other was cured by PMX-DHP and selective digestive decontamination after the diagnosis of septic shock due to bacterial translocation. We should perform surgery for the secondary pancreatic infection as soon as possible, but its diagnosis is often difficult. Even if the patients are already in septic shock, surgery could be performed after PMX-DHP improves circulatory conditions.

An Adult T-cell Leukemia Patient in Septic Shock Treated with PMX-DHP.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.176-179 (2002)
Figure&Table&Reference: FIG.1, TBL.1, REF.12
Abstract: Bacterial septicemia occurs in 3% of adult patients with T-cell leukemia, however, mortality is 33%. We describe septic shock treated with PMX-DHP in an adult T-cell leukemia patient. A 51-year-old female suffering from adult T-cell leukemia was admitted unconscious to hospital with hypercalcemia. On admission to the Intensive Care Unit, her blood pressure was 75/49mmHg, pulse rate was 88/min, and respiratory rate was 35/min. A diagnosis of septic shock was made and mechanical ventilation was instituted. PMX-DHP was performed for septic shock. Her blood pressure increased following one PMX-DHP treatment and the infusion dose of dopamine was reduced. We consider that PMX-DHP is both useful and effective for septic shock in adult T-cell leukemia patients.

A Case Report of Septic Shock Due to Enterococcus faecalis: Effective Therapy with Hemoperfusion with a Polymyxin-B Immobilized Column Direct Hemoperfusion (PMX-DHP). Trial of PMX-DHP for Clinical Deep Fungal Infection Suspected.
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Journal Code: L3418A

ISSN: 1348-821X
VOL.6; NO.1; PAGE.186-190 (2002)
Figure&Table&Reference: FIG.1, TBL.1, REF.11
Abstract: A 79-year-old man, who could not secede from steroid-therapy due to repetitive bronchial asthma, was admitted to our hospital on March 19, 2001 because of a deterioration of the attacks. Complication with acute bronchitis made his general state worse after administration. Respiratory failure and reduction of blood pressure developed on May 7, 2001. On the next day hemoperfusion with a Polymyxin-B immobilized column direct hemoperfusion (PMX-DHP) was performed against septic shock since the patient also had tachypnea and tachycardia, besides a significant increase of C reactive protein. Hemodynamic state was markedly improved during PMX-DHP. Enterococcus faecalis was detected by blood-culture. On the other hand, endotoxin was under cut-off value throughout the clinical course, .BETA.-D-glucan significantly decreased from 2,336.0pg/mL to 1,480.0pg/mL after the therapy. We report on an interesting case, for which PMX-DHP is effective for septic shock due to Enterococcus faecalis. Moreover, there is some possibility that PMX-DHP decreased the value of .BETA.-D-glucan.

A Case of Severe Pneumococcal Pneumonia Improved by PMX-DHP.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.6; NO.1; PAGE.213-218 (2002)
Figure&Table&Reference: FIG.4, TBL.3, REF.18
Abstract: A 58 year-old man was admitted for high fever and cough on July 4th in 2001. His chest X-P showed severe consolidation in bilateral middle and lower lobes and it was considered to be septic shock because of symptoms such as respiratory failure, hypotension and multiple organ failure. Despite the use of antibiotics and intensive supportive care, his condition deteriorated. Although no endotoxin was detected in his blood and only Streptococcus pneumoniae, gram-positive bacteria, were detected in his sputa, we decided to use direct hemoperfusion by polymyxin-B immobilized fiber (PMX-DHP) expecting to remove endotoxins. After that the blood pressure increased and the data improved better. Due to a further understanding of pathobiophysiological course of septic shock, we now know that the PMX-DHP is effective for septic shock caused by both gram-positive and negative bacteria, because it removes not only endotoxins but also anandamides and other unidentified bioactive-lipids. In this case, anandamides in the patient decreased after PMX-DHP administration.

2003

Inhibitory Effect of PMX-DHP on Neutrophil Oxidative Burst in Patients with Septic Shock
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.40-45 (2003)
Figure&Table&Reference: FIG.5, REF.16
Abstract: Direct hemoperfusion with Polymyxin-B immobilized fiber (PMX-DHP) was applied in patients with septic shock patients. Hemodynamic parameters, plasma NOx levels, cGMP levels, and neutrophil oxidative burst were measured before and after the treatment. There were significant increases of SVRI and LVSWI. Plasma NOx levels did not change, however plasma cGMP levels dropped significantly after the treatment. Furthermore, neutrophil oxidative burst was promoted prior to the treatment and subsequently inhibited by PMX-DHP treatment. Oxidative burst, i.e. hydrogen peroxide was recently considered to be a vascular relaxing factor as endothelium-derived relaxing factor (EDHF). Thus, our findings suggest that inhibition of neutrophil oxidative burst by PMX-DHP possibly plays an important role in improving hemodynamic instability of septic shock.

Study of Direct Hemoperfusion with Polymyxin-B Immobilized Fiber Column in a Patient with Idiopathic Interstitial Pneumonia and Complication of Acute Respiratory Distress Syndrome-Change of Marker in Bronchoalveolar Lavage Fluid and Blood-
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.54-59 (2003)
Figure&Table&Reference: FIG.9, REF.6
Abstract: Acute respiratory distress sydrome (ARDS) is often complicated by severe infection. Recently there have been a few reports that direct hemoperfusion using a polymyxin-B immobilized fiber column (PMX-DHP) is effective for ARDS. We experienced a case of ARDS of idiopathic interstitial pneumonia, using PMX. After treatment, neutrophils in the bronchoalveolar lavage fluid (BALF) decreased, and chest X-ray and CT tended to improve. But the PaO2/FIO2 ratio was not significantly changed. Concentrations of KL-6, SP-D, TNF-.ALPHA., IL-6, and IL-8 in blood showed no change. Further study on the effects of PMX-DHP using measurements of cytokines, KL-6, SP-D in BALF, is strongly merited.

A Case of Septic Shock (Klebsiella pneumoniae cholecysto-cholangitis) Successfully Treated with Combined PMX-DHP and CHDF
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.60-65 (2003)
Figure&Table&Reference: FIG.5, TBL.1, REF.12
Abstract: We encountered a patient having severe sepsis with underlying uncontrolled diabetes mellitus, who responded to combined PMX-DHP (endotoxin absorption therapy) and CHDF (continuous hemodiafiltration). The patient, a 71-year-old man, had a severe infection due to obstructive cholecysto-cholangitis, and associated septic shock and DIC. After tracheal intubation, intensive care was started, with the patient being placed on artificial ventilation. Percutaneous transhepatic gallbladder drainage (PTGBD) was performed. Klebsiella pneumoniae was detected in the drainage fluid and a blood specimen. CHDF was started approximately 10 hours after the onset, and PMX-DHP within 24 hours of the onset of septic shock. CHDF was later instituted again and continued until the 4th day of hospitalization. We used PMX-DHP and CHDF for the treatment of septic shock due to severe cholecysto-cholangitis. Consequently reduced blood levels of endotoxin and anandamide were associated with improved clinical symptoms. Therefore, we consider that combined PMX-DHP and CHDF were useful for treating severe sepsis.

Apheresis Therapy for Severe Acute Pancreatitis
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.66-72 (2003)
Figure&Table&Reference: FIG.5, TBL.4, REF.14
Abstract: The relationship between timing, period, and outcome of each apheresis therapy in 50 severe acute pancreatitis cases were examined retrospectively. Survival of 25 patients with apheresis therapy was 72%. In those cases, continuous hemodiafiltration (CHDF) (n=22), plasma exchange (PE) (n=5), or polymyxin-B immobilized fiber therapy (PMX-DHP) (n=8) was started 3, 16, or 44 days after the onset, and performed 5 days, 3 times, or 1 time, respectively (median). Survival was low if CHDF was started 3 days or more after the onset, or more than 8 times, PE did 3 days or more after the onset, or PMX-DHP did twice or more. We presented a hypertriglyceridemic necrotizing pancreatitis case, in which decision of indication, timing, and period of each apheresis therapy was very difficult. Finally, he died of multiple organ failure. We conclude that each apheresis therapy may contribute to improve outcome, but should be started immediately after the onset of disease. We should consider other treatments such as necrosectomy, if apheresis could not ameliorate the disease.

A Case of Colon Perforation with Septic Shock Treated by PMX-DHP-Evaluation of the Starting Time and Number of PMX-DHP Performed-
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.74-78 (2003)
Figure&Table&Reference: FIG.3, REF.12
Abstract: The patient was a 77-year-old woman. Right hemicolectomy and lieostomy were performed for perforating transverse colon cancer. The patient, in septic shock before surgery, was managed with vasopressors, PMX-DHP, and CHDF, but died of multiple organ failure on the 9th hospital day. The first PMX-DHP performed immediatery after surgery improved circulatory dynamics, and reduced anandamide and TNF-.ALPHA. levels, however the second PMX-DHP performed 24 hours later did not improve circulatory dynamics, and even increased anandamide and TNF-.ALPHA. levels. Since the health insurance limits the number of PMX-DHP performed to twice, the determination of the starting time and whether to further increase the number of PMX-DHP are controversial. In this case, the starting time of PMX-DHP was delayed despite the marked severity of the patient's condition, therefore, PMX-DHP should be started based on the evaluation of SOFA and APACHE-II score, and the number of times of PMX-DHP should be determined based on the overall consideration of the patient's condition and institutional judgement.

Low Body Weight Pediatric Patients Treated with Continuous Blood Purification and PMX-DHP
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.85-90 (2003)
Figure&Table&Reference: FIG.4, TBL.2, REF.7
Abstract: Treatment with PMX-DHP for pediatric septic patients is not generalized. We report 2 low body weight pediatric patients treated with PMX-DHP. Body weight of patient 1 was 1,800g and her birth weight was 646g. Because she had a septic state after poor intestinal movement at day 179, we treated her with continuous hemofiltration followed by two consecutive PMX-DHP therapies. On PMX-DHP, blood pressure was stable, and we could treat her safely. But, efficacy was not sufficient, and she died at day 197. Patient 2 was born at 3,072g and had gastric perforation. At day 3, we started continuous hemodialysis after emergency operation, and at day 5, she was treated for sepsis with additional PMX-DHP therapy twice. Soon, her blood pressure and level of consciousness improved. At day 19, we discontinued continuous blood purification. If technical difficulties related to the indications for pediatric patients who have their small body and septic state are overcome, PMX-DHP would be a very effective treatment. However, we need more experience of its application.

Efficacy of the Treatment with PMX-DHP and Plasma Exchange Combined with Steroid Pulse Therapy for Pediatric Septic MODS (Multiorgan Dysfunction Syndrome)
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.92-97 (2003)
Figure&Table&Reference: FIG.4, TBL.2, REF.7
Abstract: Recently developed immobilized polymyxin B (PMX) fibers column with low-priming volume, enabled us to apply PMX-DHP (direct hemoperfusion) to small pediatric patients. Treatment including PMX-DHP and plasma exchange combined with steroid pulse therapy was given to seven children with multiorgan dysfunction syndrome (MODS) caused by septic shock. We evaluated the efficacy of this therapy in terms of clinical improvement and elimination of humoral mediators such as cytokines. Five patients among 7 were survived. Improvement of hypotension, cardiac malfunction, oliguria and respiratory distress were achieved in 6, 4, 3, and 5 children, respectively. Inflammatory cytokines (IL-1.BETA.,IL-6,IL-8,TNF-.ALPHA.) were decreased under the treatment protocol although anti-inflammatory cytokines (s-IL-6R,s-TNF-.ALPHA.R) were preserved. Lipid peroxide levels decreased during PMX-DHP, which suggested that PMX-DHP could relieve oxidative stresses.

A Case Report on the Successful Treatment of two Low-body Weight Children with Direct Hemoperfusion Using Low-priming Volume of Polymyxin-B Immobilized Fiber (PMX-05R)
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.99-102 (2003)
Figure&Table&Reference: FIG.2, TBL.1, REF.6
Abstract: We report 2 pediatric cases of septic shock, which were successfully treated by polymyxin-adsorbed column-direct hemoperfusion (PMX-DHP). Case 1 was a 9-year-old boy, who was diagnosed with primary hypersoxaluria type 1 (body weight 16kg). He underwent living-related liver transplantation and living-related kidney transplantation. Unfortunately, his kidney graft bled and was removed 3 weeks after transplantation because of a rupture of the graft associated with rejection. Because septic shock due to perforation of the digestive tract in association with the operations for graft bleeding, PMX-DHP was immediately performed to treat this critical dondition. Case 2 was a 16-year-old boy, who was diagnosed with congenital nephrotic syndrome (body weight 14.4kg). He experienced septic shock of bacterial translocation caused by encapsulating peritoneal sclerosis associated with long term peritoneal dialysis, and PMX-DHP was applied. Low priming volume of polymyxin-B immobilized fiber (PMX-05R) allowed PMX-DHP to be performed in small children with hemodynamic stability.

The Changes of Blood Levels of Anandamide and 2-Arachidonylglycerol in Infants with PMX-DHP therapy
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.106-111 (2003)
Figure&Table&Reference: FIG.6, REF.15
Abstract: Objective: Anandamide (ANA) and 2-arachidonylglycerol (2-AG), which are endogeneous cannabinoids, induced by endotoxicin of gram-negative and peptidoglycan of gram-positive bacteria, are remarkable in sepsis. Endogeneous cannabinoids are associated with hypotension in sepsis, and when they are excluded by PMX-DHP therapy, blood pressure increased in adult cases. We have analyzed endogeneous cannabinoids in the infants with PMX-DHP therapy for sepsis. Method: In the three infants, we have measured, and analyzed heart rate (bpm), systolic and diastolic pressure (mmHg) before, during, and after PMX-DHP therapy and ANA (pmol/mL), 2-AG (pmol/mL), endotoxin (pg/mL) level before and after PMX-DHP therapy. Result: (1) Heart rate; before 132.+-.7, during 136.+-.17, after 136.+-.16. (2) Systolic/diastolic pressure; before 37.6.+-.10.2/23.6.+-.6.6, during 47.8.+-.14.6/28.8.+-.8.1, after 42.1.+-.12.8/27.2.+-.8.4. (3) ANA: Case 1; before 31, after 15.6. Case 2; before 26.7, after 24. Case 3; before 16.3, after 11.8. (4) 2-AG: Case 1; before 182.6, after 94.5. Case 2; before 76.1, after 55.7. Case 3; before 63.1, after 13.3. (5) Endotoxin: Case 1; before 2,510, after 2,000. Case 2 and Case 3; before 0, after 0 Conclusion: These results suggest that an increases of blood pressure were associated with a decrease of ANA, 2-AG adsorbed by PMX in the infants.

One Hundred Twenty Cases of Direct Hemoperfusion with Polymyxin-B Immobilized Fiber (PMX) in Single Center Experience
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.119-122 (2003)
Figure&Table&Reference: FIG.6, REF.6
Abstract: Beneficial effects of PMX were examined for severe septic MOF in our center. 120 patients were treated with PMX to manage severe septic shock. Overall survival rate after 1 month was 63.3%. In the survival (n=76) group, the dose of vasopressor was successfully reduced from 18.5 to 12.1.MU.g/kg/min. Mean arterial pressure (MAP) was increased from 75.4

to 89.5mmHg one day after blood purification. Moreover, remarkable decreases of PAI-1, and IL-6 level were demonstrated. One the other hand, the does of vasopressor could not be reduced in spite of PMX treatment in the non-survival group (n=44). PAI-1 level did not statistically decrease. severity score (SSS) of more than 40 showed poor survival. In conclusion, aggressive prophylactic use of blood purification combined with use of PMX was effective to achieve recovery from hemodynamic instability and outcome in severe MOF patients.

Treatment Results and Clinical Significance of Endotoxin Adsorption Therapy
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.126-131 (2003)
Figure&Table&Reference: FIG.1, TBL.7, REF.7
Abstract: There are many reports saying that PMX-DHP (commercial name: TORAYMYXIN; made by Toray Medical Co.) is effective for septuc cases. We examined the clinical significance of PMX-DHP in peritonitis cases with digestive canal perforation. Patients and Methods: We studied 27 cases, to whom PMX-DHP was applied, among 129 cases of peritonitis surgery, excluding cases of iatrogenicity, for whom surgery was performed between April 1997 and December 2002, and 68 large intestine perforation cases, excluding those of iatrogenicity, which included cases occurring before the introduction of PMX-DHP, i.e., during the period from 1987 to March 1997. We compared clinical factors and mortality rates of the large intestine perforation cases before and after the introduction of PMX-DHP, as well as the surviving cases to whom PMX-DHP was applied. Results and Discussion: (1) The non-surviving cases to whom PMX-DHP was applied had significantly high blood-creatinine values and APACHE-II scores. (2) The survival rate of the cases showed no increase even after the introduction of PMX-DHP. (3) NO deaths were observed among the cases with an APACHE-II score of 10 or less to whom PMX-DHP was applied. (4) The cases with abnormally high blood-creatinine values, to whom PMX-DHP was applied, showed high mortality rates. In the future, we should examine a more appropriate timing of PMX-DHP application and the possibility of using PMX-DHP in combination with other blood purifying methods, comparing their characteristics to each other.

The Study on Direct Hemoperfusion with Polymyxin-B Immobilized Fiber in Patients with Acute Respiratory Distress Syndrome Developed from Pneumonia
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Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.136-140 (2003)
Figure&Table&Reference: FIG.1, TBL.3, REF.5
Abstract: We researched the therapeutic effects of PMX-DHP for septic acute respiratory distress syndrome (ARDS). The patients with ARDS divided into two groups: survival group (n=10) and dead group (n=7). PMX-DHP was carried out twice at a rate of 80-100mL/minute for 2 hours, with a time interval of approximately 24 hours for septic ARDS, which suffered from pneumonia as underlying diseases. We monitored systolic blood pressure (BP), diastolic BP, and the PaO2/FIO2 (P/F) ratio before and after initial PMX-DHP treatment. We performed blood culture and sputum culture for all patients. Before treatment of PMX-DHP, the death group showed the delay of PMX-DHP treatment, and platelet counts showed the decrease significantly. The P/F ratio increased significantly after PMX-DHP on survival group. PMX-DHP showed good effectiveness for the subjects which underlying diseases are good control. We discussed the start and performed time of PMX-DHP treatment for the patients with bad control.

Correlation Between Changes in Mediators and Number of Dysfunctional Organs in Sepsis-associated Multiple Organ Dysfunction Syndrome (MODS)
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.146-151 (2003)
Figure&Table&Reference: FIG.6, TBL.1, REF.7
Abstract: Changes in hemodynamics and a variety of mediators such as cytokines were compared with respect to the number of dysfunctional organs in

MODS cases treated with blood purification. Subjects and Methods: This study included 116 cases of MODS, which were treated with PMX-DHP. Background factors, circulatory parameters and inflammatory mediators were measured before initiating PMX-DHP. Organ dysfunction was evaluated using the MOF score according to Goris, where organ dysfunction was judged positive when the score was more than 1 point for each organ. Results: The rate of survival for more than 28 days from the start of blood purification clearly decreased as the number of dysfunctional organs increased. The APACHE-II score and the SOFA score significantly increased with an increase of dysfunctional organs, with a significant correlation. The mean IL-6 level was highest in cases with dysfunction of 4 organs. The BNP level appeared to increase as the number of dysfunctional organs increased. Conclusion: A variety of humoral mediators, including cytokines, increased as the number of dysfunctional organ increased, while the level of the increase differed for each mediator. Possible involvement of BNP was suggested in the development of sepsis-associated MODS, and will be further studied in the future.

A Successful Case of Curing an Advanced Aged Patient with Septic Shock, Using PMX-DHP
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.177-181 (2003)
Figure&Table&Reference: FIG.2, TBL.3, REF.11
Abstract: Generally, it is difficult to save the life o an aged patient who is suffering from septic shock. But, we succeeded in curing a 90-year-old woman of septic shock completely, using PMX-DHP. She developed septic shock caused by a perforation of the ileum due to incarcerated femoral hernia. Now, she has returned to her normal life at home. This shows that PMX-DHP is an effective treatment for septic shock, and in this aged patient's case, it consequently reduced the cost of care.

Case Report of Septic Shock after Operation Improved by 4th Polymyxin-B Immobilized fiber Theraqpy (PMX-DHP)
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.190-193 (2003)
Figure&Table&Reference: FIG.2, TBL.2, REF.6
Abstract: It is well known that PMX-DHP, which removes not only endotoxins but also other unidentified bioactive-lipids, is effective for septic shock caused by both gram-positive and gram-negative bacteria. Here, we report a case who recovered from septic shock following PMX-DHP treatment. The patient is a 62 year-old man who received the partial gastrectomy due to hemorrhagic gastric ulcer. High grade fever continued for more than 4 days, and the patient was considered to be in septic shock due to an unknown infectious focus. We decided to perform direct hemoperfusion of PMX-DHP to remove endotoxins. After 4 times of PMX-DHP, blood pressure increased and the patient's condition improved. In Japan, PMX-DHP is limited to second times under the medical insurance system. But, if necessary, we consider that more than second times of PMX-DHP should be provided.

Two Patients Treated with Early Endotoxin Absorbance Therapy Survive Endotoxin Shock Associated with Hematological Malignancy
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.196-202 (2003)
Figure&Table&Reference: FIG.6, TBL.3, REF.5
Abstract: When patients with hematological malignancy develop endotoxin shock, their immunological activities decrease due to the underlying disease and chemotherapy, which can impact their survival. We report 2 patients with endotoxin shock who survived after endotoxin absorbance therapy. (Case 1) A 65-year-old man,. Chief complaint: Inguinal lymph node swelling. Present history: The patient developed inguinal lymph node swelling from end of October 1999, and general fatigue in November 1999. He also showed: WBC 71,800/.MU.L (Ly 6%); Hb 10.8g/dL; PLT 15*104/.MU.L; and peripheral lymphocyte increase. On November 25, 1999, the patient was admitted for detailed examination and treatment. Hospital course: Bone marrow aspiration and lymph node biopsy showed CD 5 negative and CD 10 positive, excluding chronic lymphocytic leukemia (CLL) as the diagnosis. Because cell surface immunoglobulin positive is not commonly associated with acute lymphocytic leukemia

(ALL), we diagnosed the patient as having non-Hodgkin's lymphoma. L-AdVP therapy on December 22, 1999 decreased WBC (1,700/.MU.L) and blood pressure (70/40mmHg) and he was diagnosed as having endotoxin shock. He responded poorly to DOA and NA, thus on December 24, 1999 we conducted endotoxin absorbance therapy with a column of TORAYMYXIN (Toray Medical Co., Ltd., Tokyo, Japan). Directly after the therapy, the patient's blood pressure returned to normal, and endotoxin level decreased from 40.8 to 9.4pg/mL. Granulocyte colony-stimulating factor (G-CSF) was administered; WBC increased and sepsis was alleviated. (Case 2) A 58-year-old woman. Chief complaint: Fever. Present history: The patient presented fever and low back pain from August 2001. On September 7, 2001, when the patient's WBC was 8,500/.MU.L (blast 2%), she was admitted for detailed examination and treatment. Hospital course: Bone marrow aspiration revealed blast, 89%, and we diagnosed the patient as having acute lymphatic leukemia (ALL)....

The Effects of Direct Hemoperfusion with Polymyxin-B Immobilized Fiber (PMX-DHP) on Septic Shock Caused by Panperitonitis
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.204-209 (2003)
Figure&Table&Reference: FIG.4, TBL.2, REF.11
Abstract: We examined the effects of PMX-DHP in a case of abdominal surgery for septic shock caused by panperitonitis. Twelve patients with postoperative panperitonitis were treated with PMX-DHP to manage septic shock. Seven cases were lower bowel perforation, 2 were duodenal ulcer perforation, 2 were small intestine necrosis, and 1 was caused by unknown etiology. Because 10 of 12 septic shock patients left ICU and 7 of these 10 patients left hospital, PMX-DHP was considered effective for septic shock caused by panperitonitis. The important effects of PMX-DHP are elevation of blood pressure and improved SIRS state. However, because of APACHE-II score for cases of mortality 21 or more and the Goris score was 6 or more, after organ insufficiency has advanced, PMX-DHP is seldom expected tobe effective.

DHP by Polymyxin B Column (PMX) improved P/F Ratio in A Patient of Septicemia-Good Correlation Between EVLW and P/F Ratio-
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.7; NO.1; PAGE.211-216 (2003)
Figure&Table&Reference: FIG.4, TBL.1, REF.3
Abstract: We experienced a case of severe pneumonia with septicemia. A 66-year-old male patient who was treated with steroid for 3 months due to nephrosis complained of fever and dyspnea. Laboratory examination revealed severe hypogranulocytosis, thrombocytopenia, and low P/F ratio. On admissioin to ICU, we started PMX-DHP therapy while monitoring hemodynamics with a PCCO system. Blood pressure and cardiac output began to rise within 30 minutes after initiating PMX-DHP, and continued to develop after cessation following 3 hours of PMX-DHP therapy. PaO2 developed just after the initiation, and decreased again after cessation of PMX-DHP. In this case, the P/F ratio correlated with extra-vascular lung water (r2=0.753), and had no correlation with hemodynamic parameters such as cardiac output and blood pressure. This correlation suggests that PMX-DHP may have a direct action on the permeability of pulmonary capillaries.

2004

Effective Period for Using Endotoxin Adsorbing Column
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.42-47 (2004)
Figure&Table&Reference: FIG.5, TBL.1, REF.11
Abstract: We conducted a retrospective study on changes in cardiopulmonary performance due to the prolongation of endotoxin adsorption therapy (PMX-DHP). We divided 12 cases of septic shock totaling 14 PMX-DHP treatments into two groups: Group S,

consisting of 8 treatments lasting 2 hours, and Group L, consisting of 6 treatments lasting more than 2 hours. No significant differences between the groups in any of the study criteria were noted at the start of PMX-DHP treatment. After 12 hours, APACHE-II scores for both groups showed declining trends. Circulation was also improved in both groups. As time passed, Group L had greater volumes of urine, and after 12 hours, the group's water balances displayed negative values. Only in Group L did the P/F ratio 12 hours post-treatment show on improvement over the measurement taken 6 hours after. Respiratory index also declined only in Group L. An approximately 50% drop in platelet counts was noted in both groups on the following day. No side effects to prolonged PMX-DHP were noted. It produced the same circulatory improvements as the 2-hour treatment, and the possibility of further respiratory amelioration was also suggested.

Effects of Free Radical Scavengers in Rat Septic Peritonitis Model
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.57-62 (2004)
Figure&Table&Reference: FIG.7, REF.11
Abstract: To assess the efficacy of scavengers on lung and liver injury during rat sepsis induced by cecal ligation and puncture, we examined the lung and liver contents of 8-oxo-deoxyguanosine (8-oxo-dG), a major product of DNA oxidative damage and the expression level of the MTH-1 gene encoding the 8-oxo-dG DNA glycosylase in lung and liver. Lung myeloperoxidase (MPO) activity and nitrotyrosine contents were measured as indices of lung injury. Liver AST, ALT, and nitrotyrosine contents were measured as indices of liver injury. In the lung, the MPO activity and ratios of nitrotyrosine/tyrosine and 8-oxo-dG/dG were significantly lower in the PEG-CAT (polyethylene glycol-absorbed catalase)-treated group than in the untreated group. In the liver, the ratio of nitrotyrosine/tyrosine was significantly lower in the PEG-CAT (polyethylene glycol-absorbed catalase)-treated group than in the untreated group. But, the ratio of 8-oxo-dG/dG did not show statistically significant difference between two groups. There were a significant differences in lung and liver histology between the PEG-CAT-treated and untreated groups. However, there was no difference in the survival rate between the 2 groups. These results suggest that other factors are responsible for mortality in rat sepsis.

Managing Endotoxemia with Naturally Derived Anticoagulants
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.63-68 (2004)
Figure&Table&Reference: FIG.5, REF.10
Abstract: The inflammatory response in severe sepsis is integrally linked to procoagulant activity and endothelial activation, and abnormalities in the microcirculation results in the development of septic organ dysfunction. Natural anticoagulants, such as antithrombin III and activated protein C are expected not only to improve the unbalanced coagulation/fibrinolysis system to modulate the endothelial function, but also to express anti-inflammatory properties. To certify these effects, numbers of preclinical studies, phase II clinical trials, and finally a large-scale, multiple center, randomized, placebo-controlled trial using recombinant human activated protein C (PROWESS trial) have been performed. The results show that APC has anti-coagulatory properties, suppresses inflammatory cytokines, and suppresses leukocyteendothelial interaction, which together lead to a statistically significant improvement in the survival of patients with sepsis-induced organ dysfunction (absolute risk reduction in 6.1%).

Study on PMX-DHP Therapy for Sepsis Using a Highly Sensitive Assay of Endotoxin
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Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.79-83 (2004)
Figure&Table&Reference: FIG.3, TBL.1, REF.5
Abstract: The therapeutic effects of PMX-DHP were investigated using a hypersensitive method for measuring endotoxin levels (hypersensitive method). The subjects were 24 patients with septic shock complicating peritonitis. Their mean age was 70.3.+-.16.0 years, and the male: female ratio was 15: 9. The mean SOFA score was 7.2.+-.2.1, and Gram-negative bacteria were cultured from ascitic fluid or blood in 12 patients (50%). PMX-DHP was conducted twice in 19 patients and once in the remaining 5 patients. The

endotoxin level in peripheral blood decreased from 7.2.+-.16.0pg/mL before PMX-DHP to 4.2.+-.9.8pg/mL after the first PMX-DHP, and 3.0.+-.5.2pg/mL to 2.2.+-.4.6pg/mL after the second PMX-DHP, indicating a significant decrease in the endotoxin level after the first and second PMX-DHP. The clinical symptoms also improved after PMX-DHP. Based on these results, PMX-DHP was confirmed to be useful in the treatment of septic shock.

Oxidative Stress in Septic Patients
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.84-88 (2004)
Figure&Table&Reference: FIG.6, REF.5
Abstract: Background: Edogenous cannabinoids (arachydonylethanolamide and 2-arachydonylglycerol) are factors causing septic shock and isoprostane (8-epi-prostaglandin F2.ALPHA.; 8-epi-PGF2.ALPHA.) as an index of oxidative stress. Polymyxin-B absorbs endogenous cannabinoids, and direct hemoperfusion therapy with polymyxin-B immobilized fiber (PMX-DHP) decreases the serum levels of endogenous cannabinoids. To investigate the features of sepsis and defermine reasonable usage of PMX-DHP, we compared the transition of perioperative endogenous cannabinoids and isoprostane in myoma uteri, esophagus cancer, and septic patients. Results: Perioperative arachydonylethanolamide was myoma uteri=esophagus cancer=septic patients. 2-arachydonylglycerol was myoma uteri

The Effects of Direct Hemoperfusion with Polymyxin-B Immobilized Fiber (PMX-DHP) in Unoperated Septic Shock Cases
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.100-105 (2004)
Figure&Table&Reference: FIG.4, TBL.2, REF.13
Abstract: We evaluated the effects of PMX-DHP in patients with septic shock who did not undergo surgery. Ten patients who did not undergo surgery were treated with PMX-DHP to manage septic shock. There were cases of postoperative multi-organs failure, severe acute pancreatitis, acute obstructive cholangitis, lung abscess, pneumonia, enteritis, Hodgkin disease, and deep fungal infection. The 2 remaining cases were of unknown etiology. Eight of 10 septic shock patients weaned from shock state, 6 of these 8 patients left ICU. Three of 10 patients left hospital. In non-survival cases, the period suffered from sepsis before induction of PMX-DHP was long, Goris score was 6 or more and APACHE-II score was 21 or more. PMX-DHP was considered to be effective for unoperated septic shock cases. PMX-DHP should be started within 24 hours after septic shock shows the symptoms before organ insufficiency progresses.

Significance and Availability of Continuous Hemodiafiltration for Severe Acute Pancreatitis-A Case Report on Continuous Arterial Infusion-
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.118-123 (2004)
Figure&Table&Reference: FIG.4, TBL.2, REF.7
Abstract: Severe acute pancreatitis is defined as a systemic inflammatory disease with infected necrosis, DIC and multiple organ failure. We encountered a patient, a 32-year-old man, having severe acute pancreatitis, who responded to combined CHDF and a continuous arterial infusion therapy. He satisfied 4 items of SIRS in our hospital initial diagnosis. He had respiratory failure and acute renal failure, and the severity score was 14 points and the grade of stage was 3 according to the severe acute pancreatitis seriousness classification of the Ministry of Health and Welfare. We started artificial breathing control, CHDF, and continuous arterial infusion with fluid therapy, infusion antibiotics, and protease inhibitor. He could leave CHDF on the 8th day of hospitalization and extubation became possible on the 14th day of hospitalization. CHDF and continuous arterial infusion for sever acute pancreatitis are still controversial regarding utility, but from the seriousness of the diagnosis and strict case selection, we consider that CHDF and continuous arterial infusion are useful for treating severe acute pancreatitis.

Efficacy of Polymyxin-B Immobilized Fiber (PMX-DHP) and Continuous Hemodiafiltration (CHDF) Therapy for Severe Acute Pancreatitis with ARDS and DIC
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.124-128 (2004)
Figure&Table&Reference: FIG.2, TBL.1, REF.11
Abstract: We report on the efficacy of PMX-DHP and CHDF therapy in a patient with severe acute pancreatitis, which was triggered by hemorrhage in the pseudocyst. A 19-year-old man was diagnosed as acute pancreatitis and admitted to another hospital. He improbed following treatment, but the condition recurred after starting meals again. He was transferred to our hospital. He experienced sudden systemic inflammatory response syndrome (SIRS) and severe acute pancreatitis because a hemorrhage occurred in the pseudocyst at the 4th day after transfer. We started respiratory control, continuous regional arterial infusion, closed drainage, volume resuscitation, and CHDF for volume control in the intensive care unit (ICU). We performed PMX-DHP because we suspected sepsis at the first and 7th day after admission to ICU. He was transfered to a general ward without surgery. We suggested that PMX-DHP was effective in this case, because serum endotoxin, body temperature, and blood pressure were normalized in spite of no evidence of bacterial infection. We also suggested that CHDF could make volume resuscitation to dehydration easier.

Using PMX-DHP, a Successful Case of Curing an Aged Patient with Septic Shock Caused by Peritonitis Due to Methicillin-resistant Staphylococcus aureus (MRSA)
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.130-135 (2004)
Figure&Table&Reference: FIG.2, TBL.3, REF.8
Abstract: It is reported that cannabinoids play substantial roles in the pathogenesis of septic shock caused not only by endotoxin but also by gram-positive infection. Recently, PMX-DHP has been found to remove cannabinoids, so some researchers consider it to be a valid remedy for gram-positive septic shock. We succeeded in curing an 87-year-old woman of septic shock using PMX-DHP. She developed septic shock caused by peritonitis due to a repture of the urinary bladder, which was cased by radiation cystitis contaminated with methicillin-resistent Staphylococcus aureus (MRSA). This means that PMX-DHP is an effective treatment for septic shock due to gram-positive infection.

Efficacy and Safety of Polymyxin-B immobilized Fiber with Direct Hemoperfusion (PMX-DHP) for Septic Shock in Neutropenia Patients after Chemotherapy for Hematological Malignancies
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.141-145 (2004)
Figure&Table&Reference: FIG.3, REF.5
Abstract: We examined the effects of PMX-DHP therapy for septic shock in neutropenia patients after chemotherapy for hematological malignancies. We experienced 4 cases among 5 patients septic shock using PMX-DHP from April to October 2003 in our institute. The mean age of all patients was 68 years old. Two cases survived but 3 cases died from septic shock or respiratory failure. Neutrophil did not increase in the 2 cases who died due to septic shock. In contrast, neutrophil increased within a few days in the surviving cases. The mean platelet count was 1.5*104/.MU.L, but all patients were safely treated with PMX-DHP without severe hemorrhage. We can conclude that PMX-DHP should be attempted in neutropenia patients with septic shock, especially if there is a chance of early neutrophil recovery.

Efficacy of PMX-DHP Therapy in Two Patients with Septic ARDS
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.147-152 (2004)
Figure&Table&Reference: FIG.6, TBL.2, REF.4
Abstract: Pulmonary oxygenation was significantly improved after long-term PMX-DHP therapy in 2 patients with septic ARDS. Case 1: A-63-year-old man suffered from respiratory insufficiency in ER due to severe bacterial pneumonia. As no improvement was observed in pulmonary oxygenation with conventional therapy, long-term PMX-DHP (total of 39.5 hours, preformed twice) was performed. Case 2: A-66-year-old man developed ARDS, which progressed to aspiration pneumonia. Conventional therapy did little to improve pulmonary oxygenation, as in case 1, Then, PMX-DHP (5 hours) was performed. The P/F (PaO2/FIO2) ratio was significantly improved by PMX-DHP in 2 cases, and the improvement of the P/F ratio had no correlation with the change of urine output and water balance. However, the mechanism that improved pulmonary oxygenation with PMX-DHP has not been clearly shown, and it remains to be examined further.

A Case that Underwent Plasma Exchange for Newborn Hemophagocytic Lymphohistiocytosis (HLH)
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.158-161 (2004)
Figure&Table&Reference: FIG.4, TBL.1, REF.2
Abstract: We report out experience of performing a plasma exchange (hereinafter PE) on a newborn who developed hemophagocytic lymphohistiocytosis (hereinafter HLH) during the fetal period. The patient was a female, 0 day of age. She was born after 39 weeks and 0 day of gestation, with the body weight of 2,954g. Because the skin over her whole body was pale with many purpura, she was given an emergency transfer to the NICU of our hospital. A definite diagnosis of HLH was made after identifying hemophagocytosis with a marrow examination. We performed PE 5 times from 12 days of age to treat hypercytokinemia, using the blood purification equipment ACH-07S, the plasma separator OP-02W, and the blood circuit CHF-704N (Asahi Medical). Cytokine values decreased before and after PE. We considered this to be an effective temporary symptomatic treatment for hypercytokinemia. Vital signs were relatively stable during the performance of PE. We need to further study technical issues of the technique as a blood purification therapy for neonates.

Evaluation of 100 Cases Treated with PMX-DHP
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.187-192 (2004)
Figure&Table&Reference: FIG.9, TBL.3, REF.8
Abstract: We evaluated data on PMX-DHP and tried to rediscover not only the effects of PMX-DHP, but also the results of examinations and measurements that are useful for understanding the state of patients in our facility. Objects: 100 cases treated with PMX-DHP in our facility. Results: There were 56 survival cases and 44 deaths. The number of patients who died within 7 days was 18, which was significantly large. We divided the patients into 3 groups for evaluation: the early death group (died within 7 days), the later death group (died within 28 days), and the long-term death group (died after 28 days). The rate of lives saved was high in G (-) infectious diseases. The later death rate was significantly high in the endotoxin positive group and the early death rate was high in sepsis witn unknown causes. APACHE-II and SOFA score were high in the death group, and peripheral lymphocyte count increased significantly in the survival group after 5 days. Conclusions: When the effectiveness of PMX-DHP is evaluated according to survival rate, a difference is seen in the rate of lives saved and time of death depending on indicated diseases. We suggest that peripheral lymphocyte count is a useful parameter of the immunodeficient state.

Two Cases of Infectious Lung Disease with Severe Respiratory Failure Improved by Direct Hemoperfusion Using a Polymyxin-B Immobilized Fiber Column (PMX-DHP)
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.199-205 (2004)
Figure&Table&Reference: FIG.9, TBL.2, REF.12
Abstract: Two cases of infectious lung disease with severe respiratory failure were successfully treated with PMX-DHP. Case 1: A 43-year-old diabetic female was admitted to our hospital with severe pneumonia caused by type A influenza virus, Staphylococcus aureus and Haemophilus influenzae infection. From day 12 after admission, she was treated twice with PMX-DHP and 7 days with continuous hemofiltration. Her blood oxygen level and chest X-ray findings improved sufficiently for her to be discharged from a respirator on day 33. Case 2: A 52-year-old male was admitted to our hospital with empyema due to an esophageal rupture. Group B Streptococcus agalactiae, Escherichia coli and Staphylococcus aureus were cultivated from his pleural fluid. Immediately after admission, cardiopulmonary resuscitation was performed, however, his oxygen level continued to decline due to ARDS. The patient was treated with PMX-DHP on days 4 and 5, and was released from the respirator on day 9. In both cases PMX-DHP was effective to improve hemodynamic condition and oxygenation.

A Case Report of a Successful Treatment of Endotoxin Shock by an Early PMX-DHP
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.207-211 (2004)
Figure&Table&Reference: FIG.2, TBL.1, REF.7
Abstract: A 37-year-old male was admitted to the hospital because of high fever. Ten days before admission, the patient complained of a sore throat and headache which persisted, but did not have any fever. The patient had a history of asthma and splenectomy at the age of three, because of a car accident. On the day he was admitted to the hospital, he had high fever, abdominal pain and nausea since morning. In the same night, the patient was found unconscious on the floor of the bathroom and was transported to the hospital in an ambulance. He had a cut on his eyelid, and while being treated, his blood pressure fell to 60mmHg. Resuscitative measures were taken and the patient was quickly transferred to the intensive care unit, where his blood pressure again dropped. Ventricular fibrillation appeared on the monitor, and DC shock was given, along with other cardiopulmonary resuscitative measures. Since the patient was suspected of being in septic shock, endotoxin absorption therapy PMX-DHP was commenced. Half an hour later, his blood pressure began to rise above 60mmHg and eventually returned to normal. Since admission to the hospital, the patient's kidney function kept falling and he was consequently put on CHDF in order to remove harmful cytokines from his blood. For a while, the blood pressure was stable at 120mmHg, but eventually fell and the patient received another PMX-DHP on the second hospital day. On the fourth hospital day, the patient's blood pressure dropped to 70mmHg. By then, he was diagnosed with endotoxic shock with the report of endotoxin level of 761.2pg/mL, from a blood sample obtained at admittance, and hence received a third PMX-DHP. CHDF was continued for five consecutive days after which his laboratory results revealed an improved organ function with sufficient urine output. On the thirteenth hospital day, he was able to come out of the mechanical ventilation....

A Case of Unsuccessfully Treated Septic Shock Due to Rectal Perforation
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.214-218 (2004)
Figure&Table&Reference: FIG.5, TBL.1, REF.12
Abstract: A 70-year-old man, who was on CAPD for renal failure, was seen at our hospital for abdominal pain and fever, and was admitted with a diagnosis of catheter infection. In spite of conservative therapy, he entered a state of pan peritonitis with septic shock. An emergency operation was performed, and revealing a perforation of the rectum. After peritoneal lavage, we resected the rectum including the perforated part and made a sigmoid colostomy. After the operation, we performed PMX-DHP (4 hours/one time) and CHDF. After 4 tiems of PMX-DHP, he recovered from SIRS, but not from CHDF and artificial ventilation. On 31 POD, we performed thoracheostomy and he had a large volume of bleeding from the digestive organ on 56 POD, leading to death. We indicate that renal failure made his clinical course more complicated and treatment more difficult.

Two Cases of Septic Shock without Endotoxemia Successfully Treated with PMX-DHP Therapy

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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.8; NO.1; PAGE.220-225 (2004)
Figure&Table&Reference: FIG.3, TBL.3, REF.12
Abstract: We experienced 2 cases who reacted quickly to PMX-DHP therapy, although plasma endotoxin levels were low. Case 1 was a 66-year-old woman. She went into a septic shock caused by urinary tract infection, and DIC, ARDS were complicated. The plasma endotoxin level, analyzed by turbidimetric kinetic assay, was 1.6pg/mL. Case 2 was a 74-year-old woman. She also went into septic shock caused by a suppurative lumber spondylitis, and her plasma endotoxin level was below the measurement sensitivity. Both reacted quickly to PMX-DHP therapy, and their circulatory dynamics improved obviously. We often experience PMX-DHP therapy producing a good responsing for clinical septic shock, although plasma endotoxin levels are low. We considered some possibilities why PMX-DHP therapy were effective for these cases. 1) Medical treatment was started at an early stage rather than after endotoxins were emitted into blood. 2) Polymyxin immobilized fiber column adsorbed mediators other than endotoxins, such as endogenous cannabinoids, Anandamide (ANA), and 2-arachidonyl glyceride (2-AG). 3) Because of the low reliability of the plasma endotoxin level current measurement methods, we might change the cut-off index or measurement methtods according to the clinical situation.

2005

PMX-DHP Therapy to Adsorb and Deplete 2-AG
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.21-27 (2005)
Figure&Table&Reference: FIG.5, REF.9
Abstract: When 2-Arachydonyiglyceol (2-AG) is decreased before and after Polymyxin-B immobilized fiber direct hemoperfusion (PMX-DHP) therapy, an increase of blood pressure is more often recognized. Assuming that the effectiveness of PMX-DHP therapy lies in controlling 2-AG, our examination centered on the time course of 2-AG. We measured 2-AG and Anandamide (ANA) as intrinsic cannabis and 8-epi-prostaglandin F 2 as oxidized stress marker using GC-MS. We examined thrombomodulin and PAI-1 as parameters of endothelial cell dysfunction, and measured IL-6 to estimate the extent of invasiveness. In 18 of 26 cases with septic shock, 2-AG blood level decreased before and after PMX-DHP therapy (2-AG decreased group) for 2 hours, and 2-AG blood level decreased significantly before and after performing PMX-DHP therapy in the 2-AG decreased group, resulting in a sustained lowering of blood levels after performing PMX-DHP therapy. The remaining 8 cases showed increased blood levels of 2-AG before and after PMX-DHP therapy for 2 hours (2-AG increased group). However, this decreased at day 1 after performing PMX-DHP therapy, and it did not increase thereafter. Controlling 2-AG with PMX-DHP therapy is an effective treatment for improving hemodynamics in septic status. Considering the transition of the inflammatory mediator, a decrease of 2-AG alleviates inflammatory reactions. Improved hemodynamics, however, did not improve the organ dysfunction score. Further investigation is necessary to clarify the clinical significance of controlling 2-AG with PMX-DHP therapy.

Planning of Blood Purification for Patients with Septic Shock
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.32-35 (2005)
Figure&Table&Reference: FIG.2, TBL.2, REF.6

Abstract: The objects of acute blood purification has moved from a single organ damage such as the acute renal failures to septic shock and multi organ failure induced by sepsis. It has been understood that there is a difficult point in the effect of the removal of key mediator though CRRT. An intermittent method of increasing the amount of the substitution such as HVH, PMX-DHP, and the plasma exchange, etc. has been paid to attention. There are two methods whether to support vital organs or to remove the key mediators positively as a role of the blood purification. Therefor, it is necessary to establish mechanism of effectiveness and the evidence of the prognosis improvement to select the blood purification.

Investigation on Blood Endotoxin Levels in Cases Who Underwent PMX-DHP Therapy
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Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.41-45 (2005)
Figure&Table&Reference: FIG.3, TBL.4, REF.6
Abstract: We evaluated an our data on PMX-DHP and investigated a correlation between plasma endotoxin level and various parameters, chronic underlying diseases, sources of infection, and severity scores. We also considered why the cases with a high plasma endotoxin level are getting decreasing. 54 cases had PMX-DHP therapy for septic shock from January 2002 to October 2004. The mean plasma endotoxin level was 56.1.+-.234.8 pg/mL. There was no correlation between plasma endotoxin level and source of infection, APACHE II score, or SOFA score. However there were some differences because antibiotics which were used at first when septic shock occurred. The possibility of antibiotics-induced endotoxin release was suggested.

Usefulness of Soluble CD 14 Subtype Which as Is a New Diagnostic Marker for Sepsis
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Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.46-50 (2005)
Figure&Table&Reference:
Abstract: CD 14 is a receptor, which exists existing on the cell membrane of endotoxin and LBP complex, and transmits a signal of endotoxin inside the cell,; but however, it is also known to exist in blood as soluble protein. We discovered soluble CD 14 subtype (sCD 14-ST, 49 kD),the molecular weight of which is different from that of traditional CD 14 among soluble CD 14, and developed an assay for sCD 14-ST using the ELISA technique. In When examining ROC curves, it was clear that the measurement of ing the sCD 14-ST value in septic patients by this method provides a superior ability to diagnose sepsis compared to factors such as CRP, endotoxin, IL-6, and procalcitonin.

Early Induction of PMX-DHP for Sepsis Can Improve Clinical Condition.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.57-61 (2005)
Figure&Table&Reference: FIG.3, REF.21
Abstract: A 53-year-old man complained of fever and malaise. Chest X-ray films showed pneumonia, and he was hospitalized. Hematology tests performed on the same day revealed a low WBC (3.3*10'3'/.MU.L). His temperature was 38.8.DEG.C., pulse rate was 120/min, and respiration rate was 30/min. He was diagnosed as having sepsis, and was transferred to the emergency center of Surugadai Nihon University Hospital. Arterial blood gas analysis showed a low PaO2/FIO2 ratio (137), so respiratory management using a ventilator was instituted after tracheal intubation. The case was diagnosed as atypical pneumonia because the causative organism was unknown. Administration of imipenem (IMP) was started. PMX-DHP was also performed because septic shock was suspected. His pneumonia could not be controlled and the causative organism remained unknown. However, hemodynamics and tissue oxygen metabolism improved after 48 hr and 72 hr, respectively. The IL-8 level showed a decrease after 120 hr and the patient's SIRS was controlled.

Endotoxin Adsorbance Therapy (PMX-DHP) Improved the Condition of Severe Psittacosis Associated with Low Blood Pressure.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.65-69 (2005)
Figure&Table&Reference: FIG.4, TBL.3, REF.12
Abstract: We encountered a case of severe psittacosis associated with low blood pressure, in which the condition was improved by PMX-DHP. The patient, a 74-year-old woman, presented with cough and nasal discharge. She was diagnosed as pneumonia. While she was in hospital, we incubated her sputa and blood. However, we could not detect microbes. We administered antibiotics without success. Her condition slowly deteriorated and her blood pressure decreased. We tried PMX-DHP; her condition got better and her blood pressure increased. We continued to administer CHDF. Subsequently, based on blood tests, we could diagnosed psittacosis, which resulted from a chlamydia psittaci infection. Chlamydia psittaci has the characteristic of multiplying within the phagosomes of the host cell like a virus. Nevertheless, it has lipopolysaccharide in its outer membrane. So, PMX-DHP was thought to be effective.

Successful Use of Blood Adsorption Therapy with Polymyxin B-Immobilized Fibers in Neonatal Pseudomonas aeruginosa Infection
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.72-76 (2005)
Figure&Table&Reference: FIG.4, TBL.2, REF.14
Abstract: We report a case of severe neonatal infection with Pseudomonas aeruginosa, which was successfully treated with blood adsorption therapy using polymyxin B-immobilized fibers (PMX-DHP). A healthy G 1 P 1 mother delivered a 3,070 g male neonate at 39 weeks gestation. Two hours after birth, the patient showed tachypnea and was admitted with a diagnosis of severe infection. He developed shock. Antimicrobial therapy, inotropic therapy, mechanical ventilation and NO inhalation, exchange transfusion and, anti-DIC therapy were all ineffective. We introduced PMX-DHP at 27 hours after birth. There was a significant increase in blood pressure immediately after initiation of blood adsorption therapy. No complication was observed with this therapy. His clinical condition improved remarkably, although serum endotoxin levels showed no correlation. Consequently, it is indicated that the PMX column removed not only endotoxins but also other substances such as anandamide. Several reports describe the effectiveness of PMX-DHP in clinical experience with adults, but few pediatric cases have been reported. We consider PMX-DHP to be an effective therapy for infants with severe sepsis.

Successful Treatment of Infant by PMX-DHP therapy Combined with Continuous Hemodiafiltration
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.85-89 (2005)
Figure&Table&Reference: FIG.2, TBL.4, REF.9
Abstract: Treatment with PMX-DHP for pediatric septic patients is not generally performed. We report an infant treated with combined endotoxin adsorption therapy (PMX-DHP, polymixin-direct hemoperfusion) and a CHDF 3-year-old male infant (9 kg body weight) with septicemia caused by severe CIIPS from shock after intubation with cardiopulmonary arrest. After cardiopulmonary resuscitation hemodynamics deteriorated and oliguresia resulted. Dialysis (PMX-DHP) was performed immediately, the hemodynamics were stabilized directly after PMX-DHP, and general condition improved. In recent years, PMX-DHP has been widely used in Japan to remove endotoxin, a causative agent of sepsis. In infants, blood flow rate is restricted, and hemodynamics readily become unstable. Therefore, small dialysis columns are necessary. It is important to improve blood access, and quality and performance of catheters.

A Case of Group A .BETA.-hemolytic Bacteremia Responding to the Second Endotoxin Absorption Therapy (PMX-DHP)
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.94-99 (2005)
Figure&Table&Reference: FIG.3, TBL.1, REF.10
Abstract: The patient was a 55-year-old man, who was admitted to ICU for septic shock following a neck infection. Blood examination showed a decrease of WBC and increases of CRP, BUN and Creatinine. APACHE-II score was 26, SOFA score was 11 and DIG score was 8 on admission to ICU. Blood culture showed infection by group A .BETA.-hemolytic streptococcus. We started fluid and inotropic therapy in ICU, but blood pressure was still low despite a high cathecolamine index. We decided to perform direct hemoperfusion using polymyxin-B immobilized fiber (PMX-DHP) six hours after admission to ICU. We started continuous bemodiafiltration (CHDF) after PMX-DHP, but we did not observe improved hemodynamics. We decided to perform the second PMX-DHP. We observed improvement of hemodynamic state and good urination after this treatment. The levels of IL-6, PAI-I and IL-ra were extremely high before PMX-DHP and decreased after PMX-DHP and PaO2/FIO2 ratio improved after the first PMX-DHP. We considered that PMX-DHP might be a good treatment for septic shock following Gram positive bacterial infection after fluid treatment.

Three Cases of Sepsis Caused by Gram-positive Bacterial Infection Improved by PMX-DHP
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.101-106 (2005)
Figure&Table&Reference: FIG.6, TBL.1, REF.13
Abstract: We report 3 cases of sepsis caused by gram-positive bacterial infection which was improved by PMX-DHP. The first case was a 65-year-old man, who had been followed after pancreato-duodenectomy. He was diagnosed as cholangitis and lung abscess from imaging and laboratory data, and Klebsiella pneumoniae and Staphylococcus haemolyticus was detected in his blood. The second case was a 66-year-old man, who had been admitted for esophageal cancer and received chemoradiation. He had an unknown high fever, and Staphylococcus capitis was detected in his blood. The third case was a 76-year-old woman, who had been admitted for thyroid cancer. She had an unknown high fever, and Staphylococcus hominis was detected in her blood. We administered PMX-DHP (4-6 hours/one time) twice to each patient and all recovered from sepsis. We indicate that PMX-DHP is also effective for sepsis caused by gram-positive bacteria.

A Retrospective Analysis of Therapeutic Strategy Using PMX-DHP for Septic Shock Due to Acute Pan-peritonitis
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.112-116 (2005)
Figure&Table&Reference: FIG.1, TBL.4, REF.15
Abstract: The efficacy of direct hemoperfusion therapy with polymyxin-B immobilized fiber (PMX-DHP) in septic patients is known, however, there are few reports regarding concrete introduction time. A chart of 23 patients who received emergency laparotomy and PMX-DHP for septic shock due to acute pan-peritonitis were retrospectively reviewed. All of the patients were divided into 2 groups, A group comprised early cases in which the time from completion of surgery until PMX-DHP initiation was less than 3 hours (10 cases) and B group comprised late cases of over 3 hours (13 cases), for which we evaluated severity and outcome. B group comprised many mortalities (6 cases/7 cases), but no significant difference was noted. Severity was significantly greater for an APACHE-II score of 20 or more (11 cases) compared to other cases (p=0.0069). Among these 11 cases, outcome was significantly better in A group compared to B group (p=0.0357). In conclusion, we propose a new strategy for patients with severe septic shock due to peritonitis. Namely, a patient whose APACHE-II score exceeds 20 PMX-DHP should receive treatment within 3 hours after laparotomy.

A Case of Colon Perforation with Septic Shock Treated by Long Time PMX-DHP
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.128-131 (2005)
Figure&Table&Reference: FIG.1, TBL.1, REF.7
Abstract: A 56-year-old woman, with a previous history of sarcoidosis, diabetes mellitus, complete AV block, and uterocervical cancer, developed septic shock caused by a perforation of the transverse colon. Emergency laparotomy was performed, and the patient was treated with vasopressors and CHDF. Because of the prolonged septic shock, we performed PMX-DHP combined with CHDF. Hemodynamics became stable after PMX-DHP and the dose of vasopressor was gradually reduced. However, the patient suffered from colonic perforation again and died of multiple organ failure on postoperative day 32. Serum IL-6 value decreased 2 hours after the start of PMX-DHP and continued decreasing for 24 hours. In conclusion, 24 hours PMX-DHP treatment may be recommended.

A Case with Severe Klebsiella pneumoniae Sepsis who Was Cured with Long-term PMX-DHP Therapy
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.143-145 (2005)
Figure&Table&Reference: TBL.1, REF.6
Abstract: It has been demonstrated that PMX-DHP is powerful therapy in patients with septic shock. In this time, we performed long-term treatment PMX-DHP in a patient with Klebsiella pneumoniae infection. Circulation was improved after 14 hours. The endotoxin level in peripheral blood decreased from 200 pg/mL before PMX-DHP to 3.1 pg/mL after the second PMX-DHP. These observations were indicated that long-term treatment with PMX-DHP may be useful therapy for patients with severe septic shock.

PMX-DHP Treatment for Severe Acute Pancreatitis without Secondary Pancreatic Infection
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.166-171 (2005)
Figure&Table&Reference: FIG.3, TBL.1, REF.15
Abstract: The effects of polymyxin-B immobilized fiber therapy (PMX-DHP) are limited without treatment for infection such as drainage. An indication of PMX-DHP for acute pancreatitis is the onset of secondary pancreatic infection, but endotoxemia by bacterial translocation (BT) or endogenous cannabinoids, which can be eliminated by PMX-DHP, might contribute to shock in sterile necrotizing pancreatitis. Therefore, we reviewed whether it could be assumed in 5 severe acute pancreatitis patients without secondary pancreatic infection who underwent PMX-DHP. Blood pressure of 4 patients (except 1 acute portal obstruction case) increased and 3 cases survived without performing drainage. Secondary pancreas infection was not proved by abdominal imaging, or fine needle aspiration culture. In addition, the presence of another site infection such as catheter or respiratory infection was not proved. Although certification is extremely difficult, mechanism such as BT might play a role in shock with sterile severe acute pancreatitis because PMX-DHP is effective in such cases.

The Effects of Direct Hemoperfusion with Polymyxin-B Immobilized Fiber (PMX-DHP) on Septic Shock Caused by Lower Bowel Perforation
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.199-204 (2005)
Figure&Table&Reference: FIG.4, TBL.1, REF.12
Abstract: We examined the effects of PMX-DHP on septic shock due to lower bowel perforation. Ten patients with postoperative lower bowel perforation were treated with PMX-DHP to manage septic shock. Because 8 of 10 septic shock patients left ICU, PMX-DHP was considered to be effective for septic shock caused by lower bowel perforation. In non-survival cases a long time passed from lower bowel perforation to diagnosis and treatment, Goris score and SOFA score did not decrease after PMX-DHP treatment.

Because the organ damage had progressed, PMX-DHP did not demonstrate the effects in non-survival cases. PMX-DHP treatment should begin from perforation within 24 hours in the case of septic shock caused by lower bowel perforation.

A Case who Underwent PMX-DHP for Sepsis after Living Donor Liver Transplantation.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.212-216 (2005)
Figure&Table&Reference: FIG.3, TBL.1, REF.6
Abstract: A 45-year-old man underwent a living donor liver transplantation for hepatic failure accompanying type B liver cirrhosis. Enterococcus faecium (VRE) was detected in urinary and fecal cultures, and Pseudomonas aeruginosa was detected in sputum culture. Pulmonary suppuration was diagnosed by chest CT. Bile peritonitis was also diagnosed by abdominal CT and cholangiography, and laparotomic drainage was performed. Pseudomonas aeruginosa was detected in the blood culture. On day 11 after drainage, the endospecy was increased to 8.3 pg/mL. The PaO2/FIO2 ratio decreased to 180 on day 12. PMX-DHP was performed for 3 hr 30 min, and the PaO2/FIO2 ratio improved to 300. Subsequently, the pulmonary oxygenation capacity did not decrease and the artificial ventilator was removed on day 19.

A Case Report: PMX-DHP (Endotoxin Absorption Therapy) and SHDF (Slow-hemodiafiltration) Is Useful in ARDS with Sepsis Due to Cervical Subepidural Abscess (SEA).
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.218-222 (2005)
Figure&Table&Reference: FIG.6, REF.5
Abstract: A case of ARDS and MOF with sepsis due to subepidural abscess treated with PMX-DHP (endotoxin absorption therapy) and SHDF (slow-hemodiafiltration) is reported. Although presenting rapidly progressive septic shock, he was discharged without any complications. The patient, a 49-year-old man, was hospitalized with persisting headache and cervical pain for 10 days. Meningitis was first diagnosed. On the second day of hospitalization, he complained of dyspnea, his respiratory function was in distress with a PaO2/FIO2 (P/F) ratio of 51. Chest roentgenograms revealed pulmonary edema with pleural effusion as ARDS. PMX-DHP and SHDF were started for 3 days following the onset of septic shock. Following this therapy, his condition; P/F ratio, blood pressure, CRP in serum laboratory data improved. On the 5 th day. PMX-DHP was discontinued, and on the 14 th day, respirator and intratracheal intubations were withdrawn, and he could breaths by himself in the oxygen provided through a nasal mask. He was discharged on the 76 th day without any complications. PMX-DHP and CHDF was effective for ARDS with septic shock as initial therapy. In conclusion the blood purification therapy was useful for ARDS.

Polymyxin-B Immobilized Fiber (PMX-DHP) Trial Performed for Acute Exacerbation of Interstitial Pulmonary Fibrosis
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.224-228 (2005)
Figure&Table&Reference: FIG.4, TBL.1, REF.6
Abstract: Acute exacerbation is one of the major causes of death among patients suffering from IPF. Although the most popular therapy for acute exacerbation of interstitial pneumonitis is Steroid Pulse Therapy or Immunosuppressive Therapy, no effective treatment. We analyzed 62 patients admitted for treatment. 19 of 62 patients had acute exacerbation; the mortality rate was 89 percent and the average survival was 36 days. PMX-DHP has been reported to be safe and effective for patients with ALI/ARDS. In this study, we tried to treat 4 patients with acute exacerbation of IPF who had no response to steroid pulse therapy using PMX-DHP. As a result of our treatment, 3 of 4 patients had improved saturation during PMX-DHP, and 2 of 4 patients no longer required a ventilator use. Peripheral blood samples were collected before and after PMX-DHP. After PMX-

DHP, both levels of serum IL-8 and serum PAI-1 dropped significantly after PMX-DHP, and the level of serum IL-10 level increased.

Hemoperfusion with an Immobilized Polymyxin-B Fiber Column Eliminates Humoral Mediators and Improves Pulmonary Oxygenation
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.231-236 (2005)
Figure&Table&Reference: FIG.3, TBL.2, REF.17
Abstract: We investigated the efficacy and the mechanism by which direct hemoperfusion with a polymyxin-B column (PMX-DHP) improved the oxygenation index in patients with adult respiratory distress syndrome (ARDS) and acute lung injury (ALI). Seven patients with ARDS and ALI due to infection were enrolled in the study. PMX-DHP was performed twice (for 3 hours each time) within a 24-hour period and PaO2/FIO2 (P/F ratio), IL-8 level, and neutrophil elastase (NE) activity were measured before PMX-DHP, as well as 24 hr, 48 hr, and 72 hr thereafter. The P/F ratio was measured at 24-hr up intervals with 120 hr afterward. The P/F ratio increased from 24 hr onward and a significant improvement was observed after 96 hr. IL-8 decreased significantly from 24 hr onward. On the other hand, NE showed a significant increase after 24 hr, but tended to decrease from 48 hr compared to the baseline value. These findings suggest possible involvement of IL-8 and NE in the effects of PMX-DHP on the oxygenation index.

Polymyxin-B Immobilized Column Is Effective for Hydrochloric Acid-induced Lung Injury in Rats.
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.239-244 (2005)
Figure&Table&Reference: FIG.9, TBL.1, REF.5
Abstract: We examined whether direct hemoperfusion of polymyxin-B immobilized column (PMX) improves circulatory and respiratory disturbances in non-endotoxic lung injury. Adult Sprague-Dawley rats weighing 300 mg underwent direct hemoperfusion using PMX for 30 minutes at a flow of 120 mL/hour after intratracheal instillation of hydrochloric acid (HCl). Rats were divided into those which underwent hemoperfusion with or without PMX 30 minutes after HCl instillation (HCl+PMX and HCl), and hemoperfusion with or without PMX 30 minutes after aqua instillation (Aqua+PMX and Aqua). Blood pressure, white blood cell count, and arterial blood gas analysis were measured before the examinations, immediately before PMX, at 3 hours after PMX. At 3 hours after PMX, bronchoalveolar lavage (BAL) was performed and neutrophils, albumin, concentrations of growth-related oncogene/cytokine-induced neutrophils chemoattractant-1 (GRO/CINC-1), ANA and 2-AG were measured in both plasma and BAL fluid. The number of neutrophils in the BAL fluid and lung tissue were significantly lower in the HCl+PMX group. The GRO/CINC-1 concentraions in the plasma and BAL fluid were also significantly lower in the HCl+PMX group. ANA and 2-AG concentrations in the plasma at 3 hours after PMX did not show differences in all groups, but ANA concentrations at 1 hour after PMX were significantly lower in the HCl+PMX group. We guess that absorption of ANA by PMX might suppress immigrant of neutrophils in lung tissue at 3 hours after PMX. PMX is an effective therapy for lung injury due to non-endotoxic lung injury.

PMX-DHP Therapy for a Patient with Infectious Endocarditis
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.247-250 (2005)
Figure&Table&Reference: FIG.4, TBL.1, REF.8
Abstract: A 52-year-old male was admitted to our hospital following congestive heart failure due to infectious endocarditis (IE). Ultrasound cardiography revealed aortic valve and mitral valve regurgitation. Vegetation and perforation were found at the mitral valve. Due to unstable hemodynamics and respiration, emergency surgery was performed to replace the aortic valve and the mitral valve with mechanical valves. The first PMX-DHP therapy was administered via the cardiopulmonary bypass. On the postoperative day, the second PMX-DHP therapy, and antibiotics and human gamma globulin were administered. The patient recovered well, showing no recurrence, and was discharged. Although the role of PMX-DHP in the therapy of IE has not been precisely clarified and further study is necessary, it promises to provide good efficacy.

A Case Successfully Treated with PMX-DHP for Septic Shock due to Peritonitis after Abdominal Aortic Aneurysm Substitution
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.9; NO.1; PAGE.252-256 (2005)
Figure&Table&Reference: FIG.5, TBL.1, REF.11
Abstract: An 80-year-old woman with abdominal aortic aneurysm, who received surgery to replace an aortic aneurysm with a Y-graft at a previous hospital, was transferred to our hospital with a colonic perforation 2 weeks after surgery. We performed a left hemi-colectomy with gauze packing, but were not able to accomplish reconstruction because of a severe clinical condition included hypotension, hypothermia, and acidosis. After the operation, she fell into septic shock, which was not responsive to blood transfusion and catecholamine infusion. PMX-DHP was performed for 3 hours after the operation. During PMX-DHP, systolic blood pressure began to rise and catecholamine dose could be reduced. Three days later, we removed the gauze packing and performed a transverse colostomy. After this second operation, she fell into a shock state again, PMX-DHP was performed. During PMX-DHP, blood pressure rose to over 100 mmHg. She recovered from Systemic Inflammatory Response Syndrome one day after the second operation. She was transferred to the previous hospital after 36 post-operational days.

2006

Severity Score and Treatment Results for Lower Gastrointestinal Perforation
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.10-18 (2006)
Figure&Table&Reference:
Abstract: Objective: Since the treatment results of digestive tract perforation may vary with the perforation site, the outcomes of lower digestive tract perforation were evaluated according to the site. Subjects and methods: The subjects were 48 patients with perforation of the lower digestive tract operated on between January, 2001 and March, 2004. They were divided into 14 patients with perforation of the right lesion of colon (Group A) and 34 with perforation of the left lesion of colon (Group B), and the severity of the condition was evaluated using the APACHE-II score and SOFA score. The relationship between the state of use of PMX-DHP and treatment results was also evaluated. Results: The number of patients who died was 2 in Group A and 6 in Group B. No significant difference was observed in the APACHE-II score or SOFA score immediately before surgery between the two groups. Also, the scores showed no significant difference in the patients who received PMX-DHP between the two groups. No improvement in APACHE-II or SOFA score was noted in those who died despite the application of PMX-DHP. Conclusions: While no significant difference was noted in the severity of the condition according to the perforation site, early additional treatment by second PMX-DHP or CHDF is considered to be necessary in patients who show increases in the each score.

Outcome of PMX-DHP Therapy in Patients with Colorectal Perforation: Comparison of Right-sided Perforation with Left-sided Perforation
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Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.20-23 (2006)
Figure&Table&Reference:
Abstract: Various factors (age, leukocyte count, duration of onset surgery, preoperative shock, and status of perforation) are known to be prognostic factors in patients with colorectal perforation. In

addition, the site (right colon or left colon and rectum) of perforation has also been reported to be a prognostic factor because the status of perforation is influenced by the site of perforation. Patients and Methods: A total of 33 patients were divided into 2 groups according to site (right colon (n=8) versus left colon or rectum (n=25)) of perforation, all of whom received direct hemoperfusion for endotoxin absorption using polymyxin-B immobilized fiber (PMX-DHP therapy) after surgery. We compared the 2 groups in relation to the background factors, postoperative complications, and prognosis, and discussed whether treatment strategy should be altered for a different site of perforation. Results: There were no significant differences between the 2 groups in relation to background factors, laboratory data, kind and frequency of postoperative complication, and postoperative survival. Conclusions: These results suggest that treatment strategy should not be altered according to site of perforation, and that it is important to treat patients individually.

Clinical Efficacy of Direct Hemoperfusion with Polymyxin-B Immobilized Fiber (PMX-DHP) for Non-Traumatic Colorectal Perforation
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.24-29 (2006)
Figure&Table&Reference:
Abstract: Although it's usefulness for colorectal perforation has been reported since introducing PMX-DHP into Japan, there is little research on prognostic improvement. 63 patients with postoperative non-traumatic colorectal perforation were examined and studied the efficacy of PMX-DHP treatment was studied. There were no differences in severity between right side and left side site of perforation among patients. In 15 cases receiving PMX-DHP treatment, APACHE-II score and SOFA score improved after PMX-DHP treatment in survivors, but no improvement was observed in fatalities. We examined whether the prognosis for colorectal perforation would have been improved by introducing PMX-DHP. The morbidity rate before PMX-DHP introduction is 96.7% and after introduction is 75.8% with significant difference between both groups. However, the mortality rate before PMX-DHP introduction is 6.7% and after introduction is 9.1% with no significant difference. We concluded that PMX-DHP did not improve the prognosis for non-traumatic colorectal perforation.

Study on Therapeutic Results of PMX-DHP for Colorectal Perforation-Including the Effects of Location of Perforation-
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.30-35 (2006)
Figure&Table&Reference:
Abstract: One hundred and forty six cases of colorectal perforation were studied before and after PMX-DHP treatment and with or without PMX-DHP treatment. The mortality rate for the colorectal perforation after initiating PMX-DHP treatment was 14.2%, which had no statistical difference compared to mortality before initiation of PMX-DHP treatment. The mortality rate for cases receiving PMX-DHP treatment was 19.2%, which was statistically different compared to cases not receiving PMX-DHP treatment, because PMX-DHP treatment was performed only for serious cases. Cases of colorectal perforation of a proximal site of the carcinoma and coprostasis were considered serious. All possible therapies were necessary for these cases. There was no difference in the rates for PMX-DHP treatment, mortality, and severity of colorectal perforation in terms of location of perforation. The mortality rate for cases with an APACHE-II score of more than 15 was over 50% regardless of PMX-DHP treatment. Conventional PMX-DHP treatment is insufficient in these cases. PMX-DHP is effective for non-serious cases. Long-term treatment with PMX-DHP or in combination with CHDF is necessary for serious cases.

Effect of Direct Hemoperfusion Using a Polymyxin-B immobilized Column for DIC in Acute Lung Injury with Severe Sepsis
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.46-51 (2006)
Figure&Table&Reference:
Abstract: Introduction: Recently, some studies have reported that direct hemoperfusion (DHP) with polymyxin-B immobilized fiber (PMX) can significantly improve the PaO2/FIO2 (P/F) ratio in patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). The mechanism was not known. The aim of this study is to determine whether disseminated intravascular coagulation (DIC) can be treated with PMX for ALI and ARDS in sepsis patients. Material and methods: 18 patients who has ALI or ARDS with sepsis were split into 2 groups, non-DIC group and DIC group, using a new criteria for DIC at an early phase. We monitored acute physiology and chronic health evaluation II (APACHE-II) score, sepsis-related organ failure assessment (SOFA) score, DIC score, and P/F ratio before and after PMX-DHP treatment. Results: There was no significant difference in severity at pre-PMX between the 2 groups, non-DIC and DIC group. In the DIC group, the P/F ratio was 163.1.+-.69.9 before PMX-DHP treatment. This increased to 236.3.+-.108.8 after treatment, with significant improvements compared to before treatment (p=0.0357), although there was no significant difference before and after PMX-DHP treatment in the non-DIC group. The survival rates of non-DIC group and DIC group were respectively 70.0% (7/10) and 75.0% (6/8) at 28 days after PMX-DHP treatment. Conclusion: It may be suggested that the PMX-DHP treatment for severe sepsis improves oxygenation in DIC patients by inhibiting deterioration of DIC.

Three Cases of Gastrointestinal Perforation and Pan-peritonitis with Effective Long-term PMX-DHP Treatment
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.64-68 (2006)
Figure&Table&Reference:
Abstract: We have experienced 3 successful cases long-term PMX-DHP treatment for gastrointestinal perforation and pan-peritonitis. We examined average blood pressure, number of platelets, and PaO2/FIO2 ratio in 1 case receiving PMX-DHP for 6 hours twice, and 2 cases receiving second PMX-DHP treatment for 6 hours after nullification of PMX-DHP treatment for 2 hours. PMX-DHP showed that average blood pressure rose in all cases, number of platelets tended to decrease, and PaO2/FIO2 ratio failed to improve. Even though adverse effects such as a decrease in platelets were recognized, it had a high degree of effectiveness for rising blood pressure and could also save the lives of all cases. It is thought that we need to carefully examine more cases in the future.

Relationship between Implementation Time of Polymyxin-B immobilized Fiber Column-Direct Hemoperfusion (PMX-DHP) and Plasma Plasminogen Activator Inhibitor type-1 (PAI-1) in Septic Shock Patients
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Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.69-73 (2006)
Figure&Table&Reference:
Abstract: Material and Methods: We treated 11 septic shock cases with direct hemoperfusion of PMX-DHP. All patients were diagnosed as sepsis according to the criteria of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference, and required intensive care for unstable circulation. We measured plasma PAI-1 level at 4 points: before PMX-DHP, after PMX-DHP, and 1 day and 3 days after. We also divided the patients into 2 groups based on the number of columns, namely, 1-column group (5 cases) and 2-column group (6 cases), and we examined clinical data: systolic blood pressure and sepsis related organ failure assessment (SOFA) score. Results: The high PAI-1 value (more than 185ng/mL) before PMX-DHP implementation occured in 8 examples (A group 4 cases, B group 4 cases) and outcome was significantly good in the B group (p=0.0286). Increased of systolic blood pressure was confirmed in 4 cases and decreased PAI-1 in 5 cases. Before and after PMX-DHP treatment, there was a significant correlation (p=0.0152) for systolic blood pressure reaction and

PAI-1 decrease. Discussion: The significance of the plasma PAI-1 value measurement as the effect determination score of PMX-DHP was suggested. Also, the PAI-1 value suggests long-term 2-column continuous use is desirable in cases with a high plasma PAI-1 value (185ng/mL over).

Evaluation of IL-18 and sFas Levels Treated with PMC-DHP
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.96-101 (2006)
Figure&Table&Reference:
Abstract: Following PMX-DHP treatment, the levels of endotoxin, TNF-.ALPHA., IL-18, IL-12, and sFas all decreased, as follows; endotoxin: 8.8.+-.14.7pg/mL to 4.3.+-.10.2pg/mL; TNF-.ALPHA.: 113.4.+-.126.4pg/mL to 86.9.+-.110.0pg/mL; IL-18: 120.2.+-.116.4pg/mL to 84.1.+-.78.0pg/mL; IL-12: 49.1.+-.52.7pg/mL to 34.2.+-.30.1pg/mL; sFas: 97.4.+-.109.9ng/mL to 43.1.+-.33.8ng/mL. There were significant correlations among serum IL-18, sFas, and TNF-.ALPHA. levels. The results suggest that PMX-DHP eliminates various humoral factors, as well as endotoxin from the blood.

One Case of the Probability of Renal Function Suggested to Improve by the Application of PMX-DHP for Acute Renal Failure after Bee Sting
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.152-158 (2006)
Figure&Table&Reference:
Abstract: Recently we know PMX-DHP only remove endotoxin, but effect of PMX-DHP for such as systemic inflammatory reactive syndrome (SIRS) descending cytokines and like that. We reported an improved case renal function using PMX-DHP for acute renal failure with rhabdomyolysis after bee sting. An 89-years-old man was admitted to the hospital for bee sting about fifty points on his head mainly. His renel function deteriorated after 2 days from admit. He was acute renal failure for the rhabdomyolysis because his serum creatine phosphokinase (CPK) and myoglobin level so elevated. We treated him continuous hemodialysis filtration (CHDF). We think he was SIRS for bee sting because his laboratory data and physical findings were like as SIRS. We used PMX-DHP for him because his pathophysiology like an endotoxisemia, he was hypercoagulability, increasing heart rate and white blood cells were recognized. Immediately after treatment of PMX-DHP, his urination dramatically improved and he does not need for CHDF treatment. Finally, he recovered fine and left our hospital. We think PMX-DHP has potential for treatment to rhabdomyolysis of bee sting.

Effective Therapy for IL-12, IL-18, and P/F Ratio Treated with PMX-DHP; A Case Report
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.162-169 (2006)
Figure&Table&Reference:
Abstract: A 58-year-old male patient. After sustaining multiple trauma, he developed Gram-negative bacillus, which led to hyperendotoxemia with septic multiple organ failure. PMX-DHP treatment was conducted twice, after which the blood endotoxin level decreased significantly (374.RAR.52pg/mL), and the pulmonary oxygenation improved markedly (P/F ratio, 198.RAR.307). The SOFA score also improved (14.RAR.11), along with decreases in the serum levels of IL-18, IL-12, and TNF-.ALPHA.. The serum NMP level, an indicator of apoptosis, also decreased along with the improvement of the SOFA score. Following PMX-DHP, the endotoxin level decreased first, followed by a decrease in the serum levels of IL-18, IL-12, TNF-.ALPHA., IL-6, NOx, and NMP, in that order. It was considered that PMX-DHP decreased the blood endotoxin level, with consequent suppression of the production of humoral factors, which might be involved in the development of the patient's pathological condition in the presence of sepsis, thereby contributing to the improvement of symptoms.

Three Cases of Using PMX-DHP for Severe Infections after Living-related Liver Transplantations
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.174-179 (2006)
Figure&Table&Reference:
Abstract: We report 3 cases for whom PMX-DHP was performed after living-related liver transplantations, and their improvement. Case 1: A 35-year-old woman who received liver transplantation for primary biliary cirrhosis. On the 21st postoperative day (p.o.d.), PMX-DHP was performed after an operation for a perforated of small intestine. Case 2: A 56-year-old woman was performed liver transplantation for cirrhosis and HCC due to hepatitis C. WBCs increased and internal treatment was not effective, so PMX-DHP was performed on the 12th p.o.d.. On the 34th p.o.d. she experienced cholangitis and was in septic shock, and PMX-DHP was performed after biliary drainage. Case 3: A 51-year-old woman who received liver transplantation for primary biliary cirrhosis. Fever and WBCs had increased, so PMX-DHP was performed on the 8th p.o.d.. On the 46th p.o.d., PMX-DHP was performed after an operation for a perforated small intestine. PMX-DHP might provide benefits for infection control after liver transplantation.

Evaluation of HMBG 1 Levels Treated with PMX-DHP
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.199-204 (2006)
Figure&Table&Reference:
Abstract: The endotoxin level decreased from 8.8.+-.14.7pg/mL to 4.3.+-.10.2pg/mL following a 2-hour session of PMX-DHP treatment. The HMGB 1 level decreased significantly from 66.5.+-.74.9ng/mL to 31.3.+-.45.6ng/mL. Comparison of patients with endotoxin levels of .GEQ.1.1pg/mL with those with endotoxin levels of <1.1pg/mL in terms of HMGB 1 revealed that the serum levels of TNF-.ALPHA., IL-18, and IL-12 were all higher in the former group, i.e., patients with endotoxin levels .GEQ.1.1pg/mL. Comparison of the HMGB 1 level before PMX-DHP treatment between group that eventually survived and group that succumbed revealed no significant difference between the surviving group (62.2.+-.71.1ng/mL) and the deceased group (84.8.+-.99.7ng/mL). In patients with ALI/ARDS, the P/F ratio increased from 193.+-.62 to 233.+-.66 following the 2-hour session of PMX-DHP. These results suggest that the mechanism underlying the efficacy of PMX-DHP involves the suppression of endotoxin-mediated production of HMGB 1, cytokines, etc.

Serial Changes in the Serum Level of High Mobility Group Box 1 (HMGB 1) in a Patient with Septic Shock Treated with Methylprednisolone and PMX-DHP
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.207-213 (2006)
Figure&Table&Reference:
Abstract: We report a case of septic shock in which serial changes in the serum level of HMGB 1 were determined, and on the association of serum HMGB 1 with treatment for septic shock. A 70-year-old female patient was admitted to our ICU with septic shock, but infectious foci were not clear. PMX-DHP was undertaken on the 2nd ICU day. However, hemodynamic derangement was not improved despite this treatment, and subsequently 125mg of methylprednisolone (MPS) was administered intravenously. This resulted in an improvement of the shock state. Concentrations of HMGB 1 were 114.3ng/mL and 129.3ng/mL before and immediately

after PMX-DHP, respectively. Serum HMGB 1 levels were 118.5ng/mL and 34.1ng/mL 12 and 36 hours after MPS administration, respectively. As shown in this case, PMX-DHP did not lower the serum HMGB 1 level by direct adsorption. On the other hand, MPS decreased requirements for vasopressor dosage, and reduced the elevated serum HMGB 1 level. The precise mechanisms underlying MPS-induced HMGB 1 reduction are not clear. It is suggested that MPS reduces cytokine production and release, resulting in the attenuation of the cytokines-HMGB 1 vicious cycle.

Studies on 20 Cases of Colorectal Perforation in Our Hospital
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.224-228 (2006)
Figure&Table&Reference:
Abstract: This retrospective study was performed to examine the outcomes of 20 patients with colorectal perforation treated between August 2004 and October 2005, with special reference to the efficacy of direct hemoperfusion for endotoxin absorption using polymyxin-B immunobilized fiber (PMX therapy). Age ranged 37 to 83 (mean, 62) years old. The male to female ratio was 7 to 3. The most frequent site of perforation was sigmoid colon (40%). Diverticulitis was the most frequent cause of perforation (11 cases), followed by colorectal cancer (6 cases). 12 patients were found to show diffuse fecal peritonitis, four of whom had been in septic shock preoperatively. 13 patients underwent resection of the perforated lesion. One of the 7 patients treated with the PMX therapy died postoperatively, whereas all 13 patients who were not treated with PMX therapy survived. Compared to patients who were not treated with PMX therapy, those who received PMX therapy showed a more severe status in relation to degree of peritonitis, leucocyte count, and platlet cell count. These results suggest that it is required in the future to select patients who are candidates for PMX therapy more precisely.

Effects of PMX-DHP for Suspected Gram-positive Sepsis. A case report
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.230-234 (2006)
Figure&Table&Reference:
Abstract: An 80-year-old man with a perforation peritonitis was admitted to our hospital. We performed emergency laparotomy, and found multiple diverticula of the sigmoid colon and perforated region. We diagnosed perforated diverticulitis. We performed peritoneal lavage drainage and Hartmann's operation. After the operation, he fell into septic shock. Low blood pressure which did not react to catecholamine sustained. PMX-DHP was performed 4 hours after the operation. Although systolic blood pressure rose temporarily during PMX-DHP, it began to decrease after PMX-DHP. The day after operation, PMX-DHP treatment was performed again. After the second PMX-DHP treatment, blood pressure rose, and became stable, and the amount of catecholamine could be reduced. He was discharged from the ICU 25 days after admission, and left our hospital at 30 days. During hospitalization, blood level of endotoxin was within normal limits. On the other hand, the Bacillus genus (Gram-positive bacillus) was positive in the blood culture. Therefore, we consider that PMX-DHP is useful for suspected Gram-positive sepsis.

The Clinical Evaluation of PMX-DHP for Septic Shock Patients with Mean Blood Pressure Below 65mmHg
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.245-251 (2006)
Figure&Table&Reference:
Abstract: EGDT, which is a sepsis resuscitation bundle, was presented in the Surviving Sepsis Campaign guideline in 2004. PMX-DHP treatment was performed for septic patients whose mean arterial blood pressure was less than 65mmHg. Changes of hemodynamics, oxygenation index, and blood level of various mediators were evaluated after being stratified by patient's prognosis. Survival rate after 28 days was

57.6% (survivors: 34 patients, fatalities: 25). The cases with mean blood pressure below 65mmHg in spite of catecholamine administration significantly improved in both groups after PMX-DHP. Procalcitonin (PCT) level was significantly decreased with PMX-DHP only in the survival group. The blood level of PCT was thought to be useful for diagnosis and prediction of patient prognosis with sepsis and severe sepsis. PMX-DHP should be considered as one of the options for early resuscitation therapy from septic shock.

A Case of Septic Shock Caused by Calculous Pyelonephritis who Was Cured with Long-term PMX-DHP Therapy
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.252-258 (2006)
Figure&Table&Reference:
Abstract: We report a case of septic shock caused by calculous pyelonephritis. We performed 6-hour PMX-DHP treatment on the patient. The endotoxin level in peripheral blood decreased from 73.7pg/mL before PMX-DHP to 17.0pg/mL after 3 hours and to 14.1pg/mL after 6 hours. But, the platelet counts decreased from 74,000/mm'3' before PMX-DHP to 49,000/mm'3' after 3 hours and to 31,000/mm'3' after 6 hours. We should examine the utility of long-term PMX-DHP treatment. Moreover, it is necessary to note the decrease in platelet counts in a DIC-complicated case and a low platelet count case.

Case Report: Remarkable Improvement in Septic Shock Patient Infected with Gram-positive Bacteria, Using Polymyxin-B Immobilized Fiber Direct Hemoperfusion (PMX-DHP)
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.275-282 (2006)
Figure&Table&Reference:
Abstract: Direct hemoperfusion therapy with polymyxin-B immobilized fiber (PMX) was developed in Japan and has gained acceptance as a treatment for endotoxic shock caused by Gram-negative bacteria. Anandamide (ANA) is a mediator of septic shock not only caused by Gram-negative bacterial infection but also by Gram-positive. It was reported that PMX absorbs and removes ANA. After reporting this case we would like to suggest this polymyxin-B immobilized fiber direct hemoperfusion (PMX-DHP) therapy as a viable option for the treatment of sepsis induced by Gram-positive bacterial infection. With reference to the timing for starting PMX-DHP therapy in a patient under septic shock, we recommend evaluating the patient's condition and considering if the treatment should be commenced.

A Case of Septic Shock Caused by MRSA Lobar Pneumonia Treated by PMX-DHP
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.283-289 (2006)
Figure&Table&Reference:
Abstract: It is said that PMX-DHP is effective not only for gram-negative bacterial infection but also for gram-positive bacterial infection by removing cannabinoids such as anandamide. We report a case of septic shock caused by MRSA pneumonia, which was effectively treated with PMX-DHP. The patient was a 49-year-old man who was admitted to ICU for respiratory dysfunction caused by lobar pneumonia and acute renal dysfunction. Because of prolonged septic shock after sufficient fluid resuscitation and injection of dopamine 10.MU.g/kg/min, noradrenaline 0.2.MU.g/kg/min, we performed PMX-DHP treatment. PMX-DHP treatment was performed for 22 hours and 30min. Mean blood pressure continued rising until after 12 hours beginning PMX-DHP treatment. We thought that long-term treatment with PMX-DHP might be a useful therapy for severe septic shock, and might be effective for septic shock caused by gram-positive infection.

Effectiveness of Polymyxin-B Immobilized Fiber-direct Hemoperfusion for Treating of a Fulminant Myocarditis Patient: A Case Report
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Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.291-298 (2006)
Figure&Table&Reference:
Abstract: The case was a 44 year-old woman. On 24th September 2005, she was admitted to our hospital for cardiogenic shock, and intra-aortic balloon pumping (IABP), and percutaneous cardiopulmonary support system (PCPS) were started immediately, for suspected fulminant myocarditis, but it did not provide a hemodynamic improvement. On the 4th hospital day, PMX-DHP was administered in expectation that it would reduce inflammatory mediators. 2 hours later, her blood pressure was elevated. PMX-DHP therapy was stopped on the 6th day. Subsequently, her hemodynamics became stable, and PCPS was stopped on the 7th day, IABP was stopped on the 8th day. There are few reports of the PMX-DHP being effective for fulminant myocarditis, so we take this opportunity to report a successful case.

PMX-DHP Improved Impaired Oxygenation in Septic ARDS: Case Study
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Journal Title: Japan Journal of Critical Care for Endotoxemia
Journal Code: L3418A
ISSN: 1348-821X
VOL.10; NO.1; PAGE.306-311 (2006)
Figure&Table&Reference:
Abstract: We report a case of septic acute respiratory distress syndrome (ARDS) in which oxygenation was improved remarkably by polymyxin B immobilized fiber direct hemoperfusion (PMX-DHP). A 51-year-old male was admitted to our ICU with septic shock and ARDS 4 months after abdominal surgery. Immediately after ICU admission, the trachea was intubated and the patient received mechanical ventilation. Chest CT revealed ground-glass opacity and consolidation. Steroid pulse therapy and prone position respiratory care did not improve impaired oxygenation. On the 4th ICU day, PMX-DHP was performed for sustained septic shock. After PMX-DHP treatment, catecholamine index (CAI) decreased from 16 to 10 (2hrs after PMX-DHP) and to 0 (13hrs after PMX-DHP). Oxygenation index (PaO2/FIO2) increased from 66 to 121 (2hrs after PMX-DHP) and to 172 (24hrs after PMX-DHP). On the 9th ICU day, the tracheal tube was extubated. It is suggested that PMX-DHP eliminates not only endotoxin but also some unknown sepsis-related mediators. This mechanism may contribute to regulating the leukocyte function, and attenuating the endothelial perturbation, resulting in improved hemodynamics and impaired oxygenation by PMX-DHP.