cervix or colon) or inflammatory disorders. Lymphomas and pelvic or colonic neoplasms with retroperitoneal involvement are causes of ureteral obstruction. As many as 50% of men over 40 years old may have lower urinary tract symptoms associated with benign prostatic hypertrophy, but these symptoms may occur without bladder outlet obstruction.

*Functional impairment of urine flow* occurs when voiding is altered by abnormal pontine or sacral centers of micturition control. It may be asymptomatic or associated with lower urinary tract symptoms such as frequency, urgency, urge and postmicturition incontinence, nocturia, straining to void, slow stream, hesitancy, or a feeling of incomplete emptying. A history should be sought for trauma, back injury, surgery, diabetes, neurologic or psychiatric conditions, and medications. Causes include neurogenic bladder, often with adynamic ureter, and vesicoureteral reflux. Reflux in children may result in severe unilateral or bilateral hydroureter and hydronephrosis. Urinary retention may be the consequence of α-adrenergic and anticholinergic agents, as well as opiates. Hydronephrosis in pregnancy is due to relaxational effects of progesterone on smooth muscle of the renal pelvis, as well as ureteral compression by the enlarged uterus.

Diagnostic tools to identify anatomic obstruction include urinary flow measurements and a postvoid residual. Cystourethroscopy and urodynamic studies may be reserved for the symptomatic patient to assess the filling phase (cystometry), pressure-volume relationship of the bladder, bladder compliance, and capacity. Pressure-flow analysis evaluates bladder contractility and bladder outlet resistance during voiding. Bladder obstruction is characterized by high pressures in women, whereas in men, a diagnosis of bladder outlet obstruction is based on flow rate and voiding pressures. A voiding cystourethrogram may be useful in evaluating incomplete emptying and bladder neck and urethral pathology.

## CLINICAL FEATURES AND PATHOPHYSIOLOGY

The pathophysiology and clinical features of UTO are summarized in Table 343-2. *Pain*, the symptom that most commonly leads to medical attention, is due to distention of the collecting system or renal capsule. Pain severity is influenced more by the rate at which distention develops than by the degree of distention. Acute supravesical obstruction, as from a stone lodged in a ureter (Chap. 342), is associated with excruciating pain, known as *renal colic*. This pain often radiates to the lower abdomen, testes, or labia. By contrast, more insidious causes of obstruction, such as chronic narrowing of the ureteropelvic junction, may produce little or no pain and yet result in total destruction of the affected kidney. Flank pain that occurs only with micturition is pathognomonic of vesicoureteral reflux.

Obstruction of urine flow results in an increase in hydrostatic pressures proximal to the site of obstruction. It is this buildup of pressure that leads to the accompanying pain, the distention of the collecting system in the kidney, and elevated intratubular pressures that initiate tubular dysfunction. As the increased hydrostatic pressure is expressed in the urinary space of the glomeruli, further filtration decreases or stops completely.

*Azotemia* develops when overall excretory function is impaired, often in the setting of bladder outlet obstruction, bilateral renal pelvic or ureteric obstruction, or unilateral disease in a patient with a solitary functioning kidney. Complete bilateral obstruction should be suspected when acute renal failure is accompanied by anuria. Any patient with renal failure otherwise unexplained, or with a history of nephrolithiasis, hematuria, diabetes mellitus, prostatic enlargement, pelvic surgery, trauma, or tumor should be evaluated for UTO.

In the acute setting, partial, bilateral obstruction may mimic prerenal azotemia with concentrated urine and sodium retention. However, with more prolonged obstruction, symptoms of *polyuria* and *nocturia* commonly accompany partial UTO and result from diminished renal concentrating ability. Impairment of transcellular salt reabsorption in the proximal tubule, medullary thick ascending limb of Henle, and collecting duct cells is due to downregulation of transport proteins including the $Na^+$, $K^+$ adenosine triphosphatase (ATPase), $NaK_2Cl$ cotransporter (NKCC) in the thick ascending limb, and the epithelial $Na^+$ channel (ENaC) in collecting duct cells. Consequences include failure to produce urine free of salt (natriuresis) and loss of medullary hypertonicity producing a urinary concentrating defect. In addition to direct effects on renal transport mechanisms, increased prostaglandin $E_2$ ($PGE_2$) (due to induction of cyclooxygenase-2 [COX-2]), angiotensin II (with its downregulation of $Na^+$ transporters), and atrial or B-type natriuretic peptides (ANP or BNP) (due to volume expansion in the azotemic patient) contribute to the decreased salt reabsorption along the nephron.

Dysregulation of aquaporin-2 water channels in the collecting duct contributes to the polyuria. The defect usually does not improve with administration of vasopressin and is therefore a form of acquired nephrogenic diabetes insipidus.

Wide fluctuations in urine output in a patient with azotemia should always raise the possibility of intermittent or partial UTO. If fluid intake is inadequate, severe dehydration and hypernatremia may develop. However, as with other causes of poor renal function, excesses of salt and water intake may result in edema and hyponatremia.

Partial bilateral UTO often results in *acquired distal renal tubular acidosis, hyperkalemia*, and *renal salt wasting*. The $H^+$-ATPase, situated on the apical membrane of the intercalated cells of the collecting duct, is critical for distal $H^+$ secretion. The trafficking of intracellular $H^+$ pumps from the cytoplasm to the cell membrane is disrupted in UTO. The decreased function of the ENaC, in the apical membrane of neighboring collecting duct principal cells, contributes to decreased $Na^+$ reabsorption (salt-wasting), decreased electronegativity of the tubule lumen, and therefore decreased $K^+$ secretion via $K^+$ channels (hyperkalemia) and $H^+$ secretion via the $H^+$-ATPases (distal renal tubular acidosis [RTA]). Proximal tubule ammoniagenesis, important to the elimination of $H^+$ as $NH_4^+$, is impaired. These defects in tubule function are often accompanied by renal tubulointerstitial damage. Azotemia with hyperkalemia and metabolic acidosis should prompt consideration of UTO.

The renal interstitium becomes edematous and infiltrated with mononuclear inflammatory cells early in UTO. Later, interstitial fibrosis and atrophy of the papillae and medulla occur and precede these processes in the cortex. The increase in angiotensin II noted in UTO contributes to the inflammatory response and fibroblast accumulation through mechanisms involving profibrotic cytokines. With time, this process leads to chronic kidney damage.

**TABLE 343-2 PATHOPHYSIOLOGY OF BILATERAL URETERAL OBSTRUCTION**

| Hemodynamic Effects | Tubule Effects | Clinical Features |
|---|---|---|
| **Acute** | | |
| ↑ Renal blood flow<br>↓ GFR<br>↓ Medullary blood flow<br>↑ Vasodilator prostaglandins, nitric oxide | ↑ Ureteral and tubule pressures<br>↑ Reabsorption of $Na^+$, urea, water | Pain (capsule distention)<br>Azotemia<br>Oliguria or anuria |
| **Chronic** | | |
| ↓ Renal blood flow<br>↓↓ GFR<br>↑ Vasoconstrictor prostaglandins<br>↑ Renin-angiotensin production | ↓ Medullary osmolarity<br>↓ Concentrating ability<br>Structural damage; parenchymal atrophy<br>↓ Transport functions for $Na^+$, $K^+$, $H^+$ | Azotemia<br>Hypertension<br>AVP-insensitive polyuria<br>Natriuresis<br>Hyperkalemic, hyperchloremic acidosis |
| **Release of Obstruction** | | |
| Slow ↑ in GFR (variable) | ↓ Tubule pressure<br>↑ Solute load per nephron (urea, NaCl)<br>Natriuretic factors present | Postobstructive diuresis<br>Potential for volume depletion and electrolyte imbalance due to losses of $Na^+$, $K^+$, $PO_4^{2-}$, $Mg^{2+}$, and water |

***Abbreviations:*** AVP, arginine vasopressin; GFR, glomerular filtration rate.