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Critical Care of the Patient with Acute Renal Failure

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THIS REVIEW examines the complex syndrome known as acute renal failure. Emphasis is placed on the diagnosis, prevention and treatment of acute renal failure as it occurs in traumatized patients, whether the initiating event is a surgical operation or a vehicular accident. Management of patients who have established acute renal failure, including the use of modalities such as hemodialysis, is discussed.

The clinical setting of acute renal failure encompasses all major branches of medicine. A review of more than 2,400 cases from eight centers around the world reveals that 43 per cent were related to surgery, 9 per cent to trauma, 26 per cent occurred in the medical setting, 14 per cent were related to pregnancy, and the remaining 8 per cent were caused by nephrotoxins.[1–8] Table 1 lists the major causes of acute renal failure according to the anatomic site of the initial insult, *i.e.*, postrenal, prerenal and renal. This method of classification is frequently used because of its prognostic significance. Acute tubular necrosis and renal failure of intrinsic renal origin carry with them a mortality rate of approximately 30 to 40 per cent. When prerenal and postrenal failure are recognized early in their course and treated, abnormal biochemical findings, in most instances, can be rapidly reversed with little or no mortality. However, when appropriate treatment is not promptly instituted, postischemic acute tubular necrosis may develop and patient management must be along lines that include hemodialysis and severe dietary, drug, and fluid restrictions. Despite such treatment, approximately 60 per cent of patients who develop acute tubular necrosis after surgery or trauma die.[1–5,9] Recognition of the factors that lead to postischemic acute tubular necrosis, then, is the key to reduced mortality from acute renal failure.

Definitions

A definition of terms used in discussing renal failure is of value. *Renal insufficiency* is a measurable reduction in renal function with normal serum biochemical values. *Renal failure* is an advanced stage of renal insufficiency in which renal function has deteriorated to such an extent that serum biochemical values are abnormal and there is a failure of homeostatic mechanisms. The onset of renal failure is acute when the initiating process extends over days or weeks, chronic when it occurs over months or years. Acute renal failure is usually reversible, whereas chronic renal failure is not. *Anuria* is a urinary output of less than 50 ml per day, *oliguria* a urinary output of 50–400 ml per day, and *polyuria* a urinary output of more than 2.5 liters per day; all values are for an individual with body surface area of 1.73 square meters. *Acute tubular necrosis* is a type of acute renal failure. There are two types of acute tubular necrosis: the ischemic type, in which shock or a shock-like state is a predominant feature, and the nephrotoxic type, in which there appears to be cellular death from a chemical poison or irritant.[10] Acute tubular necrosis is usually accompanied by *oliguric renal failure*, *i.e.*, abnormal serum biochemical values and daily urinary output between 50 and 400 ml. However, acute tubular necrosis may occur with loss of concentrating ability and in the presence of a significant nitrogen load due to catabolism or tissue necrosis; in such cases, severe renal failure may be present, accompanied by a daily urinary output between 400 ml and 2.5 liters. This is called *non-oliguric renal failure*. When urinary output is more than 2.5 liters per day, *polyuric renal failure* is said to be present. Finally, *uremia* is a multifaceted clinical syndrome affecting virtually every organ system in a varied pattern. It is often defined as symptomatic renal failure.

Acute Renal Failure in Surgical Patients

Intraoperative oliguria and renal failure cannot be diagnosed unless there is a means of monitoring urine production. Thus, the use of an indwelling urethral catheter is justified in situations where the risk of developing acute renal failure is high (table 2). During operation, urinary output should be charted on the anesthesia record, at least hourly. A sudden decrease in output or an average output of less than 15–20 ml/hour is cause for concern. A review of vital signs, blood loss, "third-space" loss, surgical manipulation and placement of packs, and the intake and output tally usually will reveal the cause of a low measured urinary volume. A word of caution: mechanical problems with catheters are common; mucous plugs, bladder-wall tissue, and blood clots may

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TABLE 1. Major Causes of Acute Renal Failure*

Classification	Examples
A. Postrenal	
1. Obstruction	Calculi, neoplasms of bladder and pelvic organs, prostatism, surgical accidents, ureteral instrumentation
2. Extravasation	Rupture of bladder
B. Prerenal	
1. Hypovolemia	Skin losses (sweating, burns) Fluid losses (diuretics, osmotic diuresis in diabetes mellitus) Hemorrhage Sequestration (burns, peritonitis)
2. Cardiovascular failure	
a. Myocardial failure	Infarction, tamponade, dysrhythmias
b. Vascular pooling	Sepsis, septic abortion, anaphylaxis, extreme acidosis
c. Vascular occlusion	
(1) Arterial	Thrombosis, embolism, aneurysm
(2) Venous	Thrombosis, vena caval obstruction, diffuse small-vein thrombosis in amyloidosis
C. Acute tubular necrosis	
1. Postischemic	All conditions causing prerenal failure (see B, above)
2. Heme pigments	
a. Intravascular hemolysis	Transfusion reactions, hemolysis due to toxins or immunologic damage, malaria
b. Rhabdomyolysis and myoglobinuria	Trauma, muscle disease, prolonged coma, seizures, heat stroke, severe exercise
3. Nephrotoxins	Methoxyflurane, CCl_4, radiographic dyes
4. Pregnancy-related	Toxic abortifacients, septic abortion, uterine hemorrhage
D. Other renal diseases (intrinsic renal failure)	
1. Glomerulitis	Post-streptococcal, lupus erythematosus
2. Vasculitis	Periarteritis, hypersensitivity angiitis
3. Malignant nephrosclerosis	
4. Acute diffuse pyelonephritis, papillary necrosis	
5. Severe hypercalcemia	
6. Intratubular precipitation	Myeloma, urates after cytotoxic drugs, sulfonamides
7. Hepatorenal syndrome	
8. Pregnancy-related	Eclampsia, postpartum renal failure

* Modified from Levinsky and Alexander.[9]

obstruct drainage holes at the catheter tip. Also, when the patient is placed in a steep head-down position, urine may pool in the bladder dome or kidneys, with subsequent scant drainage from the catheter.

In the absence of a catheter, the intraoperative diagnosis of oliguria cannot be made. When there is reason to suspect decreased urinary output, palpation of the bladder may be helpful. However, a full bladder under these circumstances may merely reflect urine formed prior to operation or prior to the oliguric insult. To make a definitive diagnosis, an indwelling catheter must be inserted and the rate of urine formation determined. Once it is established that the patient is oliguric and that collection artifacts are not to blame, the anesthesiologist should try to determine the cause of the low urinary output.

PRERENAL OLIGURIA

Etiology. In surgical patients oliguria most commonly is prerenal in origin, that is, due to inadequate renal perfusion. Poor perfusion may occur as a consequence of decreased circulating blood volume, cardiac depression and, during operation, administration of anesthetic agents.

The signs of overt hypovolemia are familiar: decreased arterial and venous pressures, tachycardia, diaphoresis, and pallor. Smaller reductions in circulating blood volume may not be accompanied by all or any of these signs, but there still may be renal hypoperfusion as blood is shunted away from the kidneys to more "vital" organs. Similarly, cardiac depression may be grossly obvious, with all of the signs of heart failure, or it may be only minimally apparent; in both instances, however, renal blood flow may be compromised. Anesthetic-induced changes in renal blood

TABLE 2. "At-risk" Situations for the Kidney*

1. Cardiopulmonary bypass or surgery of the aorta or renal vessels[12–22]
2. Major biliary tree surgery, obstructive jaundice[23]
3. Procedures in which large volumes of blood may be transfused[21,24]
4. Hypovolemic hypotension[17,19,25]
5. Lengthy or extensive surgical procedures in elderly patients[26–28]
6. Surgery in patients with pre-existing renal disease[15–18,29,30]
7. Obstetric complications such as abruptio placentae[31]
8. Major trauma[24,32,33]
9. Sepsis and administration of nephrotoxic antibiotics[33–37]

* Modified from Cousins and Mazze.[10]

flow are thought to be secondary to the profound effects these agents exert upon the cardiovascular and sympathetic nervous systems.[11,25] All potent inhalational anesthetic agents have a direct, negative inotropic effect upon the heart and cause peripheral vascular relaxation. Additionally, the kidneys are richly supplied with sympathetic constrictor fibers derived from the T4-L1 spinal cord segments via the celiac and renal plexuses; there is no sympathetic dilator or parasympathetic innervation to the kidneys. Anesthetic administration results in increased sympathetic nervous system stimulation to the kidney,[38] with increased depth of anesthesia and administration of inhalational agents that evoke a catecholamine response, such as diethyl ether and cyclopropane, associated with the greatest decreases in renal hemodynamics and function.[39–44] Anesthetic-induced changes in renal blood flow are readily reversed when administration of the agent is discontinued.

Oliguria secondary to circulatory insufficiency, whether due to hypovolemia or cardiac depression, also is reversible when promptly treated. However, at some point, functional changes develop an organic component and they can no longer be reversed by simple measures.[12] This is particularly true when hypovolemia is severe and persistent, so that renal ischemia is present. There is great variation in both the duration and the severity of circulatory insufficiency needed to transform functional renal insufficiency to organic renal failure. In some patients transient hypotension or small decreases in cardiac output may result in organic failure, while in others overt shock, or hours or even days of renal ischemia will not produce organic lesions. Since it is impossible to predict in advance into which category an individual patient will fall, circulatory insufficiency must be rapidly diagnosed and treated in all patients.

Diagnosis and Treatment. Correction of hypovolemia will, in many cases, increase cardiac output, enhance renal perfusion, and prevent organic renal ischemic changes. A diagnostic and therapeutic maneuver in the management of oliguric patients is the rapid infusion of 500 ml of balanced salt solution and the determination of the response of the kidneys to this challenge. When there is an increase in urine flow, additional fluids must be administered, since significant oliguria usually would not have occurred unless extracellular fluid volume had been depleted by 25 per cent or more. Generally, replacement fluid should match the type of fluid that has been lost, although organ perfusion may be enhanced by hemodilution. Central venous pressure measurements are invaluable in determining the total volume of fluid to be administered. However, in patients who have marked impairment of myocardial function, or severe pulmonary disease, central venous pressure may not correlate with left atrial pressure. In such patients, when volume status is uncertain or rapid infusions are necessary, the only effective way to measure left ventricular filling pressure clinically is by determination of pulmonary-artery wedge pressure using a Swan-Ganz, balloon-tipped, triple-lumen catheter.[45]

When replacement of fluid losses does not reverse oliguria, it is possible that cardiac failure may be present. In such cases inotropic agents, such as dopamine or isoproterenol, should be administered. In recent years, the use of digitalis for the treatment of cardiac failure in the operating room has become infrequent due to the greater simplicity and lesser hazard associated with administration of the sympathomimetic amines. Dopamine in low doses, 1–5 μg/kg/min, increases renal blood flow, even in the absence of heart failure. However, in doses higher than 10–20 μg/kg/min the alpha-adrenergic stimulating effect of dopamine may predominate and renal blood flow may decrease.[46,47]

Use of Diuretics. The efficacy of diuretic administration in the treatment of oliguria and the prevention of renal failure is still debated. Because these agents are potentially harmful, their mechanism of action must be understood if they are to be employed. Osmotic agents, such as mannitol, produce diuresis because they are filtered by the glomerulus but not reabsorbed by the renal tubules, thus obligating the excretion of water. Additionally, their administration results in an increase in intravascular volume, and they may block renin release.[49] Because they increase blood volume, the use of osmotic diuretics in treating oliguria secondary to congestive heart failure is contraindicated. The average initial dose of mannitol is 12.5–25 g, administered as a 20–25 per cent solution, with total daily dosage usually less than 100 g.[30] Loop diuretics, such as furosemide and ethacrynic acid, produce diuresis by blocking sodium reabsorption in the loop of Henle and distal convoluted tubule. When administered to patients with congestive heart failure, they promote profuse natriuresis with increased urine flow. This results in a decrease in intravascular volume and ultimately an improvement in cardiac performance. The use of loop diuretics is clearly beneficial in this circumstance.[50] However, these agents are contraindicated in oliguria of hypovolemic origin because they may promote excessive natriuresis and diuresis despite hyponatremia and reduced intravascular volume, thereby aggravating renal ischemic changes.[51] When, after an initial positive response to diuretic treatment, urinary flow again decreases to less than 1 ml/kg/hour, diuretic

treatment should be continued, while carefully maintaining fluid and electrolyte balance. The average initial dose of furosemide or ethacrynic acid is 20–50 mg, with total daily dosage generally less than 200–300 mg. Additionally, some patients may not respond to one class of diuretics but will respond to combined treatment with both osmotic and loop diuretics. In refractory cases of oliguria some investigators have recommended a more radical approach.[52,53] They have administered massive initial doses of furosemide, 600–1,000 mg, followed by as much as 3,200 mg daily. Generally, this approach should be discouraged because it has not been effective in reducing mortality from acute renal failure and because these high doses are associated with increased toxicity, including fluid and electrolyte disturbances, cardiac arrhythmias, ototoxicity, skin rash, gastrointestinal disturbances, thrombocytopenia, and neutropenia.

Controversy regarding the use of diuretics in the treatment of acute renal failure has not yet been resolved. One group of nephrologists states that when they are administered judiciously, diuretics may prevent functional renal failure from progressing to organic renal disease.[20,30,54,55] Even when not completely effective, they may improve the clinical situation by converting oliguric renal failure to high-output renal failure; the latter condition is more easily managed and is associated with a lower mortality rate than the former.[12,53,54,56] Other nephrologists believe that except when oliguria is secondary to heart failure, diuretic therapy is not indicated.[50] They cite the hazards of excessive salt and water loss, ototoxicity associated with the use of the loop diuretics, and the potentiating effect of furosemide on acute renal failure, both clinical and experimental, when administered concurrently with nephrotoxic antibiotics.[57–59]

On balance, it appears that diuretic agents *may* be useful in treating oliguria in *some* patients; their administration is associated with few complications when basic physiologic principles are adhered to and dosage is not excessive. A trial with the appropriate diuretic agent is indicated in most cases of oliguria.

Postrenal Oliguria

This category comprises fewer than 5 per cent of oliguric disorders in surgical patients. Obstruction of normal urinary outflow and extravasation of urine from a ruptured bladder make up the group, with obstruction, by far, the more frequent of the two. Obstruction of urinary flow produces an increase in hydrostatic pressure in the urinary tract proximal to the blockage. This leads to a marked decrease in glomerular filtration rate and, ultimately, morphologic damage to the renal parenchyma.

The passage of urine depends upon the patency of compressible structures, so that obstruction can be further divided into that due to extrinsic and that due to intrinsic causes. Extrinsic obstruction with oliguria may be caused by rapidly growing pelvic tumors, retroperitoneal fibrosis, or malignancy. Iatrogenic oliguria may follow inadvertent placement of surgical ligatures or trauma to the ureters. A review of 161 cases of ureteral injury showed that 72 per cent followed gynecologic surgery, with an additional 12 per cent occurring after obstetrical procedures.[60] The incidence of such mishaps among patients undergoing gynecologic surgery is reported to be 0.1–0.25 per cent.[61] Approximately 20–25 per cent of ureteral injuries have been bilateral and complete, resulting in immediate anuria. A common non-iatrogenic cause of obstructive uropathy and oliguria in elderly surgical patients is fecal impaction.

Intrinsic obstruction can be caused by blood clots, calculi, prostatic hypertrophy, and neoplasms.[62,63] Only 700 cases of primary ureteral tumors have been reported,[63] and metastatic tumors to the ureter are even rarer. Patients who have calculi of the genitourinary tract may have sudden anuria when stones are bilateral or are in the bladder; there may instead be intermittent anuria or oliguria when a calculus acts as a ball valve. Benign prostatic hypertrophy is a frequent cause of decreased urinary flow in older male patients, particularly following operations around the groin or rectum, when pain prevents relaxation of voluntary sphincters. Oliguria may follow ureteral catheterization due to edema of the ureteral orifices.

Extravasation of urine outside of the bladder with oliguria most frequently occurs after trauma to the pelvis. Damage to the bladder is probably rare when it is relatively empty at the time of injury; however, pelvic fractures are associated with a 9 to 15 per cent incidence of ruptured bladder.[64]

Definitive treatment of most cases of postrenal oliguria is surgical. When the obstruction is high in the genitourinary tract, percutaneous nephrostomy may be necessary in order to provide urinary drainage. When bladder calculi cause obstruction, suprapubic cystostomy or urethral catheterization is the first therapeutic maneuver. Massive diuresis occasionally follows relief of obstruction, at times resulting in hypovolemia and electrolyte imbalance. Hypotension also has occurred following rapid decompression of an overdistended bladder. When the obstruction is recognized and treated promptly, there will be a rapid return of normal renal function.

TABLE 3. Urinary Composition in Oliguria

	Physiologic Oliguria	Prerenal Failure	Acute Tubular Necrosis
Urinary sodium	<10 mEq/l	<25 mEq/l	>25 mEq/l
Urinary specific gravity	>1.024	>1.015	1.010–1.015
Urinary/plasma osmolality	>2.5:1	>1.8:1	1.1:1 or less
Urinary/plasma urea	>100:1	>20:1	3:1, rarely > 10:1
Urinary/plasma creatinine	>60:1	>30:1, rarely <10:1	<10:1

ACUTE TUBULAR NECROSIS

Oliguria in surgical patients may persist throughout operation and into the immediate postoperative period in spite of what appears to be adequate volume replacement and treatment of the cardiovascular causes of prerenal failure. In such cases: 1) the original diagnosis of prerenal failure may have been in error; 2) therapy still may have been insufficient to correct prerenal causes of oliguria; 3) treatment may not have been instituted promptly enough to prevent postischemic acute tubular necrosis. Thus, it is necessary to re-evaluate the causes of oliguric renal failure (table 1).

In many cases, it is impossible to determine the cause of oliguria and azotemia from the clinical presentation, alone. Observation of the pattern of urinary flow offers the first clue. Complete anuria is rare, for example, occurring only once in one series of 85 patients.[65] In the medical setting, cortical necrosis, vascular occlusion, the glomerulitides and the vasculitides are the likely causes of anuria; in surgical patients, vascular accidents and obstruction of urinary flow are most often responsible. Determination of urinary composition is helpful in distinguishing reversible oliguria of prerenal origin from irreversible oliguria due to established acute tubular necrosis (table 3). In this regard, the urinary/plasma osmolality ratio is the single most valuable measurement. A ratio of 1.1:1, or less, in an oliguric patient is almost pathognomonic for acute tubular necrosis.[66] However, examination of urinary composition is of value only when the patient has not received diuretics for the preceding six to 12 hours, since diuretics interfere with the ability of the kidney to reabsorb sodium and to dilute and concentrate urine. Therefore, when renal failure is suspected, it is mandatory to collect samples of urine and plasma for subsequent examination before diuretic therapy is instituted.

Examination of the urinary sediment is also of diagnostic value in differentiating the causes of oliguria. In prerenal oliguria, there is a preponderance of hyaline and finely granular casts, with coarse and cellular casts seen only rarely. When oliguria is due to acute tubular necrosis, there are many granular, brown-pigmented, cellular casts and numerous epithelial cells, both free and in casts. Few formed elements in the urine suggest that obstruction may be present. Erythrocytes or heme-pigmented casts are seen after transfusion of incompatible blood, but otherwise are rare. Proteinuria is of little diagnostic value, as it may be found in the absence of renal disease, following stress, exercise, fever, or congestive heart failure. Absence of proteinuria does suggest pre- or postrenal failure. Massive proteinuria, however, is almost always of primary renal origin.

A plain film of the abdomen and renal tomography will determine kidney size and detect calcified stones. The kidneys are normal or increased in size in patients with acute renal failure, whereas they are frequently small in the presence of chronic renal disease. Urographic studies are used to rule out obstruction and, with modern techniques, are relatively safe even in acute oliguric renal failure. Intravenous pyelography will reveal an immediate, dense and persistent nephrogram in patients with acute tubular necrosis and pyelonephritis, but not with other forms of oliguria. In oliguria of prerenal origin, a normal pyelogram is seen. In established oliguric renal failure, the pyelogram is not seen, but the nephrogram often is dense enough to detect the calyceal system and to permit observation of filling defects. However, retrograde urography may still be necessary in some cases to localize obstructing lesions precisely. When the diagnosis is still not apparent after retrograde urography, angiography may be necessary to rule out vascular lesions.

Prior administration of nephrotoxic drugs must be considered in the differential diagnosis of oliguria.[10] Methoxyflurane anesthesia may result in renal failure by virtue of its metabolism to inorganic fluoride.[67–69] The lesion is dose-related and usually accompanied by polyuria; however, approximately 10 per cent of patients with methoxyfluorane nephrotoxicity have oliguric renal failure.[70] Several antibiotics have nephrotoxic potential, especially the aminoglycoside agents (neomycin, kanamycin and gentamicin), tetracycline, cephaloridine, and methicillin.[10,71,72] Radiographic dyes also have been implicated as the cause of nephrotoxic acute renal failure.[10]

When the above-mentioned investigations do not result in a definitive diagnosis, the adequacy of the patient's cardiac function and circulating blood volume should be re-evaluated and corrective therapy instituted when appropriate. When the patient

remains oliguric or it appears from the diagnostic evaluation that acute tubular necrosis is present, a renal failure regimen should be instituted.

The Clinical Course of Acute Tubular Necrosis[9,31,73]

Oliguric Phase. Acute ischemic or nephrotoxic damage to the kidney usually is reversible when the patient can be kept alive through the period of renal failure. Occasionally, morbid renal lesions are present, and they may be irreversible, in particular, after cases of bilateral cortical necrosis or glomerulonephritis.

Most patients have an oliguric phase, which usually begins at the time of the initiating event but may be delayed for as long as a week.[65] The average duration of oliguria is approximately ten days, but low urinary flow rates may persist for only a few hours or, conversely, for several weeks.[1,4,5,65] Renal biopsy should be performed after three or four weeks of oliguria to determine whether irreversible damage has occurred. Average urinary output during the oliguric phase is 150 ml/day. Azotemia progresses at a rate determined largely by the extent of protein catabolism, which in the non-traumatized patient amounts to about 20–40 g/day, and by the reduction in glomerular filtration rate. In the well-managed case, blood urea nitrogen increases 10–20 mg/100 ml/day and plasma creatinine, 0.5–1.0 mg/100 ml/day. In traumatized patients, when infection is present, or after major surgical procedures, blood urea nitrogen may increase by as much as 100 mg/100 ml/day and plasma creatinine by 2.0 mg/100 ml/day. At least 100 g of glucose should be provided each day in order to minimize catabolism of protein. Daily water intake should be restricted to about 500 ml plus replacement of losses from gastrointestinal drainage, sweating, and formation of urine. Additionally, more than 400 ml of water are released daily from endogenous sources. In uncomplicated cases, the net result of fluid restriction is a decrease in body weight of 0.2–0.5 kg/day because of tissue catabolism. In hypercatabolic patients, daily weight loss may be 1 kg or more.

Although oliguric patients can be managed conservatively for several days without dialysis, it is most prudent to transfer the patient to a facility with hemodialysis capabilities as soon as the diagnosis of acute renal failure has been established. Dialysis involves diffusion of circulating waste products across a semipermeable membrane (peritoneum or Cuprophane in the case of hemodialysis). Presently, two techniques, peritoneal dialysis and hemodialysis, are used. The dialysate may be hypertonic or hypotonic to plasma, resulting in removal or addition of extracellular fluid. In peritoneal dialysis, a cannula is inserted into the abdomen, and the peritoneum acts as the diffusing surface. This technique does not require vascular cannulas or complex equipment. Its disadvantages are that changes in fluid and electrolyte balance occur much less rapidly than with hemodialysis, peritonitis occasionally occurs, and abdominal pain during dialysis may be severe. Primarily because of its greater efficiency, hemodialysis is more frequently employed. To connect the patient to the artificial kidney, Teflon or silicone rubber cannulas with external couplings are inserted into blood vessels of the forearm or lower leg. Local infiltration or brachial block anesthesia is usually employed for shunt insertion. The latter may be preferable because it produces vasodilation in addition to anesthesia. When hyperkalemia and acidosis are present, increased myocardial irritability may exist; therefore, local anesthetic solutions containing epinephrine should not be used. In the interval between treatments, clotting of the blood in the cannulas usually does not occur because of the nature of the material used to construct the shunt and because blood flow in the A-V conduit is rapid (150 to 300 ml/min). During hemodialysis, which requires 4–8 hours, two to five times weekly, the patient's blood is heparinized to prevent clotting within the dialyzer. Serial serum electrolyte and hematocrit determinations are performed and abnormalities corrected by altering the composition of the dialysate.

Early and frequent dialysis allows greater flexibility in dietary and drug treatment regimens of patients who have acute renal failure. Early dialysis may also reduce the incidence of complications and improve survival.[8,74,75] Nevertheless, even with optimal management, many complications develop. Hyponatremia is common, and usually reflects excessive hydration. It is prevented by appropriate restriction of fluids.[65] Hyperkalemia results from release of potassium from tissue breakdown. In uncomplicated cases, plasma potassium increases by 0.3–0.5 mEq/l/day, and after trauma or operation, 1.0–2.0 mEq/l/day.[1,33] However, the rate of increase of plasma potassium is variable; increments of 1–2 mEq/l/hour in patients with extensive tissue trauma, large hematomas, or sepsis have been recorded.[1,60] Hyperkalemia is asymptomatic until advanced, when arrhythmias, commonly ventricular fibrillation or cardiac arrest, occur. The cardiac effects of hypokalemia are potentiated by hypocalcemia, hyponatremia and acidosis. Acidosis develops because of the release of 50–100 mEq/day of fixed acid from catabolism of protein. Plasma bicarbonate decreases 1–2 mEq/l/day in uncomplicated

cases, with a much more rapid decrement in hypercatabolic states. Phosphate, sulfate, and various organic ions also accumulate in body fluids.[9]

Hypocalcemia develops with calcium concentrations ranging from 6.0 to 8.0 mg/100 ml. The mechanism of hypocalcemia in oliguric renal failure is incompletely understood; oliguric patients may be insensitive to the action of parathyroid hormone.[9] Additional factors causing hypocalcemia are hypophosphatemia and hypoalbuminemia, both very common in oliguric renal failure. Hypermagnesemia occurs in acute renal failure; however, plasma magnesium levels rarely exceed 4 mEq/l. These levels probably are not toxic.

Cardiac arrhythmias and congestive heart failure often occur in acute renal failure. These probably are complications of fluid and electrolyte imbalance rather than primary symptoms of renal failure.[1] Digitalis toxicity is an important cause of arrhythmias. Congestive heart failure is usually due to fluid excess, with anemia, hypertension, and pre-existing heart disease contributing. The incidence of these complications is decreasing as more frequent and earlier hemodialysis is performed. Similarly, the incidence of of uremic pericarditis has been reduced from almost 20 per cent to less than 1 per cent with more aggressive hemodialysis techniques.[9,50,73]

Better medical management and increased use of dialysis have decreased the numbers of neurologic and psychiatric complications of acute uremia. In earlier series, lethargy, confusion, stupor, coma, agitation, hyperreflexia, twitching and abnormal behavior, including anxiety and paranoia, were common.[1,9,65] Convulsions, often due to overhydration, have been reported.[1,76] All of these signs and symptoms of acute uremia may reverse following dialysis. Gastrointestinal symptoms are common and include anorexia, nausea, vomiting, abdominal distention and ileus. There is a tendency towards gastrointestinal hemorrhage due to the bleeding dyscrasia of acute uremia combined with the frequent occurrence of numerous gastrointestinal ulcers.[1–3,8,74] In addition to bleeding dyscrasias, other hematologic disorders include suppression of erythropoiesis, leukocytosis, and defects in platelet production and production of coagulation factors. The combination of these factors contributes to the anemia characteristic of prolonged oliguric renal failure.[77] However, a hematocrit of 20–24 per cent is usually well tolerated when it develops over a period of several weeks or months.

Infection is the most common cause of death in acute renal failure. It is estimated that infections develop in 50–90 per cent of all such patients, and that they are responsible for a third of the deaths in traumatic or surgically induced renal failure.[1,75] Infections most often occur in the respiratory tract, urinary tract, and wounds of patients who have acute renal failure, with septicemia frequently resulting. The somnolence and stupor of acute uremia may contribute to the high incidence of respiratory tract infections by interfering with normal tracheal toilet, and by increasing the risk of aspiration of vomitus. Urinary tract infections have followed the use of indwelling catheters, so that their use is less common now than in the past. Wound infections occur in about half of civilian patients and three-quarters of military patients with acute renal failure.[33,76] As many as a quarter of these patients subsequently have septicemia. *Staphylococci*, *Streptococci*, and gram-negative organisms, including *Proteus, Klebsiella, Pseudomonas,* and *E. coli*, are the organisms most commonly found in septic patients.[78] The reason for the increased number of infections in renal failure is not clear. Antibody production and phagocytic activity, the most important factors in resistance to bacterial infection, are usually normal.[78] Cellular immune responses are depressed in uremia, but their relationship to the development of bacterial infection has not been established. Other common features of acute tubular necrosis are delayed and inadequate wound healing, perhaps due to inhibition of proliferation of fibroblasts and formation of granulation tissues.

Diuretic Phase. A daily doubling of urinary volume signals that glomerular filtration rate has started to recover.[65] Although urinary output may reach one liter by the third day, renal function still is markedly abnormal in the diuretic phase. Blood urea nitrogen and plasma creatinine levels remain elevated, and actually may increase. Urinary output frequently exceeds two liters for several days; however, higher urinary volumes are rare when dialysis has been used during the oliguric phase to treat overhydration and accumulation of an osmotic load. Fluid and electrolyte intake must be carefully managed during the early diuretic phase in order to avoid over- or underhydration and abnormalities in sodium and potassium balance. Gastrointestinal bleeding and abnormal cardiac function may persist or actually first appear in the early diuretic period.[1–3,65] About a fourth of all deaths occur during this phase, even with the regular use of dialysis.[65,76]

Recovery Phase. Renal function improves for three to 12 months after an episode of acute tubular necrosis, and then stabilizes. There may be a permanent loss of 20–40 per cent of glomerular filtration rate, and concentrating ability and ability to acidify urine may also remain suboptimal.[79] However, such renal function is compatible with normal life for

most individuals. Older patients recover renal function more slowly and less completely than younger patients; prolonged oliguria tends to be followed by less complete recovery of renal function. Generally, the prognosis following an episode of acute tubular necrosis relates, most of all, to the physical condition of the patient prior to becoming ill.[1-9,31,73] Thus, the mortality rate is 10–15 per cent among obstetrical patients, 30–40 per cent among medical patients, and 60 per cent or more among surgical patients. Despite improved dialysis techniques, survival of surgical and traumatized patients has not improved. This is probably because surgical procedures, today, are performed on patients who in past years were considered to present too great an operative risk.

Anesthetic Management of the Patient with Acute Renal Failure

Patients who have acute renal failure are prone to complications, and often need urgent or emergency surgical procedures. Whenever possible, surgical procedures should be deferred until hemodialysis has been performed, so that the patient's preoperative status is optimal. Normochromic, normocytic anemia is usually present, with hemoglobin in the 6–8 g/100 ml range.[77] This may be improved during dialysis by transfusion with leukocyte-poor packed erythrocytes. However, hemoglobin values of more than 9 g/100 ml are difficult to maintain and should not be a therapeutic aim because of the danger of producing circulatory overload. Following dialysis, results of coagulation studies should be normal, and serum creatinine and blood urea nitrogen should be less than 10 and 60 mg/100 ml, respectively; serum potassium should be in the range of 4.0–5.5 mEq/l, and serum bicarbonate should be normal. Serum calcium is usually low (7–8 mg/100 ml) but rarely causes tetany. Hypertension (blood pressure higher than 160/90 torr), present in about a third of patients prior to hemodialysis, is alleviated by dialysis, as are arrhythmias. Preoperative hemodialysis of the digitalized patient requires great care because of the danger of arrhythmias associated with changes in electrolyte concentration, particularly potassium.

Choice of anesthesia should be based on the same considerations as in other surgical patients, plus a few additional precautions. Gallamine and decamethonium, muscle relaxants excreted completely by the kidney, should not be administered. The use of succinylcholine has been questioned because reductions in pseudocholinesterase have been reported to occur after hemodialysis.[80,81] However, it has been safely administered, for both intubation and intraoperative relaxation, in patients without renal function. The increment in serum potassium following succinylcholine administration in dialyzed uremic patients is no greater than that occurring in patients without renal disease.[82,83] However, it is not known whether even small increases in serum potassium in non-dialyzed, hyperkalemic patients will result in arrhythmias. *d*-Tubocurarine is primarily excreted by the kidney, but the liver provides an alternate pathway of excretion when renal function is decreased.[84] Prolonged apnea has occurred following both succinylcholine and *d*-tubocurarine, so dosage should be carefully tailored to meet patient requirements[80,81,85,86]; a nerve stimulator may be helpful in this regard. Virtually every anesthetic agent and technique has been administered to patients with absent renal function. A consensus of reports suggests that for general anesthesia: thiopental be administered for induction of anesthesia; succinylcholine for endotracheal intubation; halothane with as much as 50 per cent nitrous oxide and oxygen for maintenance of anesthesia; and *d*-tubocurarine for intraoperative relaxation.[85,87,88] Experience with pancuronium is limited, compared with experience with *d*-tubocurarine, but it is probably satisfactory.[89] Forty to fifty per cent of pancuronium is excreted, unchanged, in the urine; excessive dosage, therefore, must be avoided.[89,90] Methoxyflurane is contraindicated because it is nephrotoxic.[67-70] Enflurane probably should not be administered, since it has been reported to exacerbate renal dysfunction in patients who have pre-existing renal disease.[91-93] Whenever appropriate, regional anesthetic techniques should be employed, because muscle relaxants are not required, endotracheal intubation and the attendant possibility of respiratory infection is avoided, and fewer central nervous system depressant drugs are needed.[94]

Fluid administration during operation must be carried out with the knowledge that patients without renal function may have increased blood volume, and cannot excrete excessive water or solute loads. Five per cent dextrose in 0.45 per cent saline solution is a frequently administered solution. Systemic arterial pressure, central venous pressure, pulse rate, and auscultation of the chest should be used to determine fluid requirements.

Patients who have severely impaired renal function may require emergency surgery without sufficient time for preoperative hemodialysis. In these individuals, hyperkalemia, acidosis and overhydration may be significant hazards. Patients whose serum potassium values are greater than 5.5 mEq/l should be given 5 per cent dextrose in water, to which two

units of regular insulin have been added for each 5 g of dextrose. This solution, initially infused at a rate of 3–5 ml/min, will facilitate transfer of potassium from serum to the intracellular compartment.[95] Calcium gluconate, 2 g/100 ml, may be added to the solution to antagonize further the cardiac toxicity of potassium. Adsorption of insulin to intravenous infusion equipment has been reported, so some prefer to administer insulin subcutaneously. Rectal administration of sodium–potassium cation exchange resins also will reduce elevated potassium levels, but less rapidly than treatment with the dextrose–insulin mixture. When moderate or severe acidosis is present, bicarbonate rather than lactate should be administered, since the latter may be poorly metabolized in advanced stages of uremia.[31] When blood is needed, it should be deionized with a device such as the Travenol JB-2 Ion Exchange Blood Pack, in order to reduce its potassium content. These therapeutic maneuvers, although not a substitute for preoperative hemodialysis, may permit emergency surgical procedures to be performed with relative safety.

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