

*Current Concepts***ACUTE OLIGURIA**

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ACUTE oliguria (excretion of less than 400 ml of urine per day) is often the earliest sign of impaired renal function and poses a diagnostic and management challenge to the clinician. Early identification of potentially reversible causes of acute oliguria and institution of appropriate therapy are crucial, since the therapeutic window is often small.¹ Oliguria can have many causes. Some are overt and apparent, such as septic shock, whereas others are concealed and subtle, such as myoglobin release or drug toxicity.² The main functional derangement in patients with acute oliguria is a sudden and severe decrease in the glomerular filtration rate (acute renal failure), sufficient to result in increases in the plasma urea and creatinine concentrations, retention of salt and water, and the development of acidosis and hyperkalemia.³

Patients with acute oliguria that develops outside the hospital should be expeditiously admitted and evaluated for potentially life-threatening complications such as hyperkalemia, manifested by muscle weakness or paralysis or by electrocardiographic changes; metabolic acidosis, resulting in Kussmaul's respirations, hypotension, and hyperreflexia; and pulmonary edema, ascites, or pleural effusions due to salt and water retention. Other complications on admission to the hospital may include nausea, vomiting, drowsiness, pericarditis, confusion, and coma. Once the potentially life-threatening conditions have been ruled out or appropriately treated, a detailed history should be obtained, including drugs the patient has taken, occupation, hobbies, recent travel, and previous renal disease. When acute oliguria develops outside the hospital, there is usually a single renal cause and a good prognosis.⁴ Most episodes of acute oliguria, however, occur in the hospital and are associated with hypovolemia, decreased cardiac output, the effects of anesthesia or surgery, or the use of diuretics, nephrotoxic drugs, or radiographic contrast agents.⁵ Patients with acute oliguria that devel-

ops in the hospital usually have had multiple renal injuries. The renal insufficiency is frequently severe, and the prognosis is not as good as it is with acute oliguria that develops outside the hospital.⁶ In the intensive care setting, acute oliguria occurs late in the clinical course of severe illness with failure of multiple organs.^{7,8}

CAUSES OF ACUTE OLIGURIA

The causes of acute oliguria can be grouped into three categories: prerenal, renal or intrinsic, and postrenal (obstructive uropathy) (Table 1). Prompt identification and treatment of prerenal causes or obstructive uropathy may prevent the development of protracted acute renal failure, which is associated with high morbidity and mortality rates.⁹ Assessment of volume status, hemodynamics, and drug use may uncover potential prerenal causes of oliguria. Invasive monitoring of central venous pressure or pulmonary-capillary wedge pressure may be indicated if an accurate assessment of intravascular volume cannot be obtained by other means — for example, in patients with poor cardiac function. Renal ultrasonography is the study of choice to detect obstructive uropathy, which if present is usually manifested by dilatation of the urinary tract above the obstruction.¹⁰ In some instances, despite the presence of obstructive uropathy, dilatation of the urinary tract does not occur for various reasons: malignancy is the cause of the obstruction, the patient is severely dehydrated, retroperitoneal fibrosis is present, or there has been insufficient time for dilatation to occur.¹⁰ The absence of urinary output suggests that the patient has obstructive uropathy, renal cortical necrosis, or necrotizing glomerular disease. Alternating episodes of polyuria and oliguria-anuria strongly suggest the presence of intermittent obstruction of the urinary tract.¹⁰

URINARY SEDIMENT AND INDEXES

A careful examination of the urinary sediment and the use of urinary indexes can help distinguish prerenal failure from intrinsic acute renal failure. In prerenal failure, hyaline and fine granular casts may be seen; however, coarsely granular and cellular casts are unusual. In intrinsic renal failure (acute tubular necrosis), brown granular casts and tubular epithelial cells, singly or in casts, are present in the urine specimens of about 80 percent of patients¹¹ (Fig. 1). Measurements of sodium and creatinine concentrations in both plasma and urine may help assess renal tubular function.^{11,12} In prerenal failure due to a reduction in the glomerular filtration rate coupled with an increased stimulus for salt and water reabsorption, the ratio of urinary to plasma creatinine is usually higher and the urinary sodium concentration is lower than in cases of intrinsic acute renal failure (Table 2).

The use of urinary indexes is based on the as-

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TABLE 1. PRINCIPAL CAUSES OF ACUTE OLIGURIA.

Prerenal events

Absolute decrease in effective blood volume due to hemorrhage, gastrointestinal fluid loss (from diarrhea, vomiting, or nasogastric suction) or pooling of fluid (from pancreatitis or bowel disease), renal losses (from diuretics or glycosuria), trauma, surgery, or burns

Relative decrease in effective blood volume due to sepsis, hepatic failure, anaphylaxis, vasodilatory drugs, the nephrotic syndrome, or anesthetic agents

Myocardial failure due to myocardial infarction, pulmonary embolism, congestive heart failure, cardiac tamponade, or mechanical ventilation

Disruption of renal autoregulation due to the administration of angiotensin-converting-enzyme inhibitors

Renal-artery or renal-vein occlusion due to thrombosis, thromboembolism, severe stenosis caused by atherosclerosis, or dissecting aneurysm

Renal or intrinsic events

Small-vessel vasculitis or acute glomerulonephritis due to connective-tissue disorders (systemic lupus erythematosus or drug-related disorders), scleroderma, malignant hypertension, toxemia of pregnancy, microscopic polyarteritis, poststreptococcal glomerulonephritis, rapidly progressive glomerulonephritis, or other disorders

Interstitial nephritis related to drugs (e.g., methicillin), infection, or cancer (lymphoma, leukemia, or sarcoidosis)

Acute tubular necrosis due to ischemia (mainly as a consequence of prerenal events), nephrotoxic antibiotics (e.g., gentamicin or kanamycin), heavy metals (mercury or cisplatin), solvents (carbon tetrachloride or ethylene glycol), radiographic contrast agents, endogenous events, intratubular crystals (uric acid or oxalate), or intratubular pigments (myoglobinuria)

Postrenal events (obstructive uropathy)

Upper urinary tract obstruction: ureteral obstruction of one or both kidneys

Lower urinary tract obstruction: bladder-outlet obstruction (more common)

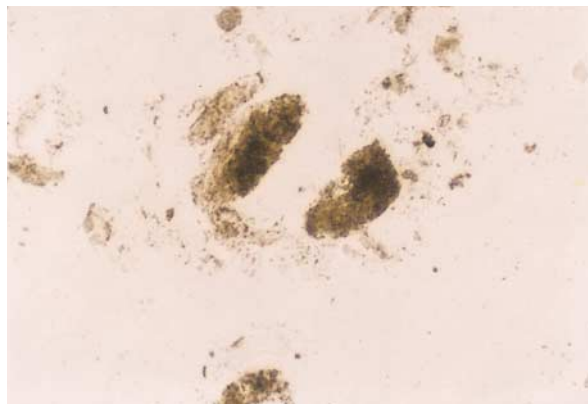


Figure 1. Photomicrograph of Urinary Sediment Obtained from a Patient with Acute Tubular Necrosis (×200).

Multiple broad, brown, granular casts are composed of Tamm-Horsfall glycoprotein, cells, remnants of shed brush border, and other cellular debris.

TABLE 2. CHARACTERISTIC URINARY INDEXES IN PATIENTS WITH ACUTE OLIGURIA DUE TO PRERENAL OR RENAL (INTRINSIC) CAUSES.

INDEX	PRERENAL CAUSES	RENAL CAUSES
Urinary sodium concentration (mmol/liter)	<20	>40
Fractional excretion of sodium (%)	<1	>1
Ratio of urinary to plasma creatinine	>40	<20
Ratio of urinary to plasma osmolarity	>1.5	<1.1

sumption that the ability of the renal tubule to reabsorb sodium and water remains intact in prerenal failure, in vascular disease of preglomerular origin, and in the early stages of glomerulonephritis, whereas these functions are impaired in tubulointerstitial disease, later in the course of glomerulonephritis, and in acute tubular necrosis. Interpretation of urinary indexes requires caution. Blood and urine specimens for these determinations should be collected before the use of fluid replacement or the administration of dopamine, mannitol, or other diuretic agents. The urine must not contain glucose or radiographic contrast material. Acute renal failure is usually considered to be due to acute tubular necrosis, but occasionally, patients have a fractional excretion of sodium of less than 1 percent. This is more common in patients with pigment nephropathy (myoglobinuria) or injury from radiographic contrast agents. Acute renal failure due to myoglobinuria should be considered in patients with trauma who

present with heme-positive urine, an elevated plasma concentration of creatine kinase, and dark urine containing dark-brown granular casts. Persistently abnormal nephrographic findings one or two days after a study with radiographic contrast agents suggest the possibility of acute renal failure induced by the agents.

PREVENTION OF INTRINSIC ACUTE RENAL FAILURE

Risk factors for intrinsic renal failure include preexisting renal disease and disorders that cause prerenal oliguria (Table 1). Prophylaxis should be considered for patients with such risk factors. Appropriate hydration and optimal preservation of intravascular volume are essential to maintain adequate renal perfusion. It is also important to maintain adequate cardiac output and prevent peripheral vasoconstriction. Hypotension should be prevented to ensure that organ ischemia and loss of renal autoregulation do not

develop. In critically ill patients, hemodynamic monitoring is required to prevent volume depletion and marked peripheral vasoconstriction. Measurements of central venous pressure, pulmonary-capillary wedge pressure, cardiac index, systemic vascular resistance, oxygen delivery, and oxygen consumption may be needed for an adequate appraisal of hemodynamics in critically ill patients.¹³

Potentially nephrotoxic substances should be avoided in patients with prerenal oliguria; these include nonsteroidal antiinflammatory drugs, aminoglycosides, radiographic contrast agents, general anesthetics, angiotensin-converting-enzyme inhibitors, amphotericin B, and many chemotherapeutic drugs. Diuretic therapy may be detrimental in patients with prerenal oliguria. If contrast agents need to be used for diagnostic reasons, saline administration may decrease their toxicity.¹⁴ Exposure to radiographic contrast agents causes vasoconstriction of the renal circulation and may precipitate acute renal failure. An increase in endothelin concentrations may account in part for the renal vasoconstriction.¹⁵ Pigment nephropathy (hemoglobinuria or myoglobinuria) can be ameliorated by maintaining a high urinary flow with the use of mannitol and volume replacement, coupled with alkalinization of the urine.

COMPLICATIONS OF ACUTE OLIGURIA

Cardiovascular, gastrointestinal, and neurologic complications may develop in the course of acute oliguria. In addition, infections occur frequently.¹⁶ Cardiovascular complications include congestive heart failure, pulmonary edema, and hypertension, mainly as a result of salt and water retention. Some degree of hypertension occurs in about 25 percent of patients with acute renal failure. However, because the oliguria is often a manifestation of other systemic illnesses, hypotension is also frequently encountered. Arrhythmias occur in 10 to 30 percent of patients. Pericarditis appears to be less frequent now than in the past.

Infections develop in 30 to 70 percent of patients with acute renal failure and are a leading cause of morbidity and mortality.¹⁶ Primary sites of infection include the respiratory and urinary tracts and sites where breaks in the normal anatomical barriers have occurred (e.g., because of indwelling catheters and intravenous needles). Impaired defenses and responses against infection due to uremia and inappropriate use of antibiotics may contribute to the high degree of infectious complications. Neurologic changes include confusion, asterixis, somnolence, and seizures. These changes may be ameliorated by dialysis.

Gastrointestinal complications include anorexia, nausea, vomiting, and ileus. Some of these complications are ameliorated by dialytic therapy. Gastrointestinal bleeding occurs in 10 to 30 percent of pa-

tients with acute renal failure. The pathogenesis of this complication is not well understood. Acute renal failure is also accompanied by anemia, with hematocrit values between 20 and 30 percent. The anemia is the result of decreased erythropoiesis and some degree of hemolysis. Gastrointestinal blood losses and frequent collection of blood samples may contribute to anemia in patients with acute renal failure.

The detection of clinical complications in patients with acute oliguria requires serial, systematic physical examinations. The development of congestive heart failure, edema, or hypertension suggests volume expansion and should be treated. Antacid therapy (nonmagnesium compounds) may decrease the incidence of gastritis. Administration of selective histamine H₂-receptor antagonists (ranitidine or cimetidine) may prevent gastrointestinal hemorrhage. However, the dose of cimetidine must be decreased to 300 mg orally twice a day. Reduced metabolism of benzodiazepines, propranolol, theophylline, and warfarin in patients receiving cimetidine may result in drug toxicity. Prevention of infection requires frequent monitoring of temperature, minimal use of instrumentation or devices that interrupt normal anatomical barriers (e.g., intravenous needles and indwelling bladder catheters), early ambulation, use of aseptic techniques, and fastidious skin and mouth care. Suspected infection should be evaluated promptly and treated without delay. Drugs excreted or metabolized by the kidneys should be avoided. These drugs include doxorubicin, allopurinol, aminoglycosides, azathioprine, cephalosporins, clofibrate, digoxin, diazepam, meperidine, procainamide, propoxyphene, propranolol, and sulfonamides. If such drugs are required, the dose should be adjusted in proportion to the decrease in renal function.

MANAGEMENT OF OLIGURIA

Acute oliguric renal failure, especially that acquired in the hospital, is associated with high morbidity and mortality rates.³ In addition, the costs of caring for patients with acute oliguria are very high.¹⁷ A variety of therapies have shown promise in animal models of acute renal injury.³ However, the results of clinical trials have been less encouraging. Several reviews have addressed this topic.^{3,18,19} In a clinical trial, 504 patients with acute renal failure were randomly assigned to receive anaritide (a synthetic form of atrial natriuretic peptide) or placebo.²⁰ Twenty-four percent of the patients had oliguria at the time of enrollment. The primary end point of the study was dialysis-free survival for 21 days after treatment. Anaritide had no apparent benefit in the patients without oliguria. Among the patients with oliguria, dialysis-free survival was 27 percent in the group receiving anaritide, as compared with 8 percent in the group receiving placebo

($P=0.008$). These results led to a follow-up study designed to enroll 250 patients with oliguric acute tubular necrosis. But this trial was discontinued after 210 patients had been randomly assigned to treatment, because it failed to demonstrate any benefit from the administration of anaritide.

Conversion from oliguria to a nonoliguric state has been considered beneficial.²⁰ This has been the rationale for using diuretics or dopamine, a selective renal vasodilator that causes natriuresis, in patients with acute oliguria.^{21,22} The potential benefits of conversion to a nonoliguric state include less stringent restrictions on salt and water intake, a decreased requirement for dialysis, and perhaps an improved prognosis.²¹

Although there is considerable controversy about the benefits of conversion to a nonoliguric state, some recommendations can be made. First, it is important to identify patients at risk for iatrogenic renal failure.²³ Second, patients should be rapidly evaluated to rule out prerenal or postrenal causes of oliguria, and nephrotoxic drugs should be discontinued when possible. Third, a fluid challenge may be appropriate in patients with oliguria who do not have a volume overload. The amount of fluid administered must be determined on an individual basis. Although the use of diuretics is controversial, if there is an inadequate response to the fluid challenge, the administration of a loop diuretic should be considered. Since the window of opportunity may be narrow, we suggest an initial intravenous infusion of 100 to 200 mg of furosemide. Some authors have recommended the use of a furosemide drip in a dose of 10 to 40 mg per hour.²¹ If urinary output fails to increase within one to two hours, the dose may be doubled, and a thiazide diuretic added. However, large doses of intravenous furosemide for prolonged periods may cause hearing loss. The therapy should be discontinued if there is no response. If there is a response, serial measurements and monitoring of volume status, hemodynamics, and electrolytes are crucial.

The benefit of dopamine therapy (1 to 3 μg per kilogram of body weight per minute) in patients with acute renal injury is controversial.²² In selected cases in which dopamine is used, a diuretic response may be evident within the first six hours of therapy. If urinary output does not increase within this time, the therapy should be discontinued.²⁴

Dialysis

Once the presence of intrinsic renal failure has been established, therapeutic interventions are confined to supportive care and the institution of dialysis in an effort to normalize extracellular volume and electrolyte concentrations and to control hyperkalemia and metabolic acidosis. The appropriate frequency and duration of dialysis for acute renal fail-

ure have not been determined. Guidelines and standards need to be developed for the use of dialysis in patients with acute renal failure.²⁵

It has been suggested that hypotension occurring during treatment with intermittent dialysis may perpetuate the renal injury and prolong the "repair" of tubular cells, which in turn may increase the risk of morbidity and mortality. It has been proposed that continuous renal-replacement therapy offers the benefit of slow and controlled ultrafiltration with a marked decrease in the frequency and duration of hypotensive episodes.²⁶ Continuous renal-replacement therapy should be used in patients whose condition is unstable and who are prone to hypotensive events.²⁷ The selection of dialysis membranes may also be important in patients with acute renal failure. Cellulose membranes may activate complement and lead to the mobilization of leukocytes, with untoward effects on the patient. Recent reports suggest that the use of biocompatible membranes in patients with acute renal failure is associated with better outcomes, including a decreased incidence of infection, than cellulose membranes.^{28,29} In a multicenter study of 153 patients with acute renal failure undergoing dialysis with biocompatible or bioincompatible membranes, dialysis with biocompatible membranes resulted in significantly better survival (57 percent, vs. 46 percent) and recovery of renal function (64 percent, vs. 43 percent).²⁹

Protein and Energy Intake

Besides the maintenance of a fluid and electrolyte balance, adequate protein and caloric intake is essential in patients with acute oliguria. Protein catabolism can be substantial (200 to 250 g per day) in patients with acute renal failure,³⁰⁻³² particularly those with shock, sepsis, or rhabdomyolysis. Increased protein degradation may accelerate the rate of increase in the concentrations of potassium, hydrogen ion, and phosphorus in patients with oliguria. A negative nitrogen balance may lead to malnutrition, with impaired immune function and an increased risk of morbidity and mortality. Aggressive nutritional therapy should be instituted early in patients with acute renal failure. In many instances, total parenteral nutrition is required. Increased caloric intake should be provided, with the use of a combined carbohydrate and fat regimen.

FUTURE DIRECTIONS

Considerable advances in our understanding of the molecular, cellular, and pathophysiologic mechanisms underlying oliguria and acute renal failure have been made since the classic description of crush injuries and consequent impaired renal function during World War II.³³ As a result, a number of new agents for the treatment of acute renal failure are now being examined or will be in the near future.

These agents target various abnormalities in the pathogenesis of acute oliguria. For example, atrial natriuretic factor, adenosine-receptor antagonists, and phosphodiesterase inhibitors target inappropriate vasoreactivity. Lazaroids and antioxidants decrease the generation or action of free radicals. Arginine-glycine-aspartic acid peptides ameliorate tubular obstruction due to the presence of casts of necrotic or viable cells in the lumen of the nephron by interfering with cell-cell adhesion mechanisms.^{34,35} Insulin-like growth factor I, epidermal growth factor, and hepatocyte growth factor facilitate the regeneration of tubular cells. Intercellular adhesion molecule 1 helps improve the immunologic response to injury. Several of these experimental drugs are currently being tested in clinical trials, and some promising results have been reported. Insulin-like growth factor I has recently been shown to preserve renal function postoperatively in patients undergoing major vascular surgical procedures requiring the interruption of blood flow to the kidneys,³⁶ and initial studies of intercellular adhesion molecule 1 in renal-allograft recipients have been completed.³⁷ These agents and others now being developed may prevent or improve adverse outcomes in patients with acute renal failure.

REFERENCES

- Levinsky NG, Bernard DB. Mannitol and loop diuretics in acute renal failure. In: Brenner BM, Lazarus JM, ed. *Acute renal failure*. 2nd ed. New York: Churchill Livingstone, 1988:841-56.
- Harrington JT, Cohen JJ. Acute oliguria. *N Engl J Med* 1975;292:89-91.
- Thadhani R, Pascual M, Bonventre JV. Acute renal failure. *N Engl J Med* 1996;334:1448-60.
- Feest TG, Round A, Hamad S. Incidence of severe acute renal failure in adults: results of a community based study. *BMJ* 1993;306:481-3.
- Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrington JT. Hospital-acquired renal insufficiency: a prospective study. *Am J Med* 1983;74:243-8.
- Elasz TA, Anderson RJ. Changing demography of acute renal failure. *Semin Dial* 1996;9:438-43.
- Wardle EN. Acute renal failure and multiorgan failure. *Nephron* 1994;66:380-5.
- Cumming AD. Sepsis and acute renal failure. *Ren Fail* 1994;16:169-78.
- Edelstein CL, Ling H, Schrier RW. The nature of renal cell injury. *Kidney Int* 1997;51:1341-51.
- Klahr S. Urinary tract obstruction. In: Schrier RW, Gottschalk CW, eds. *Diseases of the kidney*. 6th ed. Boston: Little, Brown, 1997:709-38.
- Anderson RJ, Schrier RW. Acute renal failure. In: Schrier RW, Gottschalk CW, eds. *Diseases of the kidney*. 6th ed. Boston: Little, Brown, 1997:1069-113.
- Paller MS. Pathophysiology of acute renal failure. In: Greenberg A, ed. *Primer on kidney diseases*. San Diego, Calif.: Academic Press, 1994:126-33.
- Miller SB. Renal diseases. In: Ewald GA, McKenzie CR, eds. *Manual of medical therapeutics*. 28th ed. Boston: Little, Brown, 1995:262-78.
- Solomon R, Werner C, Mann D, D'Elia J, Silva P. Effects of saline, mannitol, and furosemide on acute decreases in renal function induced by radiocontrast agents. *N Engl J Med* 1994;331:1416-20.
- Clark BA, Kim D, Epstein FH. Endothelin and atrial natriuretic peptide levels following radiocontrast exposure in humans. *Am J Kidney Dis* 1997;30:82-6.
- Finn WF. Recovery from acute renal failure. In: Lazarus JM, Brenner BM, eds. *Acute renal failure*. 3rd ed. New York: Churchill Livingstone, 1993:553-96.
- Hamel MB, Phillip RS, Davis RB, et al. Outcomes and cost effectiveness of initiating dialysis and continuing aggressive care in seriously ill hospitalized adults. *Ann Intern Med* 1997;127:195-202.
- Conger JD. Interventions in clinical acute renal failure: what are the data? *Am J Kidney Dis* 1995;26:565-76.
- Alkhunaizi AM, Schrier RW. Management of acute renal failure: new perspectives. *Am J Kidney Dis* 1996;28:315-28.
- Allgren RL, Marbury TC, Rahman SN, et al. Anaritide in acute tubular necrosis. *N Engl J Med* 1997;336:828-34.
- Majumdar S, Kjellstrand CM. Why do we use diuretics in acute renal failure? *Semin Dial* 1996;9:454-9.
- Denton MD, Chertow GM, Brady HR. "Renal-dose" dopamine for the treatment of acute renal failure: scientific rationale, experimental studies and clinical trials. *Kidney Int* 1996;50:4-14.
- Davidman M, Olson P, Kohen J, Leither T, Kjellstrand C. Iatrogenic renal disease. *Arch Intern Med* 1991;151:1809-12.
- Flancbaum L, Choban PS, Dasta JF. Quantitative effects of low-dose dopamine on urine output in oliguric surgical intensive care unit patients. *Crit Care Med* 1994;22:61-8.
- DuBose TD Jr, Warnock DG, Mehta RL, et al. Acute renal failure in the 21st century: recommendations for management and outcomes assessment. *Am J Kidney Dis* 1997;29:793-9.
- Mehta RL. Therapeutic alternatives to renal replacement for critically ill patients in acute renal failure. *Semin Nephrol* 1994;14:64-82.
- Yagi N, Paganini EP. Acute dialysis and continuous renal replacement: the emergence of new technology involving the nephrologist in the intensive care setting. *Semin Nephrol* 1997;17:306-20.
- Hakim RM, Wingard RL, Parker RA. Effect of the dialysis membrane in the treatment of patients with acute renal failure. *N Engl J Med* 1994;331:1338-42.
- Himmelfarb J, Tolkoff-Rubin N, Chandran P, Parker RA, Wingard RL, Hakim RM. A multicenter comparison of dialysis membranes in the treatment of acute renal failure requiring dialysis. *J Am Soc Nephrol* 1998;9:257-66.
- Kopple JD. Nutritional management of acute renal failure. In: Kopple JD, Massry SG, eds. *Nutritional management of renal disease*. Baltimore: Williams & Wilkins, 1997:713-53.
- Feinstein EI, Blumenkrantz MJ, Healy M, et al. Clinical and metabolic responses to parenteral nutrition in acute renal failure: a controlled double-blind study. *Medicine (Baltimore)* 1981;60:124-37.
- Feinstein EI, Kopple JD, Silberman H, Massry SG. Total parenteral nutrition with high or low nitrogen intakes in patients with acute renal failure. *Kidney Int Suppl* 1983;16:S319-S323.
- Bywaters EGL, Beall D. Crush injuries with impairment of renal function. *BMJ* 1941;1:427-32.
- Noiri E, Romanov V, Forest T, et al. Pathophysiology of renal tubular obstruction: therapeutic role of synthetic RGD peptides in acute renal failure. *Kidney Int* 1995;48:1375-85.
- Romanov V, Noiri E, Czerwinski F, Finsinger D, Kessler H, Goligorsky MS. Two novel probes reveal tubular and vascular Arg-Gly-Asp (RGD) binding sites in the ischemic rat kidney. *Kidney Int* 1997;52:93-102.
- Franklin SC, Moulton M, Sicard GA, Hammerman MR, Miller SB. Insulin-like growth factor I preserves renal function postoperatively. *Am J Physiol* 1997;272:F257-F259.
- Haug CE, Colvin RB, Delmonico FL, et al. A phase I trial of immunosuppression with anti-ICAM-1 (CD54) mAb in renal allograft recipients. *Transplantation* 1993;55:766-72.