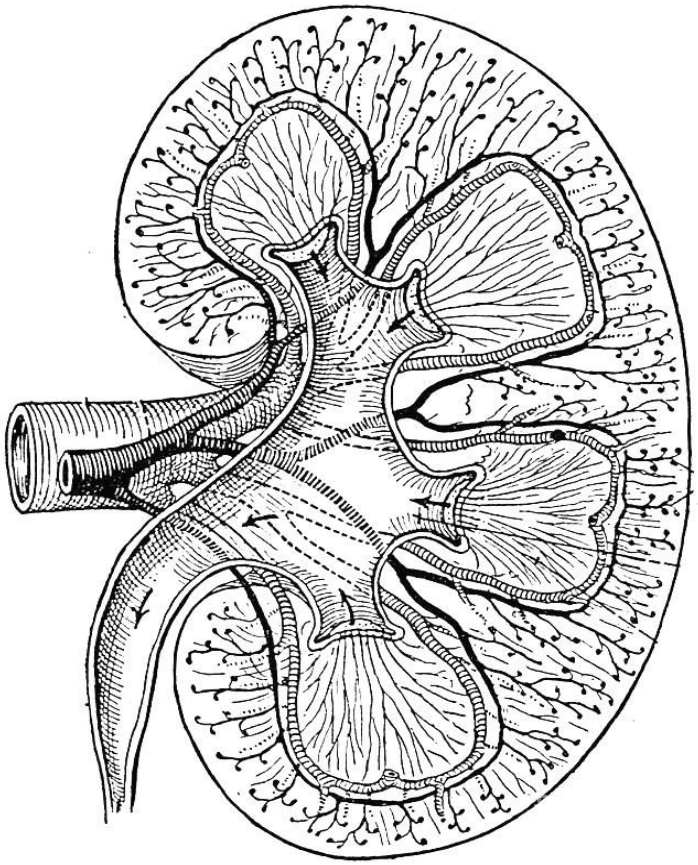
Microbiology

435's Teamwork
Renal Block



- Please contact the team leaders for any suggestion, question or correction.
- Pay attention to the statements highlighted in **bold** and\or red.
- Extra explanations are added for your understanding in grey.
- **Footnotes color code:** General | Females | Males.

Microbiology.435@gmail.com

Acute Pyelonephritis

- Lecture Three -

Introductive Video

Learning Objectives:

- **Define** the term Pyelonephritis.
- Know the **bacterial causes** of Pyelonephritis.
- Know the **pathogenesis** of Pyelonephritis.
- Know the clinical features of **acute** Pyelonephritis and **chronic** Pyelonephritis.
- State the **laboratory** and **radiological** diagnostic tests used for Pyelonephritis.
- State the **complications** of Pyelonephritis, mainly those of chronic Pyelonephritis.
- Know the **management** of Pyelonephritis (nursing / antimicrobial management).

Dr. Fauzia's introduction:

- UTIs are important because they are a category of seriously **common** diseases.
- Typically happens during **childhood**, kids are susceptible to UTIs.
- **When is it going to be considered serious?** When the kidney is involved.

One mild urinary tract infection is not enough to cause a serious kidney disease, this means that in order for it to occur, it needs a compromised kidney that with an affected function, and that usually occurs due to recurrent infections.

Acute pyelonephritis is usually a self-limiting disease that does not need aggressive treatment, however, if this infection reoccurs (becomes **recurrent)** or transferred into chronic pyelonephritis, then our prognosis becomes bad, because that leads to a very serious kidney disease that typically ends with failure.

Remember that the kidney have the ability to compensate (make up), it acts just like the heart. We learned that when the heart is affected by a disease, it takes a long time trying to compensate to its function. The kidney as well will not give up to one UTI, it will persist trying to compensate its normal function, however, recurrent infection will cause fibrosis... imagine this fibrosis happening in the glomeruli! As we know the glomeruli plays a major role in filtration, this means that there will be a defect in creatinine filtration.

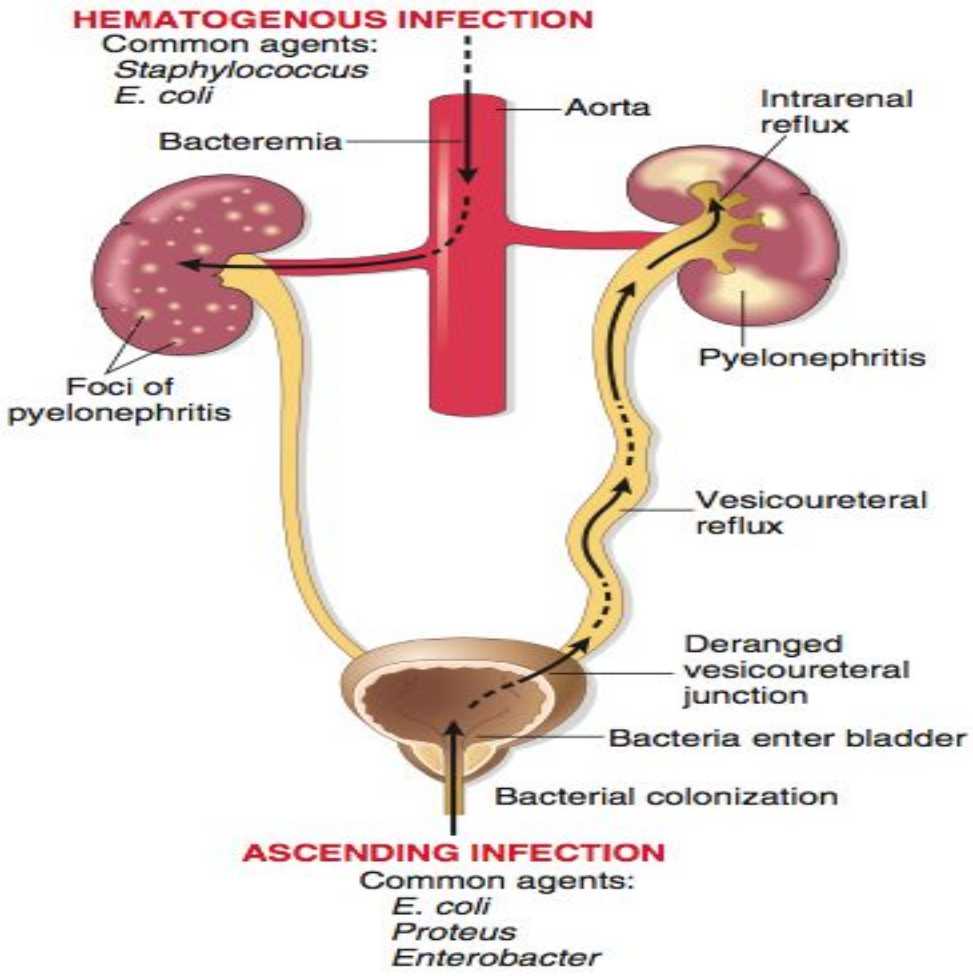
Sometimes the patient is present with no symptoms, usually complaining of any other disease at the ER, and we find out that he has a high creatinine level by taking a routine urine sample through our laboratory examination, and this, of course, indicates for renal failure.

Original Introduction:

Pyelonephritis is an inflammation (due to infection) of the **renal tubules**, **interstitial** tissue or **pelvis** of one or both kidneys. It is commonly caused by bacterial infections that:

1. **Ascended from the lower urinary tract.**
2. **Travelled through the bloodstream to the kidneys (hematogenous spread).**[1]

It can be a life-threatening semi-systemic infection that characteristically cause some **scarring** of the kidney with each infection that lead to significant damage to the kidney and hypertension[2].



[1] Most common: *Staph.aureus* and *T.B.*

[2] Kidney disease can cause 2 things: Hypertension + Renal failure. (major complications of pyelonephritis).

<table>
<tr><th colspan="3">Etiology</th></tr>
<tr><th>Ascending</th><th>Haematogenous</th><th>Nosocomial</th></tr>
<tr><td>Enteric gram-negative rods:
Escherichia coli is the most common (%80)</td><td>Gram positive bacteria:
Staphylococcus aureus[3]</td><td rowspan="2">Coliforms</td></tr>
<tr><td>Enterobacteria:
Klebsiella pneumoniae
Proteus[4] species (cause renal stone)</td><td>Mycobacterium tuberculosis</td></tr>
<tr><td>Gram negative rods:
Pseudomonas aeruginosa[5]</td><td>Gram negative rods:
Salmonella typhi</td><td rowspan="3">Enterococci</td></tr>
<tr><td rowspan="2">Gram positive bacteria:
Enterococcus faecalis
[6]Staphylococcus saprophyticus[7]</td><td>Gram-negative bacteria:
Brucella melitensis</td></tr>
<tr><td>Candida species[8]</td></tr>
</table>

Pathology:

- Pyelonephritis may be acute or chronic.
- Frequently due to ureterovesical reflux[9].
- Interstitial infiltration of inflammatory cells/Kidneys enlarge.
- Abscesses on the capsule and at corticomedullary junction.
- Result in destruction of tubules and the glomeruli.
- When chronic, kidneys become scarred, contracted and nonfunctioning.

Pathogenesis:

1. Rectal and/or vaginal reservoirs[10].
2. Colonization of perianal[11] area.
3. Bacterial migration to perivaginal[12] area.
4. Bacteria ascend through urethra to the bladder.
5. Intercourse (communication between the colonies) may contribute.
6. urethral colonization and ascending infection.
7. Asymptomatic-bacteriuria in 1st trimester[13] of pregnancy cause pyelonephritis in 3rd trimester.

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[3] Associated with pyuria (pus in urine). If the culture was positive we should look for abscess elsewhere.
[4] Can produce urease, which changes the urine pH into alkaline level + swarming appearance in culture.
[5] Hospital acquired and multidrug resistant.
[6] Nosocomial (hospital acquired infection)
[7] Why? Because it's a normal vaginal flora. It can easily cause UTI during sexual activity.
[8] Infects diabetics (the immunocompromised).
[9] Abnormal flow of urine from your bladder back up the tubes (ureters) that connect your kidneys to your bladder. Usually happens in children. Might happen asymptomatically in a child so he will have recurrent asymptomatic urinary tract infection that might end with renal disease because of this undiagnosed recurrent urinary tract infection.
[10] A place where fluid collects.
[11] Area around the anus.
[12] Area around the vagina.
[13] Pregnancy is divided into three terms of the fetus's development.

Risk factors	
Mechanical	**Constitutional**[14]

• Structural abnormalities of the kidneys and the urinary tract.
• Vesicoureteral reflux (VUR[15]) especially in young children.
• Calculi (kidney stones).
• Urinary tract catheterisation.
• Nephrostomy[16].
• **Pregnancy**.
• Neurogenic bladder[17] due to:
  - Spinal cord damage
  - Spina bifida[18]
  - Multiple sclerosis
• **Prostate** disease such as:
  - Benign prostatic hyperplasia in elderly men(usually faecalis).
• Bladder tumours.
• Urethral strictures[19].
	Diabetes mellitus
	
	Immunocompromised
	Usually without fever

Clinical Manifestations[20]		
General	**Kidney region**	**Lower tract**
Acutely ill[21]	Flank pain	**Dysuria**
Chills and Fever (>38°C)		
Nausea and vomiting	Renal angle tenderness	**Frequency**
Mental confusion in elderly		
Leukocytosis[22], Pyuria and Bacteriuria		

[14] The physical makeup of a body, including the mode of performance of its functions, the activity of its metabolic processes, the manner and degree of its reactions to stimuli, and its power of resistance to the attack of pathogenic organisms or other disease processes.

[15] It is so important that the students understand the VUR

[16] Insertion of a catheter through the skin and into the renal pelvis.

[17] Dysfunction caused by neurologic damage.

[18] Birth defect where there is incomplete closing of the membranes around the spinal cord.

[19] Abnormal narrowing of the urethra.

[20] Pyelonephritis is characterized by bacteremia so it is very important to do a blood culture.
(Any case of pyelonephritis you have to do both urine and blood culture.)

[21] General unwelling.

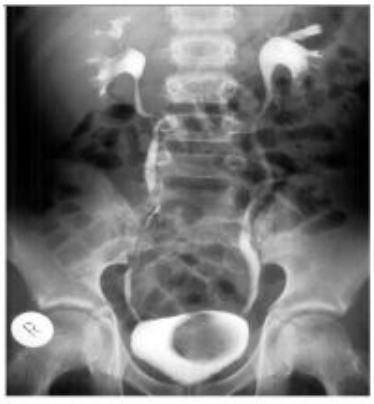
[22] It is absent in infection which caused by Enterobacteria because alkaline urine will breakdown the WBCs

Diagnosis:

It is not always straightforward.

A number of studies using **immunochemical markers** have shown that **women**, who were initially present with **lower** tract symptoms, actually have pyelonephritis. The extremes of age, the presentation may be so atypical in the very **young** (**feeding difficulty** or fever). In the **elderly**, presentation may include mental status change like **confusion** or fever.

<table>
<tr><th colspan="3">Laboratory Diagnosis of pyelonephritis</th></tr>
<tr><td rowspan="3">Urinalysis</td><td>Microscopy</td><td>Pyuria: Presence of pus cell (10 pus cells/cmm) unspun urine.</td></tr>
<tr><td>Gram stain</td><td>1 organism indicate 10^5 significant bacteriuria.</td></tr>
<tr><td>Biochemical (Dipstick test)</td><td>1) Positive Nitrate reduction to Nitrite by enterobacteriaceae e.g. E. coli
- False-negative results are common.
2) Leukocyte esterase indicate presence of pus cells.</td></tr>
<tr><td>Blood Culture</td><td colspan="2">• As acute Pyelonephritis is most accompanied by fever and Bacteremia.
• Blood culture important as this is systemic infection.</td></tr>
<tr><td>Urine culture</td><td colspan="2">To confirm your diagnosis and if there is no bacteremia</td></tr>
<tr><td rowspan="2">Radiological investigations</td><td colspan="2">• These indicate Kidneys and urinary tract abnormalities in chronic Pyelonephritis.
• CT scan or IVP (intravenous contrast pyelogram).
• Radionuclide imaging with gallium citrate and indium-111-labeled WBCs.</td></tr>
<tr><td colspan="2"> 

Micturition cystourethrogram (MCU) showing bilateral VUR, grade IV on right and grade III on left-side. There is bilateral ureteral and pelvic dilation with blunting of fornices in the right kidney.
 
Bilateral reflux extending into the pelvicalyceal systems of the kidney without dilatation of the calyces and ureters. (Note the catheter in bladder)</td></tr>
</table>

Chronic Pyelonephritis

The term "chronic pyelonephritis" is used to describe inflamed, scarred (with fibrous), contracted kidneys which are in usually in association with compromised renal function. Repeated bouts of acute pyelonephritis may lead to chronic pyelonephritis that damages the kidney and cause hypertension.

Clinical manifestations:

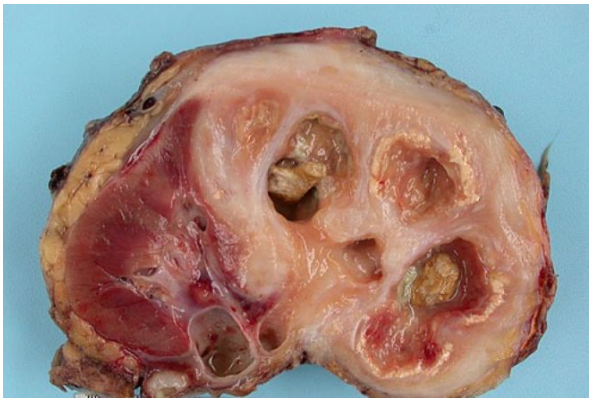
- **No symptoms** of infection unless an acute exacerbation[23] occurs.
- Progressive **scarring** that leads to renal failure.
- **Headache** and **fatigue**.
- Excessive thirst and poor appetite.
- Polyuria[24].
- Weight loss.

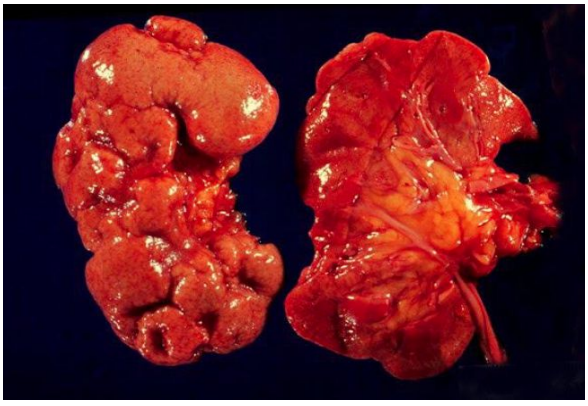
Diagnostic findings:

- Intravenous pyelogram[25] (IVP).
- **Serum creatinine**.
- **Blood urea.**
- **Culture** and **sensitivity** tests.

Complications:

- End stage renal disease.
- Hypertension.
- Kidney stones.





[23] Increase in the severity of a disease or its signs and symptoms.
[24] Production of abnormally large volumes of dilute urine.
[25] X-ray examination of the urinary tract that uses iodinated contrast material injected into veins.

Treatment of Pyelonephritis[26]

Eradicate[27] pathogens in kidney and urothelium, and treat/prevent bacteremia.

Mild or Moderate symptoms

- Outpatient treatment (total of 7–14 days).
- **Oral** treatment:
- **Fluoroquinolone**.
- TMP/SMX, if uropathogen is known to be susceptible.
- If Gram-positive pathogen: Amoxicillin or Amoxicillin-clavulanate or Ampicillin.
- Gentamicin[28] .

Hospitalized patients

- IV antibiotic first 48–72 hours followed by 7 days of oral antibiotic therapy.
  - Fluoroquinolone IV, then PO[29].
  - Aminoglycoside ± ampicillin IV, then TMP/SMX PO.
  - Third-generation cephalosporin IV, then TMP/SMX PO.

Ambulatory patients[30]

- 7–14 days of PO therapy with one of the antimicrobials above

Acute Pyelonephritis

- Treated as outpatients if there is no nausea, vomiting or dehydration and other signs and symptoms of sepsis.
- Very ill patients and all pregnant women are hospitalized at least for 2 to 3 days for parenteral therapy.
- 2 weeks course of:
  - Bactrim
  - Ciprofloxacin
  - Gentamicin with or without amoxicillin
- Another 6 weeks course if relapse
- Chronic or recurring symptomless infection persisting for months or years.
- Follow up urine culture 2 weeks after completion of therapy.

Chronic Pyelonephritis

- Medical Treatment is according to culture and sensitivity result.
- Drugs carefully titrated[31] if renal function is impaired.
- Fluids encouraged unless contraindicated.
- Bed rest, 4th hourly temperature is measured.
- Antibiotics.
- Teach how to prevent recurrent infections
- Adequate fluids, emptying the bladder regularly and performing recommended perineal hygiene taking antibiotics as prescribed.

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[26] Route of administration is important.
[27] Destroy completely.
[28] Best for gram -ve.
[29] The expression is used in medicine to describe a treatment that is taken orally.
[30] Capable of walking; not bedridden.
[31] Measure and adjust the balance of drug dosage.

Resources:
Dr Fawziya Alotaibi's 2016 lecture.
P. 868-869 Sherris Medical Microbiology.
P. 533-535 Robbins Basic Pathology.

Helpful read:
Medical news
Acute Pyelonephritis
Chronic Pyelonephritis

Additional Videos:
Acute Pyelonephritis
Chronic Pyelonephritis

PATHOGENESIS

The principal causative organisms in acute pyelonephritis are the enteric gram-negative rods. *Escherichia coli* is by far the most common one. Other important organisms are *Proteus, Klebsiella, Enterobacter,* and *Pseudomonas;* these usually are associated with recurrent infections, especially in persons who undergo urinary tract manipulations or have congenital or acquired anomalies of the lower urinary tract (see later). Staphylococci and *Streptococcus faecalis* also may cause pyelonephritis, but they are uncommon pathogens in this setting.

Bacteria can reach the kidneys from the lower urinary tract (ascending infection) or through the bloodstream (hematogenous infection) (Fig. 13–13). **Ascending infection from the lower urinary tract is the most important and common route by which the bacteria reach the kidney.** Adhesion of bacteria to mucosal surfaces is followed by colonization of the distal urethra (and the introitus in females). Genetically determined properties of both the urothelium and the bacterial pathogens may facilitate adhesion to the urothelial lining by bacterial fimbriae (proteins that attach to receptors on the surface of urothelial cells), conferring susceptibility to infection. The organisms then reach the bladder, by expansive growth of the colonies and by moving against the flow of urine. This may occur during urethral instrumentation, including catheterization and cystoscopy. Although **hematogenous spread** is the far less common of the two, acute pyelonephritis may result from seeding of the kidneys by bacteria in the course of septicemia or infective endocarditis.

In the absence of instrumentation, UTI most commonly affects females. Because of the close proximity of the female urethra to the rectum, colonization by enteric bacteria is favored. Furthermore, the short urethra, and trauma to the urethra during sexual intercourse, facilitate the entry of bacteria into the urinary bladder. Ordinarily, bladder urine is sterile, as a result of the antimicrobial properties of the bladder mucosa and the flushing mechanism associated with periodic voiding of urine. With outflow obstruction or bladder dysfunction, however, the natural defense mechanisms of the bladder are overwhelmed, setting the stage for UTI. In the presence of stasis, bacteria introduced into the bladder can multiply undisturbed, without being flushed out or destroyed by the bladder wall. From the contaminated bladder urine, the bacteria ascend along the ureters to infect the renal pelvis and parenchyma. Accordingly, UTI is particularly frequent among patients with urinary tract obstruction, as may occur with benign prostatic hyperplasia and uterine prolapse. UTI frequency also is increased in diabetes because of the increased susceptibility to infection and neurogenic bladder dysfunction, which in turn predisposes to stasis.

Incompetence of the vesicoureteral orifice, resulting in **vesicoureteral reflux** (VUR), is an important cause of ascending infection. The reflux allows bacteria to ascend the ureter into the pelvis. VUR is present in 20% to 40% of young children with UTI, usually as a consequence of a congenital defect that results in incompetence of the ureterovesical valve. VUR also can be acquired in persons with a flaccid bladder resulting from spinal cord injury or with neurogenic bladder dysfunction secondary to diabetes. VUR results in residual urine after voiding in the urinary tract, which favors bacterial growth. Furthermore, VUR affords a ready mechanism by which the infected bladder urine can be propelled up to the renal pelvis and farther into the renal parenchyma through open ducts at the tips of the papillae **(intrarenal reflux).**

MORPHOLOGY

One or both kidneys may be involved. The affected kidney may be normal in size or enlarged. **Characteristically, discrete, yellowish, raised abscesses are grossly apparent on the renal surface** (Fig. 13–14). They may be widely scattered or limited to one region of the kidney, or they may coalesce to form a single large area of suppuration.

The characteristic histologic feature of acute pyelonephritis is liquefactive necrosis with abscess formation within the renal parenchyma. In the early stages pus formation (suppuration) is limited to the interstitial tissue, but later abscesses rupture into tubules. Large masses of intratubular neutrophils frequently extend within involved nephrons into the collecting ducts, giving rise to the characteristic white cell casts found in the urine. Typically, the glomeruli are not affected.

When obstruction is prominent, the pus may not drain and then fills the renal pelvis, calyces, and ureter, producing pyonephrosis.

A second (and fortunately infrequent) form of pyelonephritis is necrosis of the renal papillae, known as **papillary necrosis.** There are three predisposing conditions for this: diabetes, urinary tract obstruction, and analgesic abuse. This lesion consists of a combination of ischemic and suppurative necrosis of the tips of the renal pyramids (renal papillae). The pathognomonic gross feature of papillary necrosis is sharply defined gray-white to yellow necrosis of the apical two thirds of the pyramids. One papilla or several or all papillae may be affected. Microscopically, the papillary tips show characteristic coagulative necrosis, with surrounding neutrophilic infiltrate.

When the bladder is involved in a UTI, as is often the case, **acute** or **chronic cystitis** results. In long-standing cases associated with obstruction, the bladder may be grossly hypertrophic, with trabeculation of its walls, or it may be thinned and markedly distended from retention of urine.

Clinical Course

Acute pyelonephritis often is associated with predisposing conditions, as described previously in the discussion of pathogenetic mechanisms. These factors include

- *Urinary obstruction,* either congenital or acquired
- *Instrumentation* of the urinary tract, most commonly catheterization
- *Vesicoureteral reflux*
- *Pregnancy*—4% to 6% of pregnant women develop bacteriuria sometime during pregnancy, and 20% to 40% of these eventually develop symptomatic urinary infection if not treated.
- *Female gender and patient age.* After the first year of life (an age by which congenital anomalies in males commonly become evident) and up to approximate age 40 years, infections are much more frequent in females. With increasing age, the incidence in males rises as a result of the development of prostatic hyperplasia, which causes urinary outflow obstruction.
- *Preexisting renal lesions,* causing intrarenal scarring and obstruction
- *Diabetes mellitus,* in which common predisposing factors are infection and bladder dysfunction
- *Immunosuppression and immunodeficiency*

The onset of uncomplicated acute pyelonephritis usually is sudden, with pain at the costovertebral angle and systemic evidence of infection, such as chills, fever, and malaise, and localizing urinary tract signs of dysuria, frequency, and urgency. The urine appears turgid due to the contained pus (pyuria). Even without antibiotic treatment, the disease tends to be benign and self-limited. The symptomatic phase of the disease typically lasts no longer than a week, although bacteriuria may persist much longer. The disease usually is unilateral, and affected persons thus do not develop renal failure because they still have one unaffected kidney. In cases in which predisposing factors are present, the disease may become recurrent or chronic, particularly when involvement is bilateral. The development of papillary necrosis is associated with a much poorer prognosis.

﴿ وَيَسْأَلُونَكَ عَنِ الرُّوحِ ۖ قُلِ الرُّوحُ مِنْ أَمْرِ رَبِّي وَمَا أُوتِيتُم مِّنَ الْعِلْمِ إِلَّا قَلِيلًا ﴾

سورة الإسراء الآية ٨٥

Team Leaders

Sara Alenezy & **A**li Alzahrani

Heartful thanks to our phenomenal team members

Fawzan Alotaibi
Shamma Alsohaili
Kowthar Almousa
Khawla Alammari
Munerah Alomari
Nojood Alhaidari
Elham Alzahrani
Shahad Alenezy
Maryam Saidan
Johara Almalki
Noura AlTawil
Ola Alnuhayer
Areeb Alogaiel
Deema Alfaris
Suha Alenazi