Intended Learning Objectives (ILOs)

- Classify tumours of the kidney and give an account of renal cell carcinoma with emphasis of presenting features and morphological appearances.
- Define Wilm'stumour of the kidney, describe its pathological features and routs of spread.
- Classify tumors of the urinary bladder.
- List the common causes of acute and chronic renal failure.
- Define haematurea and enumerate its causes.
- Define proteinurea and enumerate its causes.
- Define pyurea and enumerate its causes.
- List causes of small sized kidney.
- List causes of kidney enlargement.

Tumours of urinary tract

Tumours of the kidney

I. Primary Tumours of the Kidney:

A. Benign Tumours:

(1) ***Epithelial:*** Cortical adenoma and oncocytoma.

(2) ***Mesodermal:*** Medullary fibroma, **angiomyolipoma**, lipoma, leiomyoma, myxoma, haemangioma and lymphangioma.

B. Malignant Tumours:

(1) ***Epithelial:*** Renal cell carcinoma (hypernephroma).

(2) ***Mesodermal:*** Sarcomas, malignant lymphomas and multiple myeloma.

(3) ***Wilm'stumour*** (nephroblastoma).

C. Tumours of the Renal Pelvis:

(1) *Benign:*

(a) Haemangioma: either capillary or cavernous. Its rupture causes severe haematuria.

(b) Papilloma, inverted papilloma, and neurofibroma.

(2)*Malignant:*

(a) Transitional cell carcinoma.

(b) Squamous cell carcinoma.

II. Secondary Tumours of the Kidney:

(1) Direct or lymphatic spread from the adrenal, pancreas and large intestine.

(2) Blood stream metastases.

Adenoma of the Kidney (Cortical Adenoma):
- The tumour arises from the cortex.
- It appears as a small, rounded yellowish tumour measuring 0.5-2 cm in diameter.
- The tumour is non- capsulated.
- Malignant transformation may occur.

Renal Oncocytoma:
- Encapsulated tumour arising from the collecting ducts.
- Cut surface is homogenous tan or mahogany brown.
- Microscopically the cells are large with eosinophilic cytoplasm and small rounded benign-appearing nuclei. The cells are arranged in pseudo-alveolar pattern.

■ Renal Cell Carcinoma (Hypernephroma):

- The most common primary tumor of the kidney in the adult population, accounting for ~80% of kidney tumors
- Origin: arises from the tubular epithelium, most often in the proximal convoluted tubules or from a cortical adenoma.
- The tumour is more common in males.
- Age: occurs between 60-70 years.
- Risk factors include cigarette smoking, chronic analgesic use, asbestos exposure, chronic renal failure, acquired cystic disease, and von Hippel-Lindau disease (VHL tumor suppressor gene).

Presentation

The classic **triad of clinical symptoms** includes:
■ Painless hematuria (microscopic or macroscopic).
■ Palpable flank mass.
■ Flank pain.

Gross Picture: The tumour usually starts at one pole of the kidney and forms a variable sized rounded sharply demarcated mass. Cut surface of the tumour has a characteristic yellow colour due to high lipid content of the tumour cells and shows areas of haemorrhage, necrosis and cystic degeneration.

Microscopic Picture:

(1) ***Clear cell type*(80%):** This is the commonest type, both familial and sporadic forms are commonly associated with an underlying genetic defect in the *VHL* gene (a tumor suppressor gene on chromosome 3).
The tumors are formed of large rounded or polyhydral cells, arranged in acini or trabeculae separated by scanty stroma containing thin walled vessels. The cytoplasm is clear or vacuolated due to its high content of lipids and glycogen and the nucleus is small and darkly stained.

(2) ***Papillary type (15%):*** have a papillary growth patternand affectthe proximal tubules. The cells are columnar in shape.

(3) ***Chromophobe cell type (5%):***composed of cells with prominent cell membranes and pale eosinophilic cytoplasm, usually with a halo around the nucleus.

(4) ***Sarcomatoid type:*** The cells are undifferentiated and spindle shaped.

Diagnosis

Renal **ultrasound** shows the presence of a mass. **CT** can provide precise information on the size and location of the tumor, as well as detect enlarged lymph nodes and metastases. The most common appearance of clear-cell renal carcinoma is an upper pole mass with cysts and hemorrhage.

Spread: (1) Direct spread: To the renal pelvis, renal capsule, surrounding structures, renal vein and inferior vena cava.
(2) Blood spread: Early to the lungs, bones and liver, invasion of left renal vein can cause **left-sided varicocele** due to blockage of left spermatic vein drainage.
(3) Lymphatic spread: To the para-aortic lymph nodes.

Clinical Effects:

(1) Painless haematuria.
(2) Pain in the loin.
(3) Palpable mass.
(4) Obstruction of the spermatic veins by the tumour produces varicocele.
(5) Manifestations due to metastasis in lungs and bone.
(6) Anaemia, fever and weight loss.
(7) Polycythemia due to due to secretion of an erythropoietic stimulating substance.
(8) Hypercalcemia as a result of production of parathormone-like substance.
(9) Gynecomastia as a result of gonadotropin and placental lactogen production.

Wilm'sTumour (Nephroblastoma or Embryoma):A childhood tumour

- Origin: derived from the renal blastema due to **loss of *WT1*** (a tumor suppressor gene on chromosome 11).
- Age: The peak incidence is 2-4 years.
- The tumour constitutes 20% of malignant tumours of children.
- Bilaterality: bilateral in ***5- 10%*** of cases.

Presentation:

- Large, palpable abdominal mass that may extend into the pelvis.
- Some patients have hypertension due to excessive renin secretion.

Gross Picture: Large rounded or lobulated well circumscribed and soft in consistency. Cut section is pale gray and shows areas of cystic changes, necrosis and haemorrhages.

Microscopic Picture: The tumour consists of three components:

(1) Cellular nests and sheets of primitive blastemal cells, round to oval with scanty cytoplasm.

(2) Mesenchymal component of fibrous tissue, smooth muscle, striated muscle, bone and cartilage.

(3) Epithelial component of embryonic tubules and glomeruloid structures.

Spread: (1) Local infiltration of the kidney capsule and surrounding structures.

(2) Blood spread early to the lung, liver, bone and brainy

(3) Lymphatic spread to the para-aortic lymph nodes.

Causes of enlargement of the Kidney:

A) Marked enlargement:

1- Polycystic kidney.

2- Hydronephrosis

3- Hypernephroma & embryoma**.**

B) Mild & moderate enlargement:

1- Inflammations: ADPGN, RGN, early MGN, acute pyelonephritis & acute interstitial nephritis.

2- Degenerations: cloudy swelling, fatty change & amyloidosis.

3- Circulatory disturbances: CVC & renal vein obstruction.

4- Tumours: primary & secondary tumours.

5- Compensatory hypertophy.

Causes of small sized kidney:

1- Congenital hypoplasia.

2- Renal atrophy.

3- Chronic diffuse GN.

4- Chronic Pyelonephritis.

5- Benign nephrosclerosis.

6- Healed multiple renal infarcts.

7- Radiation nephritis.

Tumours of Urinary Bladder

About 95% of bladder tumors are of epithelial origin, the remainder being mesenchymal tumors

Benign		Malignant	
Epithelial	**Mesenchymal**	**Epithelial**	**Mesenchymal**
-Villous pap.	- fibroma	- Urothelial carc.	Rhabdomyosarcoma
-Inverted pap.	- leiomyoma	- Sq. C.C	(Botryoid sarcoma)
	-rhabdomyoma	- Adenocarc.	(in children)
	-myxoma	- Anaplastic carc.	
	- angioma		

Urothelial Neoplasms:

(A) Non invasive urothelial neoplasms:

- Urothelial papilloma
- Inverted urothelial papilloma
- Urothelial dysplasia
- Urothelial carcinoma insitu
- Non-invasive papillary urothelial carcinoma, low grade
- Non-invasive papillary urothelial carcinoma, high grade

(B)**Invasive urothelial neoplasms:**

- Infiltrating urothelial carcinoma

Squamous cell neoplasm:

- Squamous cell carcinoma

Glandular neoplasm:

-Adenocarcinoma

Benign Epithelial Tumours:

(1) Urothelial Papilloma (Villous Papilloma):

- Site: arise anywhere within the bladder, most arise from the lateral or posterior walls at the bladder base.
- Grossly: small, (0.5 to 2 cm), single, pedunculated, reddish grey in colour, friable in consistency, has multiple branching villous like projections.

- Usually recurs after removal & is considered potentially malignant.
- Microscopically: Delicate branching vascular fibrous cores covered by epithelium that is histologically identical to normal urothelium.
- Complications: Malignant transformation, Hge, obstruction of the ureteric or urethral openings.

(2)Inverted papilloma:

- A benign epithelial tumour.
- Commonly seen in adults & elderly males.
- Usually solitary and presents with haematuria.
- Grossly: Polypoid lesion with smooth contour, usually pedunculated.
- Microscopically: invagination of the epithelium in the submucosa, with absent papillae and scanty connective tissue.

Malignant Epithelial Tumours

- A common tumour.
- Age: ↑40 in non bilharzial &↓ 40 in bilharzial patients.

Predisposing factors:

1- Urinary bilharziasis due to:
   a) Mechanical irritation of the ova.
   b) Tryptophane metabolites act as a carcinogenic agents.
   c) Metaplastic changes including cystitis glandularis and squamous metaplasia.
2- Urothelial papilloma.
3- Aniline dyes used by the dye workers.
4- Cigarette smoking
5- Chronic irritation by stones or chronic cystitis.
6- Leucoplaqia.
7- Congenital anomalies (ectopia vesica & patent uracus).

A. Urothelial carcinoma (transitional cell carcinoma, TCC):

- Over 90% of bladder cancers are urothelial carcinoma.
- Common in males between 50-80 years.
- Precursors of invasive urothelial carcinoma include:
  - Non invasive papillary urothelial neoplasm.
  - Carcinoma insitu
- **Site:** Most cases affect lateral walls, posterior wall and trigone.
- **Morphology:** Urothelial transional cell neoplasm are classified into:

(1)Non-invasive p***apillary urothelial neoplasm:***They project into the limen and have a delicate papillary appearance.

They are graded into:

- Low grade papillary urothelial carcinoma.
- High grade papillary urothelial carcinoma.

(2) Invasive urothelial carcinoma:

It invades lamina propria or extends into the underlying muscle layer,
It may be:

- Associated with papillary urothelial cancer usually of high grade.
- Not associated with papillary growth, due to progression of CIS into invasive cancer.

Gross: Papillary or solid ulcerative lesions.

Microscopic Picture:

- High grade infiltrating papillary or diffuse sheets of malignant transional epithelial cells invading the lamina propria or muscle layer.
- Squamous or glandular differentiation commonly occurs.

B. Squamous cell carcinoma:

- It is common where bilharziasis is common (squamous metaplasia) or with any other lesion causing squamous metaplasia (chronic inflammation or stones).

Grossly: may form fungating, ulcerative or infiltrative mass.

Microscopically: well differentiated, moderately differentiated, poorly or undifferentiated Sq.C.C.

C- Adenocarcinoma:

May arise from:

- Urachal remnants in the dome of the bladder.
- Ectopia vesica (exostrophy)
- Areas of cystitis glandularis (glandular metaplasia).

Spread:

(1) ***Local spread:*** To the ureters, prostate, seminal vesicle, uterus, and rectum. Local spread may → a malignant fistula between the bladder and the vagina, colon or rectum.

(2) ***Lymphatic spread:*** To the hypogastric and iliac lymph nodes.

(3) ***Blood spread:*** To the lungs, liver and bones specially the lumber vertebrae and pelvic bones.

Complications: Marked haematuria, hydroureter, hydronephrosis, pyelonephritis and malignant fistulas. Complications are the common cause death.

Prognosis: The extent of invasion or spread (stage) at the time of initial diagnosis is the most important prognostic factor.

HAEMATURIA

Definition: The passage of blood with urine.

Macroscopic haematuria: Passage oflarge amount of blood.

Microscopic haematuria: Passage of scanty amount of blood.

Causes:

I. General Causes:

(1) Haemorrhagic blood diseases as haemophilia, purpura and leukemia.;

(2) Vitamin C and K deficiency.

(3) Hypertension.

(4) Anticoagulant therapy.

II. Local Causes:

(1) ***Congenital malformations:*** Polycystic kidney.

(2) ***Inflammations:*** Acute diffuse glomerulonephritis, focal glomerulonephritis, pyelonephritis, bilharzial cystitis and urinary tuberculosis.

(3) ***Vascular diseases:*** Chronic venous congestion of the kidney, renal infarct and malignant nephrosclerosis.

(4) ***Tumours:*** Of the kidney and urinary tract specially hypernephroma, embryoma, bladder carcinoma, villous papilloma and haemangioma.

(5)Mechanical trauma: e.g. by urinary stones specially the oxalate type, instrumentation as passage of a metal catheter and surgical operations.

(6) Irritation of the kidney by drugs: e.g. salicylates, sulfonamides and barbiturates.

Terminal haematuria caused by bilharzial cystitis is the commonest cause in Egypt.

Another classification:

- Early haematuria: caused by urethral lesions.
- Terminal haematuria: caused by bilharzial cystitis.
- Total profuse haematuria: cused by haemangioma and malignant tumours.

Protienuria:

Definition

Causes: Enumerate them from the previous lectures.

Types:

May be:

- Mild proteinuria.
- Massive or heavy proteinuria.

May be:

- Selective proteinuria: Albuminuria.
- Non selective proteinuria: Albumin & globulin.

Pyuria:

Definition: Presence of pus in urine.

Causes: Pyogenic inflammation of the urinary tract; pyelonephritis, pyonephrosis, pyoureter, acute (pyogenic) cystitis, gonorrhea (acute suppurative inflammation of the anterior urethra) & acute suppurative prostatitis.