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**Educational Webinars on Pediatric Nephrology &
Rare Kidney Diseases**



ERKNet

The European
Rare Kidney Disease
Reference Network



Date: January 14, 2020

Topic: Embryology of the Kidney and Urinary Tract

Speaker: Jacqueline Ho, MD

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Moderator: Elena Levtchenko (Leuven, Belgium)

Objectives

- Understand the significance of congenital anomalies of the kidney and urinary tract in pediatric kidney disease
- Discuss the embryological origins of the kidney and how that impacts on nephron number and pattern
- Describe the development of the lower urinary tract and understand how that impacts kidney function

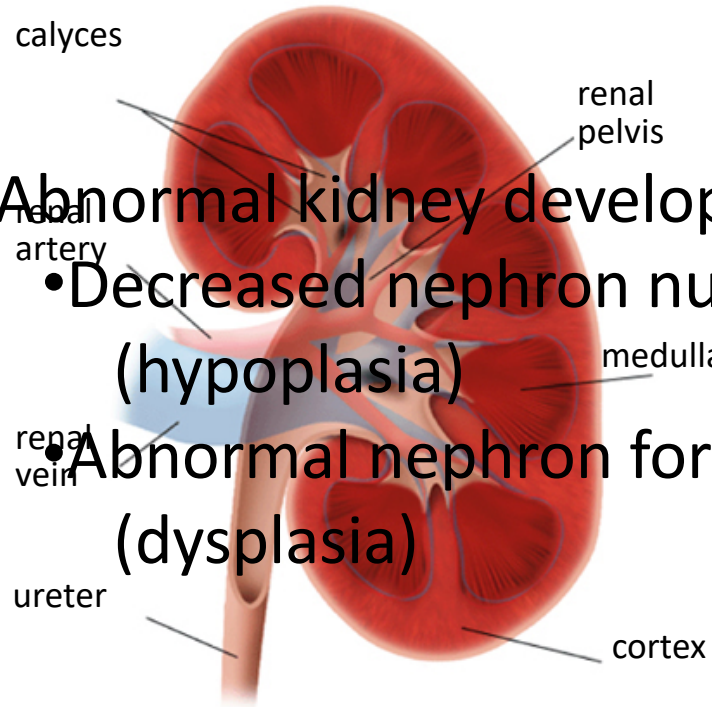
Consequences of abnormal kidney and lower urinary tract development

- Congenital anomalies of the kidney and urinary tract are the most common cause of renal failure in children
- Pediatric renal transplant patients (NAPRTCS registry):

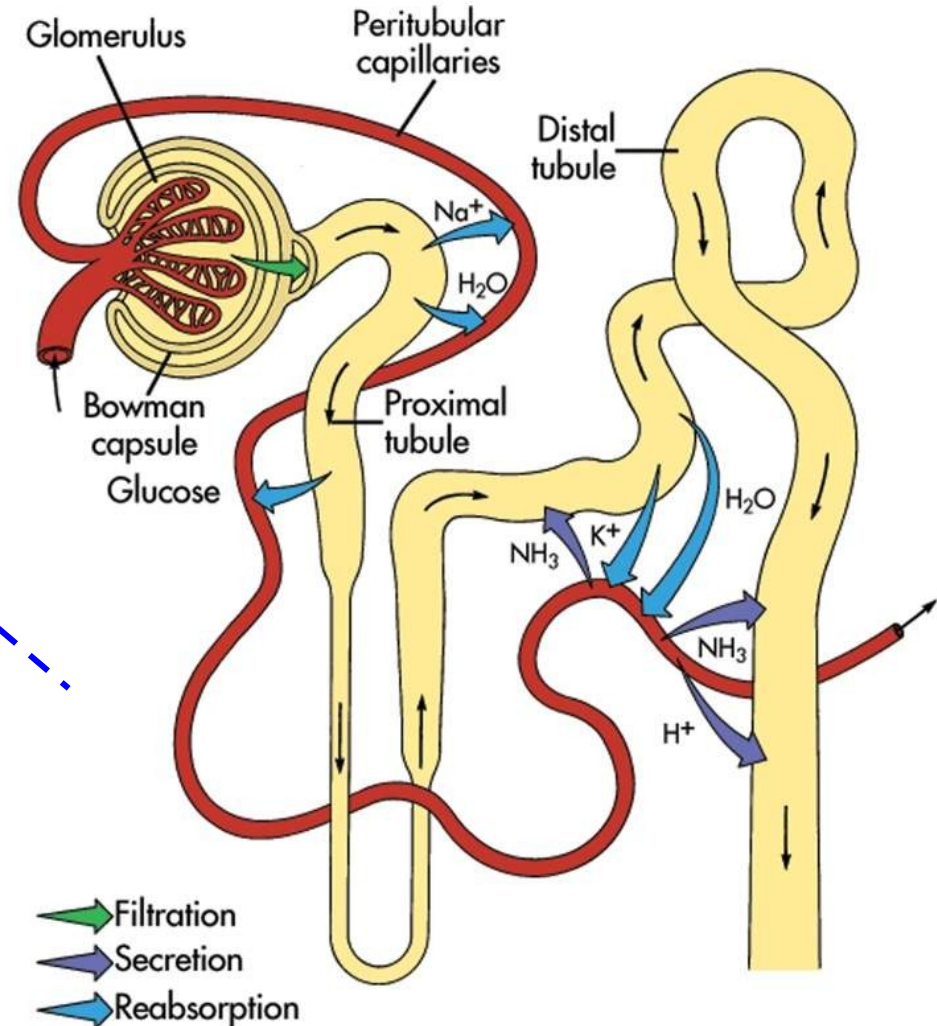
Primary Diagnosis	Percent
Renal aplasia/dysplasia/hypoplasia	15.8
Obstructive uropathy	15.3
FSGS	11.7
Other	57.1

Nephron: “functional unit” of kidney

- Abnormal kidney development:
 - Decreased nephron number (hypoplasia)
 - Abnormal nephron formation (dysplasia)



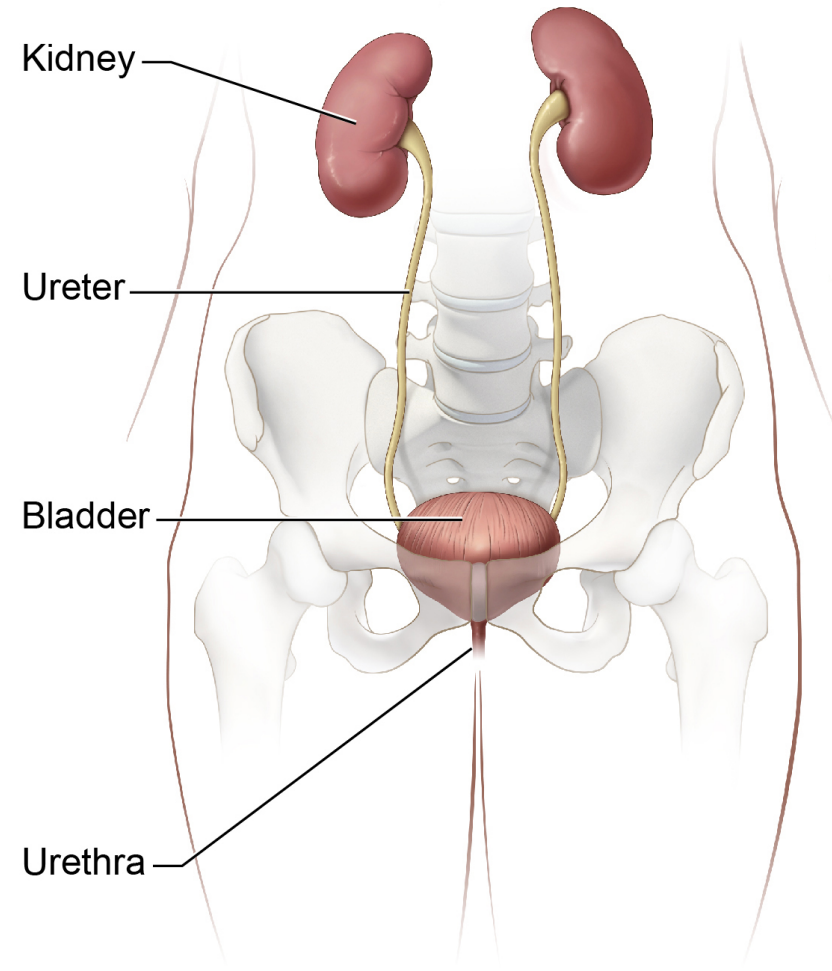
Human kidneys contain approximately 200,000 – 2,000,000 nephrons



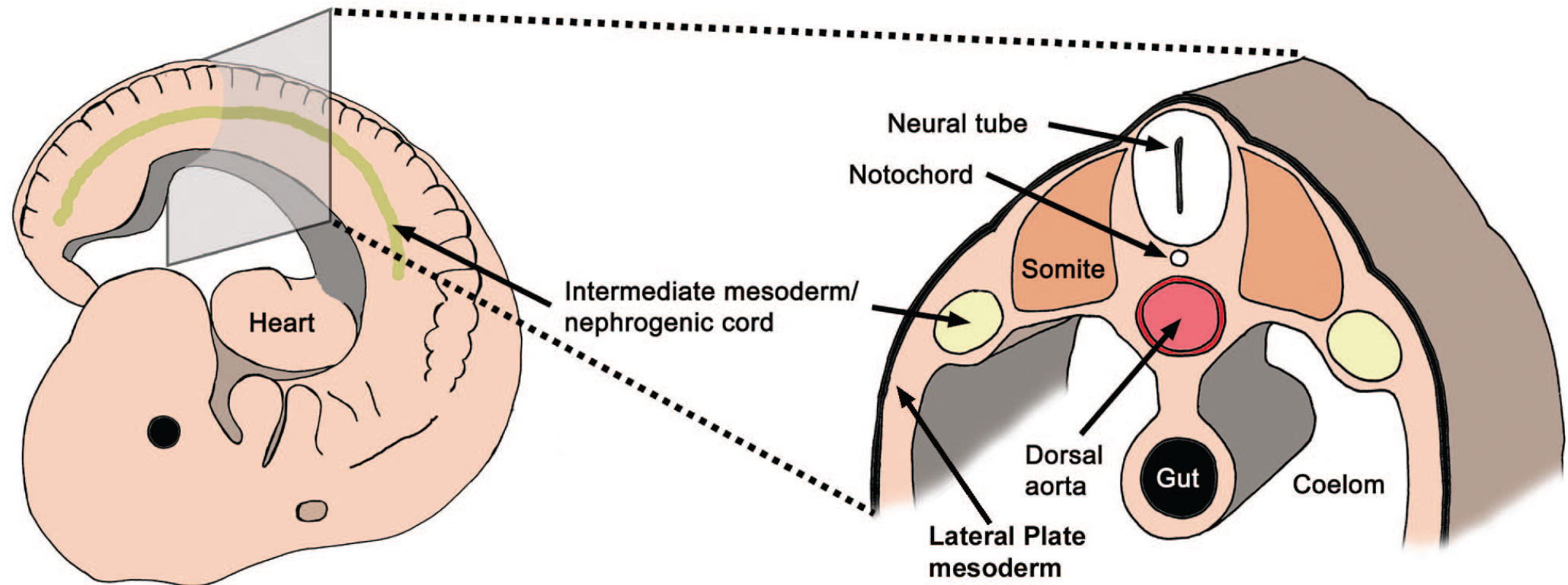
(From Thibodeau GA, Patton KT: *Anatomy & physiology*, ed 5, St Louis, 2003, Mosby.)

Lower urinary tract

- Anomalies in lower urinary tract development can result in renal hypoplasia or dysplasia
- Postnatally, urological issues influence renal outcomes
 - UTIs
 - Nephrolithiasis
 - Hydronephrosis

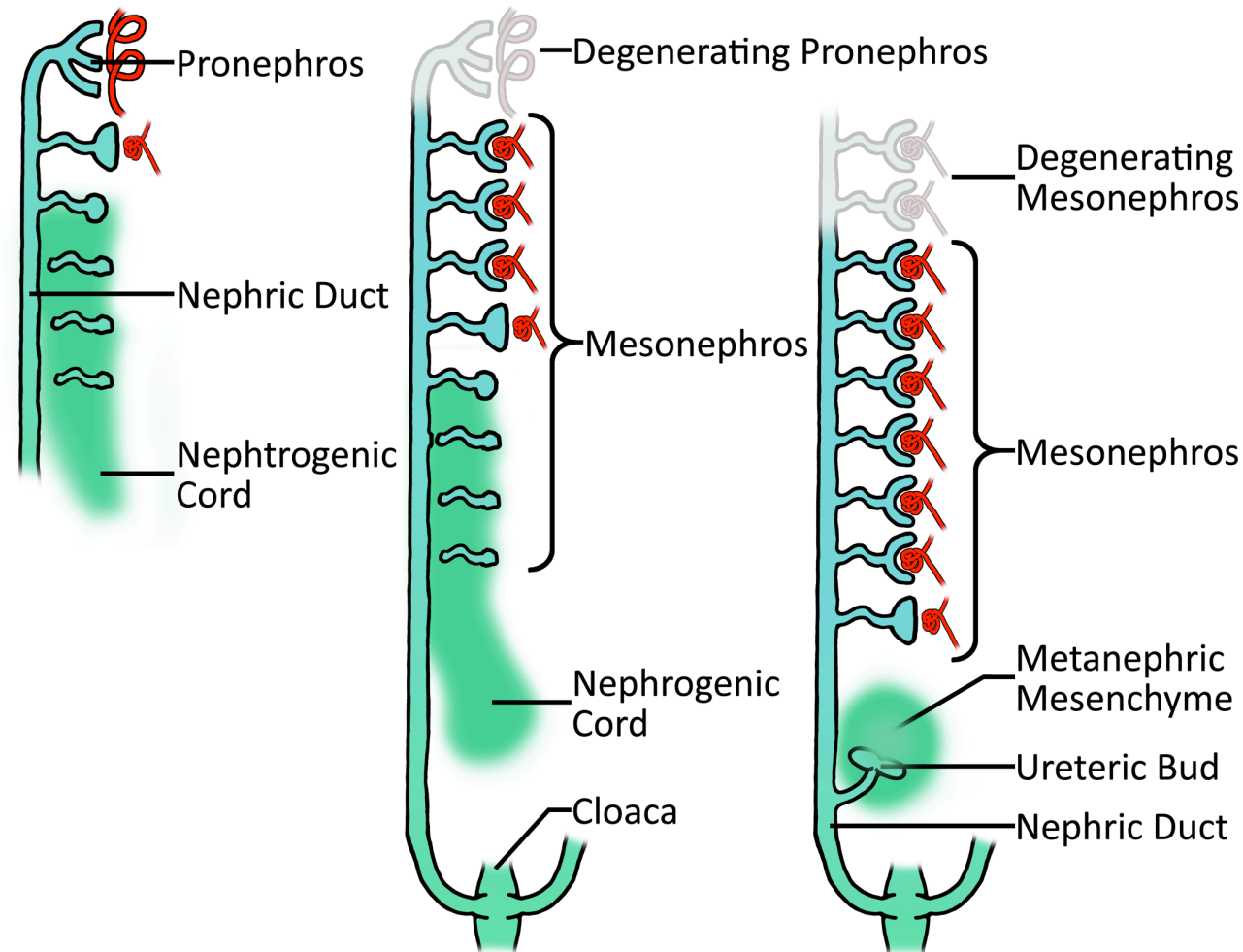


Embryological origin of the kidney and lower urinary tract: intermediate mesoderm



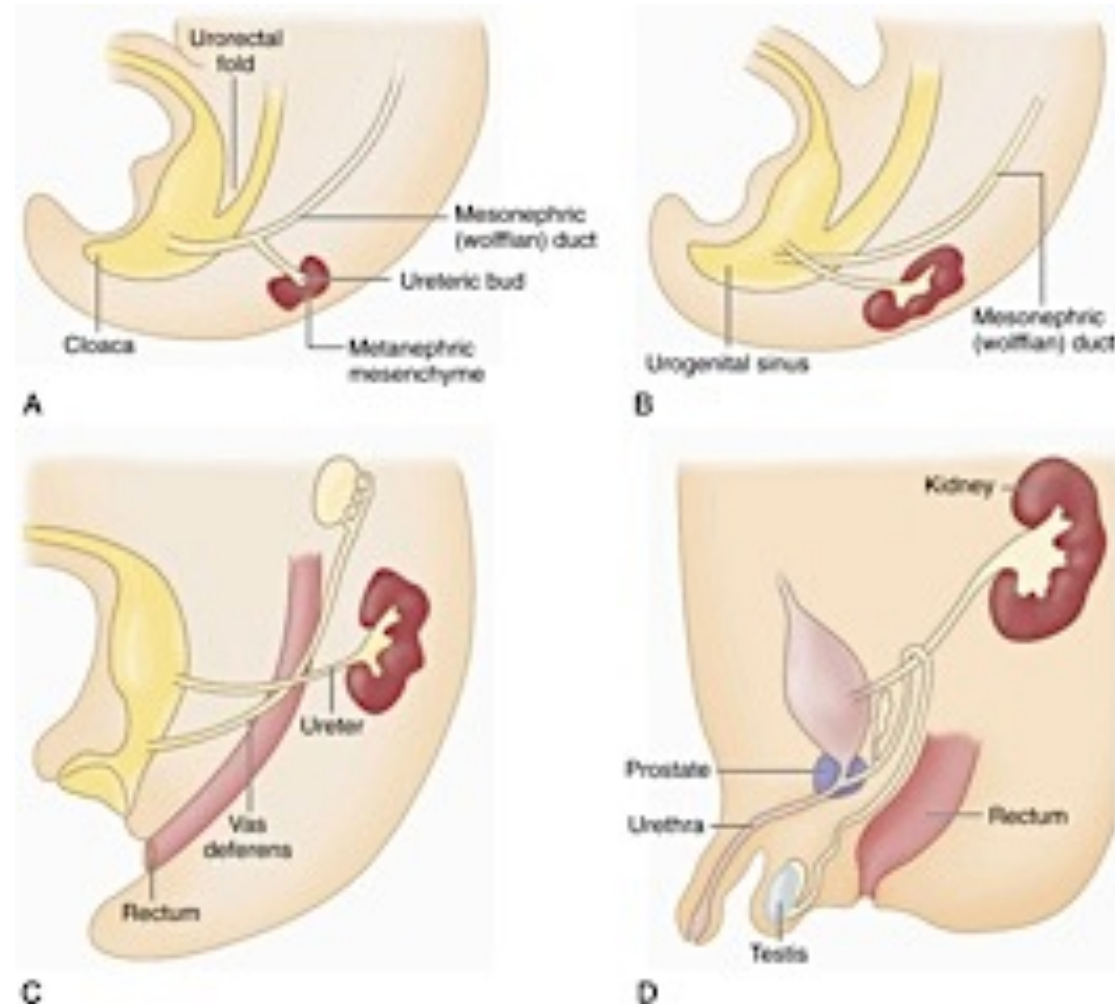
Davidson AJ. Mouse kidney development. 2009 Jan 15. In: StemBook [Internet]. Cambridge (MA): Harvard Stem Cell Institute; 2008-. Figure 2, Location of the intermediate mesoderm/nephrogenic cord. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK27080/figure/mousekidneydevelopment.F2/doi:10.3824/stembook.1.34.1>

Stages of kidney development

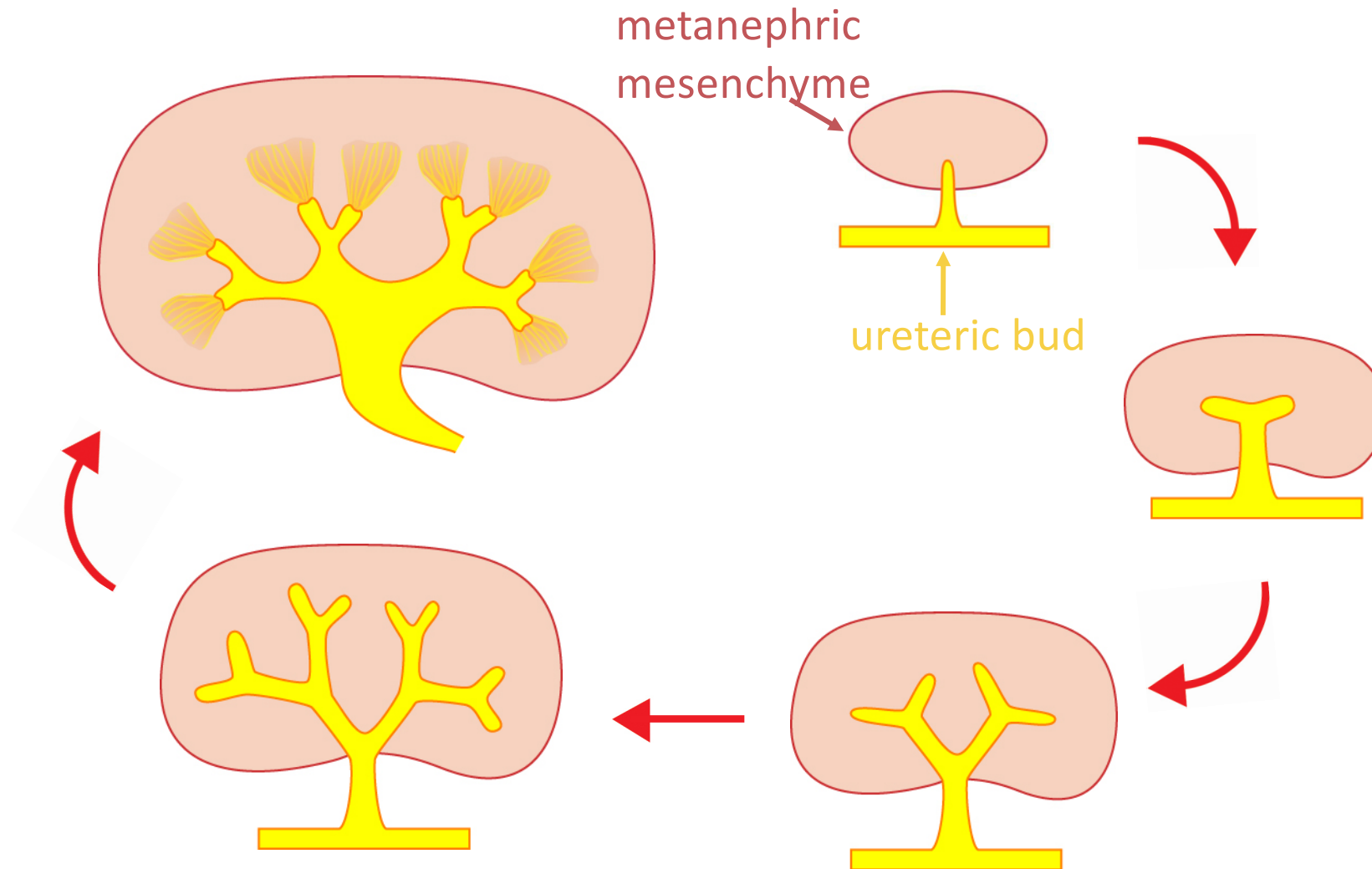


Metanephric kidney development

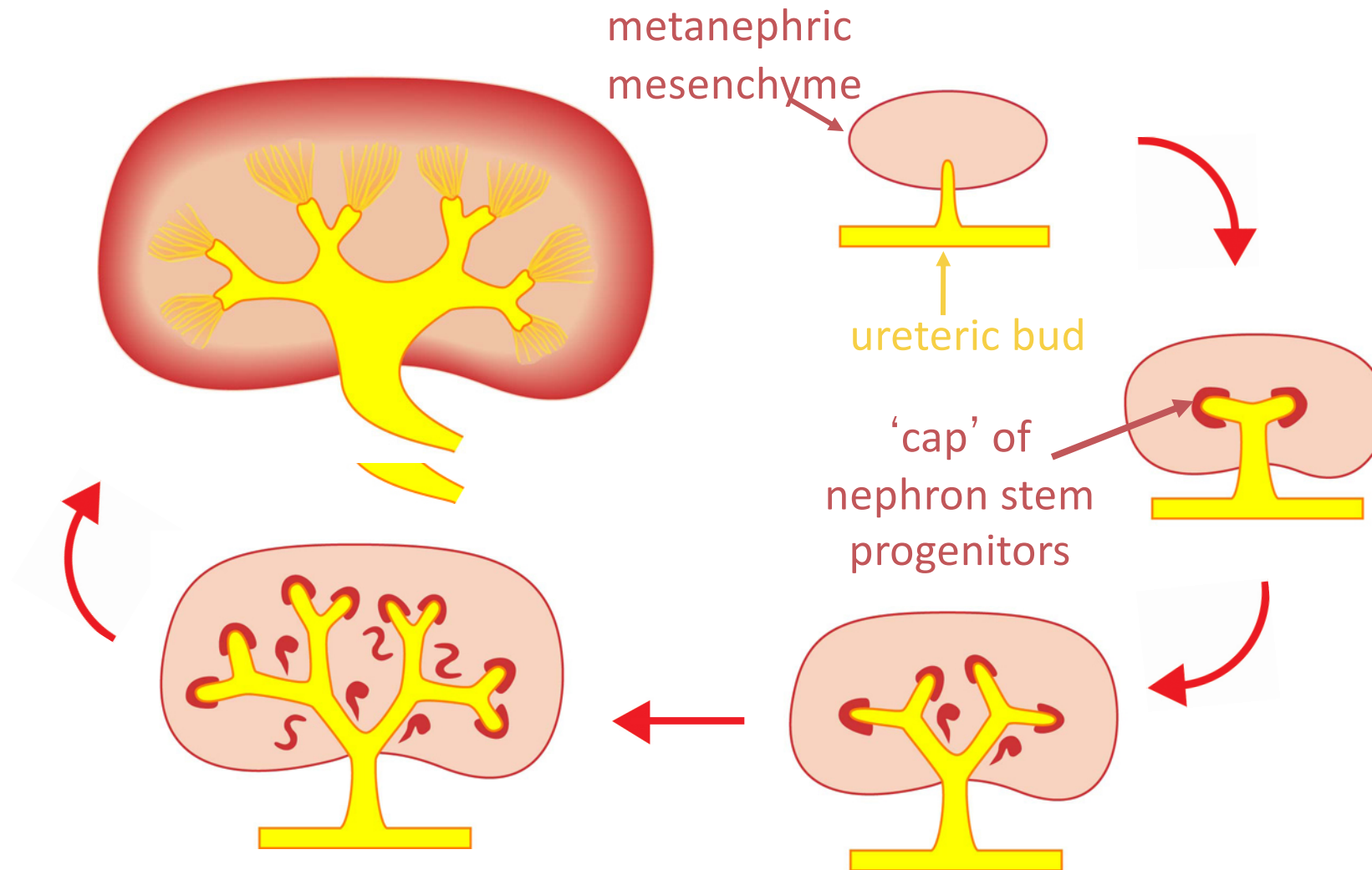
- Reciprocal induction of ureteric bud and metanephric mesenchyme
 - 5th week of gestation in humans
 - Embryonic day 10.5 in mice
- Kidneys migrate rostrally and rotate



Nephron formation

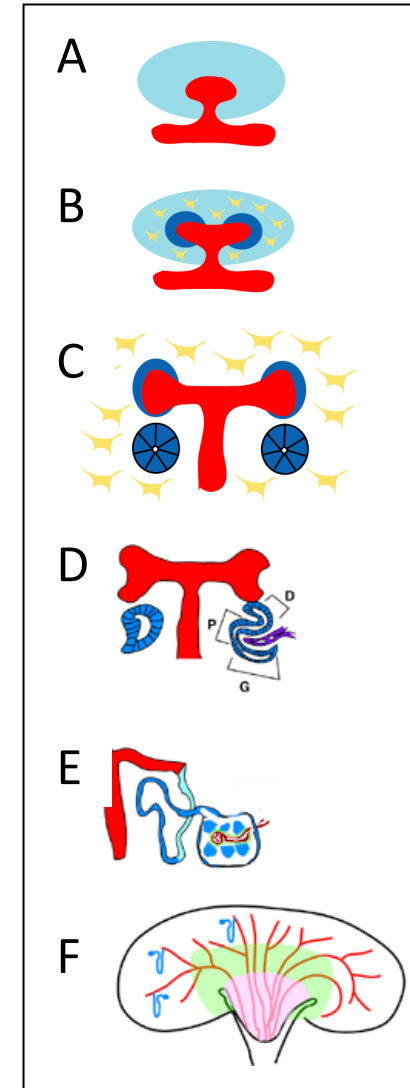


Nephron formation



Developmental lineages of nephron segments

- Ureteric bud:
 - Collecting duct
 - Ureter
- Nephron progenitor (metanephric mesenchyme, cap mesenchyme):
 - Podocytes
 - Proximal tubule
 - Loop of Henle
 - Distal tubule
- Endothelial cells
 - Glomerular endothelial cells
 - Peritubular endothelial cells



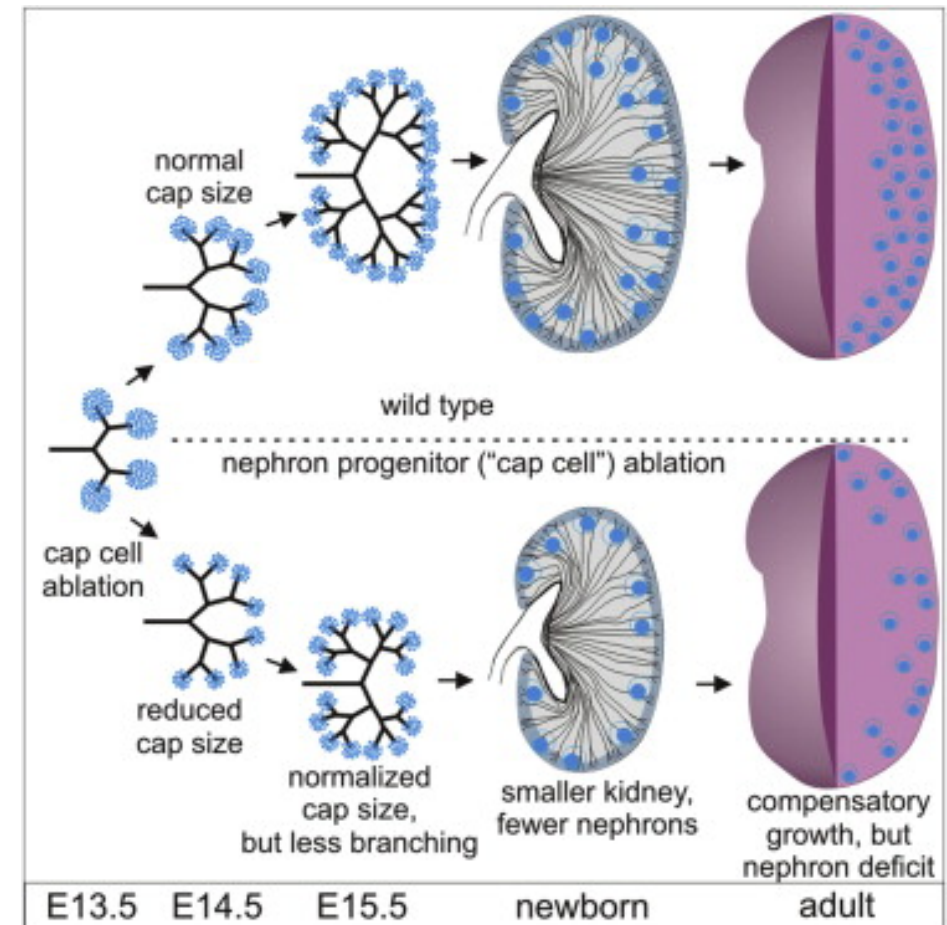
Question 1

You are seeing an infant with renal dysplasia in the clinic, and a student asks you to discuss the different stages of renal development. Which of the following is correct?

- A. The proximal tubule arises from the metanephric mesenchyme
- B. The mesonephros forms part of the mature kidney
- C. The metanephros begins to form in the second trimester
- D. The pronephros functions during early embryogenesis
- E. The ureteric bud gives rise to proximal and distal nephron segments

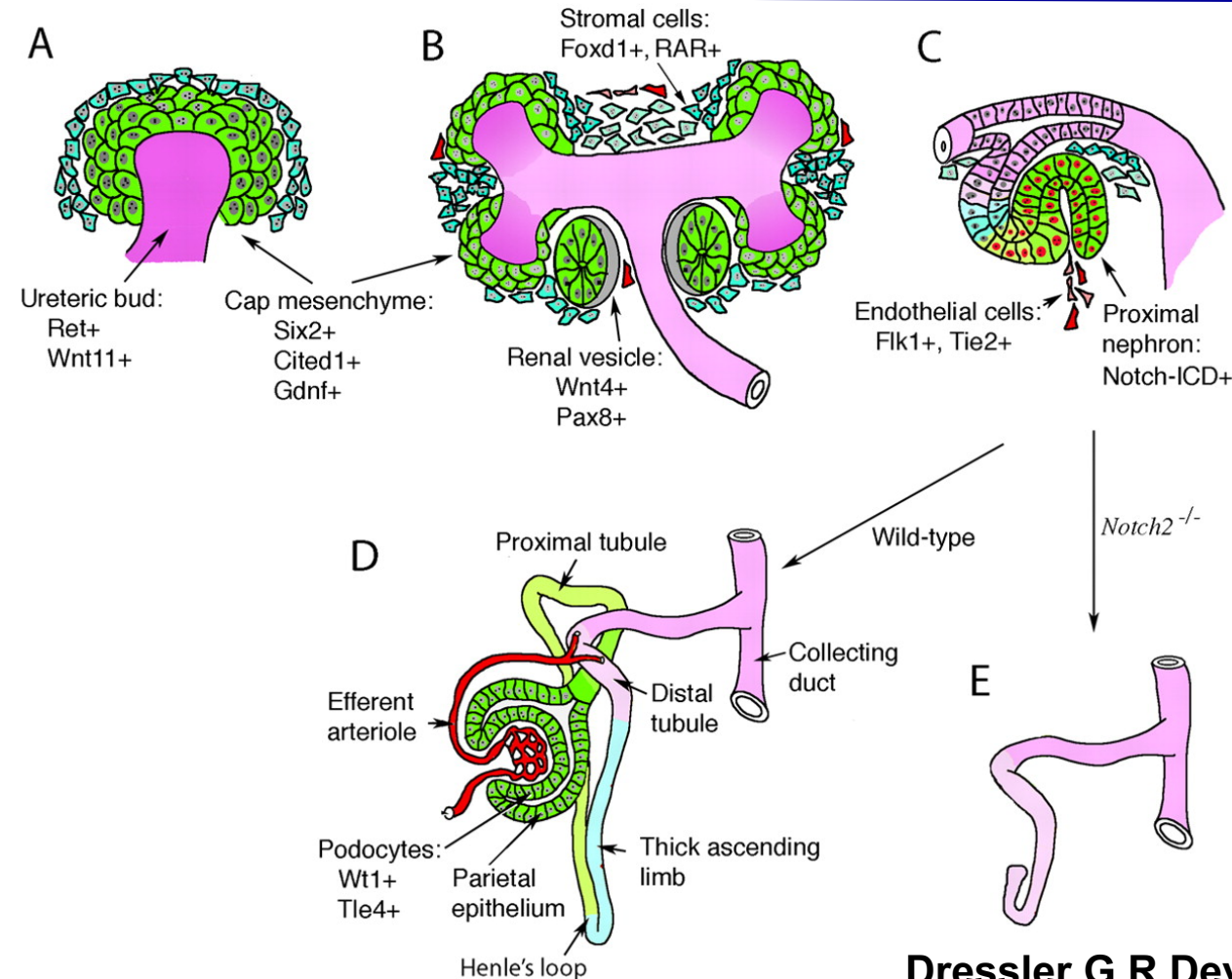
What determines nephron number?

- All nephrons are formed by around 36 weeks gestation in the human.
- The number of nephron progenitors and ureteric branching are significant contributors to how many nephrons are formed.
- The number of nephrons that are formed is impacted by genetic and environmental factors.



Cebrian et al (2014); Cell Reports: 7(1), 127-137.

What determines nephron pattern?



Dressler G R Development 2009;136:3863-3874.

Implications for kidney health and disease

- Congenital nephron endowment varies widely amongst individuals
- All nephrons are formed by 36 weeks gestational age
- Concept of “renal reserve”:
 - Progressive loss of nephrons due to age, kidney disease, hypertension
 - Decreased reserve leads to increased risk of chronic kidney disease

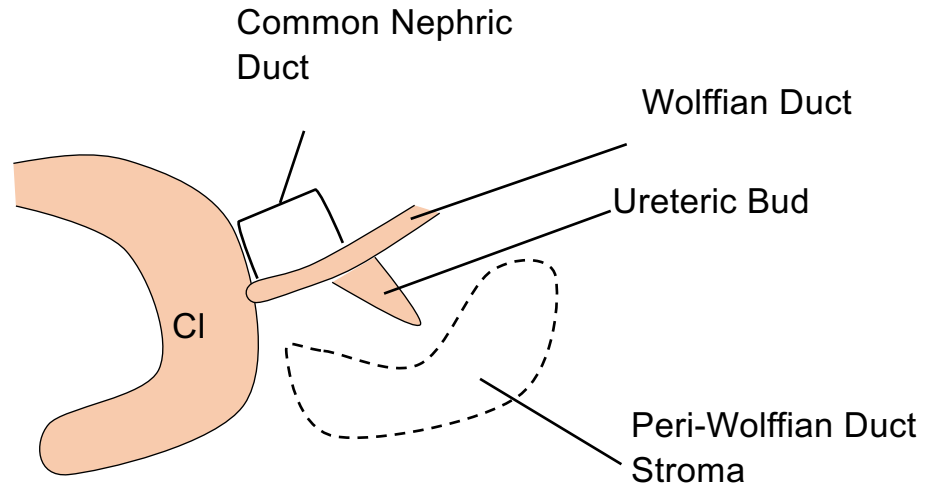
Question 2

You are seeing a family in prenatal consult regarding an antenatal ultrasound at 18 weeks gestational age demonstrating small, echogenic kidneys. The parents would like to have more information about the long-term renal outcome. Which of the following is accurate?

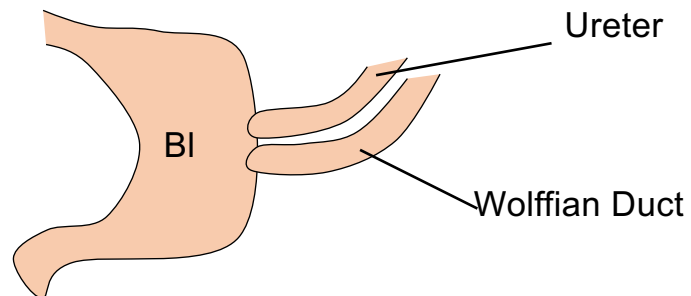
- A. Renal hypodysplasia at this age has no effect on renal outcome because nephrons are still forming.
- B. New nephrons can be made postnatally to compensate for poor kidney development in utero.
- C. The child is likely to develop chronic kidney disease and the course is variable.
- D. The child is likely to go into renal failure as an infant.
- E. Associated pulmonary hypoplasia is not a predictor of long-term outcome.

Lower urinary tract development: ureter

A (E11.5)



B (E14.0)



- Signaling between the peri-Wolffian duct stroma and ureteric bud is important in development of the ureter
- Ultimately determines the position of ureteral insertion into the bladder

Ureteral insertion into the bladder is affected by position of the ureteric bud

- Mackie-Stephens Hypothesis
- Ureteric bud positioned too high (cranial) then the ureter inserts low
- Ureteric bud positioned too low (caudal) and the ureter inserts high

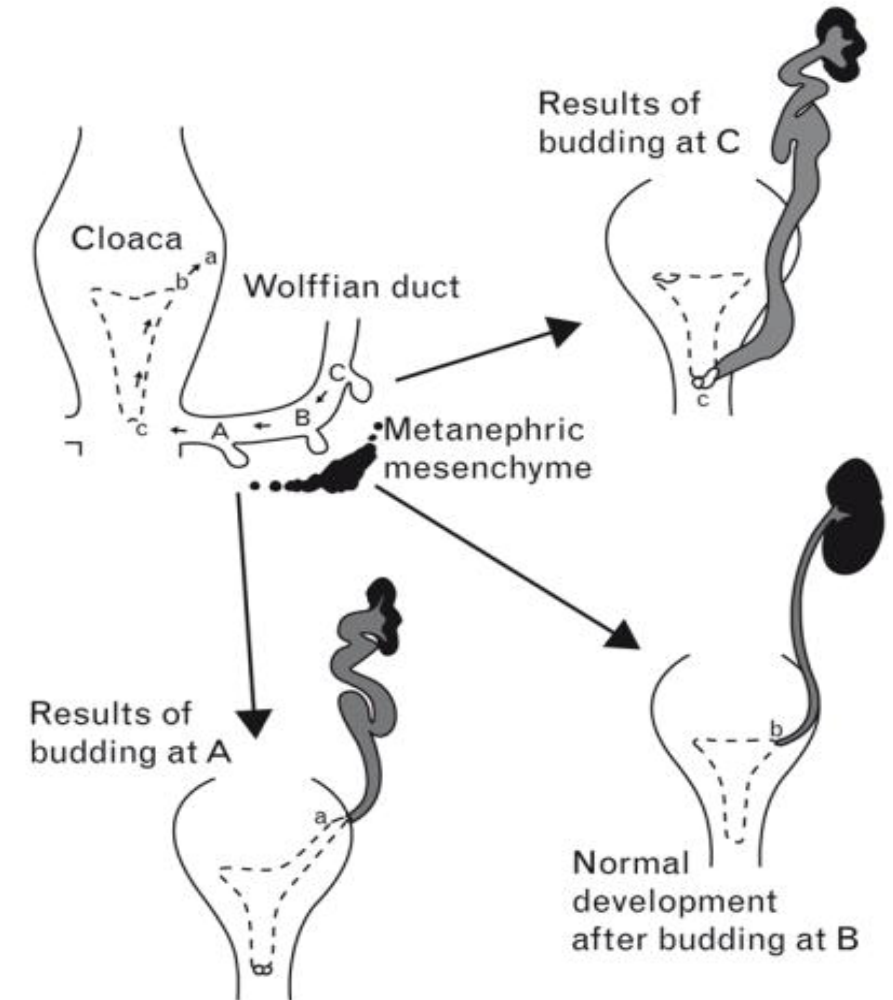
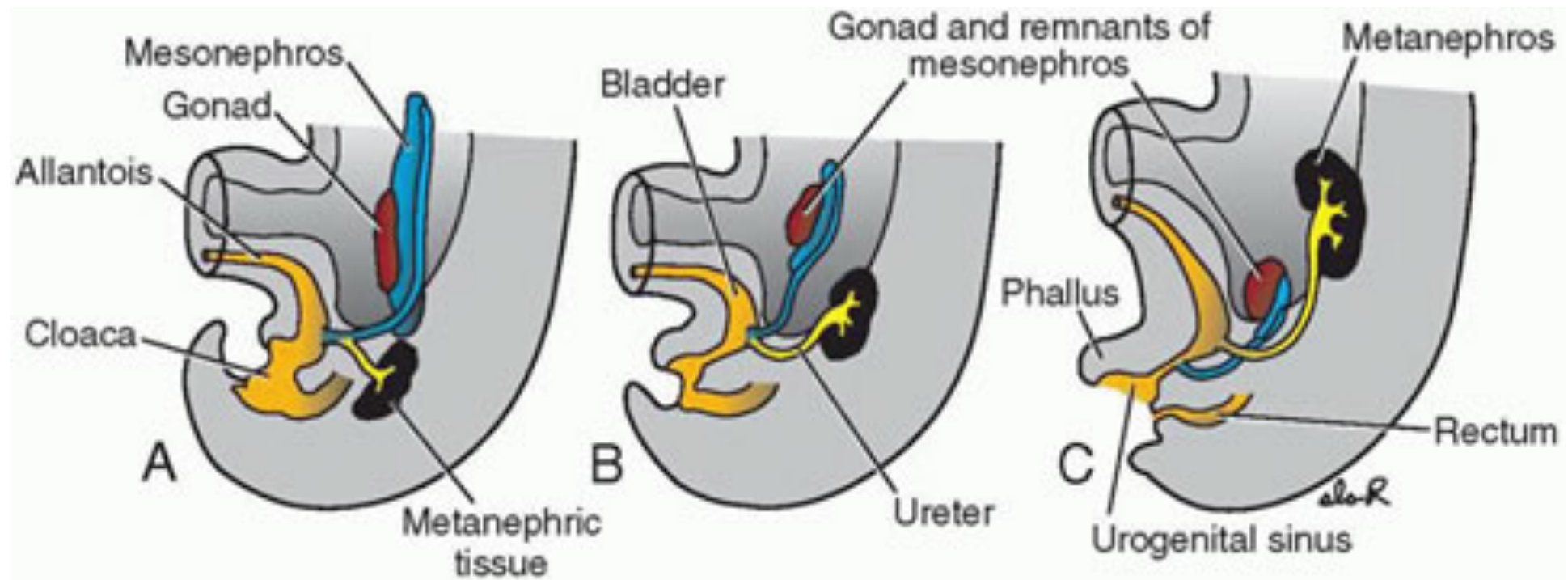
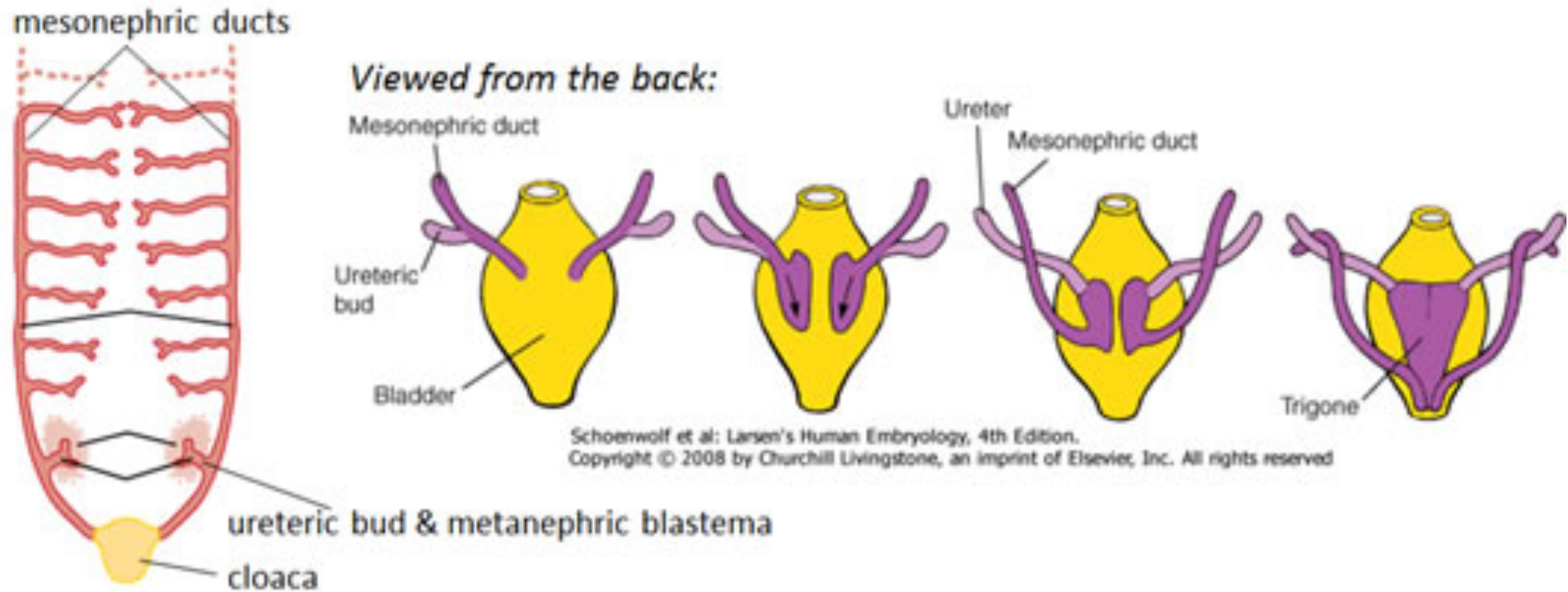


Image from Weber, 2012

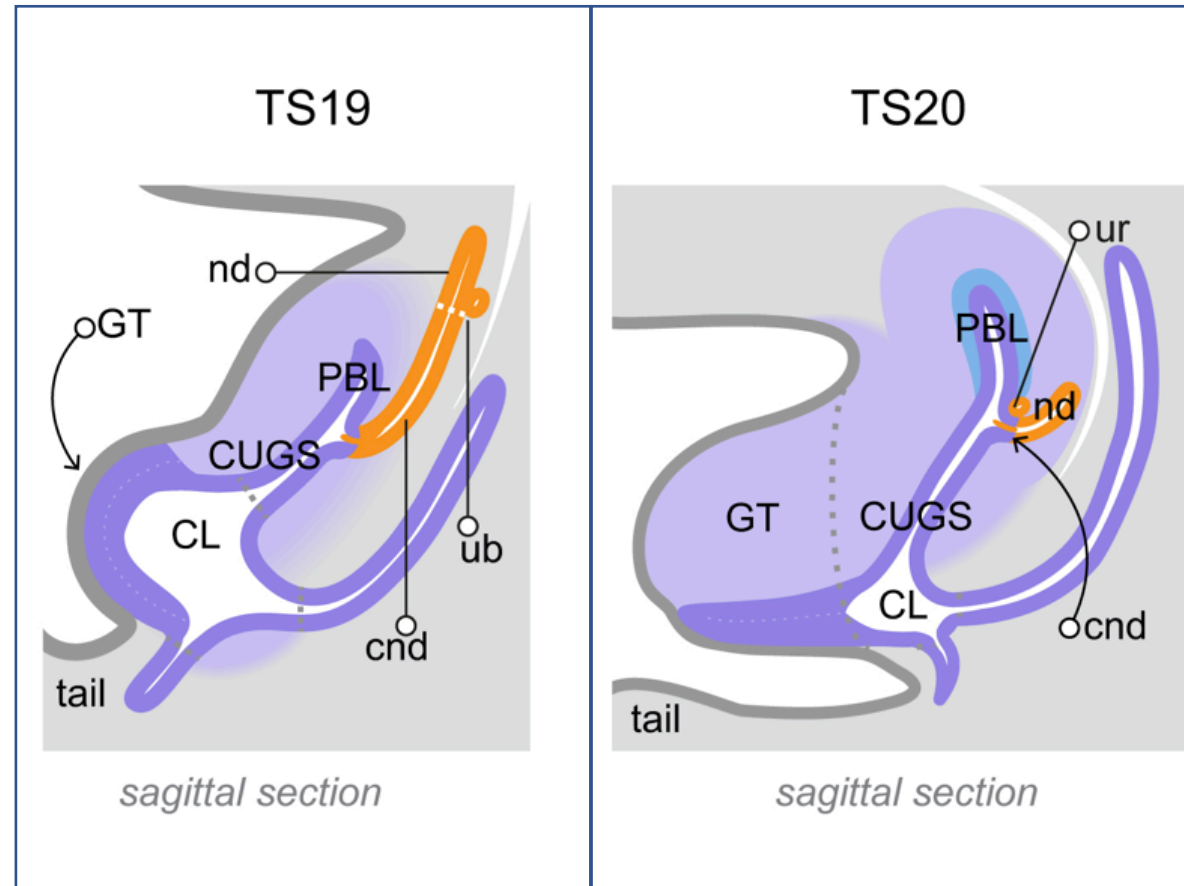
Bladder development



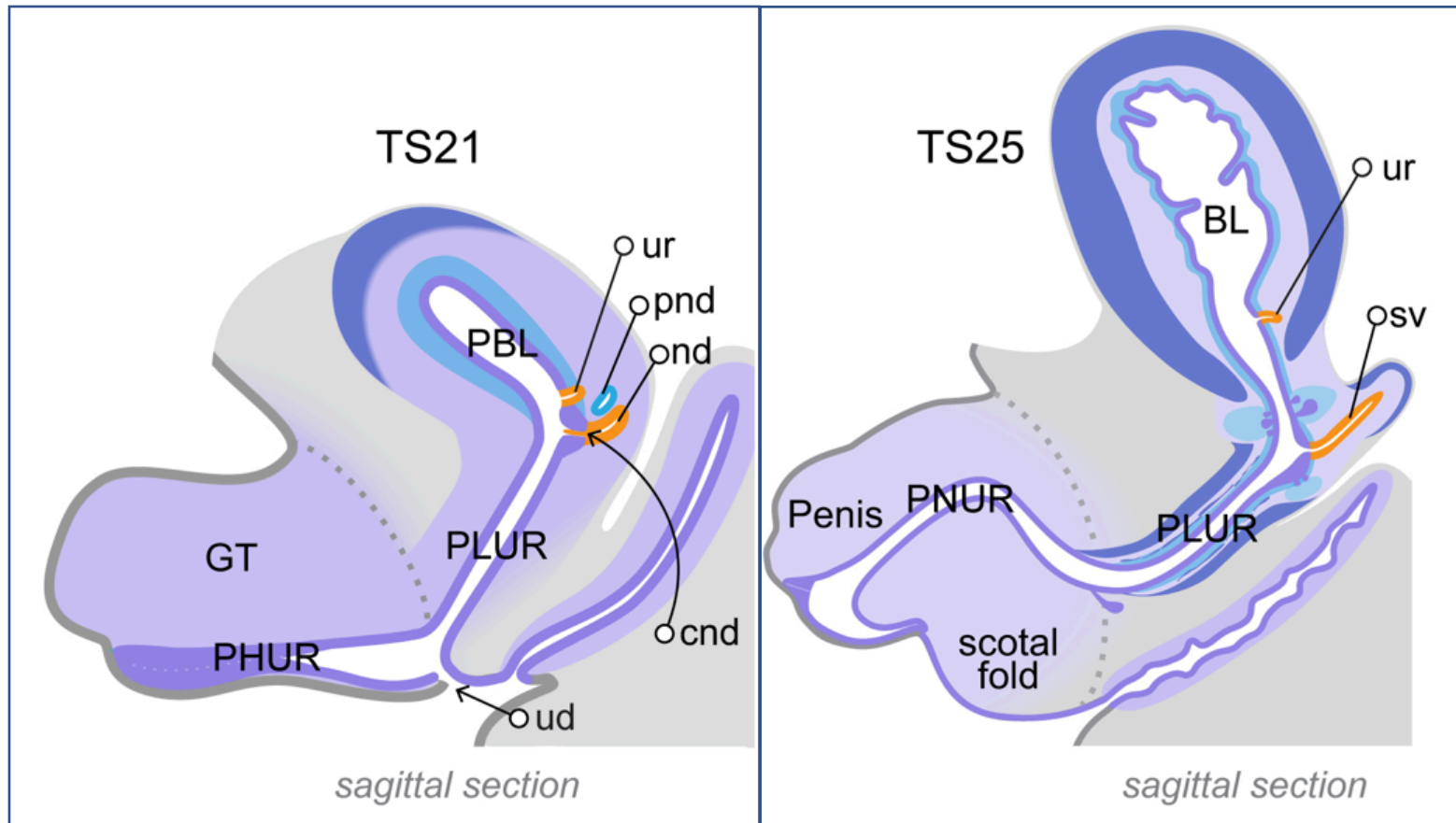
Bladder development



Urethral development



Urethral development



Question 3

The parents of a newborn infant with posterior urethral valves are asking you about the long-term renal outcome. Which of the following is the most accurate statement?

- A. Prenatal obstruction does not affect nephron pattern
- B. Prenatal obstruction does not affect nephron number
- C. The effects of prenatal obstruction on renal development are encountered in the third trimester
- D. The extent of tubular atrophy and interstitial fibrosis are major determinants of long-term outcome
- E. The long-term outcome is primarily determined by mutations in components of the renin-angiotensin system

Framework for congenital urogenital anomalies

- Abnormalities in development of the renal parenchyma
 - Renal hypoplasia
 - Renal dysplasia
- Aberrant migration of the kidneys
 - Ectopic kidneys
 - Fusion anomalies
- Abnormalities in the developing urinary collecting system
 - Obstruction
 - Vesicoureteral reflux

Next Webinars



IPNA Clinical Practice Webinars

Date: **January 16, 2020 (4 pm CET)**

Speaker: **Rukshana Shroff**

Topic: **Clinical practice recommendations for native vitamin D therapy in children with CKD stages 2-5 and on dialysis**

ERKNet Advanced Webinars on Rare Kidney Disorders

Date: **Januar 28, 2020 (4 pm CET)**

Speaker: **Francesco Emma**

Topic: **Update on the treatment of SSNS**

ESPN/ERKNet Educational Webinars on Pediatric Nephrology & Rare Kidney Diseases

Date: **February 11, 2020 (4 pm CET)**

Speaker: **Beata Lipska**

Topic: **Genetics - Basic concepts and testing**

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