URINARY SYSTEM
Part 2

OBJECTIVES:
- Cystic diseases of the kidney: including
  - Autosomal dominant polycystic kidney disease
  - Autosomal recessive polycystic kidney disease
  - Medullary cystic kidney disease
- Listing the causes and pathogenetic factor of an important cause of urinary outflow obstruction which is the nephrolithiasis and describing features and complication of its important complication which is the hydronephrosis.
- Listing the pathological features of renal cell carcinoma and its variants.
- Listing the pathological features of Wilms' tumor.
- Listing and describing the pathological features of ureteric, vesical, and urethral disorders including:
  - Congenital abnormalities
  - Inflammatory disorders
  - Tumors

CYSTIC DISEASES OF THE KIDNEY
These are a heterogeneous group comprising
- Hereditary
- Developmental but nonhereditary
- Acquired disorders.

They are important for several reasons:
1. They are practically common and often present diagnostic problems
2. Some are major causes of chronic renal failure (adult polycystic disease)
3. They can occasionally be confused clinically with malignant tumors.
4.

Simple Cysts: are a common but have no clinical significance. They can be multiple or single, commonly up to 5 cm in diameter. They are translucent; filled with clear fluid; lined by a single layer of cuboidal or flattened epithelium.

Dialysis-associated acquired cysts: occur with prolonged dialysis in those with end-stage renal disease. They may bleed, causing hematuria. Occasionally, renal adenomas or carcinomas arise in the walls of these cysts.

Autosomal Dominant (Adult) Polycystic Kidney Disease (ADPKD): is characterized by multiple expanding cysts of both kidneys that ultimately destroy the intervening parenchyma. ADPKD is responsible for 10% of all chronic renal failures. It is caused by inheritance of one of two autosomal dominant genes of very high penetrance. The kidneys may be very large (up to 4 kg for each), and thus are readily palpable abdominally. Grossly the kidney is composed of a mass of cysts of varying sizes (up to 4 cm). The cysts are filled with fluid (clear, turbid, or hemorrhagic).

Microscopically, the cysts have often atrophic, lining. The pressure of the expanding cysts leads to ischemic atrophy of the intervening renal substance.

Clinically: ADPKD in adults usually does not produce symptoms until the fourth decade, by which time the kidneys are quite large. Intermittent gross hematuria commonly occurs. The most important complications are hypertension and urinary infection.

Saccular aneurysms of the circle of Willis are present in up to 30% of patients, and these individuals have a high incidence of subarachnoid hemorrhage. Asymptomatic liver cysts occur in one-third of patients.
Autosomal Recessive (Childhood) Polycystic Kidney Disease (ARPKD) is a rare developmental anomaly that is genetically distinct from ADPKD. Perinatal, neonatal, infantile, and juvenile subcategories have been defined, depending on time of presentation and the presence of associated hepatic lesions. Both kidneys are invariably involved with numerous small cysts that give them a sponge-like appearance. The cysts are lined by cuboidal cells. ARPKD is associated with multiple epithelium-lined cysts in the liver. Young infants may die quickly from hepatic or renal failure.
**Medullary Cystic Disease (MCD)**

This is of two major types of

1. **Medullary sponge kidney** a relatively common and usually harmless condition and
2. **Nephronophthisis-medullary cystic disease complex**, which is associated with renal dysfunction (within 5-10 years). On the basis of the time of onset they are divided into, infantile, juvenile (the most common), adolescent, and adult types. Pathologic features of medullary cystic disease include small contracted kidneys with numerous small typically at the cortico-medullary junction.

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**URINARY OUTFLOW OBSTRUCTION**

**Renal Stones (Urolithiasis)** these are frequent (1% of all autopsies) and mostly form in the kidney. The majority (80%) are composed of either calcium oxalate or calcium oxalate mixed with calcium phosphate; 10% are of magnesium ammonium phosphate, and the remainder 10% are either uric acid or cystine stones. The most important cause is increased urine concentration of the stone's constituents (supersaturation). Those who develop calcium stones have

1. Hypercalciuria not associated with hypercalcemia due to either
   a. Absorption of calcium from the gut in excessive amounts (i.e. absorptive hypercalciuria)
   b. Primary renal defect of calcium reabsorption (renal hypercalciuria).

   **Hypercalcemia is present in only 5% to 10%** (due to hyperparathyroidism, vitamin D intoxication, or sarcoidosis) and consequent hypercalciuria. In 20% of this subgroup, there is excessive excretion of uric acid in the urine, which favors calcium stone formation; the urates provide a nidus for calcium deposition. A high urine pH favors crystallization of calcium phosphate and stone formation. Magnesium ammonium phosphate stones almost always occur in persistently alkaline urine due to UTIs, particularly with urea-splitting bacteria (as *Proteus vulgaris* and the *Staphylococci*).
Gout and diseases involving rapid cell turnover (as the leukemias), lead to high uric acid levels in the urine and uric acid stones. About half of the individuals with uric acid stones, however, have no hyperuricemia but unexplained tendency to excrete persistently acid urine (under pH 5.5), which favors uric acid stone formation (cf. stones containing calcium phosphate).

Common sites of formation are renal pelvis and calyces as well as the bladder. Stone may be small with smooth or jagged surface. Occasionally, progressive accumulation of salts leads to the development of branching structures known as staghorn calculi, which create a cast of the renal pelvis and calyceal system. These massive stones are usually composed of magnesium ammonium phosphate; these do not produce symptoms or significant renal damage. Smaller stones may pass into the ureter, producing a typical intense pain known as renal colic. Often at this time there is gross hematuria. The clinical significance of stones lies in their capacity to obstruct urine flow or to produce sufficient trauma to cause ulceration and bleeding. In either case, they predispose the sufferer to bacterial infection.

**Hydronephrosis** refers to dilation of the renal pelvis and calyces, with accompanying atrophy of the renal parenchyma, caused by obstruction to the outflow of urine. The obstruction may be sudden or insidious, and it may occur at any level of the urinary tract, from the urethra to the renal pelvis. The most common causes are

1. **Congenital**: e.g. urethral atresia, ureteric or urethral valves, aberrant renal artery
2. **Acquired**:
   a. **Foreign bodies**: calculi
   b. **Tumors of the prostate or bladder** (benign or malignant)
   c. **Contiguous malignant disease**: (retroperitoneal lymphoma, carcinoma of the cervix or uterus)
   d. **Inflammation**: prostatitis, ureteritis, urethritis
   e. **Neurogenic**: Spinal cord damage with paralysis of the bladder
f. **Normal pregnancy**: mild and reversible

**Bilateral hydronephrosis** occurs only when the obstruction is below the level of the ureters. If blockage is at the ureters or above, the lesion is unilateral. Sometimes obstruction is complete, allowing no urine to pass; usually it is only partial.

**Pathogenesis**

Even with complete obstruction, glomerular filtration persists for some time, and the filtrate subsequently diffuses back into the lymphatic and venous systems. Because of the continued filtration, the affected calyces and pelvis become dilated, often markedly so. The unusually high pressure thus generated in the renal pelvis, as well as that transmitted back through the collecting ducts, causes compression of the renal blood vessels. Both arterial insufficiency and venous stasis result. The most severe effects are seen in the papillae, because they are subjected to the greatest increases in pressure. Accordingly, the initial functional disturbances are largely tubular, manifested primarily by impaired concentrating ability. Thereafter the glomerular filtration begins to diminish. *Serious irreversible damage occurs in about 3 weeks with complete obstruction, and in 3 months with incomplete obstruction.*

**Gross features**

- The changes vary with the degree and speed of obstruction
  - With subtotal or intermittent obstruction, the kidney is massively enlarged consisting almost entirely of the greatly distended pelvicocalyceal system. The renal parenchyma shows compression atrophy, with obliteration of the papillae and flattening of the pyramids.
  - With sudden complete obstruction, glomerular filtration is reduced relatively early, and as a consequence, renal function may cease while dilation is still slight.
- Depending on the level of the obstruction, one or both ureters may also be dilated (hydroureter).

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**Hydronephrosis:**

There is marked dilation of the pelvi-calyceal system and thinning of renal parenchyma.
Microscopic features
- Early lesions show tubular dilation, followed by atrophy and fibrous replacement with relative sparing of the glomeruli. Eventually, in severe cases the glomeruli also become atrophic and disappear, converting the entire kidney into a thin shell of fibrous tissue.
- With sudden and complete obstruction, there may be coagulative necrosis of the renal papillae.

Course & prognosis
Bilateral complete obstruction produces anuria. When the obstruction is below the bladder, there is bladder distention. Incomplete bilateral obstruction causes polyuria rather than oliguria, as a result of defects in tubular concentrating mechanisms. Unilateral hydronephrosis may remain completely silent. Removal of obstruction within a few weeks usually permits full return of function; however, with time the changes become irreversible.

TUMORS
The kidney is the site of benign and malignant tumors. In general, benign tumors (such as small cortical adenomas or medullary fibromas) have no clinical significance. The most common malignant tumors of the kidney in descending order of frequency are
1. Renal cell carcinoma
2. Nephroblastoma (Wilms tumor)
3. Transitional cell carcinoma of the calyces and pelvis

Renal Cell Carcinoma (RCC)
This is derived from the renal tubular epithelium and represents the most common primary malignant tumor of the kidney (80%). The mean age of incidence is 50 to 70 years. Risk factors include:
- smoking,
- hypertension,
- obesity,
- occupational exposure to cadmium,
- and acquired polycystic disease complicating chronic dialysis (30-fold).

RCC are currently classified according to the molecular origins of these tumors. The three most common forms are
1. Clear Cell Carcinomas (80% of RCCs): these are made up of cells with clear or granular cytoplasm. The majority are sporadic, but may occur in familial forms or in association with von Hippel-Lindau disease (VHLD). The latter is autosomal dominant and characterized by predisposition to a variety of neoplasms including bilateral & often multiple RCC of clear cell type. Patients with VHLD inherit a germline mutation of the VHL gene on chromosome 3 and lose the second allele by somatic mutation. Thus, the loss of the normal copies of both these tumor suppressor genes gives rise to clear cell carcinoma. It has been also confirmed that homozygous loss of the VHL gene seems to be the common underlying molecular abnormality in both sporadic and familial forms of clear cell carcinomas.
2. Papillary Renal Cell Carcinomas (10%). These tumors are frequently multifocal and bilateral and like clear cell carcinomas, they occur in familial and sporadic forms. The cause is the MET proto-oncogene. It is the increased dosage of the MET gene
(due to duplications of chromosome 7) seems to encourage neoplastic growth abnormal growth in the proximal tubular epithelial cell precursors.

3. **Chromophobe RCCs**: these are the least common; they arise from intercalated cells of collecting ducts. Their name indicates that the tumor cells stain more darkly than cells in clear cell carcinomas. These tumors are unique in having multiple losses of entire chromosomes, including chromosomes 1 and 2. In general, they have a good prognosis.

**Pathologic features**

**Clear cell carcinoma**

**Gross features:**
- There is usually solitary spherical mass; large when symptomatic.
- The cut surface is variegated; yellow-orange to gray-white with red areas of hemorrhage. There are prominent areas of cystic degeneration.
- Although the margins of the tumor are well defined, with enlargement extension may occur in two directions
  1. Into the pelvicalyceal system & as far down as the ureter.
  2. Into the renal vein, then the inferior vena cava & even into the right side of the heart.
Microscopic features

- The classic lipid- & glycogen-laden clear cells have well defined cell membranes. The nuclei are usually small and round.
- These cells are mixed to varying extent with cells having granular pink cytoplasm.
- Some tumors exhibit marked degrees of anaplasia, with numerous mitotic figures and markedly enlarged, hyperchromatic, pleomorphic nuclei (sarcomatoid RCC).
- The stroma is usually scant but highly vascularized.

Papillary renal cell carcinomas
- Exhibit papilla formation with fibrovascular cores.
- They tend to be bilateral and multiple.
- The cells can have clear or, more commonly, pink cytoplasm.

The classical triad of painless hematuria (the most frequent), a palpable abdominal mass, and dull flank pain is characteristic. RCCs are well-known for their association with several paraneoplastic syndromes. Polycythemia may occur; it results from excessive secretion of erythropoietin by the tumor. Uncommonly, these tumors also produce a variety of hormone-like substances, resulting in hypercalcemia, hypertension, Cushing syndrome, etc. In many individuals the primary tumor remains silent and is discovered only after its metastases have produced symptoms. Common locations for metastases are the lungs and the bones. Forty percent of patients die of the disease.

Wilms Tumor (WT) (nephroblastoma)
This is the most common primary renal tumor of children and the third most common organ cancer in those younger than 10 years. WT may arise sporadically or be familial. Some congenital malformations are associated with an increased risk of developing Wilms' tumor such as aniridia, mental retardation, gonadal dysgenesis and renal abnormalities. These conditions are associated with inactivation of the Wilms' tumor 1 (WT1) gene, located on chromosome 11. This gene is critical to normal renal and gonadal development. Patients with the Beckwith syndrome (BWS); characterized by enlargement of individual body organs (e.g., tongue, kidneys, or liver) or hemihypertrophy of the entire body segments. In addition to Wilms' tumors, patients with BWS are also at increased risk for developing other cancers e.g. hepatoblastoma.
**Gross features**
- WT tends to be large, well-circumscribed mass with soft, homogenous, tan to gray cut section accentuated with occasional foci of hemorrhage, necrosis and cystic degeneration.

**Microscopic features**
- In WT there are attempts to recapitulate different stages of nephrogenesis.
- WT contain a variety of tissue components, but all derived from the mesoderm.
- The classic *triphasic combination* of blastemal, stromal, and epithelial cell types is observed in most lesions.
  - The blastemal component is represented by sheets of small blue cells
  - The epithelial component (differentiation) is represented by abortive tubules or glomeruli.
  - The stromal component is represented usually by fibroblastic cells or myxoid areas, although skeletal muscle "differentiation" and other mesenchymal elements may be seen.
- *The presence of anaplasia correlates with underlying p53 mutations, and the emergence of resistance to chemotherapy.*
Clinically, there is a readily palpable abdominal mass, which may extend across the midline and down into the pelvis. Fever and abdominal pain, with hematuria, are less frequent. The prognosis of Wilms' tumor is generally very good, and excellent results are obtained with a combination of nephrectomy and chemotherapy. WTs with diffuse anaplasia, especially those with extra-renal spread, have the least favorable outcome.

RENAL PELVIS, URETER, URINARY BLADDER & URTHERA URETERS

Congenital Anomalies these are rare, and mostly of little clinical significance. However, some may contribute to urine outflow obstruction. Incompetent ureterovesical junction predisposes to pyelonephritis. The majority of double ureters are unilateral and of no clinical significance. A congenital ureteropelvic junction obstruction is the most common cause of hydronephrosis in infants and children. There is agenesis of the kidney on the opposite side in a significant number of cases. Diverticula are saccular outpouchings acting as pockets of stasis and secondary infections. Hydroureter with elongation and tortuosity may be congenital leading to hydronephrosis if untreated.

Ureteritis may be one component of UTI. With long-standing chronic ureteritis, there may be aggregation of lymphocytes in the subepithelial region causing fine granular mucosal surface (ureteritis follicularis), or the mucosa may become sprinkled with tiny cysts (ureteritis cystica). Identical changes are found in the bladder. The two most common tumors and tumor-like lesions are fibroepithelial polyps and leiomyomas. Primary malignant tumors are similar to those arising in the renal pelvis, calyces, and bladder; the majority are transitional cell carcinomas. They cause obstruction and are most frequently during the sixth and seventh decades. They can be multiple and may occur concurrently with similar tumors in the bladder or renal pelvis.

Obstructive lesions of the ureters

A great variety of pathologic lesions may obstruct the ureters and give rise to hydroureter, hydronephrosis, and sometimes pyelonephritis. The more important causes include
1. impacted small stones
2. strictures (congenital or acquired),
3. primary carcinoma,
4. pregnancy,
5. retroperitoneal fibrosis & cancers of the rectum, bladder, prostate, ovaries, uterus and cervix.

Sclerosing Retroperitoneal Fibrosis is a fibrous proliferative inflammatory process encasing the retroperitoneal structures including the ureters and causing hydronephrosis. Two thirds of the cases are idiopathic. The remaining cases are attributed to drugs (ergot derivatives, β-adrenergic blockers), adjacent inflammatory conditions or malignant disease. It may be associated with mediastinal fibrosis, sclerosing cholangitis, and Riedel thyroiditis. This suggests that the disorder is systemic in distribution but preferentially involves the retroperitoneum. An autoimmune reaction, sometimes triggered by drugs, has been proposed.

URINARY BLADDER

Congenital anomalies

Diverticula are pouch-like evaginations of the bladder wall that may be congenital, but more commonly acquired due to persistent urethral obstruction (e.g. prostatic
hyperplasia or neoplasia). In both forms, there are frequently multiple sac-like pouches that range from less than 1 cm to 10 cm in diameter. Most diverticula are small and asymptomatic, but may be sites of urinary stasis that predispose to infection and the formation of bladder calculi.

**Exstrophy** is a developmental failure in the anterior wall of the abdomen and the bladder, so that the bladder communicates directly through a large defect with the surface of the body. The exposed bladder mucosa may undergo colonic glandular metaplasia and is subjected to infections. There is an increased risk of carcinoma.

**Vesicoureteral reflux** is the most common and serious anomaly that contributes to renal infection and scarring.

**Congenital fistulas** are abnormal connections between the bladder and the vagina, rectum, or uterus.

**Persistent urachus** refers to failure of the urachus to close in part or in whole. When it is totally patent, a fistulous urinary tract is created that connects the bladder with the umbilicus. Sometimes, only the central region of the urachus persists, giving rise to urachal cysts. Carcinomas, mostly adenocarcinomas, may arise in such cysts.

**ACUTE & CHRONIC CYSTITIS**

The common etiologic agents of **bacterial cystitis** are the E. coli, followed by Proteus, & Klebsiella. Women are more likely to develop cystitis due to their shorter urethras. Bacterial pyelonephritis is frequently preceded by cystitis, with retrograde spread of microorganisms into the kidneys and their collecting systems. **Tuberculous cystitis** is almost always a consequence of renal tuberculosis. **Fungal cystitis** is usually due to Candida albicans. It is particularly seen in immunosuppressed patients or those receiving long-term antibiotics. **Schistosomal cystitis** (Schistosoma haematobium) is common in certain Middle Eastern countries, notably Egypt. Viruses (e.g., adenovirus), Chlamydia, and Mycoplasma may also be causes of cystitis.

**Predisposing factors of cystitis include**

1. Urinary obstruction e.g. prostatic hyperplasia, bladder calculi, tumors
2. Cystocele or diverticula
3. Diabetes mellitus
4. Instrumentation
5. Immune deficiency.

**Hemorrhagic cystitis** sometimes complicates cytotoxic antitumor drugs (e.g. cyclophosphamide). **Radiation cystitis** is due to radiation of the bladder region. Most cases of cystitis take the form of nonspecific acute or chronic inflammation of the bladder. **Gross features**

- There is hyperemia of the mucosa.
- **Hemorrhagic cystitis** shows in addition a hemorrhagic component; this form is sometimes follows radiation injury, antitumor chemotherapy, or adenovirus infection.
- **Suppurative cystitis** is characterized by the accumulation of large amounts of suppurative exudate.
- **Ulcerative cystitis** refers to cystitis associated with ulceration of large areas of the mucosa, or sometimes the entire bladder mucosa.
- Persistence of the infection leads to chronic cystitis, which shows red, friable, granular, sometimes ulcerated mucosa. Chronicity is also associated with fibrous thickening and inelasticity of the bladder wall.

**Microscopic features**

- In acute cystitis there are the expected features of acute inflammation.
- In chronic forms there is chronic inflammatory cells infiltration with fibrosis.
Variants of chronic cystitis include *Follicular cystitis* and *Eosinophilic cystitis*

**Schistosomal cystitis:** urogenital bilharziasis is caused by *S. haematobium*. Eggs are deposited in the superior rectal vein. From there, they pass through anastomoses into the veins of the wall of urinary bladder. There they cause granulomatous cystitis with eosinophilic infiltrate & fibrosis. These granulomas are visible under endoscopy as minute granules referred to as “sand grain” cystitis. The eggs eventually die in the tissue with regressive calcification. The condition may be complicated by:

a. Extensive fibrosis that may impinge on the ureteric orifices with eventual hydronephrosis
b. Carcinoma of bladder that is frequently squamous in type; as this form of cystitis can be associated with squamous metaplasia of the native transitional epithelium.

**Special Forms of Cystitis**

These are distinctive by either their morphologic appearance or their causation.

1. **Interstitial Cystitis (Hunner Ulcer):** a painful form of chronic cystitis occurring most frequently in women. Cystoscopy shows fissures and punctate hemorrhages in the mucosa, sometimes with chronic mucosal ulcers (Hunner ulcers). Infiltration by mast cells is characteristic of this disease. The condition may be of autoimmune origin.

2. **Malakoplakia** is characterized macroscopically by soft, yellow, slightly raised mucosal plaques 3 to 4 cm in diameter and histologically by infiltration with large, foamy macrophages with debris of bacterial origin (mostly E. coli) (Fig. 21-27). In addition, laminated mineralized concretions (Michaelis-Gutmann bodies) are typically present. Similar lesions have been described in other organs e.g. colon, lungs, bones. It occurs with increased frequency in immuno-suppressed transplant recipients and as a result of defects in phagocytic or degradative function of macrophages.

3. **Polypoid Cystitis** is an inflammatory condition resulting from irritation to the bladder mucosa mostly by indwelling catheters. The urothelium is thrown into broad, bulbous, polypoid projections as a result of marked submucosal edema.

**METAPLASTIC LESIONS**

**Cystitis Glandularis and Cystitis Cystica:** these terms refer to common lesions in which nests of transitional epithelium (*Brunn nests*) grow downward into the lamina propria and undergo transformation of their central epithelial cells into columnar epithelium lining (**cystitis glandularis**) or cystic spaces lined by urothelium (**cystitis cystica**).
cystica). The two processes often coexist. In a variant of cystitis glandularis, goblet cells are present (intestinal metaplasia). Both variants are common microscopic incidental findings in relatively normal bladders and are not associated with an increased risk of adenocarcinoma. Two forms of metaplasia occur in response to injury:

1. Squamous Metaplasia
2. Nephrogenic Metaplasia (Nephrogenic Adenoma): the urothelium may be focally replaced by cuboidal epithelium, which can assume a papillary growth pattern with subjacent tubular proliferation.

TUMORS OF THE URINARY BLADDER AND COLLECTING SYSTEM (Renal Calyces, Renal Pelvis, Ureter, and Urethra)

The entire urinary collecting system from renal pelvis to urethra is lined with transitional epithelium, so its epithelial tumors assume similar morphologic patterns. Tumors in the collecting system above the bladder are relatively uncommon; those in the bladder, however, are a more frequent cause of death than are kidney tumors. 

**Gross features**

Four morphologic patterns are recognized that range from small benign papillomas to large invasive cancers. These tumors are classified into:

1. Benign papilloma (rare)
2. Papillary urothelial neoplasms of low malignant potential, and
3. Urothelial carcinoma (low and high grade)

**Papillomas** are very rare, small (up to 1 cm) benign tumors with frondlike structures having a delicate fibrovascular core covered by multilayered, well-differentiated
transitional epithelium. Such lesions are usually solitary. They rarely recur once removed. **Urothelial (transitional) cell carcinomas** range from papillary to flat, noninvasive to invasive and low grade to high grade. **Low-grade carcinomas** are always papillary and are rarely invasive, but they may recur after removal.

*High-grade carcinoma* can be papillary or occasionally flat; they may cover larger areas of the mucosal surface, invade deeper, and have a shaggier necrotic surface than do low-grade tumors. Occasionally, these cancers show foci of squamous cell differentiation, but only 5% of bladder cancers are true **squamous cell carcinomas**. Carcinomas of grades II and III infiltrate surrounding structures, spread to regional nodes, and, on occasion, metastasize widely.
Painless hematuria is the dominant clinical presentation of all these tumors. They affect men three times more frequently than women and usually develop between the ages of 50 and 70 years.

Risk factors of bladder cancer are:
1. Exposure to β-naphthylamine (50 times increased risk).
2. Cigarette smoking
3. Chronic cystitis
4. Schistosomiasis of the bladder
5. Certain drugs (cyclophosphamide).

A wide variety of genetic abnormalities are seen in bladder cancers; of these, mutations involving several genes on chromosome 9, p53, and FGFR3 are the most common.

The prognosis of bladder tumors depends on their histologic grade and the depth of invasion of the lesion; the latter is much more important. Except for benign papillomas, all tend to recur after removal. Lesions that invade the ureteral or urethral orifices cause urinary tract obstruction. Overall 5-year survival is 57%. With deep penetration of the bladder wall the 5-year survival rate is less than 20%.

Papillary tumors occur much less frequently in the renal pelvis than in the bladder, they nonetheless make up to 10% of primary renal tumors. Patients present with painless hematuria, and may develop hydronephrosis. Infiltration of the walls of the pelvis, calyces, and renal vein worsens the prognosis. Despite removal of the tumor by nephrectomy, fewer than 50% of patients survive for 5 years.

Cancer of the ureter is fortunately the rarest of the tumors of the collecting system. The 5-year survival rate is less than 10%.