Congenital anomalies of the kidney

Objectives:

1. To understand the presentations and management of congenital anomalies.

Embryology of kidney and ureter

The pronephros: derived from an intermediate plate of mesoderm. The mammalian pronephros *is a transitory, nonfunctional* kidney, analogous to that of primitive fish, the first evidence of pronephros is seen late in the third week, and it completely degenerates by the start of the fifth week**.**

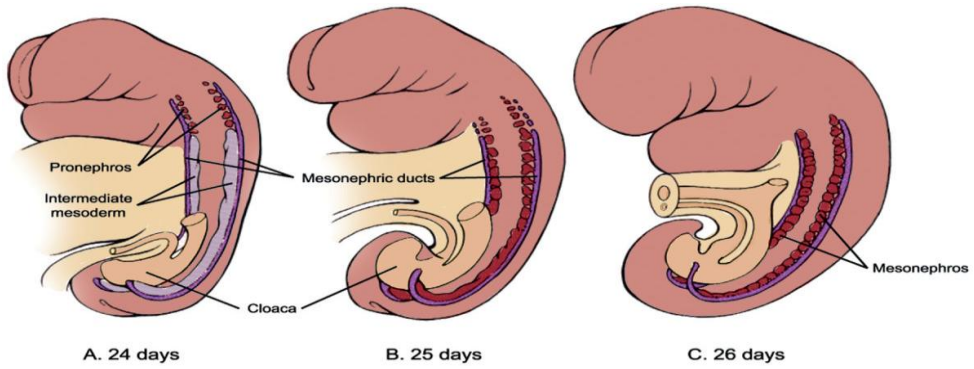
The mesonephros: functions from weeks 4and 8, and is associated with 2 duct systems of the mesonephric duct and, adjacent to this, the paramesonephric duct. The mesonephric (Wolffian) ducts develop laterally, and advance downwards to fuse with the primitive cloaca (hindgut).It is also transient, it serves as an excretory organ for the embryo while the definitive kidney, the *metanephros,* begins its development.

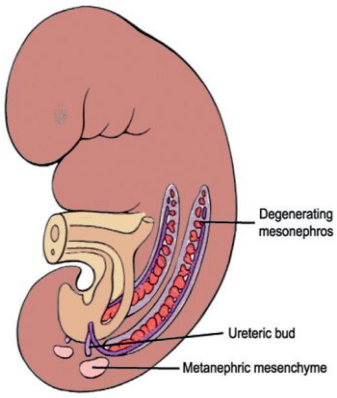
The metanephros: The definitive kidney, or the *metanephros,* forms in the sacral region as a pair of new structures, called the *ureteric buds,* sprout from the distal portion of the mesonephric duct and come in contact with the condensing blastema of *metanephric mesenchyme* at about the 28th day.

Branching of the ureteric bud forms the renal pelvis, calyces, and collecting ducts. Glomeruli and nephrons are created from metanephric mesenchyme. During weeks 6 and 10, the caudal end of the fetus grows rapidly and the fetal kidney effectively moves up the posterior abdominal wall to the lumbar region**.**

Urine production starts at week 10

Thus, in both males and females, the mesonephric duct forms the ureters and renal collecting system. The paramesonephric essentially forms the female genital system (fallopian tubes, uterus, upper vagina); in males, it regresses. The mesonephric duct forms the male genital duct system (epididymis, vas deferens, seminal vesicles, central zone of prostate); in the female, it regresses.





28 days

CONGENITAL ANOMALIES OF THE KIDNEY

1) ANOMALIES OF NUMBER

A. Agenesis: Absence of the renal tissue either bilateral (only about 500 cases having been reported and it is incompatible with life) or unilateral Renal Agenesis(unilateral agenesis occurs once in 1100 births)

B. Supernumerary Kidney: 3-4 separated kidneys

2) ANOMALIES OF VOLUME AND STRUCTURE

Hypoplasia**,** Multicystic kidney**,** polycystic kidney (Infentile and Adult type), Medullary cystic disease.

3) ANOMALIES OF ASCENT

A. Simple Renal Ectopia: refers to a low kidney in proper side that failed to ascend (pelvic kidney, or at pelvic brim)

B. Cephalic Renal Ectopia

C. Thoracic Kidney

4) ANOMALIES OF FORM AND FUSION

1- Crossed Renal Ectopia With and Without Fusion, **Inferior Ectopic Kidney, Sigmoid or S-Shaped Kidney, Lump Kidney L-Shaped Kidney, Superior Ectopic Kidney**

2-Horseshoe kidney:

Most common example of renal fusion. Prevalence 1 in 400 persons(0.25%).

Male to female ratio 2:1.

The kidneys lie vertically (instead of obliquely) and are joined at their lower poles (in 95%) by midline parenchymal tissue (the isthmus).

The inferior mesenteric artery obstructs ascent of the isthmus. Consequently, the horseshoe kidney lies lower in the abdomen (L3 or L4 vertebral level).

Normal rotation of the kidney is also prevented and therefore the renal pelvis lies anteriorly, with the ureters also passing anteriorly over the kidneys and isthmus (but entering the bladder normally).

Blood supply is variable, usually from one or more renal arteries or their branches, or from branches off the aorta or inferior mesenteric artery.

Associated anomalies: A proportion of individuals with horseshoe kidneys have associated congenital abnormalities (Turner's syndrome, trisomy 18, genitourinary anomalies, ureteric duplication); vesicoureteric reflux; UPJ obstruction; and renal tumours (including Wilms tumours).

Clinical features: most patients with horseshoe kidneys remain asymptomatic; however, infection and calculi may develop and cause symptoms.

The diagnosis: is usually suggested on renal **ultrasound** and confirmed by **IVU** (calyces of the lower renal pole are seen to point medially, and lie medially in relation to the ureters) or **CT**. Renal function is usually normal.

5) ANOMALIES OF ROTATION; The adult kidney, as it assumes its final position in the "renal" fossa, orients itself so that the calyces point laterally and the pelvis faces medially. When this alignment is not exact, the condition is known as ***malrotation***

6) ANOMALIES OF RENAL VASCULATURE

A. ***Aberrant, Accessory, or Multiple Vessels***
   "aberrant vessels" should be reserved for those arteries that originate from vessels other than the aorta or main renal artery**.** The term **"accessory vessels"** denotes two or more arterial branches supplying the same renal segment.
B. ***Renal Artery Aneurysm***
C. ***Renal Arteriovenous Fistula***

7) ANOMALIES OF THE COLLECTING SYSTEM

Calyceal Diverticulum, Megacalycosis, Bifid Pelvis

Cystic kidney disease

Congenital cystic kidney disease can be classified into genetic and non-genetic types:

Genetic (Inheritable)	**Non-genetic (Noninheritable)**
Autosomal recessive (infantile) polycystic kidney disease	Multicystic kidney (multicystic dysplastic kidney)
Autosomal dominant (adult) polycystic kidney disease	Benign multilocular cyst (cystic nephroma)
Juvenile nephronophthisis/medullary cystic disease complex	Simple cysts
Juvenile nephronophthisis (autosomal recessive)	Medullary sponge kidney
Medullary cystic disease (autosomal dominant)	Sporadic glomerulocystic kidney disease
Congenital nephrosis (familial nephrotic syndrome) (autosomal recessive)	Acquired renal cystic disease

Familial hypoplastic glomerulocystic disease (autosomal dominant)	Calyceal diverticulum (pyelogenic cyst)
Multiple malformation syndromes with renal cysts (e.g., tuberous sclerosis, von Hippel-Lindau disease)	

Autosomal recessive polycystic kidney disease (ARPKD)

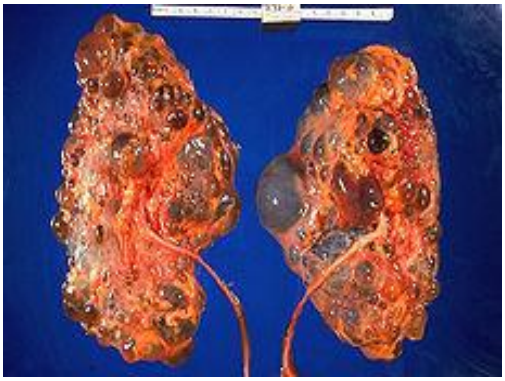
A disease of infancy and childhood, where renal collecting tubules and ducts become cystically dilated and numerous small cysts form in the renal cortex and medulla.

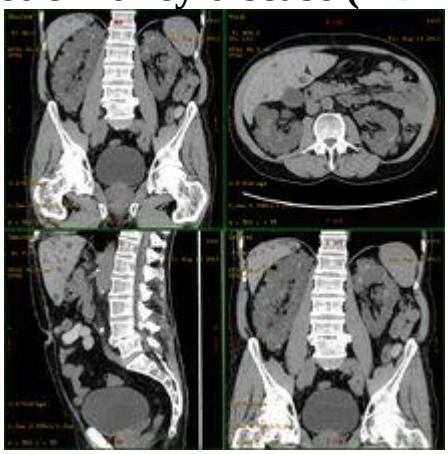
Genetics: **a single gene, named *PKHD1* and located on chromosome 6r, are responsible for the disease.**

Clinical Features: Severe forms present early and have a poor prognosis. Prenatal USS demonstrates oligohydramnios (amniotic fluid <200ml) and large, bright homogeneously hyperechogenic kidneys, which can cause obstructed labour and respiratory problems. Neonates have large flank masses, limb and facial anomalies. All cases are associated with congenital hepatic fibrosis. Infants develop fatal uraemia and respiratory failure; older children present with renal failure, hypertension, and portal hypertension.

Treatment: No cure. Most develop end-stage renal failure by adulthood, requiring haemodialysis and renal transplantation.

Autosomal dominant polycystic kidney disease (ADKD)





Autosomal dominant polycystic kidney disease is by far the most common inheritable form of renal cystic disease,

Typically presents in adulthood, although older children can present with complications of haematuria, flank pain, flank mass, UTI, proteinuria, hypertension, and intracerebral bleeds (secondary to berry aneurysm rupture). It is characterized by multiple expanding cysts of both kidneys that ultimately destroy the intervening parenchyma, and accounts for 10% of all chronic renal failure.

Epidemiology

Incidence is about 0.1% with an incidence of approximately 1 in 400 to 1000 live births ; 95% are bilateral. Symptoms manifest in the 4th decade. **Pathology**

The kidneys reach an enormous size due to multiple fluid-filled cysts and can easily be palpated on abdominal examination. Expansion of the cysts results in ischaemic atrophy of the surrounding renal parenchyma, and obstruction of normal renal tubules. End-stage

renal failure is inevitable and occurs around the age of 50 yrs. The incidence of RCC in patients with ADPKD is no higher than that in the general population.

Associated disorders

10 to 30% incidence of Circle of Willis berry aneurysms (associated with subarachnoid haemorrhage); cysts of the liver (33%), pancreas (10%), and spleen (<5%); renal adenoma; cardiac valve abnormalities; aortic aneurysms and diverticular disease.

Aetiology

PKD-1 gene defects (chromosome 16) account for 90% of cases; PKD-2 gene defects (chromosome 4) cause 10%, and now a third gene, PKD-3 is also implicated. Pathogenesis theories include intrinsic basement membrane abnormalities; tubular epithelial hyperplasia (causing tubular obstruction and basement membrane weakness), and alterations in the supportive extracellular matrix due to defective proteins, all of which may cause cyst formation.

Presentation

Positive family history (50% inheritance); palpable abdominal masses; flank pain (due to mass effect, infection, stones, or following acute cystic distension due to haemorrhage or obstruction); macroscopic (and microscopic) haematuria; UTI; and hypertension (75%). Renal failure may present with lethargy, nausea, vomiting, anaemia, confusion, and seizures.

Differential diagnosis

Renal tumours; simple cysts; von Hippel-Landau syndrome (cerebellar and retinal haemangioblastomas; renal, adrenal, and pancreatic cysts); tuberous sclerosis (adenoma sebaceum, epilepsy, learning difficulties, with polycystic kidneys and renal tumours).

Investigation

This depends on the presenting symptoms.

- For suspected UTI-culture urine.
- For haematuria-urine cytology, flexible cystoscopy, and renal ultrasound. On ultrasound the kidneys are small and hyperechoic, with multiple cysts of varying size, many of which show calcification. If the nature of the cysts cannot be determined with certainty on ultrasound, arrange a renal CT.
- Renal failure will be managed by a nephrologist. Anaemia may occur, though ADPKD may cause increased erythropoietin production and polycythaemia.
- Renal imaging (ultrasound and CT are useful for investigation of complications).

Treatment

– The aim is to preserve renal function as long as possible (control hypertension and UTI). Upper tract urinary tract infections are common in patients with ADPKD, especially women and the only dependable antibiotics were those that were lipid soluble, namely, trimethoprim-sulfamethoxazole, fluoroquinolones, and chloramphenicol.Infected cysts (abscesses) should be drained. Persistent, heavy haematuria can be controlled by embolisation or nephrectomy. Progressive renal failure requires dialysis and, ultimately, renal transplantation.

Multicystic dysplastic kidney

The most common cystic kidney disorder and **is the second most common cause of an abdominal mass in infants after hydro**nephrosis. The cysts of a multicystic

kidney are not due to dilatation of renal collecting ducts (as in polycystic disease) but, instead, the entire kidney is dysplastic, with immature dysplastic stroma and cysts of various sizes.

Clinical features:

Bilateral disease is incompatible with life. Unilateral disease is often associated with contralateral reflux seen in 18% to 43% of infants or ureteropelvic junction obstruction in 3% to 12% of infants. Affected kidneys may undergo renal aplasia, where they spontaneously shrink to a tiny remnant.

Diagnosis:

- MDCK is most often identified by prenatal ultrasonography, and,in newborns, ultrasonography is usually repeated (one within the first few days of life and another one month later) to confirm the diagnosis and to evaluate the contralateral kidney and bladder In general, the multicystic kidney has a haphazard distribution of cysts of various sizes without a larger central or medial cyst and without visible communications between the cysts. Frequently, very small cysts appear between the large cysts. By comparison, in ureteropelvic junction obstruction, the cysts or calyces are organized around the periphery of the kidney; connections usually can be demonstrated between the peripheral cysts and a central or medial cyst that represents the renal pelvis; and there is an absence of small cysts between the larger cysts
- In these difficult cases, radioisotope studies may be helpful. Hydronephrotic kidneys usually show some function on a dimercaptosuccinic acid (DMSA) or technetium-99m mercaptoacetyltriglycine (99mTc MAG3) scan, whereas renal uptake is seldom seen in multicystic kidney

Treatment:

Most can be treated conservatively with close surveillance for the associated risks of hypertension and Wilms tumour, which would be indications for surgery.

Simple cysts

Simple cysts are single or multiple renal masses ranging from a few to many centimetres in diameter that do not communicate with any part of the nephron or the renal pelvis.

They are mainly confined to the renal cortex, are filled with clear fluid, and contain a membrane composed of a single layer of flattened cuboidal epithelium.

They can be unilateral or bilateral, and often affect the lower pole of the kidney. In comparison, parapelvic cysts are simple parenchymal cysts located adjacent to the renal pelvis or hilum.

The prevalence of simple cysts increases with age. The precise prevalence depends on the method of diagnosis. On CT, 20% of adults have renal cysts by age 40 years and 30% by the age of 60. At postmortem, 50% of subjects aged >50 have simple cysts. Most reports show no gender predilection. Cysts do not usually increase in size with age, but may increase in number.

Aetiology

Both congenital and acquired causes have been suggested. Chronic dialysis is associated with the formation of new simple cysts.

Presentation

Simple cysts are most commonly diagnosed following a renal ultrasound or CT (less commonly, nowadays, after IVU) done for other purposes, and as such they represent an incidental finding. Very large cysts may present as an abdominal mass or cause dull flank or back pain. The great majority of simple renal cysts are asymptomatic. Acute, severe loin pain may follow bleeding into a

cyst (causing sudden distension of the wall). Rupture (spontaneous or following renal trauma) is rare. Rupture into the pelvicalyceal system can produce haematuria. Infected cysts (rare) present with flank pain and fever. Very occasionally, large cysts can cause obstruction and hydronephrosis.

Differential diagnosis;

- Renal cell carcinoma
- Early autosomal dominant polycystic kidney disease (ADPKD)- diffuse, multiple, or bilateral cysts; presence of hepatic cysts
- Complex renal cysts (i.e. those which contain blood, pus, or calcification)

Investigation

- Renal ultrasound

  Simple cysts are round or spherical, have a smooth and distinct outline, and are anechoic (no echoes within the cyst i.e. sound waves are transmitted through the cyst). Evidence of calcification, septation, irregular margins, or clusters of cysts requires further investigation (CT ±aspiration, MRI). In the absence of these features no further investigation is required.
- CT

  Simple cysts are seen as round, smooth-walled lesions with homogenous fluid in the cavity (with a typical density of -10 to +20 Hounsfield units), and with no enhancement after contrast (enhancement implies that the mass contains vascular tissue or communicates with the collecting system i.e. that it is not a simple cyst). Hyperdense cysts have a density of 20-90 Hounsfield units, do not enhance with contrast media, and are <3cm in diameter.

Treatment

A simple cyst (round or spherical, smooth wall, distinct outline, and no internal echoes) requires no further investigation, no treatment, and no follow-up. In the rare situation where the cyst is thought to be the cause of symptoms (e.g. back or flank pain) treatment options include percutaneous aspiration ±injection of sclerosing agent or surgical excision of the cyst wall. In the rare event of cyst infection, percutaneous drainage and antibiotics are indicated.

Cysts with features on ultrasound suggesting possible malignancy (calcification, septation, irregular margins) should be investigated by CT with contrast.

Calyceal diverticulum

A calyceal diverticulum is an outpocketing from the pelvicalyceal system, with which it communicates by way of a narrow neck. It is lined by a smooth layer of transitional epithelium and is covered by a thin layer of renal cortex. The aetiology of calyceal diverticula is unknown. They are usually asymptomatic and are discovered incidentally on an IVU. Symptoms may result from the development of a stone or infection within the diverticulum, presumably caused by urinary stasis.

Medullary sponge kidney (MSK)

Definition

A cystic condition of the kidneys characterized by dilatation of the distal collecting ducts associated with the formation of multiple cysts and diverticula within the medulla of the kidney.

Presentation

The majority of patients are asymptomatic. When symptoms do occur, they include ureteric colic, renal stone disease (calcium oxalate ¡± calcium phosphate), UTI, and haematuria (microscopic or macroscopic). Up to 50% have hypercalciuria due to renal calcium leak or increased gastrointestinal calcium absorption. Renal function is normal, unless obstruction occurs (secondary to renal pelvis or ureteric stones).

Differential diagnosis

Other causes of nephrocalcinosis (deposition of calcium in the renal medulla) (e.g. TB, healed papillary necrosis).

Investigation

Intravenous urogram (IVU)

The characteristic radiological features of MSK, as seen on IVU, are dilatation of the distal portion of the collecting ducts with numerous associated cysts and diverticula (the dilated ducts are said to give the appearance of (bristles on a brush). The collecting ducts may become filled with calcifications, giving an appearance described as a (bouquet of flowers)or (bunches of grapes).

Biochemistry

24-h urinary calcium may be elevated (hypercalciuria). Detection of hypercalciuria requires further investigation to exclude other causes (i.e. raised serum parathyroid hormone levels (PTH) indicate hyperparathyroidism).

Treatment

Asymptomatic MSK disease requires no treatment. General measures to reduce urine calcium levels help reduce the chance of calcium stone formation (high fluid intake, vegetarian diet, low salt intake, consumption of fruit and citrus fruit juices). Thiazide diuretics may be required for hypercalciuria resistant to dietary measures designed to lower urine calcium concentration. Intra-renal calculi are often small and, as such, may not require treatment, but if indicated this can take the form of ESWL or flexible ureteroscopy and laser treatment. Ureteric stones are again usually small and will therefore pass spontaneously in many cases, with a period of observation. Renal function tends to remain stable in the long term.