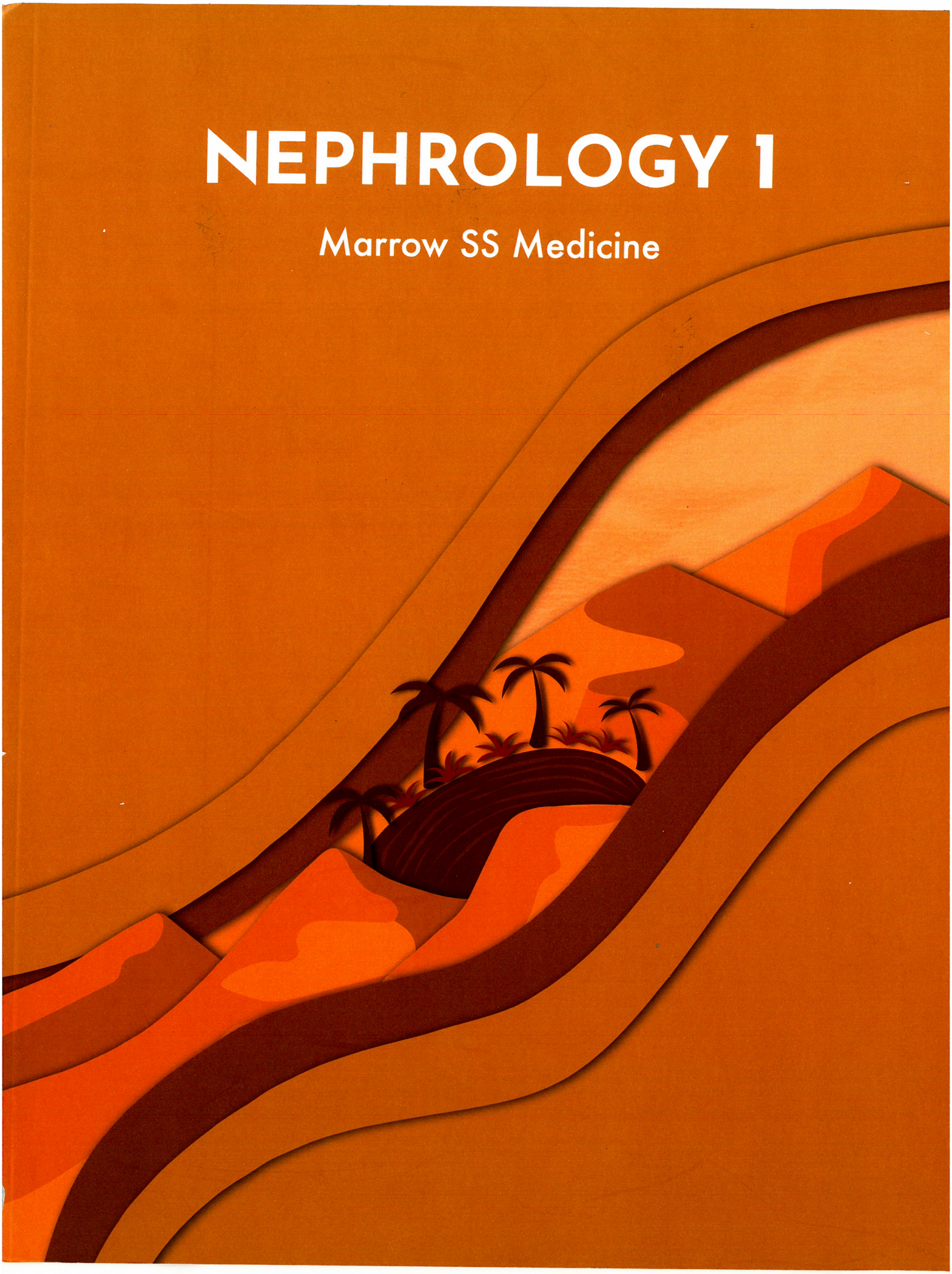
NEPHROLOGY 1

Marrow SS Medicine



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Nephrology

Volume - 1

MARROW
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RENAL EMBRYOLOGY

Development of urogenital system

00:00:38

Mesoderm :

- Intermediate mesoderm : Gives rise to kidneys.
- Paraxial mesoderm : Gives rise to somites (muscles).
- Lateral plate mesoderm : Cavities (Pleura, peritonium, pericardium).
  - Somatopleuric gives rise to parietal pleura, parietal pericardium, etc.
  - Splanchnopleuric gives rise to visceral pleura, visceral pericardium, etc.

Development of urogenital system :

Entire urogenital system is derived from :

- Intermediate mesoderm : Entire kidney is derived from this.
- Cloaca.

Cloaca :

- Cloaca is part of the hindgut that is distal to the allantois.
- Cloaca is completely endodermal in origin.
- It gives rise to two structures namely :
  a. Primitive urogenital sinus :
  Gives rise to vesicourethral canal → Bladder and urethra.
  The upper part gives rise to the bladder.
  Pelvic part gives rise to prostatic and membraneous urethra.
  Phallic part gives rise to sponge urethra.
  b. Primitive rectum :
  Gives rise to rectum and anal canal up to pectinate line.
  Anal canal below pectinate line is ectodermal in origin.

Intermediate mesoderm :

Gives rise to :

- Genital ridge (Gonads).
- Paramesophric duct (mullerian duct).
- Mesonephric duct/wolffian duct.
- Urogenital ridge (Nephrogenic cord) : It extends from the cervical to sacral region of the embryo. It is very closely aligned to the wolffian duct.

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Structures derived from mesonephric duct :

- Seminal vesicle.
- Ejaculatory duct.
- Vas deferens.
- Trigone of bladder (Entire bladder is endodermal in origin except trigone).
- Appendix of epididymis.
- Ureteric bud.

Note :

Remnants of mesonephric duct are Gartner's cyst, epoophoron and paroophoron.
Remnants of paramesophric duct are appendix of testis and hydatid of morgagni.

Timelines of development :

- Day 22 : Pronephros appears and regresses in 2-3 days.
- Day 24 : mesonephros appears and regresses in 4 months.
- 5th week :
  - metanephric mesenchyme (Forms the excretory part of the kidney).
  - Ureteric bud develops from the mesonephric duct (Forms the collecting part of the kidney).
- Between 6th to 8th week : Epithelial mesenchymal interaction occurs.
- End of the 8th week : First fully formed nephron.
- 9-10th week : Urine formation starts.
- 32-26 weeks : Nephrogenesis is completed.
- 18 months : Fetal kidney reaches adult concentrating capacity.
- After birth :
  - New nephrons are not formed, and lost nephrons cannot be replaced.
  - Concentrating capacity is increased even after the birth.
- At 18 months : Adult concentrating capacity is reached.
- metanephros (Adult kidney) :
  - It is initially formed at the level of S1-S2.
  - At around 9-10th week, ascend with rotation occurs and reaches T12-L3 level.

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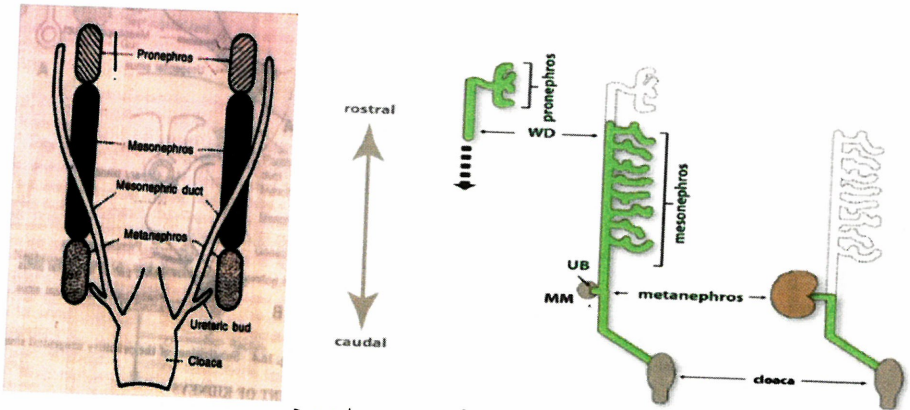

Development of renal system

Importance of nephron number :

- 60% of nephrons are formed in third trimester.
- GFR = Single nephron GFR x Number of nephrons.
- CKD is decrease in nephron number.
- 3 Kg at birth : 9,00,000 nephrons in each kidney.
- 2 Kg at birth : 2,25,000 nephrons in each kidney.
- Birth weight determines the number of nephrons at birth, after which new nephrons are not formed.
  Therefore premature babies are prone to CKD.
- Mother's average BP during pregnancy determines birth weight → Determining risk of CKD.

EMI & associated anomalies

00:16:33

Epithelial mesenchymal interaction (EMI) :

- Epithelial mesenchymal interaction (EMI) is made possible by transcription factors which is expressed from the ureteric bud side or metanephric mesenchyme side.
- Transcription factor required for are ureteric bud induction : PAX-2 (mutation causes unilateral renal agenesis).
- VEGF is produced by the podocytes and is required for this progression.
- Homozygous mutation leads to bilateral renal agenesis.
- Transcription factors expressed by :
  - Metanephric mesenchyme : WT1, WNT4 and WNT6.
  - Ureteric bud : FGF, BMP-7.
- WT1 gene on chromosome 11p :
  Mutation leads to :
  - WAGR syndrome.
  - Denys Drash syndrome.

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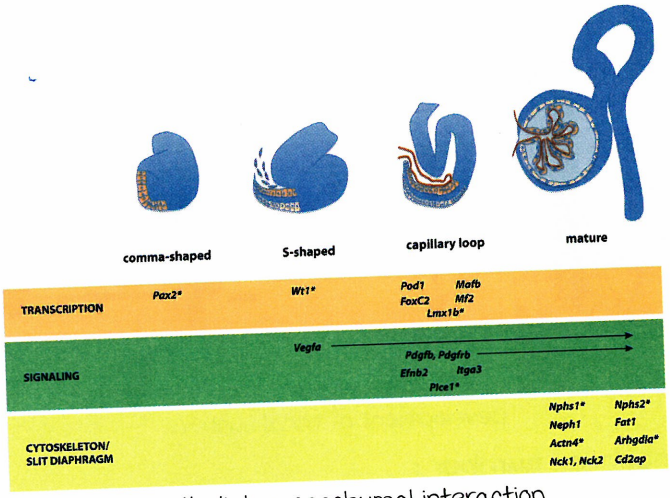
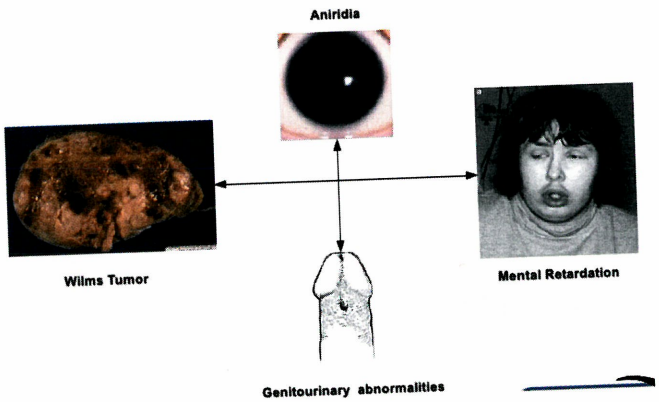


Epithelial mesenchymal interaction

WAGR syndrome :

- Wilms tumour.
- Aniridiia.
- Genitourinary abnormalities.
- Mental retardation.

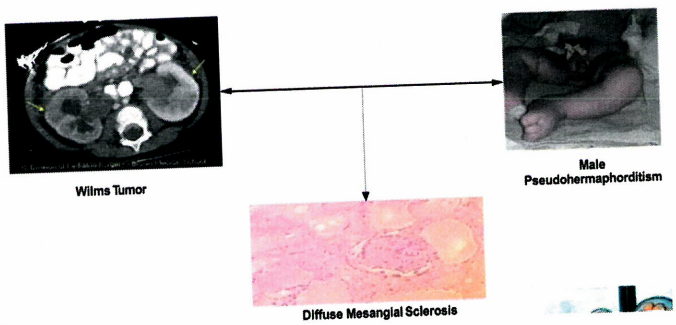


WAGR syndrome

Denys Drash syndrome :

Characterized by :

- Wilms tumor.
- Male pseudohermaphrodism
- Early onset renal failure (Diffuse mesangial sclerosis).



Denys Drash syndrome

Beckwith-Wiedmann syndrome :

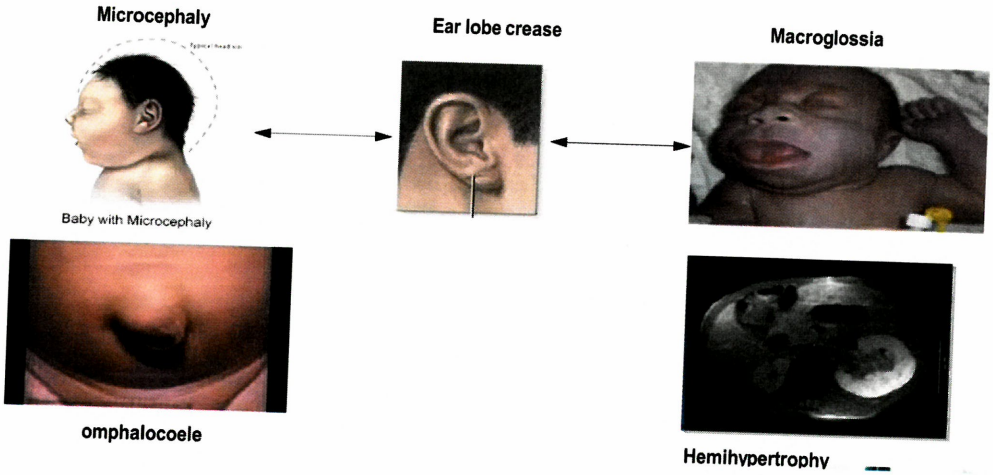
Beckwith-Wiedmann syndrome is not a part of EMI.

Due to WT2 gene mutation on chromosome 11.

Genomic imprinting abnormalities are present.

Clinical features :

- Organomegaly (Renomegaly, nephromegaly, adrenomegaly, hepatomegaly).
- Omphalocele/umbilical hernia.
- Macroglossia.
- Hemihypertrophy of testes (very closely associated with medullary sponge kidney).



Beckwith-Wiedmann syndrome

Other mutations :

- WNT4 and WNT6 mutation :
  - Renal hypodysplasia (<2 SD size).
  - Hyperandrogenism
  - Mullerian aplasia.
- ACE mutations are associated with tubular dysgenesis.
- HNF1B mutations are associated with MODY 5, renal cysts, genital abnormalities.

Renal agenesis :

Unilateral renal agenesis :

- Heterozygous PAX-2 mutation : Unilateral renal agenesis with optic coloboma.
- Incidence : 1 in 1000 live births.
- Common in females >> males.
- HTN is only the clinical feature.

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Malformations associated with unilateral renal agenesis :

- Single umbilical artery.
- Absent uterus.
- Absent ipsilateral vas deferens.
- Contralateral vesico-ureteral reflex.
- Contracted kidneys from birth : Multicystic dysplastic kidney.

Bilateral renal agenesis :

- RET/GDNF gene mutation.
- Associated with : Oligohydramnios and Potter's syndrome (Bilaterally absent renal artery, disc shaped adrenals).

CAKUT anomalies

00:27:56

TABLE 50.1 Monogenic Causes of CAKUT

Stage of Nephrogenesis	Gene	Associated Phenotype
Ureteric bud induction	*EYA1*	Branchio-oto-renal syndrome
	GATA3	HDR syndrome
	PAX2	Renal coloboma syndrome, FSGS
	RET	Renal agenesis and Hirschsprung disease
	ROBO2	VUR
	SALL1	Townes-brocks syndrome
	SIX1, SIX5	Branchio-oto-renal syndrome
Mesenchymal to epithelial transition	*WNT4*	Renal hypodysplasia, müllerian aplasia, hyperandrogenism
	SIX2	Renal hypodysplasia
Branching morphogenesis	*ACE*	All associated with renal tubular dysgenesis
	AGT	
	AGTR1	
	REN	
As yet unknown	*HNF1B*	Renal cysts and diabetes syndrome, genital malformations, hypomagnesaemia, abnormal LFTs, gout, autism
	DSTYK	CAKUT
	TNXB	VUR, joint hypermobility
	SOX17	VUR
	KAL1	Kallman syndrome
	FRAS1	Fraser syndrome
	FREM2	Fraser syndrome
	GRIP1	Fraser syndrome

Common congenital anomalies of kidneys and urinary tract.

m/c ESRD in children.

It includes :

- Agenesis : It can be unilateral or bilateral.
- Dysplasia : Abnormal differentiation.
  Eg : Multicystic dysplastic kidney (Unilateral).
- Hypoplasia : Decrease in size of kidney.
  Associated with :
  - Normal nephron number.

- Oligomeganephronia (Decreased nephron number) : Remaining glomeruli undergo hypertrophy).
- Segmental hypoplasia : Associated with HTN in young (Ask up mark Kidney).

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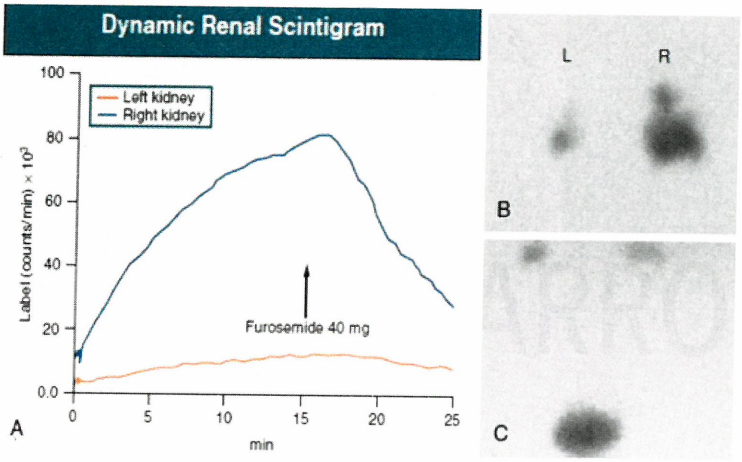
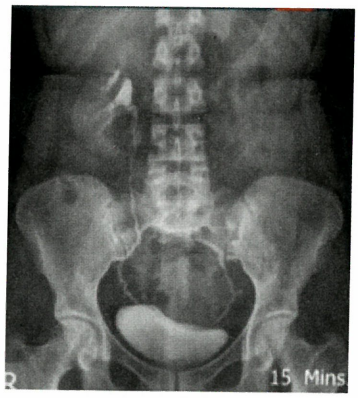
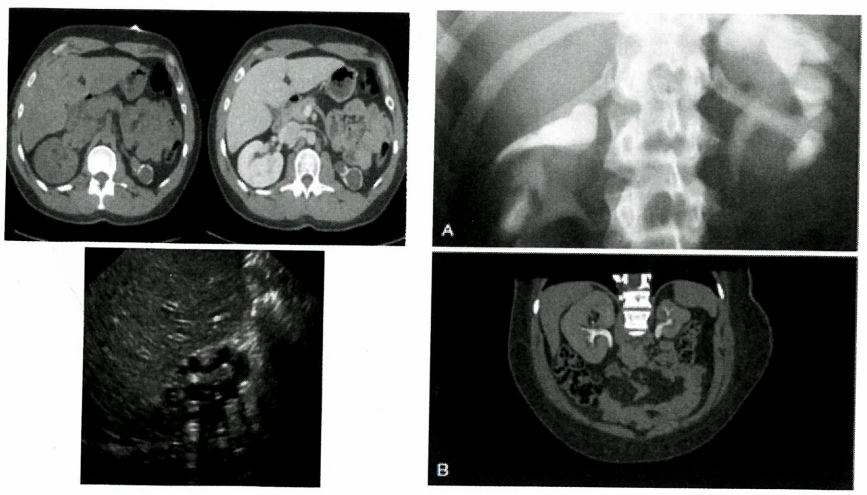
Note :

Technetium-99m MAG3 scintigram : used to detect PUJ stenosis.





Ectopic Kidney



Multicystic dysplastic Kidney

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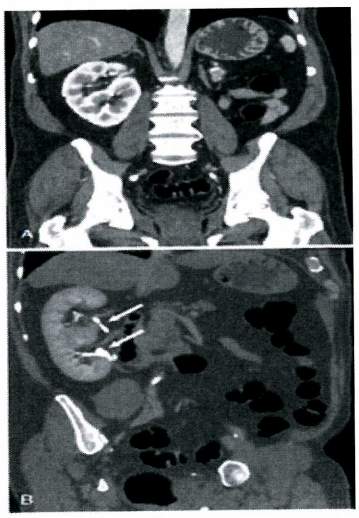
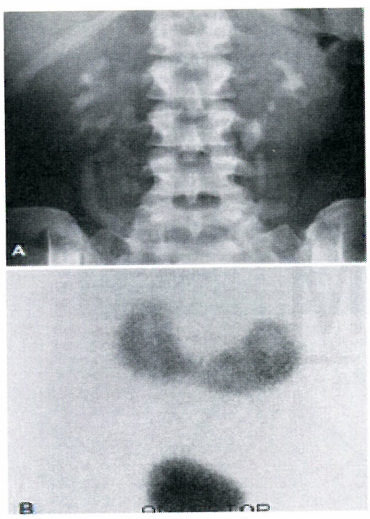
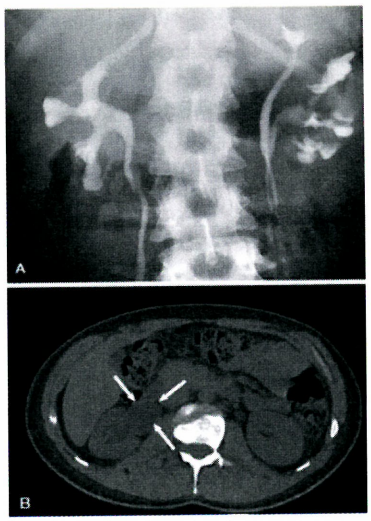
Other Kidney anomalies :



Crossed fused ectopic kidney



Horseshoe Kidney



Duplex system

RENAL ANATOMY

Definitions

00:00:21

Nephron

Renal corpuscle :

- Glomerulus : The term used most frequently to refer to the entire renal corpuscle.
- Bowman's capsule

Proximal tubule

- Convoluted part.
- Straight part (pars recta) or thick descending limb of Henle's loop.

Intermediate tubule

- Descending part or thin descending limb of Henle's loop.
- Ascending part or thin ascending limb of Henle's loop.

Distal tubule

- Straight part or thick ascending limb of Henle's loop : Subdivided into medullary and a cortical part; the latter contains in its terminal portion the macula densa.
- Convoluted part.

Collecting duct system

Connecting tubule :

- Includes the arcades in most specie

Collecting duct

- Cortical collecting duct : Outer medullary collecting duct subdivided into an outer and an inner stripe portion.
- Inner medullary collecting duct subdivided into basal, middle, and papillary portions.

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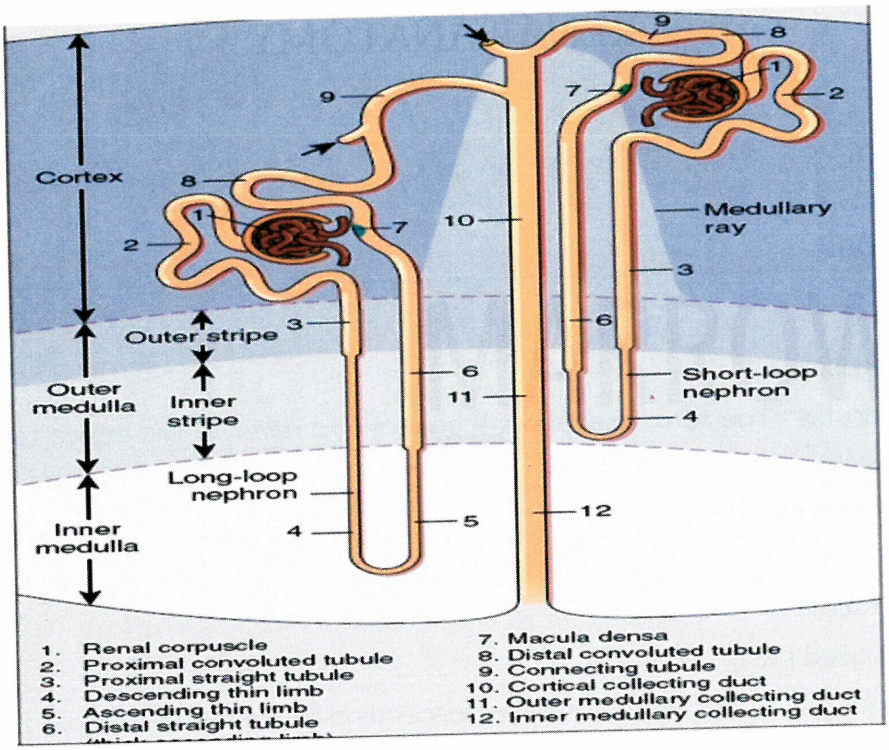

Structures in the excretory part of kidney

1. Glomerulus + Bowman's capsule (renal corpuscle).
   - PCT or pars convoluta.
2. The S1 and S2 segments are parts of PCT. Present in the cortex.
3. PST or pars recta :
   - S3 segment is present in PST. It is present in the medulla.
   - 2 + 3 is called proximal tubule.
   - The main function of proximal tubule is reabsorption.
   - It contains abundant number of mitochondria.
   - The tubule is lined by cuboidal epithelium containing brush border microvilli.
   - PST is the most susceptible to acute tubular injury because of high oxygen requirement needed for reabsorption.
   - Ischemia is the most common cause for acute tubular injury.
4. Thin descending limb of Henle's loop.
5. Thin ascending limb of Henle's loop.
   - 4 + 5 is called intermediate tubules.
   - 85% of nephrons are cortical nephrons and 15% of nephrons are juxtamedullary nephrons.
   - Cortical nephrons are short looped and juxtamedullary ones are long looped based on the location of tip of the loop of Henle.
   - When the tip is at the junction of inner and outer medulla, it is called short looped cortical nephrons.