Trauma Rounds

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Acute Renal Failure in Trauma Patients

WILLIAM COPELAND, MD:* A 28-year-old man was admitted to the emergency room in profound shock with two stab wounds in the abdomen. The patient had been found in Golden Gate Park and it is not known at what time he was injured. Examination showed the patient to be unresponsive with poor peripheral perfusion. Blood pressure was unobtainable and the pulse was 120 beats per minute and thready. After immediate resuscitation with three liters of Ringer's acetate, blood pressure became palpable at 90 mm of mercury and the pulse was 110 beats per minute.

There were two stab wounds each 1 cm in length in close proximity to the umbilicus in the left lower quadrant. The patient's vital signs deteriorated again and he was promptly taken to surgery. On exploratory laparotomy, 2 liters of free blood was noted in the peritoneal cavity and injuries were seen to consist of multiple penetrating wounds of the small bowel and a single, 1 cm laceration of the infrarenal aorta.

The aorta was repaired by lateral suture and the small bowel injuries were closed with a single layer technique. During operation and in the postoperative period there was no urine output. By the fourth postoperative day serum creatinine was 7.6 and potassium was 6.1. Hemodialysis was instituted and discontinued on the 24th postinjury day following return of renal function.

In the postoperative period the patient gave a history of having stabbed himself with a pair of scissors and it was estimated that he had been in the park for at least 8 hours.

GEORGE SHELDON, MD:† We have presented this case today because the statement has recently been made that acute renal failure is no longer a problem in trauma patients. This patient sustained renal failure because of prolonged untreated shock. Renal dialysis has indeed proved to be an effective means of supporting patients with acute renal failure. Its use is not without its problems, however. Dr. Michael Humphreys has reviewed our experience with acute renal failure at San Francisco General Hospital and will review the indications for dialysis and describe current methods of management.

MICHAEL HUMPHREYS, MD:‡ We have reviewed our experience with dialysis for acute renal failure in the past 21 months. A total of 85 patients was seen during this time with a clinical diagnosis of acute renal failure. In 38 of these patients, either peritoneal or hemodialysis related to the

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renal failure was required. Eleven patients had dialysis because of renal failure developing in the setting of trauma; there was massive trauma in 8 of these, and in the other 3 renal failure developed related to myoglobinuria from ischemia injury to an extremity. Six of the eight patients with massive trauma died, but all of the patients with myoglobinuria and ischemia injury survived, so that mortality for all 11 patients was 55 percent. These patients as a group averaged 12 hemodialyses per patient before renal function recovered or death occurred.

With this as background, it may be useful to talk for a minute about the pathogenesis and differential diagnosis of acute renal failure. Oliguria, the most common manifestation of acute renal failure, can be defined as urine output which is less than 500 ml per day in an average adult. As to functional assessment, it is a rate of urine output which is insufficient to permit excretion of the daily load of solute delivered to the circulation from body metabolism; any rate of urine flow which results in a solute accumulation in the body can be defined as oliguria. Therefore, the differentiation between oliguric and nonoliguric renal failure is a semantic one, although nonoliguric renal failure appears to be more benign and carries a better prognosis. The initial clinical insult, whether severe shock, sepsis or massive trauma, initiates a series of events which results in inadequate renal perfusion either as a result of compromise of the systemic circulation or due to changes in the blood itself. The effects of renal ischemia are manifest in a variety of ways, from mild renal dysfunction reflected as mild azotemia to severe renal damage which requires extensive supportive therapy.

The primary problem that the clinician faces when impaired renal function develops in association with oliguria is to differentiate between prerenal and renal azotemia. Table 1 shows the criteria which are used to differentiate between these two groups. In both forms of renal failure the urine output is decreased and there is solute accumulation in the blood. With prerenal azotemia, tubular function is intact and urine osmolality is usually higher than plasma osmolality. If the ratio of urine-to-plasma osmolality is 1.5 or greater, then the renal insufficiency may well be prerenal in origin. The kidneys perceive this situation as pronounced volume depletion, and react by trying to conserve sodium; the result is that urine sodium concentration will be less than 20 mEq per liter and often less than 10 mEq per liter. Urine potassium will be high, reflecting hyperaldosteronism. In prerenal azotemia the urine-to-plasma ratio for creatinine concentration is greater than 14 to 1. The urine sediment may be relatively benign, only a few granular casts being seen. If the problem is renal parenchymal failure, there is oliguria but the urine-to-plasma osmolality ratio approaches one, the urine sodium concentration is greater than 20 mEq per liter and the urine potassium concentration is low. The ratio of urine-to-plasma creatinine is also low, and the urine sediment may contain larger number of epithelial cells.

None of these diagnostic indices is absolute; in fact, values from patients with prerenal azotemia may overlap with those from patients with established acute tubular necrosis. This was well illustrated in a study by Handa and Morrin (Canad. Med. Assoc. J. 96:78-82, 1967). They reviewed the values of diagnostic indices in 10 patients with acute tubular necrosis compared with 13 patients with functional renal failure (prerenal azotemia). Neither the urine sodium concentration nor the urine-to-plasma creatinine ratio alone provided very complete separation of the two groups of patients. However, when these indices were combined by dividing the urine sodium by the urine-to-plasma creatinine ratio, near-perfect separation occurred. All patients with acute tubular necrosis had values of this fraction above 2, while all but

TABLE 1.—*Diagnostic Indices in Oliguric Acute Renal Failure*

	Pre-Renal Azotemia	*Parenchymal Renal Damage (Acute Tubular Necrosis)*
Urine Volume	<500 ml/24°	<500 ml/24°
Urine Osmolality	>400 mOsm/kg (U/P_{osm}>1.5)	±300 mOsm/kg (U/P_{osm}±1)
Urine Sodium	<10 mEq/l	>20 mEq/l
Urine Potassium	>50 mEq/l	<40 mEq/l
Urine-to-plasma creatinine	>14	<14
Urine Sediment	Benign; hyaline and granular casts	Epithelial cells and epithelial cell casts

one patient with functional renal failure had a value less than 1.3. These results have subsequently been confirmed by other investigators, and they showed the importance of early urine measurements in patients with oliguria and rising levels of blood urea nitrogen (BUN) and creatinine. When these measurements are used properly, accurate diagnosis of the cause of the oliguria can be made in most cases.

One of the standard means of treating a patient with oliguric acute renal failure has been by mannitol diuresis. This is still generally accepted as being of benefit in preventing renal failure although its effectiveness has not been unequivocally proven. Mannitol is confined to the extracellular space. An intravenous bolus injection expands the vascular compartment, increases the cardiac output, decreases renal vasoconstriction and improves renal blood flow, thereby improving renal function and urine output.

DR. SHELDON: *How do you determine whether mannitol is going to work?*

DR. HUMPHREYS: A patient in whom there is evidence of prerenal azotemia is most apt to respond and this can be defined using the tests I previously described. However, it is our feeling that any patient who has renal failure of recent onset should receive an infusion of mannitol, on the chance that urine flow may increase regardless of what the indices show. One ampule containing 12.5 grams of mannitol is administered intravenously over a period of 10 minutes or so. If the cardiovascular system is not compromised, usually there will be an increase in urine flow to some 50 ml an hour for the next four hours. If the response is less, we usually repeat the injection, and if there is no response accept the fact that acute renal failure is established.

The potent diuretic furosemide has been used in an effort to produce diuresis in patients with oliguric acute renal failure. However, there is no evidence that administration of furosemide is of any benefit in preventing renal failure. Moreover, there is now experimental evidence suggesting that the converse may be true and that this drug may actually aggravate the renal problem by worsening any preexisting hypovolemia. Another aspect of the problem is that the diagnostic features are confused by the administration of a diuretic. Following administration of furosemide, even though the patient remains oliguric, the effect on the renal tubule is such that urine sodium concentration will increase. The ability to assess the nature of the renal failure is thus impaired. So I would like to emphasize that diuretics should be avoided because they are not therapeutic and can compound the problem of making a diagnosis as to the cause of the oliguria.

In a relatively large percentage of patients seen in our hospital, myoglobinuria-related renal failure due to extensive muscle damage is present. The tip-off to this diagnosis involves examination of the urine. Myoglobin produces a urine which is red-brown in color and which gives a positive test for blood. However, results of testing the urine sediment are negative for red blood cells. The usual laboratory test for myoglobin is relatively crude and a negative finding on a laboratory test for myoglobin does not necessarily rule it out. Correlated with the findings of abnormally colored urine is the determination that the normal BUN-to-creatinine ratio in plasma of 10:1 no longer exists. In patients with myoglobinuria due to muscle damage, the serum creatinine rises more rapidly than the BUN, so the ratio is less than 10:1. This reflects a release of creatinine phosphate from the damaged muscle. Usually results of other tests of muscle damage, such as of the enzymes creatine phosphokinase (CPK) and serum glutamic oxaloacetic transaminase (SGOT), show elevated levels.

The treatment of myoglobinuria consists of a cocktail which we use in an effort to prevent the renal failure from becoming established. It is composed of a liter of 5 percent dextrose and water solution from which 200 ml have been removed and two ampules of sodium bicarbonate and two ampules of mannitol have been added. This reconstituted liter contains 100 mEq of sodium bicarbonate plus 25 grams of mannitol. The sodium bicarbonate helps to alkalinize the urine and maintain myoglobin solubility, the mannitol and water restore vascular volume and enhance renal perfusion. One liter of this is given at the rate of 250 ml per hour over a period of four hours. If there is a response, judged by urine output, administration of the cocktail is continued at a rate equal to the urine output. If at the end of four hours, there is no response to the cocktail, then the assumption has to be made that renal parenchymal damage is present and the patient's condition will not respond to further trials.

In every patient with acute renal failure, careful monitoring of fluid balance is indicated. Intake, output and daily weights should be recorded;

these should include estimates of the increased insensible losses due to fever and wounds. Phosphate retention is a result of renal failure, and can be treated by administration of oral antacids which are phosphate binders. Rarely, calcium supplements may be indicated; serum calcium levels should be measured several times weekly.

Another aspect of treatment is to avoid administering compounds containing magnesium because magnesium levels can rise to alarming levels in patients with renal failure. In addition, administration of drugs that have renal toxicity such as some of the antibiotics like kanamycin or those that are excreted by the kidney must be avoided, since toxic blood levels may result. Acidosis can be treated with sodium bicarbonate administration. Vigorous treatment of infection is indicated because sepsis is associated with the potential for further damage to the kidney. Although these patients become anemic, transfusions are not necessarily needed. The hematocrit usually stabilizes in the low 20's and this is perfectly adequate for oxygen transport. Patients in the diuretic phase of recovery from renal failure should be watched carefully since shifts in fluids and electrolytes can be profound, and all the previous considerations must be kept in mind.

DR. SHELDON: *Dr. Humphreys, would you discuss the indications for hemodialysis or for peritoneal dialysis?*

DR. HUMPHREYS: The chief indications for the institution of dialysis are hyperkalemia (serum potassium $>$ 7 mEq per liter), heart failure from fluid overload, severe metabolic acidosis and, in general, a rise in BUN above 120 and creatinine above 10—although the numbers by themselves rarely dictate when dialysis should commence. Other indications for dialysis consist of toxic or uremic complications such as pericarditis, nausea and vomiting, bleeding, seizures or coma.

One question often asked is: When do you select hemodialysis as opposed to peritoneal dialysis? Obviously, the answer relates to what is available—not all hospitals having facilities for acute hemodialysis. If only one or two dialyses may be required, peritoneal dialysis may be the method of choice. The best patients for peritoneal dialysis are those in whom rates of catabolism are low.

Hemodialysis should be the method of treatment for rapidly deteriorating patients and those who will in all probability require repeated dialysis. The absolute indications for hemodialysis are rapid catabolism—particularly in patients with burns, major trauma or severe crushing injuries—or recent abdominal surgical operation which would contraindicate introduction of a peritoneal catheter. Finally, the removal of toxins and poisons is a situation in which peritoneal dialysis is relatively ineffective and hemodialysis is preferred.

Relative contraindications to hemodialysis are systemic hypotension or limited myocardial reserve, as blood flow through the artificial kidney may be poor. Since anticoagulation must be carried out while dialysis is being done, those patients who have severe bleeding problems present formidable difficulties for hemodialysis. In the patients in whom systemic anticoagulation is contraindicated—such as patients with head trauma —regional heparinization can be used and may permit dialysis without greatly risking bleeding complications.

Some of the complications associated with hemodialysis are bleeding and rapid changes in blood volume which can result in shock and hypotension. Abrupt shifts in fluid balance and electrolyte concentrations can produce cardiac arrhythmias. Although the dialyzing membrane may rupture, blood loss is usually not a major problem, as current machines limit this potential. Occasionally, due to technical errors, the composition of the dialysate may be such that hemolysis results. A final complication which can arise is the dialysis disequilibrium syndrome. When high levels of BUN and creatinine are lowered abruptly during dialysis, a syndrome may develop characterized by central nervous system abnormalities, such as headache, nausea, vomiting, coma, seizures and occasionally even death. The mechanism for this syndrome is unknown, but may be related to the rapid removal of solutes from the spinal fluid, resulting in cerebral edema. In order to avoid this complication we make the first dialysis a short one to minimize unduly rapid solute removal.

DR. SHELDON: The incidence of renal failure in trauma patients is approximately equal to the incidence of the respiratory distress syndrome of shock and trauma. When we make vigorous attempts to avoid pulmonary failure by restricting fluids we may inadvertantly trade this for renal failure. Since our mortality rate for renal failure

as documented by Dr. Humphreys is between 55 and 75 percent and our mortality rate in those patients who develop severe respiratory failure is approximately 20 percent, treatment directed toward preventing renal failure is well advised even though respiratory problems may be aggravated.

In patients with renal failure, one goal of treatment should be to cut back on the catabolic nature of the injury so that the muscle breakdown is lessened. The problem relates to the fact that when muscle breaks down, the products of this breakdown cannot be excreted. Attempts to nourish these patients are limited by the need to limit fluids. Measure of catabolism in battle casualties shows the faster the rise in BUN levels, the greater the catabolic rate. Almost all of the nitrogen in nitrogen balance studies is excreted in urine. In the acute post-trauma period, muscle rather than fat breaks down preferentially to supply nutritional needs. It has been shown that in dogs in which kidneys have been removed, increases in BUN levels occur quickly. If amino acids and hypertonic glucose are administered, the rate of rise of BUN levels can be slowed by about 50 percent. The primary problem related to protein administration is the need to limit fluids. If too much fluid is administered, dialysis may be required to get rid of extra fluid.

During the initial catabolic phase following trauma, a patient may lose 10 grams of nitrogen a day. During the recovery or anabolic period, the return to normal is much slower than in the initial catabolic phase, and takes approximately three times as long. We advise that parenteral nutrition using an amino acid mix be started immediately after renal failure is recognized. Concentrated solutions of dextrose are administered simultaneously to cut down on the nitrogen loss. It requires approximately 4,000 calories to cut off protein catabolism and to establish positive nitrogen balance. If we were able to cut off catabolism, the urea rise would decrease and it is possible actually to put muscle mass back into the patient.

In a study at Massachusetts General Hospital, with patients in acute tubular necrosis (ATN) treated in double blind fashion, gross survivals were better in the group treated with hyperalimentation. Although their dialysis needs were lessened only slightly, their nutritional status was improved and this was probably the factor which increased survival.

J. ENGLEBERT DUNPHY, MD:* I concur based on a personal experience in battle casualties sent to us for treatment of renal failure. The prognosis was dismal in these patients in whom renal failure developed after trauma. In most there were associated sepsis, major trauma and wound complications. These survival rates have not seemed to change much over the years despite the enthusiasm for dialysis.

LAWRENCE WAY, MD:† *Dr. Humphreys, what is the best mechanism for handling the nutritional status of a patient in renal failure? Do you agree with Dr. Sheldon's recommendations?*

DR. HUMPHREYS: I am a convert to Dr. Sheldon's program. Within the restraints of fluid balance, attempts should be made to establish caloric balance in these patients. I believe this will shorten the time on dialysis and provide a better nutritional reserve. We do not need to be concerned with limiting the protein intake and can let these patients take as much protein as they can handle. We are concerned about fluid and potassium loads, however, and fluid and electrolyte balance should be monitored carefully.

F. WILLIAM BLAISDELL, MD:‡ I would like to reemphasize that the mortality from renal failure is higher than that for respiratory failure. From a clinical point of view, when dealing with trauma patients a fall in renal output within the first 24 hours following a critical clinical insult is due to inadequate renal perfusion from one of two factors—hypovolemia or cardiac failure. If the venous pressure is low to normal, a fluid load is indicated until renal output is established, or central venous pressure rises above normal. If necessary, I do not mind putting a patient in pulmonary edema, for under this circumstance I know where I am. Acute water-load pulmonary edema is relatively easily treated and readily reversible. If central venous pressure rises or pulmonary edema ensues without establishing good renal output, then attention directed toward improving cardiac function is warranted.

Once we have a patient in a stable environment such as the intensive care unit, the use of a Swan-Ganz catheter in these critical situations will permit careful titration of vascular volume and cardiac functions. A pulmonary wedge pressure in

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excess of 10 to 15 mm of mercury with no urine output directs attention toward cardiac resuscitation. A low wedge pressure is an indication for more volume. Once the initial 24 hour period has passed, the lack of response to these measures suggests the possibility of renal damage. At this point we have time to obtain consultation and apply the sophisticated tests Dr. Humphreys advocated to differentiate between prerenal failure due to inadequate circulation and renal tubular damage. I believe that most of the 11 cases of renal failure which developed in our trauma population were preventable had adequate volume been administered early and had volume therapy been maintained at optimal levels.

DR. HUMPHREYS: Dr. Blaisdell touched on the issue of pulmonary as opposed to renal consequences of hydration—a point over which the Nephrology Service gets into disagreement with our medical respiratory unit very frequently. Rather than get too far into the controversy, I will say that this has to be decided in each individual case. However, in most instances we would agree with the point that volume is needed in these patients to improve renal function. I have seen a number of cases in which there is a general overall capillary leak syndrome; under these situations, the volume titration with the Swan-Ganz catheter is essential. In most of these patients, there are vascular volumes which when measured are found to be on the low side, and therefore volume replacement is needed.

DR. BLAISDELL: We might conclude from the discussion that attempts to straddle the fence between pulmonary failure on one hand and renal failure on the other may result in inadequate volume resuscitation and may result in the worst outcome of all: a combination of respiratory and renal failure which in our experience has a 70 to 95 percent fatality.