PATHOLOGY of URINARY SYSTEM

 Approximately 10% of infants are born with potentially significant malformations of the urinary system. These abnormalities can range from bilateral renal agenesis, which is incompatible with life, hypogenesis of one kidney, which usually causes no problems unless the function of the remaining kidney is impaired, to polycystic kidney disease which greatly depends on type of its inheritance. The developmental process can result in kidneys that lie outside their normal position.

**Polycystic kidney diseases**

The disease is characterized by tubular dilatation with cyst formation in between normally functioning nephrons. The cysts may be single or multiple and can vary in size from microscopic to several centimeters in diameter. The polycystic kidney disease is of two types:

**I// autosomal recessive:** which is present at birth. It is rare disorder and inherited as a recessive AR trait, meaning that both parents are carriers of the gene and that there is a one in four chance of the parents having another child with the disorder. The condition includes bilateral and significant renal dysfunction accompanied by variable degrees of liver fibrosis and portal hypertension. The disorder can be diagnosed by ultrasonography. There is no known treatment for the disease. Approximately 75% of infants die during the perinatal period.

**II//*Autosomal dominant polycystic kidney disease*:** affects children and adults and also called *adult polycystic kidney disease*, this disorder is transmitted as an autosomal dominant trait. There is considerable variability in gene expression. The symptoms occur later in life and three types of genes are implicated: first gene is **polycystic kidney disease gene called PKD1,** located on chromosome 16, is responsible for approximately 85% of cases. Second gene, **called *PKD2***, which is located on chromosome 4, is responsible for a milder form of the disease. Third gene, ***PKD3*,** located on chromosome 11 is responsible for a minority of cases.

**OBSTRUCTIVE DISORDERS**

Urinary obstruction can occur in persons of any age and can involve any level of the urinary tract from the urethra to the renal pelvis. The two most damaging effects of urinary obstruction are (1) **stasis of urine**, which predisposes to infection and stone formation, and **(2) development of backpressure**, which interferes with renal blood flow, destroys kidney tissue, tubules are distended with urine and predisposes to **hydronephrosis**: (Hydronephrosis refers to dilation of the renal pelvis and calices, with atrophy of renal tissue, that is caused by obstruction to the outflow of urine. The obstruction may be sudden or insidious in onset and may occur at any level of the urinary tract). The destructive effects of urinary obstruction on kidney structures are determined by the **degree of obstruction** (*i.e.*, partial vs. complete, unilateral vs. bilateral) and the **duration of the obstruction**.

**Causes of UrinaryTract Obstruction**

|  |  |
| --- | --- |
| Renal pelvis | Renal stones |
| Papillary necrosis |
| Ureter | Renal stones |
| Pregnancy |
| Tumors that compress the ureter |
| Ureteral stricture |
| Congenital disorders of the ureterovesical junction and ureteropelvic junction strictures |
| Bladder and urethra | Bladder cancer |
| Neurogenic bladder |
| Bladder stones |
| Prostatic hyperplasia or cancer |
| Urethral strictures |
| Congenital urethral defects |

**Renal stones (Calculi**)

Kidney stones are crystalline structures that form from components of the urine. The most common cause of upper urinary tract obstruction is urinary stones. Although stones can form in any part of the urinary tract, most develop in the kidneys. Men are more frequently affected than women, with a ratio of 4/1. Kidney stones require a nidus, or nucleus, to form and a urinary environment that supports continued precipitation of stone components to grow.

Predisposing factors for stone formation:

1. Increases blood and urinary levels of stone components ca++ stones associated with hypercalcemia
2. Anatomic changes in urinary tract structures.
3. Metabolic and endocrine influences
4. Dietary factors.
5. Renal obstructive disorders.
6. Urinary tract infections.

**Types of Stones:** There are four basic types of kidney stones:

1. Calcium stones(*i.e.*, ca-oxalate or ca-phosphate)
2. Magnesium ammonium phosphatestones
3. Uric acid stones
4. Cystine stones.

**Calcium Stones**. Most kidney stones (70% to 80%) are calcium stones—calcium oxalate, calcium phosphate, or a combination of the two materials. Calcium stones usually are associated with increased concentrations of calcium in the blood and urine. Excessive bone resorption caused by immobility, bone disease, hyperparathyroidism, and renal tubular acidosis all are contributing conditions.

***Magnesium Ammonium Phosphate Stones.*** Magnesium ammonium phosphate stones, also called *struvite stones*, form only in alkaline urine and in the presence of bacteria that possess an enzyme called *urease*, which splits the urea in the urine into ammonia. The ammonia that is formed takes up a hydrogen ion to become an ammonium ion, increasing the pH of the urine so that it becomes more alkaline. Because phosphate levels are increased in alkaline urine and because magnesium always is present in the urine, struvite stones form. These stones enlarge as the bacterial count grows, and they can increase in size until they fill an entire renal pelvis. Because of their shape, they often are called *staghorn stones*. Struvite stones in usually are too large to ben passed and require lithotripsy or surgical removal.

***Uric Acid Stones.*** Uric acid stones develop in conditions of gout and high concentrations of uric acid in the urine. Unlike radiopaque calcium stones, uric acid stones are not visible on x-ray films. Uric acid stones form most readily in urine with a pH of 5.1 to 5.9. Thus, these stones can be treated by raising the urinary pH to 6 to 6.5 with potassium alkali salts.

***Cystine Stones.*** Cystine stones are rare. They are seen in cystinuria, which results from a genetic defect in renal transport of cystine. These stones resemble struvite stones except that infection is unlikely to be present.

**Theories of urinary stones formation:**

1. *The saturation theory* states that the risk of stone formation is increased when the urine is supersaturated with stone components (e.g., calcium salts, uric acid, magnesium ammonium phosphate, cystine).
2. The *matrix theory* proposes that organic materials, such as mucopolysaccharides derived from the epithelial cells that line the tubules, act as a nidus for stone formation. This theory is based on the observation that organic matrix materials can be found in all layers of kidney stones.
3. The *inhibitor theory* suggests that persons who have a deficiency of proteinsthat inhibit stone formation in their urine are at increasedrisk for stone formation. Kidney cells produce at least three proteinsthat are thought to slow the rate of calcium oxalate crystallization:**nephrocalcin, Tamm-Horsfall mucoprotein, anduropontin.** Nephrocalcin inhibits nucleation, aggregation,and growth of calcium oxalate stones. *Tamm-Horsfall mucoprotein*is impair crystal aggregation.Uropontin inhibits the growth of calcium oxalate crystals.

**Pathogenesis of renal obstructive disorders in calcium stone formation:**

Urinary obstruction and stagnation of urine predisposes to infection. If calculi formed first, it serves as foreign bodies and contribute to the infection. Once established, the infection is difficult to treat. If infection occur first it often caused by urea-splitting organisms (e.g., Proteus, staphylococci) that increase ammonia production and cause the urine to become alkaline. Calcium salts precipitate more readily in stagnant alkaline urine and calcium stone formed.

**URINARY TRACT INFECTIONS**

Urinary tract infections (UTIs) are the second most common type of bacterial infections seen by health care providers (respiratory tract infections are first).

**Etiologic bacteria**

Most UTIs are caused by *Escherichia coli*. Other common pathogens include gram *negative enterbacteriacae,* *Proteus, Klebsiella pneumoniae*, and gram positive *Staphylococcus saprophyticus and Enterococcus* species. Normal flora of skin can cause infection in immune compromised patients or after instrumentation. Bacteria can enter the kidneys either through the bloodstream or as an ascending infection from the lower urinary tract. Most infections are of the ascending type. Among the factors that contribute to bacterial virulence is the type of fimbriae (pili) that the bacteria possess.

**Risk (predisposing factors):**

1. Urinary obstruction: renal stones, neurogenic bladder a disorder that impair bladder emptying, men with diseases of the prostate benign prostatic hyperplasia BPH) .
2. Urine reflux: Reflux occurs when urine from the urethra moves into the bladder (i.e., urethrovesical reflux) or from the bladder into the ureters (i.e., vesicoureteral reflux).
3. Sexual activity: women more affected than men because of short urethra.
4. Urinary catheterization is the most common predisposing factors for nosocomial UTIs.

**Host Defenses against UTI:**

1. washout phenomenon,in which bacteria are removed from the bladder and urethraduring voiding
2. protective mucin layer that protects mucosa against bacterial invasion
3. peristaltic movements of ureter facilitate the movement of urine
4. secretory immunoglobulin A (IgA)
5. Phagocytic blood cells further assist in the removal of bacteria from the urinary tract.

**Signs and symptoms of urinary tract infections:**

* **Urgency: A strong, persistent urge desire to urinate**
* **Dysuria: A burning sensation when urinating**
* **Frequency: Passing frequent, small amounts of urine**
* **Hematuria: urine that appears red a sign of presence of blood in the urine**
* **Pelvic pain— suprapubic in lower UTI and loin pain radiate to the back (costovertebral) in upper UTI**

| **Part of urinary tract affected** | **Signs and symptoms** |
| --- | --- |
| Kidneys (acute pyelonephritis) | * Upper back and side (flank) pain
* High fever
* Shaking and chills
* Nausea
* Vomiting
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| Bladder (cystitis) | * Pelvic pressure
* Lower abdomen discomfort
* Frequent, painful urination
* Blood in urine
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| Urethra (urethritis) | * Burning with urination
* Discharge
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**Classification UTI:**
• *Lower UTI*

 Infections of the lower urinary tract (urethra, bladder). The most prominent symptoms are dysuria, frequency, urgency and urinary incontinence.

Cystitis: This type of UTI is usually caused by Escherichia coli (E. coli), a type of bacteria commonly found in the gastrointestinal (GI) tract. Other common pathogens include *gram negative enterobacteriacae* eg *Proteus, Klebsiella pneumoniae*, *or grame positive Staphylococcus saprophyticus* and *Enterococcus* species.

Honey moon cystitis: cystitis due to sexual activity of newly married couples.

Urethritis:sexually transmitted infections, such as herpes, gonorrhea, chlamydia and mycoplasma, are the most common cause of urethritis. G-ve enterobact. also cause of urethritis

* **Upper UTI**

**Pyelonephritis**

Refers to an inflammation of the kidneys and renal pelvis. There are two forms of pyelonephritis: acute and chronic.

*Acute pyelonephritis* represents a patchy interstitial suppurative inflammatory process. Infection may occur through bloodstream or ascend from the bladder. Bacteria such as *E. coli* often cause the infection. However, any serious infection in the bloodstream can also spread to the kidneys and cause acute pyelonephritis.

The onset of acute pyelonephritis typically is abrupt, with chills, fever, headache, back pain, tenderness over the costovertebral angle, and general malaise. It usually is accompanied by symptoms of bladder irritation, such as dysuria, frequency, and urgency.

Complications:

1. Chronic pyelonephritis
2. abscess formation
3. tubular necrosis

*Chronic pyelonephritis* represents a progressive process usually associated with unresolved obstructive renal diseases. There is scarring and deformation of the renal calices and pelvis due to chronic pyelonephritis.