Chapter 72

Anesthesia and the Renal and Genitourinary Systems

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Key Points

• Innervation of the intraabdominal components of the genitourinary system—the kidney and the ureter—is primarily thoracolumbar (T8-L2). The nerve supply of the pelvic organs—the bladder, the prostate, the seminal vesicles, and the urethra—is primarily lumbosacral with some lower thoracic input.

• The spinal level of pain conduction for the external genitourinary organs is S2-4, except for the testes (T10-L1).

• The kidneys receive 15% to 25% of the total cardiac output, with most of this blood directed to the renal cortex. Renal medullary papillae are more vulnerable to ischemic insults. Kidneys successfully autoregulate their blood flow between 60 and 160 mm Hg mean arterial pressures.

• The glomerular filtration rate (GFR) is the best measure of glomerular function. Creatinine clearance is a good measure of the GFR; urine output is not.

• Hypervolemia, acidemia, hyperkalemia, cardiorespiratory dysfunction, anemia, and bleeding disturbances are manifestations of chronic renal failure.

• Although renal transplantation reverses most of the abnormalities in end-stage renal disease, dialysis improves only some, and introduces additional complications of its own.

• Newer techniques, such as laser prostatectomy, are making transurethral resection of the prostate (TURP) syndrome a rare event. TURP syndrome is a constellation of symptoms caused by the absorption of hypotonic bladder irrigants. Cardiovascular and neurologic changes are due to hypoosmolality, hyponatremia, hyperglycinemia, hyperammonemia, and hypervolemia.

• Regional anesthesia offers several advantages over general anesthesia for standard, but not laser, TURP. Yet, 30-day mortality rates remain unchanged at 0.2% to 0.8%.

• Laparoscopic surgery in urology frequently requires insufflation of carbon dioxide into the retroperitoneal space. In lengthy procedures, pneumomediastinum and subcutaneous emphysema of the head and neck may occur.

• Extracorporeal shock wave lithotripsy (ESWL) causes significant physiologic changes related to immersion if a water bath is used. Shock waves can cause arrhythmias and injury to the lungs. Pregnancy and untreated bleeding disorders are contraindications to ESWL.

• Regarding renal tumors, 5% to 10% extend into the renal vein, inferior vena cava, and right atrium. Complications ranging from circulatory failure to embolization of tumor during surgery may occur. Cardiopulmonary bypass may be necessary for surgery.

• Radical prostatectomy causes significant blood loss sometimes including intraoperative venous air emboli. Regional anesthesia with spontaneous ventilation is associated with less blood loss than general anesthesia and intermittent positive-pressure ventilation. Other advantages of epidural anesthesia include a decreased incidence of deep vein thrombosis and preemptive analgesia. Whether outcomes are dependent on the choice of anesthesia is not clear.

• Robotic radical prostatectomy is associated with reduced blood loss and postoperative pain compared with open radical prostatectomy. Anesthetic concerns are related to steep head-down tilt (also see Chapter 41) and pneumoperitoneum and include hypercarbia, hypoxemia, increased intraocular and intracranial pressures, decreased perfusion pressure to lower extremities, and positional injuries.
Patients requiring anesthesia for renal and genitourinary surgery are frequently at the extremes of age. In addition to the physiologic changes of aging in older patients (see also Chapter 80), concomitant cardiovascular and respiratory comorbidity is common. A medical history, physical examination, and appropriate laboratory tests are necessary to evaluate concomitant disease. In pediatric urologic patients, a careful history should exclude other nonurologic congenital lesions (see Chapter 93).

Urologic procedures are performed mostly on the kidneys, adrenals, ureters, urinary bladder, prostate, urethra, penis, scrotum, testis, and spermatic cord. Because their sensory nerve supply is primarily thoracolumbar and sacral outflow (Table 72-1), these structures are well adapted for regional anesthesia.

**INNERVATION OF THE GENITOURINARY SYSTEM**

The parts of the genitourinary system that are in the abdomen receive their nerve supply from the autonomic nervous system by means of sympathetic and parasympathetic pathways. The pelvic urinary organs and genitalia are supplied by somatic and autonomic nerves. Table 72-1 summarizes the pain conduction pathways and spinal levels of the genitourinary system.

**KIDNEY AND ABDOMINAL URETER**

Sympathetic nerves to the kidney originate as preganglionic fibers from the eighth thoracic through the first lumbar segments and converge at the celiac plexus and aorticorenal ganglia (Fig. 72-1). Postganglionic fibers to the kidney arise mainly from the celiac and aorticorenal ganglia. Some sympathetic fibers may reach the kidney via the splanchnic nerves. Parasympathetic input is from the vagus nerve.1 Sympathetic fibers to the ureter originate from the tenth thoracic through the second lumbar segments and synapse with postganglionic fibers in the aorticorenal and superior and inferior hypogastric plexuses. Parasympathetic input is from the second through fourth sacral spinal segments.1 Nociceptive fibers travel along the sympathetics to the same spinal segments.

Pain from the kidney and ureter is referred mainly to the somatic distribution of the tenth thoracic through the second lumbar segments—the lower part of the back, flank, ilioinguinal region, and scrotum or labia. Effective neural block of these segments is necessary to provide adequate analgesia or anesthesia.

**BLADDER AND URETHRA**

Sympathetic nerves to the bladder and urethra originate from the eleventh thoracic to the second lumbar segments, travel through the superior hypogastric plexus, and supply the bladder through the right and the left hypogastric nerves.2 Parasympathetic nerves arise from the second through the fourth sacral segments.
and form the pelvic parasympathetic plexus, which is joined by the hypogastric plexus. Vesical branches proceed toward the bladder base, where they provide the nerve supply to the bladder and proximal part of the urethra (Fig. 72-2). Parasympathetic fibers are the main motor supply to the bladder (with the exception of the trigone) and far outnumber sympathetic fibers in the bladder.\(^2\)

The afferents carrying sensations of stretch and fullness of the bladder are parasympathetic, whereas pain, touch, and temperature sensations are carried by sympathetic nerves. Sympathetic fibers are predominantly \(\alpha\) adrenergic in the bladder base and urethra, and \(\beta\) adrenergic in the bladder dome and lateral wall. Knowledge of these aspects of neuroanatomy is important to appreciate the pharmacologic effects on the urologic system of neural ablation or regional block and drugs with adrenergic or cholinergic effects.\(^2\)

**PROSTATE AND PROSTATIC URETHRA**

The prostate and the prostatic urethra receive sympathetic and parasympathetic supply from the prostatic plexus arising from the pelvic parasympathetic plexus, which is joined by the hypogastric plexus. The spinal origin of the nerve supply is primarily lumbosacral (see Fig. 72-2).\(^2\)

**PENIS AND SCROTUM**

The autonomic supply to the penile urethra and the cavernous tissue comes from the prostatic plexus. Somatic fibers from the pudendal nerve (S2-4) supply the external sphincter. The dorsal nerve of the penis, the first branch of the pudendal nerve, is its main sensory supply. The scrotum is innervated anteriorly by the ilioinguinal and genitofemoral nerves (L1 and L2) and posteriorly by perineal branches of the pudendal nerve (S2 and S4).\(^2\)

**TESTES**

The testes descend from their intraabdominal location to the scrotum during fetal development. Because they share their embryologic origin with the kidney, their nerve supply is similar to that of the kidney and upper part of the ureter and extends up to the T10 spinal segment.\(^2\)

**RENALE BLOOD FLOW**

The kidneys receive approximately 15% to 25% of total cardiac output, or 1 to 1.25 L/min of blood through the renal arteries, depending on the state of the body. Most of the blood is received by the renal cortex, with only 5% of cardiac output flowing through the renal medulla, which
makes the renal papillae vulnerable to ischemic insults. Renal blood flow is regulated by various mechanisms that control the activity of vascular smooth muscle and alter vascular resistance. Sympathetic tone of renal vessels increases during exercise to shunt renal blood flow to exercising skeletal muscle; similarly, renal blood vessels relax during the resting condition of the body. Sympathetic stimulation resulting from surgery can increase vascular resistance and reduce renal blood flow, whereas anesthetics may reduce renal blood flow by decreasing cardiac output.

Glomerular capillaries separate afferent arterioles from efferent arterioles. Glomerular capillaries are high-pressure systems, whereas peritubular capillaries are low-pressure systems. Consequently, the glomerular capillaries are a fluid-filtering system, whereas the peritubular capillaries are a fluid-absorbing system. The vasa recta, a specialized portion of peritubular capillaries formed from efferent arterioles, are important in the formation of concentrated urine by a countercurrent mechanism. An intrinsic mechanism that causes vasodilation and vasoconstriction of renal afferent arterioles regulates the autoregulation of renal blood flow. A decrease in mean arterial pressure also decreases renal blood flow and eventually affects the glomerular filtration rate (GFR) when the pressure decreases to less than 60 mm Hg. A persistently low mean arterial pressure greater than 60 mm Hg affects renal blood flow, but does not affect the GFR because of the intrinsic mechanism of autoregulation (Fig. 72-3). Autoregulation maintains mean arterial pressure between 60 mm Hg and 160 mm Hg in intact and denervated kidneys.3

Although knowledge of neuroanatomy and renal blood flow is essential to provide adequate anesthesia, a thorough understanding of renal physiology and pharmacology is equally important. Genitourinary surgical patients frequently have mechanical or functional renal disease. Anesthetics and surgery can significantly alter renal function. Conversely, renal dysfunction significantly affects the pharmacokinetics and pharmacodynamics of anesthetics and adjuvant drugs. Evaluation of a patient with renal disease is discussed later.

### EVALUATION OF RENAL FUNCTION

Renal disease can be discovered incidentally during a routine medical evaluation, or patients may exhibit evidence of renal dysfunction, such as hypertension, edema, nausea, and hematuria (see Chapter 23). The initial approach in both situations should be to assess the cause and severity of renal abnormalities. In all cases, this evaluation includes (1) an estimation of disease duration, (2) a careful urinalysis, and (3) an assessment of the GFR. The history and physical examination, although equally important, are variable among renal syndromes; specific symptoms and signs are discussed in sections on each disease entity. Further diagnostic categorization is based on anatomic distribution: prerenal disease, postrenal disease, and intrinsic renal disease. Intrinsic renal disease can be divided further into glomerular, tubular, interstitial, and vascular abnormalities. Laboratory tests useful in evaluating renal function are described next (Table 72-2).

### TABLE 72-2 COMMONLY ORDERED RENAL FUNCTION TESTS

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Reference Range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea nitrogen</td>
<td>5-25 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.5-1.5 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>133-147 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td>3.2-5.2 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Chloride</td>
<td>94-110 mmol/L</td>
<td></td>
</tr>
<tr>
<td>CO₂</td>
<td>22-32 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td>2.5-7.5 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>8.5-10.5 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Phosphorus</td>
<td>2.2-4.2 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Urinalysis, routine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Color</td>
<td>Straw-amber</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Appearance</td>
<td>Clear-hazy</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Protein</td>
<td>0</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Blood</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>0</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Ketones</td>
<td>0</td>
<td>mg/dL</td>
</tr>
<tr>
<td>pH</td>
<td>4.5-8.0</td>
<td></td>
</tr>
<tr>
<td>Specific gravity</td>
<td>1.002-1.030</td>
<td></td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Urinalysis, microscopic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red blood cells</td>
<td>0-3 per high-power field</td>
<td></td>
</tr>
<tr>
<td>White blood cells</td>
<td>0-5 per high-power field</td>
<td></td>
</tr>
<tr>
<td>Casts</td>
<td>0-2 per low-power field</td>
<td></td>
</tr>
</tbody>
</table>

GLOMERULAR FUNCTION

Glomerular Filtration Rate

The GFR is the best measure of glomerular function. Normal GFR is approximately 125 mL/min. Manifestations of reduced GFR are not seen, however, until the GFR has decreased to 50% of normal. When GFR decreases to 30% of normal, a stage of moderate renal insufficiency sets in. Patients remain asymptomatic with only biochemical evidence of a decline in GFR (i.e., an increase in serum concentrations of urea and creatinine). Further workup usually reveals other abnormalities, such as nocturia, anemia, loss of energy, decreasing appetite, and abnormalities in calcium and phosphorus metabolism.

As the GFR decreases further, a stage of severe renal insufficiency begins. This stage is characterized by profound clinical manifestations of uremia and biochemical abnormalities, such as acidemia; volume overload; and neurologic, cardiac, and respiratory manifestations. At the stages of mild and moderate renal insufficiency, intercurrent clinical stress may compromise renal function further and induce signs and symptoms of overt uremia. When the GFR is 5% to 10% of normal, it is called end-stage renal disease (ESRD), and continued survival without renal replacement therapy becomes impossible. Although most clinical abnormalities of corticotropin-releasing factor are reversed by renal transplantation, the response to dialysis is highly variable (Table 72-3).

Blood Urea Nitrogen

The blood urea nitrogen (BUN) concentration is not a direct correlate of reduced GFR. BUN is influenced by nonrenal variables, such as exercise, bleeding, steroids, and massive tissue breakdown. The more important factor is that BUN is not elevated in kidney disease until the GFR is reduced to almost 75% of normal.4

Creatinine and Creatinine Clearance

Measurements of creatinine provide valuable information regarding general kidney function. Creatinine in serum results from turnover of muscle tissue and depends on daily dietary intake of protein. Normal values are 0.5 to 1.5 mg/100 mL; values of 0.5 to 1 mg/100 mL are present during pregnancy. Creatinine is freely filtered at the glomerulus, and apart from an almost negligible increase in content because of secretion in the distal nephron, it is neither reabsorbed nor secreted. Serum creatinine measurements reflect glomerular function (Fig. 72-4),4 and creatinine clearance is a specific measure of GFR. Creatinine clearance can be calculated by the following formula derived by Cockcroft-Gault that accounts for age-related decreases in GFR, body weight, and sex:

Creatinine clearance (mL/min) = [(140 – Age) × Lean body weight (kg)]/[Plasma creatinine (mg/dL) × 72]

This value should be multiplied by 0.85 for women because a lower fraction of body weight is composed of muscle.

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| TABLE 72-3 CLINICAL ABNORMALITIES IN CHRONIC RENAL FAILURE AND THEIR RESPONSE TO DIALYSIS AND ERYTHROPOIETIN TREATMENT |
|---|---|---|---|---|
| Improved by Dialysis | Improved by Adding Erythropoietin | Variable Response | Not Improved | Develop after Dialysis Therapy |
| Volume expansion and contraction | Fatigue | Secondary hyperparathyroidism | Increased lipoprotein level | Adynamic osteomalacia |
| Hypernatremia and hyponatremia | Impaired mentation | Hyperuricemia | Decreased high-density lipoprotein level | β2-Microglobulinemia |
| Hyperkalemia and hypokalemia | Lethargy | Hypertriglyceridemia | Impaired growth and development | Muscle cramps |
| Metabolic acidosis | Pallor | Protein-calorie malnutrition | Infertility and sexual dysfunction | Dialysis dysequilibrium syndrome |
| Hyperphosphatemia | Anemia | Headache | Amenorrhea | Hypertension and arrhythmias |
| Hypocalcemia | Bleeding diathesis | Peripheral neuropathy | Sleep disorders | Hepatitis |
| Vitamin D-deficient osteomalacia | | Restless legs syndrome | Pruritus | Idiopathic ascites |
| Carbohydrate intolerance | | Paralysis | Lymphocytopenia | Peritonitis |
| Hypothesis | | Seizures | Splenomegaly and hypersplenism | Leukopenia |
| Asterixis | | Myopathy | | Hypocomplementemia |
Because there is such a wide range in normal values, a 50% increase in serum creatinine concentration, indicative of a 50% reduction in GFR, may go undetected unless baseline values are known. Also, excretion of drugs dependent on glomerular filtration may be significantly decreased despite what might seem to be only slightly elevated serum creatinine values (1.5 to 2.5 mg/100 mL). The serum creatinine concentration and clearance are better indicators of general kidney function and GFR than are similar measurements of urea nitrogen (Box 72-1). There are disease states, however, in which even the serum creatinine can be affected independent of the GFR (Table 72-4).

TUBULAR FUNCTION

Concentration

Urinary specific gravity is an index of the kidney’s concentrating ability, specifically, renal tubular function. Determination of urinary osmolality (i.e., measurement of the number of moles of solute [osmoles] per kilogram of solvent) is a similar, more specific test. Excretion of concentrated urine (specific gravity, 1.030; 1050 mOsm/kg) is indicative of excellent tubular function, whereas a urinary osmolality fixed at that of plasma (specific gravity 1.010; 290 mOsm/kg) indicates renal disease. The urinary dilution mechanism persists after concentrating defects are present, so a urinary osmolality of 50 to 100 mOsm/kg still may be consistent with advanced renal disease.

Protein

Patients without renal disease can excrete 150 mg of protein per day; greater amounts may be present after strenuous exercise or after standing for several hours. Massive proteinuria (i.e., >750 mg/day) is always abnormal and usually indicates severe glomerular damage.

Glucose

Glucose is freely filtered at the glomerulus and is subsequently reabsorbed in the proximal tubule. Glycosuria signifies that the ability of the renal tubules to reabsorb glucose has been exceeded by an abnormally heavy glucose load and is usually indicative of diabetes mellitus. Glycosuria also may be present in hospitalized patients without diabetes who are receiving intravenous glucose infusions.

ADDITIONAL DIAGNOSTIC TESTS

Urinalysis and Appearance

Gross and microscopic observation of urine and its sediment, along with determination of urinary pH, specific gravity, protein content, and glucose content, is one of the most readily available, inexpensive, and informative laboratory tests. The gross appearance of urine may indicate the presence of bleeding or infection in the genitourinary tract. Microscopic examination of urinary
sediment may reveal casts, bacteria, and various cell forms, supplying diagnostic information in patients with renal disease.

**Serum and Urine Electrolytes**

**pH AND BLOOD GASES.** Sodium, potassium, chloride, and bicarbonate concentrations should be determined if impairment in renal function is suspected. The results of these tests usually remain normal until frank renal failure is present, however, and hyperkalemia does not occur until patients are uremic. Measuring urinary sodium or chloride excretion is especially useful when attempting to differentiate between causes of hyponatremia, as seen in volume contraction (whether a decrease in total circulatory volume or a decrease in effective arterial blood volume), versus conditions associated with increased salt loss, such as the syndrome of inappropriate secretion of antidiuretic hormone, salt-losing nephropathy, or adrenal insufficiency. If significant renal disease is present, patients consuming a diet high in animal protein may have metabolic acidosis.

**Electrocardiogram.** The electrocardiogram (see Chapter 47) reflects the toxic effects of potassium excess more closely than determination of the serum potassium concentration.

**Imaging Studies**

**Computed Tomography Scan of Kidneys.** A stone protocol computed tomography (CT) scan of the kidneys, ureter, and bladder has become the study of choice for the detection of kidney stones because of its ability to detect stones of all kinds, including uric acid stones and nonobstructing stones in the ureter. Masses in the kidney can be evaluated using either contrast-enhanced CT or renal ultrasound.

**Computed Tomography Angiography.** Computed tomography angiography is used for the evaluation of renal artery stenosis and is emerging rapidly as a useful study. Although it is comparable to magnetic resonance angiography as a noninvasive tool, it requires the use of iodinated contrast material, which may cause renal dysfunction in patients with chronic kidney disease.

**Magnetic Resonance Imaging with Magnetic Resonance Angiography.** The use of magnetic resonance imaging (MRI) with magnetic resonance angiography has revolutionized the evaluation of renovascular disease. The test is highly sensitive, but tends to overestimate the degree of stenosis. Its accuracy in detecting fibromuscular dysplasia causing renal artery stenosis has not been well validated. MRI also can be used to evaluate renal masses. The main advantages of MRI are that it is a noninvasive test and does not require iodinated contrast material.

**IMPORTANT PATHOPHYSIOLOGIC MANIFESTATIONS OF CHRONIC RENAL FAILURE** (See also Chapter 23)

**Hypervolemia.**

Total-body contents of Na⁺ and H₂O are increased in chronic renal failure (CRF), although this increase might not be clinically apparent until the GFR is reduced to very low levels. Weight gain is usually associated with volume expansion and is offset by the concomitant loss of lean body mass. The combination of loop diuretics with metolazone, which acts by inhibiting the Na-CI cotransporter of the distal convoluted tubule, can overcome diuretic resistance.

**Acidemia.**

Although urine can be acidified normally in most patients with CRF, these patients have a reduced ability to produce ammonia. In the early stages, the accompanying organic anions are excreted in urine, and the metabolic acidosis is of the non-anion gap variety. With advanced renal failure, a fairly large “anion gap” can develop (to approximately 20 mmol/L), however, with a reciprocal decrease in plasma HCO₃⁻ concentration. This acidemia is usually corrected by hemodialysis. Although acidemia is well compensated in moderate CRF, patients can become acidic and hyperkalemic in the postoperative period (Table 72-5).

**Hyperkalemia.**

The approximate daily filtered load of K⁺ is 700 mmol. Most of this filtered load is reabsorbed in tubule segments, and most of the K⁺ excreted in the final urine reflects events governing K⁺ handling at the level of the cortical collecting tubule and beyond. K⁺ excretion in the gastrointestinal tract is augmented in patients with CRF. Hyperkalemia may be precipitated, however, in numerous clinical situations, including protein catabolism, hemolysis, hemorrhage, transfusion of stored red blood cells (see Chapter 61), metabolic acidosis, and exposure to various medications that inhibit K⁺ entry into cells or K⁺ secretion in the distal nephron.

**Cardiac and Pulmonary Manifestations.**

Hypertension is a common complication of CRF and ESRD (see Chapter 39). Because hypervolemia is the major cause of hypertension in uremia, normotension

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**TABLE 72-5 METABOLIC ACIDOSIS IN CHRONIC RENAL FAILURE**

<table>
<thead>
<tr>
<th></th>
<th>Paco₂ (mm Hg)</th>
<th>pH</th>
<th>HCO₃⁻ (mEq/L)</th>
<th>K⁺ (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>32</td>
<td>7.32</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>Intraoperative</td>
<td>40</td>
<td>7.25</td>
<td>18</td>
<td>5.3</td>
</tr>
<tr>
<td>Postoperative</td>
<td>44</td>
<td>7.21</td>
<td>19</td>
<td>5.6</td>
</tr>
<tr>
<td>48</td>
<td>7.18</td>
<td>19</td>
<td>5.9</td>
<td></td>
</tr>
</tbody>
</table>

The patient is a 36-year-old man with severe diabetic nephropathy and end-stage renal failure undergoing cadaver renal transplantation. Preoperatively, the patient has a chronic metabolic acidosis (HCO₃⁻, 17 mEq/L) with partial respiratory compensation (PaCO₂, 32 mm Hg; pH 7.32). Potassium is high normal at 5 mEq/L. Intraoperatively, he is given “standard” mechanical minute ventilation, and with “normal” PaCO₂ (40 mm Hg), the metabolic acidosis is unmasked (pH 7.25), and potassium increases to 5.3 mEq/L. His trachea is extubated at the end of the procedure, but graft function is sluggish, and the metabolic acidosis remains unchanged. With residual opioid-induced narcosis, moderate CO₂ retention occurs (Paco₂, 44 mm Hg and 48 mm Hg), pH decreases further to 7.18, and a dangerous degree of hyperkalemia develops (K⁺, 5.9 mEq/L).
is usually restored by the use of diuretics in predialysis patients or by dialysis in ESRD patients. Despite therapy, patients continue to be hypertensive because of the vaso-dilators required for the management of overwhelming hyperreninemia. Patients generally have left ventricular hypertrophy and accelerated atherosclerosis (disordered glucose and fat metabolism). Pericarditis can be observed in patients with inadequate dialysis versus patients with CRF who undergo regular dialysis.

A unique form of pulmonary congestion and edema can occur even in the absence of excessive intravascular volume and is associated with normal or mildly increased intracardiac and pulmonary capillary wedge pressure. This entity, characterized radiologically by peripheral vascular congestion giving rise to a “butterfly wing” distribution, is due to increased permeability of alveolar capillary membranes. This “low-pressure” pulmonary edema and the cardiopulmonary abnormalities associated with excessive intravascular volume usually respond promptly to vigorous dialysis.9

Hematologic Manifestations

Chronic renal failure usually causes a normochromic, normocytic anemia. Anemia is generally observed when the GFR decreases to less than 30 mL/min and is due to insufficient production of erythropoietin by the diseased kidneys. Other factors are iron deficiency, either related to or independent of blood loss from repeated laboratory testing, blood retention in the dialyzer, or gastrointestinal bleeding.10 Treatment of anemia with iron, darbepoetin alfa, and human recombinant erythropoietin (Table 72-6) restores a normal hematocrit and avoids repetitive red blood cell transfusions, reduces the requirement for hospitalization, and decreases cardiovascular mortality by about 30%.11

Prolongation of the bleeding time because of decreased activity of platelet factor 3, abnormal platelet aggregation and adhesiveness, and impaired prothrombin consumption contributes to the clotting defects. The abnormality in platelet factor 3 correlates can be corrected with dialysis, although prolongation of the bleeding time can be observed in well-dialyzed patients. Abnormal bleeding times and coagulopathy in patients with renal failure may be managed with desmopressin, cryoprecipitate, conjugated estrogens, blood transfusions, and erythropoietin use.10

EFFECTS OF DRUGS IN PATIENTS WITH REDUCED RENAL FUNCTION

Most anesthetic drugs are weak electrolytes and are lipid soluble in the un-ionized state; they are extensively reabsorbed by renal tubular cells (see Chapters 26 and 30). Termination of their action does not depend on renal excretion; redistribution and metabolism produce this effect. After biotransformation, these drugs are excreted in urine as water-soluble, polar forms of the parent compound. They are usually pharmacologically inactive, and their retention is harmless.10 Most drugs with prominent central and peripheral nervous system activity in this category include most narcotics, barbiturates, phentothiazines, butyrophenone derivatives, benzodiazepines, ketamine, and local anesthetics.12 Several drugs are lipid insoluble or are highly ionized in the physiologic pH range, however, and are eliminated unchanged in urine. Their duration of action may be extended in patients with impaired renal function. Drugs in this category include muscle relaxants, cholinesterase inhibitors, thiazide diuretics, digoxin, and many antibiotics (Table 72-7).13

Opioids

Renal failure has implications of major clinical importance with respect to morphine and meperidine (see Chapter 31). For the fentanyl congeners, the clinical importance of renal failure is less marked.14 Morphine is an opioid with active metabolites that depend on renal clearance mechanisms for elimination. Morphine is principally metabolized by conjugation in the liver, and the water-soluble glucuronides (morphine-3-glucuronide and morphine-6-glucuronide) are excreted via the kidney. The kidney also plays a role in the conjugation of morphine, accounting for nearly 40% of its metabolism.15 Patients with renal failure can develop high levels of morphine-6-glucuronide and life-threatening respiratory depression.14 In view of these changes induced by renal failure, morphine might not be a good choice in patients with severely altered renal clearance mechanisms.

The clinical pharmacology of meperidine also is significantly altered by renal failure. Normeperidine, the chief metabolite, has analgesic and central nervous system (CNS) excitatory effects.16 Because the active metabolites

| TABLE 72-6 MANAGEMENT GUIDELINES FOR CORRECTION OF ANEMIA OF CHRONIC RENAL DISEASE |
|---------------------------------|---------------------------------|
| **Erythropoietin**               | **Starting dosage**             |
|                                 | 50-150 U/kg/wk IV or SC (once, |
|                                 | twice, or three times per week) |
| **Target hemoglobin**            | 11-12 g/dL                      |
| **Optimal rate of correction**   | Increase hemoglobin by 1-2 g/dL  |
|                                 | over 4 wk                       |
| **Darbepoetin alfa**             | **Starting dosage**             |
|                                 | 0.45 mg/kg administered as single |
|                                 | IV or SC injection once weekly |
| **Target hemoglobin**            | 12 g/dL                         |
| **Optimal rate of correction**   | Increase hemoglobin by 1-2 g/dL  |
|                                 | over 4-wk period                |
| **Iron**                        | Monitor iron stores by TSat and serum ferritin |
|                                 | If patient is iron-deficient (TSat <20%; serum ferritin <100 g/L), administer iron, 50-100 mg IV twice per week for 5 wk; if iron indices are still low, repeat the same course |
|                                 | If iron indices are normal but hemoglobin is still inadequate, administer IV iron as outlined above; monitor hemoglobin, TSat, and ferritin. |
|                                 | Withhold iron therapy when TSat >50% or ferritin >800 ng/mL (>800 g/L) |

IV, Intravenous; SC, subcutaneous; TSat, percent transferrin saturation.
are subject to renal excretion, this potential CNS toxicity secondary to normeperidine accumulation is especially a concern in patients in renal failure.

The clinical pharmacology of the fentanyl congeners is not grossly altered by renal failure, although a decrease in plasma protein binding potentially can alter the free fraction of the fentanyl class of opioids. Fentanyl clearance is not altered by renal failure. As with fentanyl, sufentanil pharmacokinetics are not altered in any consistent fashion by renal disease, although greater variability exists in the clearance and elimination half-life of sufentanil when patients have impaired renal function. An increased clinical effect is likely with alfentanil in renal failure because of a decreased initial volume of distribution and an increased free fraction of alfentanil. No delay in recovery after alfentanil administration should be expected, however. Neither the pharmacokinetics nor the pharmacodynamics of remifentanil are altered by impaired renal function.

Hydromorphone, as the parent drug, does not substantially accumulate in hemodialysis patients. Conversely, an active metabolite, hydromorphone-3-glucuronide, quickly accumulates between dialysis treatments, but seems to be effectively removed during hemodialysis. With careful monitoring, hydromorphone can be used safely in patients who require dialysis. It should be used with caution, however, in patients with a GFR less than 30 mL/min and who have yet to start dialysis or who have withdrawn from dialysis.

### Inhaled Anesthetics

All inhaled anesthetics (see Chapters 25, and 26) are biotransformed to some extent, with the nonvolatile products of metabolism eliminated almost entirely by the kidney. Reversal of the CNS effects of inhaled anesthetics depends on pulmonary excretion; therefore, impaired kidney function would not alter the response to these anesthetics. From the viewpoint of selecting an anesthetic that would not be harmful to patients with mild or moderate impairment of renal function, all the modern potent anesthetics are suitable. Enflurane is biotransformed to inorganic fluoride, but levels after 2 to 4 hours of anesthesia average only 19 μM in patients with mild to moderate kidney disease, significantly lower than the nephrotoxic threshold of 50 μM, which is frequently reported after the administration of methoxyflurane. This level of fluoride should not cause further renal impairment. Fluoride levels after isoflurane increase by only 3 to 5 μM, and by only 1 to 2 μM after halothane; therefore, these anesthetics have no nephrotoxic potential.

Desflurane and sevoflurane, two newer inhaled anesthetics, are remarkably different in their molecular stability and biotransformation. Desflurane is highly stable and resists degradation by soda lime and the liver. The mean inorganic fluoride concentration after 1 minimum alveolar concentration (MAC)-hour exposure to desflurane was less than 1 μM. The safety of desflurane in renal failure patients has been confirmed. In addition, more sensitive indices of renal function—urine retinol-binding protein and β-N-acetylglucosaminidase—showed no evidence of renal damage. Prolonged exposure to desflurane (7 MAC-hours) has been associated with normal renal function.

Sevoflurane is not very stable. Soda lime causes it to decompose, and it is biotransformed by the liver. Plasma inorganic fluoride concentrations approaching nephrotoxic levels (50 μmol/L) have been reported after prolonged inhalation of sevoflurane. No evidence of gross changes in renal function was found in humans, however. In one study, sevoflurane was used at low flow (1 L/min), and there was no relationship to compound A and renal function.

Inhaled anesthetics cause a transient reversible depression in renal function. GFR, renal blood flow, urine output, and urinary excretion of sodium are decreased (Table 72-8). Probable mechanisms include reduced renal blood flow, loss of renal autoregulation, neurohumoral factors (e.g., antidiuretic hormone, vasopressin, renin), and neuroendocrine responses. Although most inhaled anesthetics have been shown to reduce GFR and urinary excretion of sodium, their effects on renal blood flow have yielded conflicting results, which can be explained by differences in experimental methodology. Data suggest that renal blood flow is maintained with halothane, isoflurane, and desflurane, but it is decreased with enfurane and sevoflurane.

### Intravenous Anesthetics

Reversal of CNS effects after the administration of ultra-short-acting barbiturates such as thiopental and methohexitol occurs as a result of redistribution, and hepatic metabolism is the sole route of elimination of these drugs (see Chapter 30). Thiopental is 75% to 85% bound to albumin, the concentration of which may be markedly reduced in uremia. Because it is a highly bound drug, reduced binding permits a greater proportion of an administered dose of thiopental to reach receptor sites. In addition, thiopental is a weak acid, with its pKₐ in the

<table>
<thead>
<tr>
<th>TABLE 72-7 DRUGS USED OR ENCOUNTERED IN ANESTHESIA PRACTICE THAT SIGNIFICANTLY DEPEND ON RENAL ELIMINATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Completely Dependent</strong></td>
</tr>
<tr>
<td>Digoxin, inotropes (used frequently; monitoring of blood levels indicated in chronic renal failure)</td>
</tr>
<tr>
<td>Others—aminoglycosides, vancomycin, cephalosporins, and penicillins</td>
</tr>
<tr>
<td>Others—milrinone, hydralazine, cycloserine, sulfonamides, and chloropropamide</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

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Muscle Relaxants and Their Antagonists

(See Chapters 34 and 35)

Succinylcholine has been used without difficulty in patients with decreased or absent renal function. Its metabolism is catalyzed by pseudocholinesterase to yield the nontoxic end products succinic acid and choline. The metabolic precursor of these two compounds, succinylmonocholine, is excreted by the kidneys. Large doses of succinylcholine, which might result from prolonged infusion, should be avoided in patients with renal failure. Although pseudocholinesterase levels are reduced in uremia, these reductions are insufficient and cause a prolonged block. Hemodialysis has been reported to have no effect on cholinesterase levels.

Administration of succinylcholine causes a rapid, transient increase of 0.5 mEq/L in the serum potassium concentration. In traumatized, burned, or neurologically injured patients, the increase may be 5 to 7 mEq/L, probably as a consequence of denervation supersensitivity of the muscle membrane to succinylcholine and to acetylcholine, which can result in cardiovascular collapse. An exaggerated increase in serum potassium could be particularly dangerous in uremic patients with hyperkalemia; therefore, the use of succinylcholine is inadvisable, unless the patient has undergone dialysis within 24 hours before surgery. If the patient has recently undergone dialysis or has normal serum potassium, the use of succinylcholine is reportedly safe.

The disposition of nondepolarizing muscle relaxants has been well studied. Renal failure influences the pharmacology of nondepolarizing muscle relaxants by producing either decreased elimination of the drug or its metabolites by the kidney or decreased activity of enzymes that metabolize the drug, such as in the case of mivacurium (Table 72-9). Consequently, the duration of action of muscle relaxants may be prolonged in patients with renal failure.

Approximately 40% to 50% of pancuronium is excreted in urine. A portion of this excretion occurs after biotransformation to the less active metabolite 3-hydroxypancuronium. Pancuronium has a prolonged terminal elimination half-life in patients with reduced renal function (see Table 72-9); therefore, it should be administered cautiously, particularly when several doses are required.

Two nondepolarizing muscle relaxants, atracurium and vecuronium, were introduced into clinical practice during the early 1980s. Atracurium is degraded by enzymatic ester hydrolysis and nonenzymatic alkaline degradations (Hofmann elimination) to inactive products that are not dependent on renal excretion for termination of action. Predictably, their terminal elimination half-life and indices of neuromuscular blockade (onset, duration, and recovery) are the same in patients with normal and absent renal function.

Approximately 30% of a dose of vecuronium is eliminated by the kidneys. Lynam and colleagues found that the duration of neuromuscular blockade after the administration of vecuronium was longer in patients with renal failure than in patients with normal renal function (99 versus 54 minutes) because of a longer elimination half-life (83 versus 52 minutes) and lower plasma clearance.

<table>
<thead>
<tr>
<th>TABLE 72-8 EFFECTS OF VARIOUS ANESTHETICS ON RENAL FUNCTION</th>
<th>RBF</th>
<th>GFR</th>
<th>Urine Output</th>
<th>Urine Solutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>General anesthesia</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Intravenous anesthetics</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Thiopental</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Midazolam</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Fentanyl/droperidol</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Fentanyl (high dose)</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Inhaled anesthetics</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Halothane</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Enflurane</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>PEEP</td>
<td>¡</td>
<td>¡</td>
<td>¡</td>
<td>¡</td>
</tr>
<tr>
<td>Regional anesthesia</td>
<td>¡</td>
<td>¡</td>
<td>¡</td>
<td>¡</td>
</tr>
<tr>
<td>Epidural (with epinephrine)</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Epidural (without epinephrine)</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Spinal</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>


GFR, Glomerular filtration rate; PEEP, positive end-expiratory pressure; RBF, renal blood flow; −, no significant change; ø, significant data; ¡, decrease.

Although conflicting reports of anesthetic effects on RBF have been reported because of different investigative methods, the current literature seems to support these data.

Physiologic range; acidosis results in more un-ionized, nonbound, active thiopental. In combination, these changes produce an increase in the free fraction of thiopental from 15% in normal patients to 28% in patients with CRF. With thiopental metabolism essentially unchanged in renal disease, the dose to produce and maintain anesthesia should be reduced. The same considerations are true for methohexital, although metabolism plays a slightly greater part in the termination of its therapeutic effect.

Propofol does not adversely affect renal function as reflected by measurements of creatinine concentration. Prolonged infusions of propofol may result in the excretion of green urine because of the presence of phenols in the urine. This discoloration does not affect renal function. Urate excretion is increased after the administration of propofol and is usually manifested as cloudy urine when urate crystallizes under conditions of low pH and temperature.

There are no reports of the disposition of narcotics and tranquilizers when used in large dosage for anesthesia in uremic patients. These drugs are extensively metabolized before excretion; therefore, when combined with 30% to 50% nitrous oxide, they should not have a particularly prolonged effect. The benzodiazepines, especially diazepam, have a long half-life and tend to accumulate. Because of the greater ease of reversibility of the potent inhaled anesthetics versus intravenous drugs, inhaled anesthetics may offer some advantages for the induction of general anesthesia in uremic patients.
(3.1 mL/kg/min versus 5.3 mL/kg/min). In a related area, an interaction between the solvent of cyclosporine (Kolliphor EL) with atracurium and vecuronium has been reported, with the action of these muscle relaxants potentiated in cats, but it is unknown whether such potentiation also occurs in human renal transplant recipients.

Cisatracurium is the single cis isomer of atracurium. Organ-independent mechanisms (Hofmann elimination) account for 77% of the total clearance of cisatracurium. Because renal excretion accounts for only 16% of the elimination of cisatracurium, renal failure should have little effect on its duration of action.

The short-acting drug mivacurium is metabolized by plasma pseudocholinesterase. Its effect has been shown to be lengthened by 10 to 15 minutes in patients with ESRD, most likely because of a decrease in plasma cholinesterase activity in these patients associated with uremia or hemodialysis and a decrease in the mivacurium requirement by infusion in anephric patients.

The elimination half-life of rocuronium is increased in renal failure because of an increase in the volume of distribution with no change in clearance. This explanation might account for a longer duration of action in anephric patients, although its clinical significance is uncertain.

Pharmacokinetics data for the cholinesterase inhibitors neostigmine, pyridostigmine, and edrophonium for normal, anephric, and renal transplant patients are presented in Table 72-10; there are no major differences among the three drugs. Renal excretion is of major importance for the elimination of all three reversal drugs, with approximately 50% of neostigmine and 70% of pyridostigmine and edrophonium excreted in urine. Excretion of all the cholinesterase inhibitors is delayed in patients with impaired renal function to the same or perhaps to a slightly greater extent than is elimination of muscle relaxants. Reappearance of neuromuscular blockade after pharmacologic reversal of neuromuscular blockade in a patient with renal failure is, in most cases, due to some other cause. Table 72-10 contains data indicating that the pharmacokinetics of all the cholinesterase inhibitors is similar in healthy patients and in patients with well-functioning newly transplanted kidneys.

### Tables

**Table 72-9** Pharmacokinetics Data for Nondepolarizing Muscle Relaxants in Normal and Anephric Patients

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patients Studied</th>
<th>Elimination Half-life (hr)</th>
<th>Clearance (mL/kg/min)</th>
<th>Volume of Distribution (L/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vecuronium</td>
<td>Normal</td>
<td>0.9</td>
<td>5.3</td>
<td>0.20</td>
</tr>
<tr>
<td></td>
<td>Anephric</td>
<td>1.4</td>
<td>3.1</td>
<td>0.24</td>
</tr>
<tr>
<td>Atracurium</td>
<td>Normal</td>
<td>0.3</td>
<td>6.1</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>Anephric</td>
<td>0.4</td>
<td>6.7</td>
<td>0.22</td>
</tr>
<tr>
<td>Pancuronium</td>
<td>Normal</td>
<td>1.7</td>
<td>1</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>Anephric</td>
<td>8.2</td>
<td>0.3</td>
<td>0.14</td>
</tr>
<tr>
<td>Rocuronium</td>
<td>Normal</td>
<td>0.71</td>
<td>2.9</td>
<td>0.264</td>
</tr>
<tr>
<td></td>
<td>Anephric</td>
<td>0.97</td>
<td>2.9</td>
<td>0.264</td>
</tr>
<tr>
<td>Cisatracurium</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
<td>0.031</td>
</tr>
<tr>
<td></td>
<td>Anephric</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mivacurium</td>
<td>Normal</td>
<td>0.03</td>
<td>106</td>
<td>0.278</td>
</tr>
<tr>
<td></td>
<td>Anephric</td>
<td>0.06</td>
<td>80</td>
<td>0.478</td>
</tr>
</tbody>
</table>

*P < .05 versus normal.

**Table 72-10** Pharmacokinetics Data for Cholinesterase Inhibitors in Normal, Anephric, and Renal Transplant Patients

<table>
<thead>
<tr>
<th>Drug</th>
<th>Patients Studied</th>
<th>Elimination Half-life (hr)</th>
<th>Clearance (mL/kg/min)</th>
<th>Volume of Distribution (L/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neostigmine</td>
<td>Normal</td>
<td>1.3</td>
<td>8.4</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>Anephric</td>
<td>3*</td>
<td>3.9*</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>Renal transplant</td>
<td>1.7</td>
<td>9.4</td>
<td>1.1</td>
</tr>
<tr>
<td>Pyridostigmine</td>
<td>Normal</td>
<td>1.9</td>
<td>8.6</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>Anephric</td>
<td>6.3*</td>
<td>2.1*</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Renal transplant</td>
<td>1.4</td>
<td>10.8</td>
<td>1</td>
</tr>
<tr>
<td>Edrophonium</td>
<td>Normal</td>
<td>1.9</td>
<td>8.2</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>Anephric</td>
<td>3.6*</td>
<td>2.7*</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>Renal transplant</td>
<td>1.4</td>
<td>9.9</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Vasopressors and Antihypertensive Drugs

(See Chapter 16)

Patients with severe renal disease are frequently given antihypertensive and other cardiovascular medications. More than 90% of the thiazides and 70% of furosemide are excreted by the kidneys and they have prolonged durations of action in patients with abnormal or absent renal function. Propranolol is almost completely metabolized in the liver, and esmolol is biodegraded by esterases in the cytosol of red blood cells; therefore, their effects are not prolonged in patients with abnormal or absent renal function. The calcium channel–blocking agents nifedipine, verapamil, and diltiazem are extensively metabolized in the liver to pharmacologically inert products; they can be administered in usual doses to patients...
with renal insufficiency. Nitroglycerin is useful because it is metabolized rapidly, with less than 1% excreted unchanged in urine.

Sodium nitroprusside has had a resurgence in use since its initial introduction as a hypotensive drug in the 1920s. Cyanide is an intermediate in the metabolism of sodium nitroprusside, with thiocyanate being the final metabolic product. Although cyanide toxicity as a complication of sodium nitroprusside therapy is well described, it is less well appreciated that thiocyanate is also potentially toxic. The half-life of thiocyanate is normally more than 4 days, and it is prolonged in patients with uremia; therefore, caution is required when it is administered. After a single intravenous dose of 0.5 mg/kg of labetalol, the volume of distribution, clearance, and elimination half-life were similar in patients with ESRD and in healthy volunteers. Esmolol is independent of renal function because it is metabolized by red blood cell cytosol esterases.

Hydralazine is slower acting than the other three drugs discussed previously. Its action is terminated by hydroxylation and subsequent glucuronidation in the liver, with approximately 15% excreted unchanged in urine. The elimination half-life of hydralazine is prolonged in patients with uremia; therefore, caution is required when it is administered. After a single intravenous dose of 0.5 mg/kg of labetalol, the volume of distribution, clearance, and elimination half-life were similar in patients with ESRD and in healthy volunteers. Esmolol is independent of renal function because it is metabolized by red blood cell cytosol esterases.

If administration of a vasopressor is necessary, a direct β-adrenergic–stimulating drug such as phenylephrine would be effective. This type of vasopressor causes the greatest interference with renal circulation. Although β-adrenergic–stimulating drugs such as isoproterenol maintain heart and brain perfusion without renal vasoconstriction, they also increase myocardial irritability. When possible, it is best to substitute simple measures such as blood volume expansion for drug therapy. If these measures are inadequate, β-adrenergic–stimulating drugs or dopamine should be used.

### ACUTE KIDNEY INJURY AND HEMODIALYSIS

Until recently the definition of acute kidney injury (AKI) was not standardized. Authors have used terms such as renal insufficiency, renal dysfunction, acute renal failure (ARF), and renal failure requiring dialysis somewhat interchangeably. Parameters used to define these terms include (Fig. 72-5) absolute and percentage changes in creatinine values, absolute and percentage changes in estimated GFRs, and reduction in output. The incidence of AKI depends on the type of surgery and preexisting kidney function. In cardiac surgery, incidence is between 7.7% and 11.4% when defined broadly, whereas frequency of AKI requiring dialysis is generally lower, ranging between less than 1% and 5%. In gastric bypass surgery, the incidence is 8.5% and after aortic aneurysm surgery, it is around 15% to 16%. Similarly, liver transplant is also associated with a high frequency of AKI. It is reported that 48% to 94% of patients suffer from acute worsening renal function after liver transplantation.

In noncardiac surgery, several independent risk factors for AKI have been identified by Kheterpal and co-workers: age, emergent surgery, liver disease, body mass index, high-risk surgery, peripheral vascular disease, and chronic obstructive pulmonary disease (requiring chronic bronchodilator therapy). Based on incremental score, the frequency of renal failure increased, ranging between 0.3% and 4.5%, respectively.

#### Parameters used to define acute kidney injury

<table>
<thead>
<tr>
<th>RIFLE class</th>
<th>Serum creatinine*</th>
<th>Urine output</th>
<th>AKIN class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk</td>
<td>1.5 × baseline</td>
<td>&lt; 0.5 mL/kg/hr × 6 hours</td>
<td>Stage 1</td>
</tr>
<tr>
<td>Injury</td>
<td>2 × baseline</td>
<td>&lt; 0.5 mL/kg/hr × 12 hours</td>
<td>Stage 2</td>
</tr>
<tr>
<td>Failure</td>
<td>3 × baseline or creatinine &gt; 4 mg/dL or acute rise of ≥ 0.5 mg/dL</td>
<td>&lt; 0.3 mL/kg/hr × 24 or anuria × 12 hours</td>
<td>Stage 3**</td>
</tr>
<tr>
<td>Loss*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* RIFLE criteria include changes in glomerular filtration rate (GFR): RISK: 25% reduction in GFR INJURY: 50% reduction in GFR FAILURE: 75% reduction in GFR **AKIN Stage 3 is automatically designated for any patient receiving renal replacement therapy.

The incidence of AKI depends on the type of surgery and preexisting kidney function (Box 72-2 and Table 72-11).

In cardiac surgery, incidence is between 7.7% and 11.4% when defined broadly, whereas frequency of AKI requiring dialysis is generally lower, ranging between less than 1% and 5%. In gastric bypass surgery, the incidence is 8.5% and after aortic aneurysm surgery, it is around 15% to 16%. Similarly, liver transplant is also associated with a high frequency of AKI. It is reported that 48% to 94% of patients suffer from acute worsening renal function after liver transplantation.

In noncardiac surgery, several independent risk factors for AKI have been identified by Kheterpal and co-workers: age, emergent surgery, liver disease, body mass index, high-risk surgery, peripheral vascular disease, and chronic obstructive pulmonary disease (requiring chronic bronchodilator therapy). Based on incremental score, the frequency of renal failure increased, ranging between 0.3% and 4.5%, respectively.

---

PERIOPERATIVE MANAGEMENT OF PATIENTS WITH ACUTE KIDNEY INJURY

Although many factors have been shown to contribute to AKI in surgical patients, there are few interventions demonstrated to prevent AKI. Of these interventions, there is no obvious cure for perioperative renal injury. Although a complete review of such interventions is beyond the scope of this chapter, some deserve mention.64

Dialysis

Dialysis may not decrease perioperative AKI; however, it can treat the associated acidosis, hyperkalemia, and hypervolemia. For certain surgeries, such as aortic, dialysis actually reduces 30-day mortality rates in patients who develop loss of renal function.70 As many as 75% of these survivors regain kidney function and become independent of dialysis.

Nondialytic Management

Optimal therapy for renal dysfunction is not clear as to whether such as ACE-I therapy or diuretic therapy prevents decline in kidney function around the time of surgery.65

Normal hemodynamic variables probably should be preserved during the operative period in an attempt to prevent AKI. Scavengers of oxygen free radicals such as mannitol and N-acetylcysteine have been given to prevent ischemia-reperfusion injury. Recent studies, however, have failed to show benefit in reduction of AKI in cardiac surgery patients. For years, mannitol was administered before aortic clamping, especially suprarenal clamping, during abdominal aortic aneurysm surgery. It is not clear whether this approach reduces the incidence of renal failure in this population of patients.71

Both dopamine72 and atrial natriuretic peptide initially showed promise in the prevention of AKI because of their vasoactive effects leading to increased renal blood flow. Studies have shown neither dopamine nor atrial natriuretic peptide to be associated with improved mortality. Likewise, fenoldopam, a selective renal dopamine receptor agonist, initially showed potential renoprotective benefit. In large studies, fenoldopam was not beneficial in prevention of AKI.73

| BOX 72-2 Risk Factors for Development of Postoperative Acute Kidney Injury |
|-----------------------------|------------------|
| **PREOPERATIVE FACTORS**    | **RENAL AND GENITOURINARY PROCEDURES** |
| • Preoperative renal dysfunction | **TRANSURETHRAL RESECTION OF THE PROSTATE** |
| • Increasing age             | Pathophysiology of Prostate Hypertrophy |
| • Heart disease (ischemic or congestive) | The prostatic gland consists of four closely integrated zones—the anterior, peripheral, central, and preprostatic zones. Each zone consists of secretory, smooth muscle, and fibrotic tissue. All four zones are enclosed in one capsule. The gland is rich in blood supply. Arteries and veins penetrate the prostatic capsule and branch inside the gland. The venous sinuses adjacent to the capsule are particularly large. Nodules begin to develop by the fourth decade of life in the preprostatic zone and form middle, lateral, and posterior lobes. The middle and posterior lobes are most often associated with symptoms of urinary tract obstruction.74 |
| • Smoking                   | |
| • Diabetes mellitus         | |
| • ASA PS 4 or 5             | |
| **INTRAOPERATIVE FACTORS**  | |
| • Emergency surgery or intraperitoneal, intrathoracic, suprarenal vascular surgeries | |
| • Erythrocyte transfusion   | |
| • Inotrope use              | |
| • Aortic cross-clamp time   | |
| • CPB: furosemide use, urine output, need for a new pump run | |
| • Postoperative Factors     | |
| • Erythrocyte transfusion   | |
| • Vasocostrictor use        | |
| • Diuretic use              | |
| • Antiarrhythmic drug use   | |


ASA PS, American Society of Anesthesiologists Physical Status classification; CPB, cardiopulmonary bypass.

<table>
<thead>
<tr>
<th>TABLE 72-11 COMMON CAUSES OF POSTOPERATIVE DECREASED URINE OUTPUT AND ACUTE KIDNEY INJURY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Site of Defect</strong></td>
</tr>
<tr>
<td><strong>Prerenal</strong></td>
</tr>
<tr>
<td>Hypotension</td>
</tr>
<tr>
<td>Absolute</td>
</tr>
<tr>
<td>Relative</td>
</tr>
<tr>
<td>Hypovolemia</td>
</tr>
<tr>
<td>Absolute</td>
</tr>
<tr>
<td>Relative (e.g., IAH)</td>
</tr>
<tr>
<td><strong>Renal</strong></td>
</tr>
<tr>
<td>Acute tubular necrosis</td>
</tr>
<tr>
<td>Ischemia-reperfusion</td>
</tr>
<tr>
<td>Radiocontrast</td>
</tr>
<tr>
<td>Acute interstitial nephritis</td>
</tr>
<tr>
<td><strong>Postrenal</strong></td>
</tr>
<tr>
<td>Urinary catheter obstruction</td>
</tr>
<tr>
<td>Catheter kinking</td>
</tr>
<tr>
<td>Debris</td>
</tr>
<tr>
<td>Prostatic hypertrophy</td>
</tr>
<tr>
<td>Bladder spasm</td>
</tr>
<tr>
<td>Urinary retention</td>
</tr>
</tbody>
</table>

From Chenitz KB, Lane-Fall MB: Postoperative oliguria, Anesth Clin 2012;513-526.
Surgical Procedures

Transurethral resection of the prostate (TURP) is performed by inserting a resectoscope through the urethra and resecting prostatic tissue with an electrically powered cutting-coagulating metal loop or using laser-vaporization energy. This can be accomplished with either a monopolar TURP (M-TURP) or bipolar TURP (B-TURP) technique. Laser energy for TURP has also been used for many years. With each technique, as much prostatic tissue as possible is resected, but the prostatic capsule is usually preserved. If the capsule is violated, large amounts of irrigation solution can be absorbed into the circulation via the periprostatic, retroperitoneal, or peritoneal space.

Bleeding during TURP is common, but usually controllable; however, when large venous sinuses are opened, hemostasis becomes difficult. If bleeding becomes uncontrollable, the procedure should be terminated as quickly as possible, and a Foley catheter should be passed into the bladder and traction applied to it. The catheter’s inflated balloon exerts lateral pressure on the prostatic bed and reduces bleeding. Bleeding requiring transfusion occurs in approximately 2.5% of TURP procedures.75

Irrigation Solutions

Ideally, an irrigation solution for TURP should be isotonic, electrically inert, nontoxic, transparent, easy to sterilize, and inexpensive. Such a solution does not exist. Distilled water is electrically inert and inexpensive and has excellent optical properties, but it is extremely hypotonic. When absorbed into the circulation in large amounts, plain water causes hemolysis, shock, and renal failure.

Numerous nearly isotonic irrigation solutions are available. Commonly used solutions are glycine 1.2% and 1.5%, mannitol 3% to 5%, glucose 2.5% to 4%, sorbitol 3.5%, Cytal (a mixture of sorbitol 2.7%, and mannitol 0.54%), and urea 1% (Table 72-12). These solutions are purposely moderately hypotonic to preserve their transparency.

Although these irrigation solutions cause no significant hemolysis, excessive absorption of them can lead to other complications, such as pulmonary edema and hyponatremia. In addition, the solutes can have adverse effects. Glycine can cause cardiac and retinal toxic effects, mannitol rapidly expands the blood volume and can cause pulmonary edema in cardiac patients, and glucose can cause severe hyperglycemia in diabetic patients. These complications are discussed in detail later.

<table>
<thead>
<tr>
<th>Solution</th>
<th>Osmolality (mOsm/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycine, 1.2%</td>
<td>175</td>
</tr>
<tr>
<td>Glycine, 1.5%</td>
<td>220</td>
</tr>
<tr>
<td>Sorbitol, 3.5%</td>
<td>165</td>
</tr>
<tr>
<td>Mannitol, 5%</td>
<td>275</td>
</tr>
<tr>
<td>Cytal (see text)</td>
<td>178</td>
</tr>
<tr>
<td>Glucose, 2.5%</td>
<td>139</td>
</tr>
<tr>
<td>Urea, 1%</td>
<td>167</td>
</tr>
</tbody>
</table>

Replacement of distilled water with nearly isosmotic solutions has eliminated hemolysis and its sequelae as a complication of M-TURP. The incidence of severe CNS problems associated with extreme hyponatremia, such as convulsions and coma, has been reduced. The other major problem associated with the absorption of large volumes of irrigating solution, overhydration, still remains, however. With B-TURP and laser-TURP (L-TURP) techniques normal saline as the bladder irrigating solution can be used which significantly helps to minimize or eliminate TURP syndrome.

Anesthetic Techniques

Previously, spinal anesthesia was the most frequently used anesthetic for TURP in the United States, and it is believed to be the technique of choice when traditional M-TURP is performed. Spinal anesthesia provides adequate anesthesia for the patient with good relaxation of the pelvic floor and the perineum for the surgeon. The signs and symptoms of water intoxication and fluid overload can be recognized early because the patient is awake. Accidental bladder perforation also is recognized easily if the spinal level is limited to T10 because the patient would experience abdominal or shoulder pain. Satisfactory regional anesthesia for TURP involves achieving an anesthetic block level that interrupts sensory transmission from the prostate and bladder neck. In addition, the uncomfortable sensation of bladder distention must be considered.76,77

As explained earlier, the visceral pain sensation from the prostate and bladder neck is transmitted by afferent parasympathetic nerve fibers derived mostly from the second and third sacral roots traveling with the pelvic splanchnic nerves. Bladder sensation is supplied by sympathetic nerves of the hypogastric plexus, derived from nerve roots extending inferiorly from T11 to L2. Regional anesthesia resulting in a sensory level to T10 is required to eliminate the discomfort caused by bladder distention and other aspects of this procedure; however, slightly lower sensory levels often suffice for smaller lesions. In one study in which bladder pressure was monitored and kept low, anesthetic levels to T12 or L1 were adequate, but midlumbar blocks to L3 were not.79 Sensory levels above T9 should not be sought because the capsular sign (i.e., pain on perforation of the prostatic capsule) would not be present should perforation occur.

Subarachnoid anesthesia is generally preferred over continuous epidural anesthesia for the following reasons. It is technically easier to perform in elderly patients, and the duration of surgery is generally not long. The incomplete block of sacral nerve roots that occasionally occurs with the extradural technique is usually avoided with subarachnoid anesthesia.

Caudal and sacral blockade also has been used effectively for prostate surgery, and bladder distention is avoided with the use of continuous irrigation. Caudal anesthesia has been used effectively in high-risk patients undergoing laser prostatectomy.79 Hemodynamic stability is the main advantage with this technique. Local infiltration of the perineum and the prostatic fossa also has been advocated by some anesthesiologists for limited TURP procedures, although the operative analgesia afforded
Anesthesia and the Renal and Genitourinary Systems

Chapter 72: Anesthesia and the Renal and Genitourinary Systems

Fluid during the procedure produces numerous problems with cardiovascular and neurologic implications. A change in the patient’s mental status provides an early indication that excessive absorption of irrigating fluid has occurred. These changes are described more fully in the next section.

Visual disturbances, such as blurred vision and transient blindness, have been reported in association with TURP (see Chapter 100). The biotransformation of absorbed glycine to ammonia has been implicated in these and other CNS abnormalities. Another potential complication during TURP is bladder perforation secondary to overdistention with irrigation fluid or contact of the bladder wall with the surgeon’s resectoscope. Conscious patients might experience symptoms related to perforation well before it becomes apparent to the surgeon, alerting the operating team early on. Signs and symptoms of bladder perforation include bradycardia, hypotension, restlessness, diaphoresis, nausea, abdominal pain, dyspnea, shoulder pain, and hiccups. Extraperitoneal perforation may be manifested as pain in the periumbilical, inguinal, or suprapubic area. Intrapерitoneal bladder perforation, a less frequent event, may cause symptoms related to diaphragmatic irritation (i.e., pain referred to the upper part of the abdomen, precordial area, shoulder region, or neck).81

Regional anesthesia for TURP offers some advantages over general anesthesia. Although laboratory monitoring of electrolytes is useful intraoperatively, a change in mental status in a conscious patient provides an early indication of electrolyte disturbances. Bladder perforation is recognized earlier in a conscious or lightly sedated patient, as noted previously.

Sensory levels above T9 are undesirable because pain caused by perforation of the prostatic capsule (capsular sign) would not be apparent to the patient if this complication occurs. Another benefit of regional anesthesia for TURP is a decreased requirement for analgesics in the immediate postoperative period compared with general anesthesia.82

Morbidity and Mortality after Transurethral Resection of the Prostate

Although spinal anesthesia offers certain distinct advantages over general anesthesia for TURP surgery, mortality and many markers of patient outcome have been similar for both groups. What constitutes the safest anesthetic for prostatectomies was debated in 1924, with proponents of regional anesthesia gaining ground quickly thereafter.83 The 30-day mortality rate associated with M-TURP is reported to be 0.2% to 0.8%.77 Mortality rates are similar in patients receiving regional anesthesia or general anesthesia.84 With mortality rates as low as 0.2%, however, many more patients need to be studied than previously examined in any of the studies to draw a meaningful and statistically significant conclusion. The postoperative morbidity rate in one study was 18%77. Increased morbidity was found in patients with resections exceeding 90 minutes, gland size larger than 45 g, acute urinary retention, and age older than 80 years.77 Ashton and co-workers85 studied 250 men undergoing TURP and observed one postoperative myocardial infarction (0.4%) resulting in one death. The incidence of postoperative complications, including myocardial infarction, pulmonary embolism,
COMPLICATIONS OF TRANSURETHRAL RESECTION OF THE PROSTATE

Absorption of Irrigating Solution

Because the prostate gland contains large venous sinuses, it is inevitable that irrigating solution would be absorbed. Simple principles govern the amount of absorption: (1) The height of the container of irrigating solution above the surgical table determines the hydrostatic pressure driving fluid into prostatic veins and sinuses, and (2) the time of resection is proportional to the quantity of fluid that is absorbed. On average, 10 to 30 mL of fluid is absorbed per minute of resection time, with 6 to 8 L absorbed in some procedures lasting up to 2 hours. Whether patients experience complications as a consequence of the absorption of irrigating fluid depends on the amount and type of fluid absorbed.

Excessive Circulatory Volume, Hyponatremia, and Hypoosmolality

Solutions such as normal saline and lactated Ringer’s solution would be well tolerated when absorbed intravascularly, but these electrolyte solutions are highly ionized and facilitate the dispersion of high-frequency current from a monopolar resectoscope. Solutions of nonelectrolytes, such as glucose, urea, glycine, mannitol, sorbitol, and Cytal, have replaced distilled water. Of all the irrigating solutions available today (see Table 72-12), glycine and Cytal, have replaced distilled water as the two most commonly used.

Replacement of distilled water with nearly isosmotic solutions has eliminated hemolysis and its sequelae as a complication of TURP. The incidence of severe CNS problems associated with extreme hyponatremia, such as convulsions and coma, has been reduced; however, the other major problem associated with the absorption of large volumes of irrigating solution, overhydration, remains. Under usual conditions, only 20% to 30% of a load of crystalloid solution remains in the intravascular space; the remainder enters the interstitial space. When intravascular pressure is increased, movement of fluid into the interstitial space and the development of pulmonary edema are favored. Whether symptoms of circulatory overload develop in a given patient depends on the patient’s cardiovascular status, the amount and rapidity of absorption of irrigating fluid, and the extent of surgical blood loss.

The situation is dynamic, and patients must be monitored carefully. In this regard, spinal or epidural anesthesia, supplemented with only light intravenous sedation, has the advantage of allowing the patient’s subjective judgment to contribute to assessment of his condition during surgery. In addition, the cardiovascular depression associated with the administration of potent inhaled anesthetics is avoided. Another advantage of regional anesthesia is that the sympathetic block that it produces increases venous capacitance and tends to mitigate intraoperative fluid overload. When the block dissipates, venous capacity acutely decreases, and circulatory overload can occur.

Concomitant with the excessive intravascular volume caused by significant absorption of irrigating fluid are usually hyponatremia and hypoosmolality. TURP syndrome has been typically described as being caused by hyponatremia and subsequent water intoxication. It is now recognized that the classic CNS signs of TURP are not caused by hyponatremia per se, but are due to the accompanying acute serum hypoosmolality that allows movement of water into cells and causes cerebral edema.

The use of nonelectrolyte isosmotic irrigating solutions has reduced the incidence of severe CNS complications because extreme extracellular fluid hypoosmolality does not occur, and the subsequent development of cerebral edema is avoided. That CNS symptoms occur at all is probably due to the fact that the incidence and extent of hyponatremia are unchanged. The concentration of extracellular sodium must be in the physiologic range for depolarization of excitable cells and production of the action potential. CNS symptoms, which include irritability, apprehension, confusion, and headache, provide early warning signs of rapidly developing hyponatremia. Further progression of hyponatremia (sodium ≤ 102 mEq/L) and decreased serum osmolality lead to the development of seizures and coma. The CNS effects become apparent at sodium levels less than 120 mEq/L. The cardiovascular effects of severe hyponatremia include negative inotropy, hypotension, and dysrhythmias. At sodium levels less than 115 mEq/L, electrocardiogram changes are made manifest by QRS widening and ST-segment elevation. When extracellular sodium levels are less than 100 mEq/L, consciousness is lost, and convulsions may ensue. Signs and symptoms of cardiovascular dysfunction secondary to hyponatremia also may occur, including arrhythmias, hypotension, and pulmonary edema.

It is often impossible, however, to separate the latter events from events attributable to fluid overload.

Glycine Toxicity

Since the early 1980s, attention has turned to the absorption of glycine (HO₂—CCH₂—NH₂), a nonessential amino acid, as a possible cause of some CNS symptoms associated with TURP. In one publication, five cases of transient blindness were attributed to glycine toxicity. Glycine has a distribution similar to that of aminobutyric acid, the latter being an inhibitory transmitter in the brain; it has been suggested that glycine is a major inhibitory
transmitter acting in the spinal cord and brainstem. Normal plasma glycine levels are 13 to 17 mg/L, whereas levels of 1029 mg/L were measured during one episode of blindness. Twelve hours later, the glycine level in this case had declined to 143 mg/L, by which time vision had returned; however, an overall correlation between plasma glycine levels and CNS toxicity has not been established. This relationship, although interesting, still must be considered speculative. Glycine also has been implicated in the myocardial depression and hemodynamic changes associated with TURP syndrome.

Ammonia Toxicity
Absorption of glycine can result in CNS toxicity because of oxidative biotransformation of glycine to ammonia. In a report of delayed awakening after TURP in three patients, an association with elevated blood ammonia concentrations was noted. Blood ammonia levels of 500 M were noted in this and another case report. Deterioration of CNS function is said to occur when ammonia levels are greater than 150 M. In a prospective study examining glycine metabolism, blood ammonia levels were increased postoperatively in 12 of 26 patients in whom 1.5% glycine was used as the irrigating solution for TURP. Blood glycine levels also were measured. Glycine and ammonia levels did not correlate; the opposite relationship was prevalent. High ammonia levels were not associated with CNS symptoms of toxicity. Although the investigators postulated that delayed awakening and other CNS symptoms were due to ammonia toxicity, it is unclear whether this hypothesis is correct.

Perforation
Another common complication of TURP is perforation of the bladder. Perforations usually occur during difficult resections and are most often made by the cutting loop or knife electrode. Some are made by the tip of the resectoscope, whereas others result from overdistention of the bladder with irrigation fluid. Most perforations are extraperitoneal, and in a conscious patient they result in pain in the periumbilical, inguinal, or supra- pubic regions. The urologist may also note the irregular return of irrigating fluid. Less often, the perforation is through the wall of the bladder and is intraperitoneal, or a large extraperitoneal perforation may extend into the peritoneum. In such cases, pain may be generalized in the upper part of the abdomen or be referred from the diaphragm to the precordial region or the shoulder. Other signs and symptoms, such as pallor, sweating, abdominal rigidity, nausea, vomiting, and hypotension, have been reported; the number and severity depend on the location and size of the perforation and the type of irrigating fluid. In an early series of 2015 cases in which the incidence of complications of TURP was examined, perforation occurred in 25 patients (1.2%). Four deaths and five additional major complications occurred in 12 patients in whom suprapubic cystostomy was delayed more than 2 hours after perforation. Distilled water was the bladder irrigant in most of these cases; therefore, it is unclear whether these morbidity and mortality data are still relevant.

Transient Bacteremia and Septicemia
The prostate harbors many bacteria, which can be a source of intraoperative and postoperative bacteremia through the prostatic venous sinuses. This risk is increased further by the presence of an indwelling urinary catheter. Bacteraemia is usually asymptomatic and easily treated with commonly used antibiotic combinations that are effective against gram-positive and gram-negative bacteria; however, septicemia may occur in 6% to 7% of patients. Common manifestations include chills, fever, and tachycardia. In severe cases, bradycardia, hypotension, and cardiovascular collapse can occur, with mortality rates of 25% to 75%. Aggressive treatment with antibiotics and cardiovascular support is warranted.

Hypothermia
Irrigating fluids stored at room temperature are frequently used during TURP. Heat loss as a result of irrigation and significant absorption of this fluid can lead to a decrease in the patient’s body temperature and cause shivering. The use of warmed irrigating solutions has been shown to be efficacious in reducing heat loss and the resultant shivering. Although one may believe that warming of fluids might cause increased bleeding because of vasodilation, such is not the case, as shown by study of Heathcote and Dyer. The use of systemic and intrathecal opioids decreases postoperative shivering from cold.

Bleeding and Coagulopathy
A hypertrophied prostate is highly vascular, and operative bleeding can be significant. The blood is washed into the draining bucket and mixed with ample quantities of irrigant fluid. Estimation of blood loss is inaccurate and extremely difficult. Efforts have been made to quantify blood loss based on resection time (2 to 5 mL/min of resection time) and size of the prostate in grams (20 to 50 mL/g); however, these guidelines are rough estimates at best, and the patient’s vital signs and serial hematocrit values should be monitored to assess the blood loss and need for transfusion. Because adrenergic receptors are abundant in prostate tissue, the use of adrenergic agonists would cause vasoconstriction of prostatic blood vessels and a decrease in blood loss.

Abnormal bleeding after TURP occurs in less than 1% of cases; it is believed by some clinicians to be due to systemic fibrinolysis secondary to plasmin. The prostate releases plasminogen activator, which converts plasminogen to plasmin. Other clinicians believe that the fibrinolysis is secondary to disseminated intravascular coagulation triggered by the systemic absorption of resected prostate tissue, which is rich in thromboplastin. If primary fibrinolysis is suspected, aminocaproic acid can be effective when given intravenously in a dose of 4 to 5 g during the first hour, followed by 1 g/hr.

Treatment of Transurethral Resection of the Prostate Syndrome
Treatment of TURP syndrome (Table 72-13) consists of fluid restriction and a loop diuretic such as furosemide. Hypertonic saline (3% sodium chloride) is rarely, if ever, necessary and should be considered only in patients with severe hyponatremia. CNS complications of hypertonic
saline include cerebral edema and pontine myelinolysis.\textsuperscript{76,89} Cardiovascular support should be provided as necessary.

Anesthetic considerations for TURP should include positioning (see Chapter 41). TURP is usually performed in the lithotomy position with a slight Trendelenburg tilt. This positioning results in changes in pulmonary blood volume; a decrease in pulmonary compliance; a cephalad shift of the diaphragm; and a decrease in lung volume parameters such as residual volume, functional residual volume, tidal volume, and vital capacity. Cardiac preload may increase. Nerve injuries to the common peroneal, sciatic, and femoral nerves can occur.\textsuperscript{76}

### B-TURP, L-TURP, AND MICROWAVE ABLATION OF PROSTATE

Traditional M-TURP electrode prostate surgery has been challenged with new urethral prostate resection techniques. B-TURP offers the advantage of a bipolar electrode resection, which allows normal saline to be used as the bladder irrigating fluid. The electrical current is self-contained in the bipolar design, which prevents it from dispersing through the bladder irrigating fluid or patient. Using normal saline avoids the morbidity associated with hypoosmolar bladder irrigants, such as glycine if absorbed, but does not prevent the possibility of volume overload.

Issa\textsuperscript{100} reviewed 16 studies conducted over a 10-year period comparing the safety properties of M-TURP and B-TURP. They found a statistically significant decrease in overall complication rate, transfusion rate, and TURP syndrome with B-TURP. A randomized outcome study by Chen and colleagues,\textsuperscript{101} in which M-TURP and B-TURP were compared, found that B-TURP was associated with significantly less fluid absorption, less change in serum sodium and in hemoglobin, and comparable urologic efficacy in prostate symptom scores. Two meta-analytic studies comparing M-TURP and B-TURP also reported favorable outcomes in the B-TURP groups.\textsuperscript{102,103} A prospective, randomized trial comparing complications and clinical outcomes 18 months after TURP, concluded that fewer postoperative readmissions, faster postoperative recovery, and equivalent long-lasting results were found in B-TURP than in M-TURP.\textsuperscript{104}

L-TURP is replacing conventional TURP. Laser therapy delivers vaporization energy creating a thin resecting coagulation treatment zone during prostate resection. The neodymium:yttrium-aluminum-garnet (Nd:YAG) laser has been replaced by holmium and potassium-titanyl-phosphate lasers. The laser incorporates a 532-nm wavelength energy that is selectively absorbed by hemoglobin. When directed to the prostate, the laser vaporizes a layer of tissue in millimeter resection zones. An evolution of these lasers has occurred from 80 to 120 watts, to the currently available 180-watt laser. The increased wattage provides more efficient tissue ablation resulting in a decreased TURP resection time. These lasers produce varying degrees of coagulation and vaporization of prostate tissue. The main advantages over M-TURP include minimal blood loss (50 to 70 mL) and minimal fluid absorption, which should nearly eliminate these two major complications of TURP; however, other potential complications are introduced, including coagulation through the prostatic fossa and sloughing of prostatic debris in the postoperative period, with subsequent urinary obstruction and urinary retention.\textsuperscript{105-109} Protective eyewear and a means to evacuate the smoke plume are needed.\textsuperscript{110} In critically ill patients, caudal anesthesia has been used successfully for L-TURP because the use of continuous irrigation combined with minimal bleeding obviates the need for copious irrigation and minimizes bladder distention.\textsuperscript{79}

Hanson and associates\textsuperscript{111} reviewed the anesthetic implications of the newer prostate laser resection therapies. The described advantages included minimal bladder irrigating fluid absorption, a minimized risk of TURP syndrome, potential to perform the procedure on anticoagulated patients, delivery in an outpatient setting, and less emphasis on describing regional as the preferred anesthetic technique. General anesthesia is acceptable because of the decreased risk of TURP syndrome.

In a systematic review of randomized, controlled trials evaluating the efficacy and safety of L-TURP techniques versus conventional TURP for symptomatic benign prostatic obstruction, the authors observed that L-TURP provided slightly greater improvement in urinary symptoms and flow. Laser procedures resulted in fewer transfusions and strictures and shorter hospitalizations. Reoperation was required more often after laser procedures.\textsuperscript{112} As suggested, L-TURP is feasible when anticoagulation therapy withdrawal is considered a significant patient risk perioperatively.\textsuperscript{113}

When M-TURP, B-TURP, and bipolar plasma vaporization TURP were compared in a prospective, randomized long-term comparison study, capsular perforation and intraoperative bleeding were less in bipolar plasma vaporization TURP. Postoperative hematura, blood transfusion, and clot retention rates were higher in M-TURP.\textsuperscript{114}

Transurethral microwave thermotherapy (TUMT) ablation of the prostate is considered a minimally invasive office-based technique that can be performed under local or sacral block. High-energy TUMT has received

| TABLE 72-13 SIGNS AND SYMPTOMS OF TRANSURETHRAL RESECTION OF THE PROSTATE SYNDROME |
|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|
| Cardiovascular and Respiratory | Central Nervous System | Metabolic | Other |
| Hypertension | Agitation/confusion | Hyponatremia | Hypoosmolality |
| Bradycardias, tachycardias | Seizures | Hyperglycinemia | Hemolysis |
| Congestive heart failure | Coma | Hyperammonemia | |
| Pulmonary edema and hypoxemia | Visual disturbances (blindness) | |
| Myocardial infarction | | |
| Hypertension | | |

Hypertension Agitation/confusion Hyponatremia Hypoosmolality

Bradyarrhythmias, tachyarrhythmias Seizures Hyperglycinemia Hemolysis

Congestive heart failure Coma Hyperammonemia

Pulmonary edema and hypoxemia Visual disturbances (blindness)
reconsideration for use instead of current TURP techniques in certain patient populations. It can be performed as an outpatient procedure and lacks significant side effects. Although it is still reported to be less effective than TURP in relieving urinary outflow obstruction long term, it is an option especially in elderly or high-risk patients.115

LASER LITHOTRIPSY

Laser lithotripsy is used for ureteral stones that are low in the ureter and not amenable to extracorporeal shock wave lithotripsy (ESWL). A pulsed dye laser is generated with a laser beam of 504-nm wavelength passing through an organic green dye.116 This laser beam is easily absorbed by the stones, and pulsatile energy is released that causes disintegration of the stones. The beam is carried over a bare wire passed through a rigid ureteroscope, which is longer and more pointed than a cystoscope, so the risk of ureteral perforation exists. Ideally, general anesthesia with paralysis should be maintained to avoid patient movement. If regional anesthesia is chosen, a spinal level of T8 to T10 is required. The bare laser wire is sharp and can cause mucosal injury to the ureter. These lasers are not well absorbed by red blood cells or other tissues, however, which provides safety against tissue coagulation or thermal injury. Because the laser beam is reflective, the user, other personnel, and the patient should wear protective eyeglasses. Some hematuria always occurs; good intravenous hydration is recommended.116

LAPAROSCOPIC SURGERY IN UROLOGY

Urologic laparoscopic surgery continues to pioneer new surgical approaches for treatment of diseases previously performed by an open surgery. Advances in this area now routinely include laparoscopic varicocelectomy, hernia repair, adrenalectomy, partial adrenalectomy, renal pelvis or ureter percutaneous stone retrieval, nephrectomy, radical prostatectomy, extra-adrenal pheochromocytoma, nephropexy, pyleoplasty, nephrectomy, partial nephrectomy, and cystectomy. Many of these surgeries are robot assisted for tumor resection and reconstruction. During robotic laparoscopic surgery, the surgeon is stationed in the operating room away from the operating room table while working at a computer console with a three-dimensional view of the operating field and manual controls at the console for robotic instruments placed in the abdomen via laparoscopic trocars.

For radical prostatectomy, the objectives of laparoscopic surgery are to reduce perioperative morbidity compared with conventional surgery and allow a more precise operative procedure. The quality of surgery can be improved by better visualization of the operative site as a result of optical magnification and the maneuverability of the laparoscope, which provides a hitherto unattainable anatomic view. The laparoscopic approach not only improves the postoperative course, but also allows better preservation of periprostatic vascular, muscular, and neurovascular structures.117

A unique challenge in nephron-sparing laparoscopic surgery is achieving successful renal hypothermia for renal preservation during renal artery occlusion. Techniques described for renal hypothermia include laparoscopic deployed ice slush kidney surface cooling (preferred option), endoscopic retroperitoneal cold saline infusion, and transarterial renal hypothermia via femoral artery catheter approach.

Although all the conventional complications and concerns associated with laparoscopy are applicable to urologic procedures, two unique problems also are identified. First, because the urogenital system is mainly retroperitoneal, the large retroperitoneal space and its communications with the thorax and subcutaneous tissue are exposed to the insufflated carbon dioxide. Significant subcutaneous emphysema can occur in these patients and may extend all the way up to the head and neck.118 The upper airway is at risk for compromise in the most severe cases because of pharyngeal swelling secondary to submucous carbon dioxide. This complication should be kept in mind before extubation of the trachea in these patients. Second, the procedures can be lengthy, allowing for sufficient absorption of carbon dioxide to result in acidemia and marked acidosis.118 Because of significant increases in intra-abdominal and intrathoracic pressure as a result of insufflated carbon dioxide, a steep Trendelenburg position, and lengthy procedures, general anesthesia with controlled ventilation is the method of choice. Despite adequate intravascular hydration, intraoperative oliguria may occur and be followed by diuresis in the immediate postoperative period. Although the exact mechanism is unclear, increased perirenal pressure exerted by the insufflated gas in the retroperitoneal space is a likely explanation.

EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY

Extracorporeal shock wave lithotripsy has become the treatment of choice for disintegration of urinary stones in the kidney and upper part of the ureter. The first clinical model of the lithotripter introduced into common practice (Dornier HM-3) used a water bath in a steel tub and a metal gantry chair to support the patient suspended in a sitting position. This first-generation lithotripter is still used in some institutions and presents complex challenges of immersion physiology and monitoring difficulties. Second-generation and third-generation lithotripters (e.g., Siemens, Lithostar, Wolf Piezolith, Dornier HM-4, MFL 5000, MPL 9000) have evolved mainly in the direction of eliminating the water bath and minimizing patient discomfort. All lithotripters share similar technology in having three main components: (1) an energy source, most commonly a spark plug (alternatively, an electromagnetic membrane or piezoelectric elements); (2) a system to focus the shock wave, such as ellipsoid or reflecting mirrors; and (3) fluoroscopy or ultrasound to visualize and localize the stone in focus.119

Technical Aspects

An electrode (or spark plug) located in an ellipse creates a spark causing explosive vaporization of water. The sudden expansion of air bubbles created sets up a pressure wave (shock wave) which is focused by the ellipse to a
Biomechanical Effects of Shock Wave Therapy

For shock waves to be most effective, the stone should remain in the F2 focus during treatment. Pressure energy measurements show an exponential decrease beyond this small focal zone. The kidneys and the kidney stone follow the up-and-down movements of the diaphragm during respiration. The stone is likely to move in and out of focus during respiration. In the past, ventilatory techniques such as decreased tidal volumes with increased respiratory rates and high-frequency jet ventilation have been used to increase the efficacy of the treatment. However with contemporary lithotripsy machines, sedation and therefore spontaneous ventilation is the only option.

For effective stone disintegration, shock waves should reach the stone unimpeded. The flank area should be kept free of any medium that would provide an interface for the dissipation of shock wave energy. Nephrostomy dressings should be removed, and the nephrostomy catheter should be taped clear of the blast path. Although shock waves pass through most tissues relatively unimpeded, they do cause tissue injury, the extent of which depends on the tissue exposed and the shock wave energy at the tissue level. Skin bruising and flank ecchymoses can occur at the entry site. Painful hematoma in the flank muscles may occur. Hematuria is almost always present at the end of the procedure and results from shock wave–induced endothelial injury to the kidney and ureter. Adequate hydration is necessary to prevent clot retention. Lung tissue is especially susceptible to injury by shock waves. Air trapped in alveoli presents a classic water (tissue)-air interface to the shock wave and causes dissipation of energy. Massive hemoptysis and death from pulmonary damage have been reported in laboratory animals after a single exposure of the thorax to a shock wave. Shock wave–induced hemoptysis in a child and a pulmonary contusion with life-threatening hypoxemia in an adult have been reported. Children are more likely to sustain pulmonary damage from shock waves because of the shorter distance of the lung bases from the kidneys than in adults. It is recommended that a Styrofoam sheet or Styrofoam board be placed under the back in children to shield the lung bases from shock waves during ESWL.

Shock wave–induced cardiac arrhythmias previously reported in 10% to 14% of patients undergoing lithotripsy are extremely rare nowadays. Artifacts on electrocardiogram also are common. Artifacts and arrhythmias usually disappear when the lithotripsy is stopped.

Physiologic Changes during Immersion Lithotripsy

Water immersion with the Dornier HM-3 lithotripter produces significant changes in the cardiovascular and respiratory systems (Box 72-3).

Anesthetic Choices for Lithotripsy

Anesthetic regimens used successfully for lithotripsy include general anesthesia, epidural anesthesia, spinal anesthesia, and analgesia-sedation, including patient-controlled analgesia. General anesthesia offers the advantages of rapid onset and control of patient movement. Ventilatory variables can be controlled to decrease stone movement with respiration. With epidural anesthesia using loss of resistance to air to identify the epidural space, only the smallest amount of air necessary should be injected. Air in the epidural space provides an interface and can cause dissipation of shock wave energy and local tissue injury. Korb and associates found a decrease in epidural compliance and pain on injection with repeat epidurals for subsequent lithotripsies in their patients. In animal experiments, they were able to show epidural tissue damage after injection of air and exposure to shock waves. It is reassuring, however, that in most lithotripsies performed under epidural anesthesia worldwide, neurologic injury has not been a problem.

The main disadvantage of epidural anesthesia is its slow onset. Spinal anesthesia offers a reasonable alternative with its rapid onset. The incidence of hypotension (the patient is in a sitting position for treatment) is higher, however. In one series, the incidence of hypotension with general, epidural, and spinal anesthesia was 13%, 18%, and 27%, respectively. Local anesthetic infiltration of the flank with or without intercostal blocks provides adequate anesthesia when combined with intravenous sedation and avoids hypotension. Intravenous analgesia-sedation in various combinations has been used successfully.

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**BOX 72-3 Changes on Immersion during Lithotripsy**

<table>
<thead>
<tr>
<th></th>
<th>Increased</th>
<th>Central blood volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td></td>
<td>Central venous pressure</td>
</tr>
<tr>
<td>Increased</td>
<td></td>
<td>Pulmonary artery pressure</td>
</tr>
<tr>
<td>Increased</td>
<td></td>
<td>Pulmonary blood flow</td>
</tr>
<tr>
<td>Decreased</td>
<td></td>
<td>Vital capacity</td>
</tr>
<tr>
<td>Decreased</td>
<td></td>
<td>Functional residual capacity</td>
</tr>
<tr>
<td>Decreased</td>
<td></td>
<td>Tidal volume</td>
</tr>
<tr>
<td>Increased</td>
<td></td>
<td>Respiratory rate</td>
</tr>
</tbody>
</table>
Newer Lithotripters

Newer lithotripters have no water bath, and they tend to use multifunctional tables that allow other procedures, such as cystoscopy and stent placement, to be accomplished without moving the patient off the table. The shock waves are tightly focused; therefore, they cause less pain at the entry site, and intravenous analgesia-sedation is the mainstay of anesthesia with these newer lithotripters. Other incidental interventions, such as cystoscopy, stone manipulation, or stent placement, alter anesthetic requirements. Many of these newer lithotripters have a much smaller focal zone for the shock waves. It is even more imperative that adequate analgesia and sedation be provided, so that stone excursion with respiration is limited to the focal zone. Most analgesia-sedation combinations are adequate. Even patient-controlled analgesia with alfentanil and a combination of propofol and alfentanil has been used. Many centers routinely use general anesthesia with short-acting inhaled or intravenous anesthetics and use laryngeal mask airway for ventilation.

Contraindications

Pregnancy and untreated bleeding disorders are the only contraindications to lithotripsy. Women of childbearing age must have a pregnancy test that is documented to be negative before lithotripsy. Standard tests of coagulation, such as the platelet count, prothrombin time, and partial thromboplastin time, should be obtained as indicated by medical history. Pacemakers, automatic implanted cardioverter-defibrillators (AICDs), abdominal aortic aneurysm, orthopedic prostheses, and obesity are no longer considered contraindications. Patients with pacemakers can be treated safely if the pacemaker is pectorally placed and the following precautions are observed (see Chapter 48). Pacemaker programmability should be established before the treatment, and the pacemaker should be switched to a non-demand mode in case the shock waves interfere with pacemaker function. Alternative means of pacing should be available. Although most pacemakers located pectorally are at a safe distance from the blast path, some may be damaged. Weber and co-workers examined 43 different pacemakers and found that 3 were affected. Dual-chamber pacemakers tend to be more sensitive to interference. Treatment should be started at a low energy level and gradually increased while observing pacemaker function.

Manufacturers of AICDs and lithotripters have considered an AICD a contraindication for lithotripsy; however, patients with AICDs have been treated successfully with lithotripsy. AICD devices should be shut off immediately before lithotripsy and then reactivated immediately after treatment.

Patients with small aortic aneurysms have been treated safely, provided that the stone is not close to the aneurysm. Orthopedic prostheses, such as hip prostheses and even Harrington rods, are not a problem if they are not in the blast path, which is usually the case. Positioning of obese patients may be problematic at times. Not only do extremely obese patients present anesthetic challenges related to obesity, but also focusing of the stone may be extremely difficult in the very obese. It is prudent for focusing of the stone to be attempted before administering any anesthetic in this high-risk population.

RADICAL SURGERY IN UROLOGY

Radical surgery includes radical nephrectomy, radical cystectomy, and radical retropubic prostatectomy. Common features include lengthy procedures, associated sudden and significant blood loss, and attention to renal function preservation. With radical nephrectomy, significant cardiorespiratory changes attendant to the flank position are a concern. Respiratory changes include decreases in thoracic compliance, tidal volume, vital capacity, and functional residual capacity. Dependent atelectasis is common and can lead to hypoxemia. Pneumothorax may occur and can have significant respiratory and hemodynamic consequences intraoperatively. It is common to see a decrease in blood pressure when the kidney rest is raised. This decrease is usually due to compression of the inferior vena cava. In addition, hepatic encroachment on the vena cava and mediastinal shift may reduce venous return and stroke volume further. Cervical plexus, brachial plexus, and common peroneal neuropathies can occur because of stretch or compression of nerves in the lateral position.

Radical Nephrectomy for Renal Cell Carcinoma

The most common malignancy of the kidney is renal cell carcinoma; 85% to 90% of all solid renal masses are renal cell carcinoma. Because renal cell carcinoma is refractory to chemotherapy and radiation therapy, surgical resection or ablation can offer curative treatment of localized disease (Box 72-4). Recently, resection of the ipsilateral adrenal gland has been reserved for patients with large upper pole lesions or when the adrenal gland is enlarged or appears abnormal. Partial nephrectomy (nephron-sparing surgery) is considered for patients with small lesions or bilateral tumors or for patients at risk because of other diseases, such as diabetes or hypertension.

In 5% to 10% of patients, the tumor extends into the renal vein and the inferior vena cava and right atrium.

**BOX 72-4 Anesthetic Implications of Radical Nephrectomy for Tumors**

- 85%-90% are for renal cell cancer
- 5%-10% extension to the IVC and right atrium
- Large-bore IV access, A-line, IJV line (preferably on left side if IVC is involved)
- Paraneoplastic syndrome
- Hypercalcemia, eosinophilia; increased prolactin, erythropoietin, and glucocorticoids
- Occurs more frequently in men than women
- Chronic smoking history usually associated
- CAD, COPD
- Renal failure

CAD, Coronary artery disease; COPD, chronic obstructive pulmonary disease; IJV, internal jugular vein; IVC, inferior vena cava.
Tumor extension into the inferior vena cava and atrium occurs more frequently with right-sided renal cell carcinoma. Several problems can occur in these patients, ranging from circulatory failure as a result of complete occlusion of the vena cava by tumor to acute pulmonary embolization of tumor fragments during surgery. To operate on these patients safely, the extent of the lesion must be defined preoperatively. Cardiopulmonary bypass can be required. Central venous pressure in such cases might not reflect intravascular volume accurately, because venous return through the inferior vena cava is impaired by the thrombus and intraoperative transesophageal echocardiography may be of value.150 A decrease in venous return also predisposes the patient to hypotension during induction of anesthesia. Venous obstruction can lead to dilation of the epidural veins and the development of abdominal wall and retroperitoneal collaterals. The emphasis is on appropriate preoperative preparation, which is possible only when the full extent of the lesion has been defined.149

Radical Prostatectomy

Localized prostate cancer is treated by either radiation therapy or radical prostatectomy (Box 72-5). Radical prostatectomy has become more commonly performed because of routine prostate-specific antigen testing in men older than 50 years and popularization of the nerve-sparing surgery to reduce the risk of impotence. Although originally described in 1905 via the transperineal approach, the retropubic approach is mostly used now. The prostate, the ejaculatory ducts, the seminal vesicles, the bladder neck, and the pelvic lymph nodes are removed along with the pubic symphysis.

Traditionally, the procedure was performed by open laparotomy, but laparoscopic and robotic surgery are being used more frequently. A potential intraoperative problem with open radical prostatectomy is hemorrhage and massive blood loss requiring blood transfusion. Autologous predonation, preoperative recombinant erythropoietin therapy, intraoperative isovolemic hemodilution, and cell salvage are commonly practiced to reduce the patient’s exposure to allogeneic blood. Early postoperative complications, including deep vein thrombosis, pulmonary embolism, hematoma, seroma, and wound infection, occur in 0.5% to 2% of cases.151 Late complications include incontinence, impotence, and bladder neck contracture.152 Patients undergoing radical prostatectomy are placed supine in steep Trendelenburg position with the back extended, which places the pubis above the head. Air embolism from the prostatic fossa caused by a gravitational gradient between the prostatic veins and the heart has been reported.153

**Comparison of Anesthetic Techniques for Radical Prostatectomy**

Epidural anesthesia, spinal anesthesia, general anesthesia, and combined epidural and general anesthesia have been used for this surgery. For the epidural component of combined techniques, a thoracic or a lumbar approach to anesthesia or analgesia has been used, and spontaneous ventilation or intermittent positive-pressure ventilation (IPPV) has been used for the general anesthesia component. Many investigators have reported their findings in comparing the three anesthetic techniques for radical retropubic prostatectomy,154-157 and certain trends emerge.

Intraoperative blood loss is significantly less if epidural anesthesia or a combined epidural and general anesthetic with spontaneous ventilation is used. In one study, blood loss in the general anesthesia and the combined anesthesia group with IPPV was significantly more than in the epidural anesthesia group despite little difference in arterial pressure among the three groups.154 It was postulated that the increased venous pressure as a result of IPPV was the most likely cause of increased bleeding in the general and the combined anesthesia groups during radical prostatectomy. Previous studies have shown that central and peripheral venous pressure is lower in patients during spontaneous ventilation under epidural anesthesia or combined epidural-general anesthesia than in patients receiving IPPV during general anesthesia.158 Epidural anesthesia alone or when added to a general anesthetic decreases the risk of thromboembolism,159 decreases postoperative pain and analgesic requirements,160 and speeds recovery of bowel function. The length of stay and the cost of hospitalization can be decreased with the judicial use of epidural anesthesia and established clinical pathways.161,162 In one study, 80% of patients were satisfactorily discharged after 1 day, and the mean length of stay was 1.34 days.163

Possible differences in patient outcome with general versus epidural anesthesia are not clear. Local practices are therefore based on the preferences of the urologist, the anesthesiologist, and the patient.

**Robotic Assisted Radical Prostatectomy**

Many surgical advantages of robotic assisted radical prostatectomy (RARP) are described, including better visualization, more controlled finer movements of robotic arms allowing better dissection, decreased blood loss, less scarring and pain, shorter recovery time, faster return to daily activity, and possibly improved continence and potency.

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**Box 72-5 Anesthetic Implications of Radical Prostatectomy**

- Disease of the elderly
- CAD, COPD, and renal dysfunction
- Significant blood loss
- Wide-bore IV access and invasive monitoring
- Acute normovolemic hemodilution versus autologous blood donation
- Hyperextended position
- Nerve injuries, soft tissue injury, joint dislocations
- Venous air embolism
- Anesthesia
- Benefits of regional anesthesia versus general anesthesia debated
- Not known to influence mortality
- Epidural anesthesia with spontaneous ventilation decreases blood loss
- General or combined anesthesia with IPPV increases blood loss

CAD, Coronary artery disease; COPD, chronic obstructive pulmonary disease; IPPV, intermittent positive-pressure ventilation; IV, intravenous.
rates (although these last outcomes have been suggested only given the short-term follow-up at this time). Anesthetic concerns are primarily related to steep head-down tilt and pneumoperitoneum required for surgery.

Ventilatory and respiratory changes resulting from pneumoperitoneum include decreased compliance, increased airway pressures, and increased ventilation-perfusion mismatch. Application of positive end-expiratory pressure improves oxygenation in these patients. Hypercapnia develops within 15 to 30 minutes of carbon dioxide insufflation with resultant hypercarbia, acidosis, tachycardia, arrhythmias, and other deleterious hemodynamic and CNS effects. Increase in mechanical ventilation can obviate these changes in most patients, and most healthy patients tolerate the changes even though they are clinically significant. Extraperitoneal insufflation of carbon dioxide is associated with larger increases in arterial P\textsubscript{a}CO\textsubscript{2} than in intraperitoneal insufflation. Hemodynamic changes include decreased venous return with decreased cardiac output despite an increase in filling pressures indicative of increased intrathoracic pressures.

Physiologic changes resulting from steep Trendelenburg position include hemodynamic effects such as decreased perfusion pressure of lower extremities, increased mean arterial pressure at the circle of Willis, increased central blood volume, decreased cardiac output, and a decreased perfusion of vital organs in a normovolemic patient. Increased myocardial oxygen consumption, ischemia, arrhythmias, and decreased oxygen delivery are potential risks in patients with cardiac disease. Despite an observed twofold to threelfold increase of right- and left-sided filling pressures in ASA I and II patients during RARP, Lester and colleagues observed no significant changes in cardiac performance. Respiratory effects of steep head down tilt—decreased compliance, reduced vital capacity and functional residual capacity, 20% decrease in lung volumes, and ventilation-perfusion mismatch—compound the effects of pneumoperitoneum. Pulmonary congestion and edema have been reported in susceptible patients. A transient increase in serum creatinine secondary to pneumoperitoneum during robotic prostatectomy has been reported. Regurgitation in this position in patients with history of reflux increases their risk of aspiration of gastric contents. Maintaining normothermia may be a problem in some cases because of prolonged pneumoperitoneum with dry cold gases.

Other significant effects of steep head down tilt include increased intracranial pressure, increased intracranial pressure, venous air embolism, brachial plexopathy, arthralgias, compartment syndrome, and finger injuries. It has been recommended to perioperatively assess the function of a patient with a ventriculoperitoneal shunt scheduled for any laparoscopic procedure. Issues of increased intracranial pressure or consequences of a malfunctioning shunt with pneumoperitoneum in steep Trendelenburg position need to be realized. Kalmar and associates concluded patients overall clinically tolerated the influence of prolonged steep Trendelenburg position with CO\textsubscript{2} pneumoperitoneum on cardiovascular, cerebrovascular (including cerebral perfusion pressure and oxygenation), and respiratory homeostasis during robotic prostatectomy. Significant increases in intraocular pressure have been reported in robotic prostatectomy, but the clinical significance is unknown. Of concern is the reporting of at least six cases of postoperative visual loss following radical prostatectomy, three open and three robot-assisted laparoscopic prostatectomy cases. Chemosis (conjunctival edema) is common in RARP, but is usually self-limiting once the patient is taken out of the steep Trendelenburg position.

Compared with retropubic radical prostatectomy, RARP is usually associated with much less blood loss, except for one study. Mild to moderate pain is expected postoperatively, and low pain scores of 0 to 4 have been reported after retropubic radical prostatectomy and robotic assisted radical prostatectomy using preemptive analgesia with ketorolac given intraoperatively combined with rescue opiate or nonopiate analgesia. Most patients are discharged home the day after surgery. The use of robots in urologic surgery has been extended to include radical cystectomy, pyeloplasty, and renal and adrenal surgery in adults and children, and newer indications are developing. Other considerations in robotic surgery focus on the rigidly placed intraabdominal trocars attached to the robotic arms. Patient movement during the surgery could result in visceral or vascular injury. A constant need to assess degree of muscle relaxation intraoperatively is suggested. A plan among the perioperative team to dismantle the robotic arms in the unlikely event of cardiac arrest and need for advanced cardiac life support measures needs to be rehearsed.

### UROGENITAL PAIN SYNDROMES

Pain syndromes of the urogenital system can result from infection, anatomic anomaly, obstructive uropathy, nerve entrapment, or malignancy. The site, referral pattern, and quality of pain aid the clinician in identifying the source of pain—visceral, somatic, or neuropathic—and appropriate treatment (see Chapter 98).

### BENIGN RENAL TUMORS

Flank pain is a common symptom in adults with angiomyolipomas, which consist of abnormal growth of blood vessels, smooth muscle, and fat. This benign neoplasm can create a mass effect that affects renal function and acute worsening of pain should raise suspicion for rupture and hematoma formation. Angiomyolipomas can be associated with tuberous sclerosis, but are more commonly found in otherwise healthy individuals. Treatment is symptomatic with acetaminophen and neuromodulatory agents. Care should be taken with nonsteroidal anti-inflammatory drug (NSAID) use because renal function can be compromised.

### PEDIATRIC TUMORS

Wilms’ tumor (nephroblastoma) generally occurs unilaterally and is painless on initial presentation (see Chapter 93). It may be associated with congenital malformations such as Beckwith-Wiedemann syndrome. Treatment consists of surgical resection most often
supplemented by chemotherapy, because the tumor is highly responsive to this modality. Perioperative pain can be addressed with epidural anesthesia, acetaminophen, and opioids. Chemotherapy-induced neuropathy can best be treated with antineuropathic agents.

**RENAL CELL CARCINOMA**

Renal cell carcinoma is described as having a classic triad of hematuria, flank pain, and renal mass; however, pain can be a late presentation and may indicate metastatic disease. In cases of metastasis, prognosis is often poor and pain is widespread. Early consideration of an intrathecal catheter for continuous delivery of opioids, local anesthetic, or ziconotide can improve patient quality of life. Flank pain may be due to stretching of the Gerota fascia, and metastasis is primarily local along the renal vein and inferior vena cava or into the intercostal nerves, which produces segmental neuralgia. In these cases, intercostal nerve blocks and neurolysis or radiofrequency can be of use and accomplished under fluoroscopic or ultrasound guidance.

**INFECTIOUS RENAL DISEASES**

Infectious renal diseases producing flank pain include pyelonephritis and perinephric abscess. Fever is an important associated finding that suggests the presence of infection. Because the kidneys are retroperitoneal organs, peritoneal signs are absent. Differential diagnosis must include inflammatory or infectious disease of surrounding organs, including lower lobe pneumonia, pancreatitis, appendicitis, and cholecystitis. Oral or parenteral narcotics are effective for pain control in the acute setting. Systemic antibiotics are curative in most cases, although surgical intervention may be warranted, and a focal nidus for infection (stone, urethral reflux, recurrent urinary tract infections) should be pursued.

**NEURALGIAS**

Pseudorenal pain syndromes are caused by entrapment of nerves colocalized with the urinary system in the lower abdomen and groin. Neuralgia of the genitofemoral nerve is common after hernia surgery, given its close proximity and variable relation to the spermatic cord. Pain radiates to the inguinal ligament via the femoral branch and to the testicle via the genital branch. Injury to the iliohypogastric or ilioinguinal nerves can occur with lower abdominal incisions or trocar placement for laparoscopy, resulting in neuralgia radiating to the lower abdomen and groin. Pain sensation is generally neuropathic in these conditions and dermatomal testing will reveal sensory deficits. Nerve blocks can be performed under ultrasound guidance to help establish the diagnosis, differentiate from urogenital pain, and for therapeutic benefit. Antineuropathic drugs are also of help should nerve injury be confirmed (see Chapter 64).

**POLYCYSTIC KIDNEY DISEASE**

Polycystic kidney disease is most often inherited in an autosomal dominant manner and can lead to massive enlargement of the kidneys with compromised renal function. Renal pain is caused by distention of the cysts and stretching of the Gerota fascia. Hemorrhage into the cysts, rupture of the cysts, or infection can exacerbate pain. Percutaneous drainage of renal cysts can relieve the symptoms. Opioids are appropriate in the acute phase.

**OBSTRUCTIVE UROPATHY**

Obstruction of the urinary tract causes severe, spasmatic pain in the flank. Pain from the upper third of the ureter may be referred to the lower abdomen and back, pain from the middle third to the iliac fossa, and pain from the lower third to the suprapubic and groin area. Minimal fluid intake and a high concentration of stone-forming salts predispose to nephrolithiasis. Renal colic, hematuria, and radiopaque stones on radiography (70% to 75% of calculi) or noncontrast CT confirms the diagnosis. Opioids and NSAIDs are best for severe symptoms. Ketorolac through the intramuscular or intravenous route may be of use if oral medications are not tolerated. Of note, intravenous hydration has not demonstrated benefit despite widespread use.

**URINARY RETENTION**

Bladder pain is most commonly described as a poorly localized ache in the suprapubic region, typical of visceral pain. Acute bladder distention is manifested as severe suprapubic pain with associated urinary frequency. This can occur postoperatively after surgery without Foley catheter placement or after neuraxial local anesthetic and opioid administration resulting in urinary retention. Initial presentation can include emergence delirium. Drainage of the bladder, either by voiding or by catheterization, is recommended when volume exceeds 600 mL to avoid overdistention of the bladder with associated sequelae. Obstruction from urethral stone or prostatic hypertrophy should be addressed if present.

**INTERSTITIAL CYSTITIS**

Interstitial cystitis (painful bladder syndrome) is a chronic pain condition marked by suprapubic pain related to bladder filling and symptoms of increased frequency and urgency in the absence of infection or malignancy. Pathologic features of interstitial cystitis that may be evident, but are not necessary to make the diagnosis, include Hunner ulcers (discrete, bleeding areas on the bladder wall) and glomerulations (petechial bleeding after distention). The proposed pathophysiology is thought to be a deficient glycosaminoglycan layer that allows increased permeability of the bladder wall, resulting in inflammation and pain. Options for pain control include pentosan polysulfate (intended to repair the glycosaminoglycan layer), amitriptyline, antihistamines, dimethyl sulfoxide instillation, sacral nerve stimulators, and cystectomy.

**UROTHELIAL TUMORS**

The most common urothelial tumor is transitional cell carcinoma of the bladder. Painless hematuria is the most
common manifestation, although patients may complain of bladder irritability if there is involvement of the muscular layers. Surgical treatment includes fulguration, transurethral resection, or cystectomy. Pain control is best accomplished with NSAIDs, acetaminophen, opioids, and neuromodulatory agents.

**TESTICULAR PAIN**

Testicular pain can be the result of trauma, torsion, infection, or neoplasm. Trauma or torsion necessitate immediate restoration of blood flow, and emergency surgical exploration is the treatment of choice. Orchitis or epididymitis should be suspected based on a thorough history and if signs of localized or systemic infection accompany pain. Tumors of the testes are most often malignant; however, extratesticular tumors within the scrotum are usually benign. The earliest sign of tumor is usually a painless testicular mass. Pain is a late sign and is usually described as a dull ache or heaviness owing to mass effect, and it is most effectively addressed through debulking via surgery or radiotherapy.

**PROSTATITIS**

Acute prostatitis is usually caused by a bacterial infection and responds to antibiotic therapy. Chronic prostatitis has been more recently referred to as *chronic pelvic pain syndrome* to reflect that there is little certainty that inflammation of the prostate is responsible for symptoms. Symptoms include genital/pelvic pain and sexual dysfunction, often accompanied by lower urinary tract symptoms. Moderate improvement has been noted with antibiotics, α-blockers, antiandrogens, NSAIDS, and pelvic floor physiotherapy.

**PROSTATE CANCER**

Adenocarcinoma of the prostate is the most common male cancer and is usually painless and discovered incidentally through routine physical examination. Epidural anesthesia can be of use for acute pain control if brachytherapy with seeding is part of treatment. Lumbar or sacral pain with prostatic cancer may be a sign of metastatic disease to bone. High-dose opioids and bisphosphonates are indicated, and placement of an intrathecal catheter should be considered early.

**PRIAPISM**

Priapism is a prolonged erection over 4 hours in duration and can be ischemic (veno-occlusive) or nonischemic (arterial). The former represents an acute emergency, and prompt therapy should be instituted to control pain and prevent subsequent impotence from fibrosis of the corpora cavernosa. Treatment consists of a penile dorsal nerve block (performed at the pubic symphysis with needle entry into the subpubic space), which must be performed with local anesthetic without epinephrine, after which aspiration of blood or intercavernosal phenylephrine can be performed. Nonischemic priapism is most commonly posttraumatic and results from creation of an arteriolar-sinusoidal fistula. This type of priapism is typically not as painful and responds to conservative management. Sickle cell priapism is treated with hydration, alkalinization, and blood transfusion to increase hemoglobin to more than 10 mg/dL.

**PEYRONIE DISEASE**

Peyronie disease is a condition that causes severe penile pain during sexual intercourse because of excess curvature. The treatment of choice is surgery and NSAIDs as necessary for pain.

**FEMALE GENITAL PAIN**

Vulvodynia is a chronic pain condition associated with sexual inactivity or dysfunction because of vulvar pain. *Vestibulitis* refers to vulvodynia confined to the vestibule. Some success with tricyclic antidepressants, Sitz baths, local estrogen creams, and pudendal nerve blocks has been reported. Vaginismus is associated with increased tone of the muscles of the pelvic floor (pubococcygeus and levator ani) producing spasms and painful sexual dysfunction. Dyspareunia is defined as recurrent and persistent genital pain before or after intercourse not solely explained by infection, trauma, lubrication, or vaginismus. Psychological factors often play a major role. Treatment involves pelvic floor physiotherapy and desensitization techniques. Opioids are not indicated.

**CHRONIC PELvic PAIN**

Chronic dysmenorrhea can be addressed with ovulation suppression or use of NSAIDs, which decrease uterine lining thickness and cramping via an antiprostaglandin effect. Chronic pelvic pain may also be due to endometriosis, pelvic congestion, adhesions, or pelvic inflammatory disease—each of which is most responsive to correction of the underlying disorder for relief of pain. Cancer of the cervix or uterus can cause severe lower abdominal pain and requires aggressive opioids and referral for superior hypogastric plexus neurolysis or intrathecal medications.

**ROLE OF SYMPATHETIC BLOCKS**

The pelvic viscera in men and women—the urogenital organs, the distal colon, and the rectum—are supplied by afferent fibers from the distal lumbar sympathetic chain. Interruption of these pathways can be achieved with a superior hypogastric plexus block. The superior hypogastric plexus is a retroperitoneal structure situated along the anterior surface of the L5 and S1 vertebrae. It can be blocked using fluoroscopic guidance and instillation of phenol or ethanol. The ganglion impar is another promising target for neurolysis, supplying mixed somatic, autonomic, and visceral fibers to the distal urethra, vulva, perineum, and distal third of the vagina. It can be blocked along the anterior surface of the sacrococcygeal junction.

**GENERAL CONSIDERATIONS**

Specific to renal compromise, meperidine and morphine should be avoided because of the accumulation of renally
excreted metabolites, including normeperidine and morphine-3-glucuronide, which lower the seizure threshold, and morphine-6-glucuronide, which maintains activity at the μ-opioid receptor. The antiprostaglandin effect of NSAIDs can also decrease renal blood flow in susceptible patients. These agents must be used with caution.

General considerations for genitourinary pain management follow the same principles of pain management elsewhere in the body. For nonmalignant acute pain, nonnarcotic medications such as acetaminophen, aspirin, and NSAIDs are indicated as first line drugs. Tricyclic antidepressants and anticonvulsant agents are useful adjuncts, particularly for neuropathic pain. Opioids may be indicated in the short term. For malignancy, opioids are often necessary and in high doses. When oral administration is not feasible, parenteral administration of narcotics should be used.

Interventional techniques are an integral part of pain control in chronic urogenital pain syndromes and particularly for malignancy. Appropriate blocks can obviate or greatly reduce the need for systemic analgesics. If intractable pain persists despite optimized oral or intravenous therapy, a tunneled catheter trial can be performed and an implantable drug delivery system should be considered. Continuous intrathecal infusions minimize fluctuation of drug levels in cerebrospinal fluid and allow for significant analgesia and use of spinal adjuncts (local anesthetic, ziconotide) and opioids with significantly lessened dose-limiting side effects.

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Complete references available online at expertconsult.com.

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