Artificial Organs: Thoughts & Progress

Artificial Organ Support Strategies in Combined Renal, Circulatory, Pulmonary and Liver Failure


This information presented has been derived from patients in acute renal failure and treated with hemodialysis. The renal failure had been the result of very severe medical or surgical emergency, predominantly multiple trauma. Multiple trauma was usually the result of road accidents or extensive and repeated surgical procedures. Acute renal failure had only been one of several complicating events. In addition to the correction of electrolyte, water and acid-base balances and the elimination of waste products by hemodialysis several other important aspects had to be considered. Therefore, special strategies to prevent a chain of life-threatening complications were developed.

The type and the sequence of the complicating events after acute renal failure is relatively uniform: fluid overload, shock lung, septic bronchopneumonia, paralytic ileus, peritonitis and severe sepsis, toxic liver damage, gastro-intestinal and other hemorrhages, consumptive coagulopathy, and irreversible cerebral edema in cases of severe brain trauma.

In the following paragraphs we describe our procedures in typical situations with regard to artificial organ therapy.

Problem No. 1: Heparinization and control of bleeding

There have been significant changes in recent years in our approach to hemodialysis, hemofiltration, or hemoperfusion of patients threatened by bleeding episodes. While it had been customary to adhere to conservative management even in cases of established renal failure, because of the risk of hemorrhage, we now start out with hemodialysis at the earliest signs of renal failure (BUN of 40-60 mg%, creatinine of 3-5 mg%). The patients can be dialyzed immediately after insertion of a Scribner shunt. This has been rendered possible through the development of a monitoring system for anticoagulant management during hemodialysis. It has thereby been possible to define a safe, though narrow zone of inhibition of plasmatic coagulation by measuring the activated thromboplastin time (APTT). With the use of intermittent single injections of 500 USP of heparin, coagulation can be inhibited sufficiently to forestall thrombus formation in the extracorporeal circulation. Within the body itself the heparin effect is insufficient to cause bleeding, even in the immediate postsurgical period.

The first APTT determination is undertaken prior to giving heparin: it enables us to detect coagulation disturbances caused by medication, e.g., Carbenicillin. Thereafter, a test dose of 500 USP heparin is administered; the resultant prolongation of the APTT value is an indication of the sensitivity of a particular patient to heparin. Subsequent doses of 500 USP are administered during dialysis whenever the APTT test approximates normal values. In cases of poisoning, we usually apply a combination of hemodialysis and hemoperfusion. A column of activated carbon or of absorptive resin is inserted into the dialysis circuit. This results in a marked increase of the foreign surface to which the blood is exposed. In such cases, the APTT test needs to be done also on the venous limb of the extracorporeal circulation since, in view of the prolonged extracorporeal sojourn of the blood, the heparin effect may have largely disappeared and coagulation may occur. Extracorporeal coagulation may also occur when blood units are added to the extracorporeal circulation before the dialyser. The added blood undergoes recalcification during passage through the dialyser cartridge, and this alters the coagulative state in an uncontrollable way. For this reason, when transfusions are needed, the blood is administered either to the venous limb of the extracorporeal circulation or directly at another unrelated site. In this manner, we have undertaken during the past two years over 2000 dialyses on about 100 patients with a high risk of bleeding. On the basis of this experience we have ceased to consider hemodialysis to be contraindicated because of the risk of giving heparin. The Lee-White method, as well as several other coagulation tests, have been found to be unsuitable for anticoagulation control of the extracorporeal circulation. Regional heparinization is likewise inferior to minimal intermittent heparinization in conjunction with the monitoring of APTT. Only occasionally did peritoneal dialysis appear to be indicated. If so, usually only at a later date in as much as many of our patients had already undergone other intraperitoneal procedures.
Problem No. 2: Control of shock lung, fluid lung and pulmonary edema

As part of the postagression syndrome, patients in general are in need of artificial respiration, natural respiratory activity being deficient. As part of the initial shock treatment they usually are subjected to excess amounts of extracellular fluid, more than the kidneys can excrete in sufficient time. This results in a disturbance of the electrolyte and acid-base balances. The excess volume becomes manifest as a raised central venous and pulmonary artery pressure. There may also be simultaneous left heart failure. This represents an immediate threat to life in patients with primary cardiac problems, e.g. myocardial infarction or coronary surgery. It usually leads to fulminant bronchopneumonia and sepsis within a few days, in spite of antibiotic therapy.

We therefore use ultrafiltration dialysis or hemofiltration at an early date in order to achieve isotonic dehydration of these patients. The most important parameter is the central venous and pulmonary artery pressure, although the systemic arterial pressure needs to be carefully monitored at the same time. The presence of a reliable bed scale is absolutely necessary in order to control the weight of the patient. Also of help is thoracic impedance cardiography since it permits the continuous monitoring of the fluid content of the thorax, and the degree of the pulmonary edema. The respiratory pressure (which can be checked at the ventilator) and the oxygen concentration needed for a satisfactory blood gas analysis are also direct indicators of the fluid content of the lungs. Either ultrafiltration dialysis or hemodilution are undertaken daily and result in a weight loss of about 2 and maximally 3 kg. If the withdrawal of fluid proceeds gently, over a period of 3 to 4 hours, significant difficulties with the systemic arterial pressure can be avoided. A distinct improvement of the respiratory state or the arterial oxygen saturation and also the general circulation is usually observed already during this procedure. With this fluid loss we aim at a central venous pressure of near zero. By this therapy, symptoms of interstitial and intraalveolar fluid collections diminish and usually disappear radiologically. Intravenous administration of 100 to 300 ml of 20% human albumin during ultrafiltration or hemofiltration will aid in mobilizing tissue fluid sequestered in the “third space”.

The just described “drying out” of the patient will often prevent the development of serious septic pulmonary complications. Likewise, we have observed a significant reduction in the development of the so called “respiratory lung”. Frequently we could progress to an assisted or an oxygen-enriched spontaneous respiration at an early date.

Problem No. 3: Adequate parenteral nutrition

The daily elimination of fluid just described opens the way for the administration of fluid sufficient for parenteral nutrition. The daily input of 2500-3000 calories, 150-500 gm glucose, evenly distributed over 24 hours is needed in our experience to satisfy the energy requirement of patients suffering from the postagression syndrome. Except in the case of diabetics, insulin administration is not necessary if the glucose is given evenly over a 24 hour period. However, we like to add a daily dose of 100 gm amino acids dissolved in 1000 ml of fluid. If fluids and electrolytes are added up in this fashion, it will amount to 2-3 liters of IV fluid per day. Unless there is a rigid and consistent daily withdrawal of fluid by means of hemofiltration or ultrafiltration, adequate parenteral nutrition in our opinion, is not feasible. We are paying increasing heed to one particular aspect of parenteral nutrition, namely depletion of phosphates. We have regularly observed this depletion which goes hand in hand with an equally pronounced 2,3 DPG depletion of the erythrocytes. The oxygen supply of the tissues is critically dependent on this 2,3 DPG content. For this reason we regularly infuse 20 mEq/l of inorganic phosphate during dialysis when patients have lowered serum phosphorus levels. In this manner, we raise the serum phosphorus level to normal and also the 2,3 DPG level of the erythrocytes.12-14 Correction of metabolic acidosis is just as important during the early phase of acute renal failure. For this reason the dialysate used by us in acute dialyses has for many years contained sodium bicarbonate as a buffer. The customary concentration of 35 mEq/L has in our hands proven inadequate in many cases to compensate for the metabolic acidosis. We therefore increased dialysate bicarbonate to reach a level of 45 mEq/L; the potassium balance remains mostly positive during dialysis, without producing hyperkalemia in the patient.

Problem No. 4: Gastrointestinal complications

Gastrointestinal complications consist of profuse hemorrhages, paralytic ileus, ruptured suctions and incisions, septic peritonitis leading to generalized sepsis, acute pancreatitis, toxic liver damage and endotoxin shock. On the basis of our experience with acute poisonings and gastrointestinal activated carbon treatment, we have begun to apply similar therapeutic regimens to prevent the above sequence of abdominal complications. It is very important to carry an adequate amount of activated carbon suspended in lactulose into the gastrointestinal tract at the earliest possible moment. There are about 150 g of pulverized activated carbon to 500 ml of lactulose; they are administered by gastric tube over 24 hour periods until rectal emergence of the suspended carbon. This interferes effectively with the intestinal
absorption of highly toxic degradation products, and also with the formation of putrefying gases which cause abdominal distension. In one particular case of grade IV coma and hypothermia of 24°C, subsequent to drug intoxication, the described type of therapy was not followed by pancreatic necrosis which otherwise happens as a rule.

Problem No. 5: Elimination of poisons after drug-induced or accidental intoxication.

Hemodialysis is a very effective method of detoxification which has to be applied especially in situations of renal failure. As previously stated, we like to combine hemodialysis with hemoperfusion utilizing either activated carbon or resins, depending on the type of toxic substance. As an alternative, we have used 2 hemodialysers hooked to each other in order to increase the active membrane surface (e.g. 2 Gambro major = 3 m² of membrane surface). In this manner we were able to successfully treat cases of bromcarbamide poisoning, which usually are resistant to conventional hemodialysis. Whenever the intoxicated patients have not yet reached a state of renal failure, we enrich the dialysate with urea, up to a concentration of 50 mg%; hereby we can achieve forced diuresis. Whenever we use activated carbon or resins, we insert it before the blood reaches the dialyser, in order to better regulate body temperature, electrolyte, water and acid-base balances.

In cases of oral intoxication it is to be expected that considerable amounts of unabsorbed material are still present in the gastrointestinal tract for a long period of time. We therefore have undertaken whole gut irrigation in several cases. This was done with lactated Ringer's solution having a potassium content of 10 mEq L⁻¹ and of body temperature. It has been possible to successfully treat a case of phenacyclidine poisoning, subsequent to oral ingestion of a lethal dose, without later complications. This was accomplished by a combination of whole gut irrigation, hemodialysis, and hemoperfusion with activated carbon. One typical and presumably organ specific complication, namely lethal pulmonary fibrosis, was avoided, largely because of the retarded and diminished absorption of paracetamol bound to the gastrointestinal tract.

Problem No. 6: Acute hepatic failure

Our cases of acute hepatic failure usually have been complicated by simultaneous renal failure. Hemodialysis was aimed at both. Occasionally we used extracorporeal balloon liver perfusion; however, the benefit derived was only temporary. One resultant complication was extreme derangement of the water, electrolyte and acid-base balances which required immediate hemodialysis. In view of this experience, any chance of success probably rests with a combined and simultaneous application liver perfusion and hemodialysis.

Problem No. 7: CNS trauma and cerebral edema

Acute renal failure in cases of CNS trauma carries a poor prognosis. A vicious cycle develops on the basis of cerebral edema, overhydration, and the accumulation of osmotically effective substances. The ensuing rising intracerebral pressure means almost certain death. Added are the osmotic shifts associated with hemodiagnosis, and an unmanageable situation is bound to arise. Only rarely did we achieve a partial success by adding urea to the dialysate at the same concentration as the patient's serum, and followed this up with cautious hemofiltration.

SUMMARY

Within recent years we have significantly broadened the indication for the treatment of acute renal failure in intensive care patients, even in the presence of multiple organ failure. This was made possible by:

1. safe heparinization of the extracorporeal circulation while avoiding bleeding tendencies
2. hemofiltration of patients threatened by pulmonary complications early during renal failure and
3. the simultaneous use of various special intensive care measures.

By this approach we have succeeded in a number of cases to break the chain of complications leading to multiple organ failure and death.

REFERENCES