Kidney Development and Function in the Fetus

Bob Caruthers, CST, PhD

The kidneys produce urine, a blood filtrate, and regulate urinary volume and composition. These regulatory activities involve balancing water and solute transport, conserving nutrients, eliminating waste products, and regulating acid and bases. The primary purpose of kidney function is to maintain a stable environment in which cellular and tissue metabolic activity can proceed at an optimal level. The kidneys secrete the hormone renin, erythropoietin and 1,25-dihydroxy vitamin D. Renin helps regulate blood pressure. Erythropoietin helps regulate erythrocyte production. 1,25-dihydroxy vitamin D plays a role in calcium metabolism. This article will discuss the development of the kidney, and its role in the fetus.[8,9]

Since the kidneys are bilateral structures, development involves both right and left kidneys. During fetal development, three separate nephric structures develop in succession: pronephros, mesonephros and metanephros (Figure 1). The associated urinary bladder and urethra both develop from a derivative of the embryonic hindgut, the urogenital sinus. The pronephros forms first, is not active in urine production, and rapidly undergoes complete regression. The mesonephros forms the second kidney. The body of the mesonephros regresses, but parts of the mesonephric duct remain to form the drainage system of the male gonad. While existing, the mesonephros is thought to produce urine in the human fetus. The third and definitive kidney, the metanephros, forms two rudiments that make up the complete adult kidney and ureter. The metanephros produces urine during fetal development.[8]

PRONEPHROS

The pronephros is a transient structure which originates in the intermediate mesoderm associated with the cranial and cervical somites. Component parts, cords of tissue or vesicles, can be seen in the fourth week. The pronephros is completel regressed by the start of the fifth week. The pronephros form and regresses in a cranial-to-caudal sequence. No pronephric glomeruli (cluster of capillaries) have been observed, and no vesicles are associated with the pronephric duct. The pronephros is, therefore, not active in urine production.[8]

MESONEPHROS

The mesonephros originates in the nephrogenic cord that is part of the intermediate mesoderm. Early mesonephric formation is evident before the pronephros has completed its regres sion. The mesonephros also degenerates in a cranial-to-cauda sequence. Some of the cranial structures are degenerating in the fifth week of fetal development while the caudal structur are still differentiating. By the eighth week of fetal development, most of the mesonephric structures have disappeared.[8]

The nephrogenic cord elongates caudally. As it grows caudal ly, the nephrogenic cord differentiates into mesonephric vesicle These vesicles form from the first thoracic to the third lumbar segment and quickly increase in number by the means of bifurc tion and/or subdivision. The vesicles elongate and appear as either pear-shaped or S-shaped vesicles. These vesicles form rud mentary nephrons. The S-shaped vesicles develop communication with the mesonephric duct (Wolffian), and branches from the dorsal aorta grow toward these S-shaped vesicles. The bodi of the S-shaped vesicles form a rudimentary type Bowman's cap sule. Blood vessels form capillary tufts that push against the developing Bowman's capsule and connect to vessels from the dorsal aorta. Portions of the S-shaped vesicle not involved in tl previously described development become more convoluted an associate with efferent arterioles that carry blood from the glomeruli (capillary tufts) to the posterior cardinal vein.[8]

Unlike the pronephros, not all of the mesonephric structures disappear. About the sixth week, the remaining mesonephros forms an ovoid mass just lateral to the midline that, with the developing gonad, helps form the urogenital ridge. The mesonephric duct courses along the lateral border of the urogenital ridge and connects with the urogenital sinus where it serves to drain the mesonephrons. This urogenital sinus will later develop into the adult urinary bladder and urethra. In the male, the mesonephric tubules that lie close to the developing gonad remain as the efferent ductules of the testis and other minor structures. The mesonephric ducts give rise to the duct of the epididymis, the vas deferens, the seminal vesicles and the ejaculatory duct in the male. In the female, the mesonephric ducts degenerates for the most part, while the associated paramesonephric duct (Müllerian) duct forms the uterine tubes, uterus, cervix and part of the vagina. One branch of the mesonephric duct, the ureteric bud, remains as part of the urine collection portion of the metanephros.[8]

There is evidence to support but not yet prove that the mesonephros produces hypotonic urine.[8]

METANEPHROS

The third nephric structure to form is the metanephros, the definitive kidney. The metanephros originates from the metanephric blastema and the ureteric bud. The metanephric blastema evolves in the caudal portion of the nephrogenic cord and develops into the components of the metanephric kidney associated with excretion: Bowman's capsule, proximal convoluted tubule, loop of Henle and distal convoluted tubule. The ureteric bud, a branch of the mesonephric duct, forms the urine collecting components: collecting tubules in the kidney, papillary ducts, and major and minor calyces. The ureteric bud contributes to the ureters, also.[1,8,12,14]

The nephrons are formed from the metanephric blastema. Local condensations of cells of the metanephric blastema form around dilated sections of the ureteric bud. The caps of metanephric blastema differentiate into vesicles, which evolve into S-shaped tubules. These nephrons continue to mature, and new ones are formed. As the nephrons mature there is an increase in the convolutions in the proximal and distal portions of the tubules and an increase in the length of the loop of Henle.[8,12,14]

The metanephros forms at the level of the upper sacral segment and receives its blood supply from sacral branches of the dorsal aorta. Between the sixth to eighth week of fetal development, the sacral segments elongate, which creates an appearance that the metanephros is

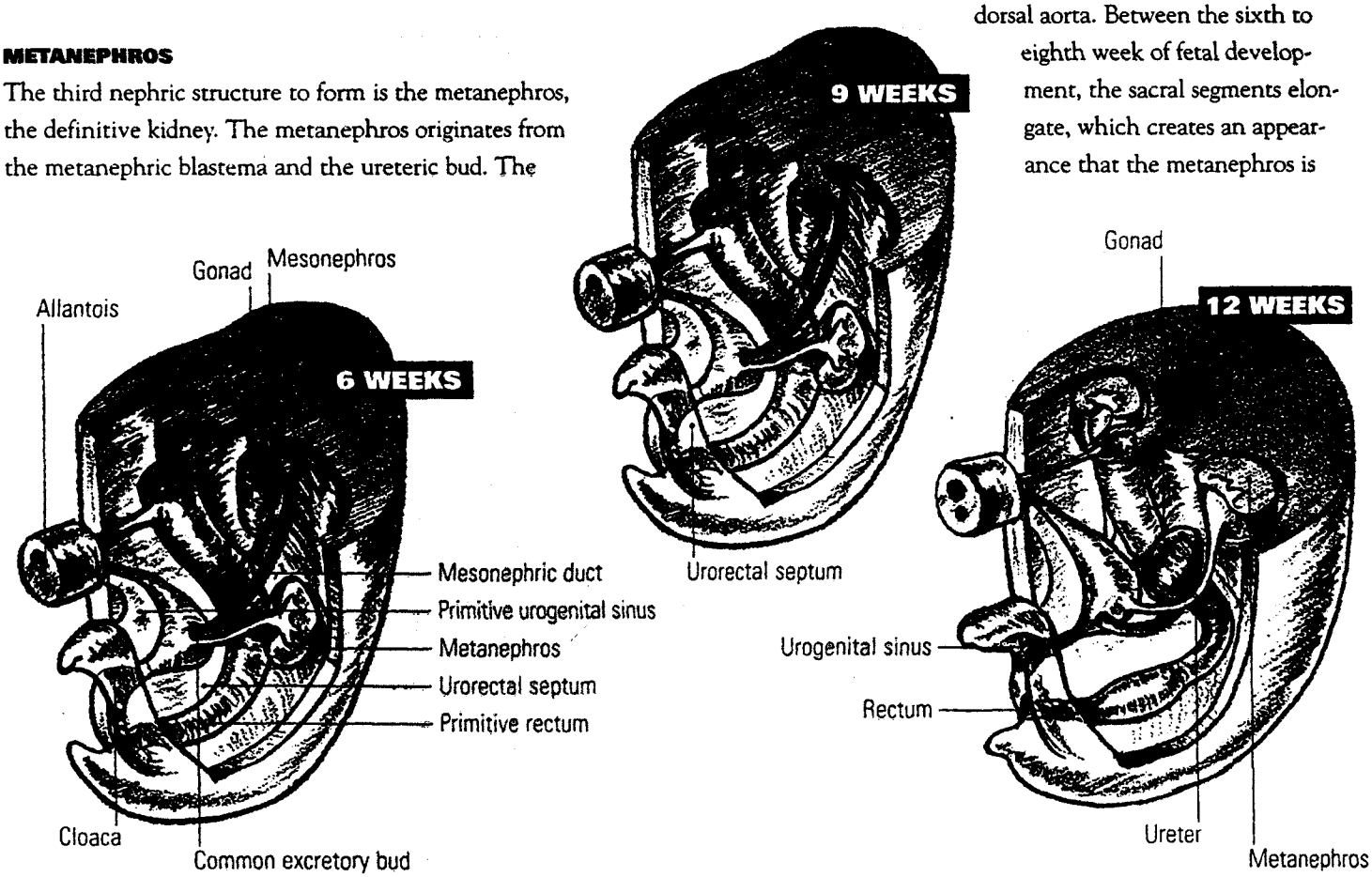

FIGURE 1—Mesonephros, gonad and metanephros during their formation.

ascending. Along with this apparent but illusionary ascension, the metanephros actually does move cephalad. The end result is a repositioning in the lumbar area. As the metanephros ascends, it takes on a new blood supply. At the level of the second lumbar segment, the renal arteries become the definitive supplier of blood to the kidney.[8]

CONGENITAL ANOMALIES OF THE KIDNEY

As with all organ development, congenital mishaps occur. Renal agenesis, the failure of the kidneys to form, is related to a failure in the development of the ureteric bud or failure of the interactive mechanism between the ureteric bud and the metanephric blastema to produce nephrons. Renal agenesis may be unilateral or bilateral. There are several types of congenital cystic disease. While the mechanisms for each type vary, the common outcome is the production of multiple renal cysts. Congenital abnormalities of final location occur. This abnormality results from some failure during the ascent of the metanephros from the sacral to lumbar position. One variant of this is a horseshoe shaped kidney in which the two kidneys are fused at the caudal poles.[8,9]

FETAL URINE PRODUCTION AND AMNIOTIC FLUID REGULATION

As previously mentioned, the mesonephric kidneys probably produce some urine. However, by the end of the twelfth week of fetal development, the mesonephros is completely degenerated, and the metanephros assumes the sole role of urine producer. It is capable of producing large quantities of urine. This fetal urine is hypotonic to fetal plasma in its sodium and chloride concentrations. The average pH is 6.0, slightly acidic. Fetal urine has more urea and creatinine that fetal plasma but it contains little protein or glucose.[4,5,8,9]

Urine production in the fetus is related to regulation of the amniotic fluid volume. Amniotic fluid provides some protection from pathogenic bacteria during fetal life. The amniotic fluid compartment provides the fetus space to grow, move about and develop. Without this space, the uterus would close down on the fetus and restrict development. In cases of first trimester amniotic fluid leakage, a fetus may develop structural abnormalities secondary to uterine compression. By midpregnancy, the amniotic fluid plays a critical role in pulmonary development. Successful pulmonary development requires that the respiratory tract be filled with fluid and that the fetus be

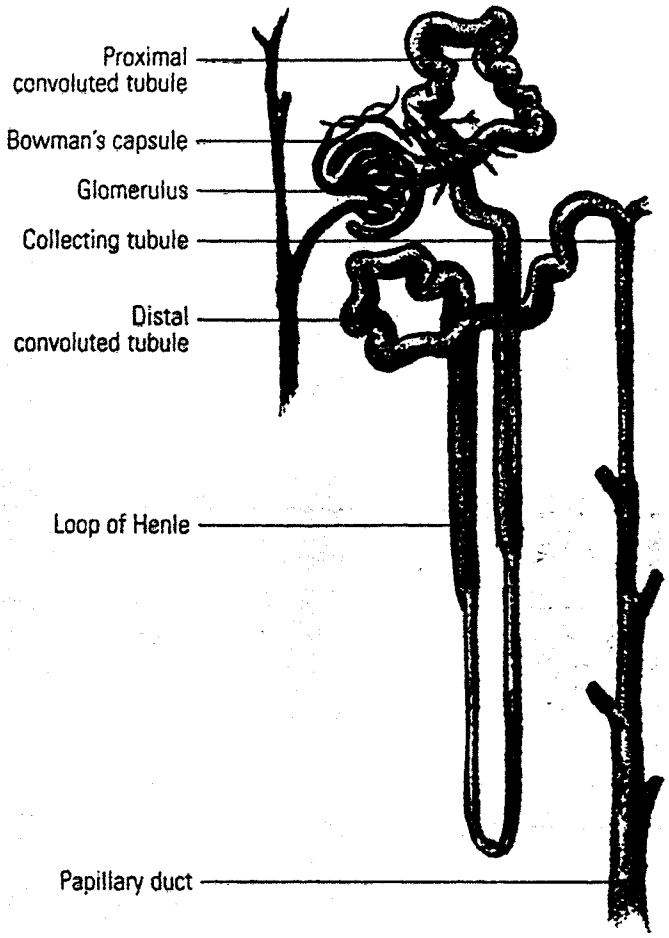

FIGURE 2—Major components of the uriniferous unit in the adult kidne

able to move the fluid in and out of the lungs. Low levels of amniotic fluid during this period of fetal development are ass ciated with pulmonary hypoplasia. Recent intrauterine therapeutic techniques may reduce fetal morbidity and mortality rates secondary to obstructive uropathy. During labor and delivery, the amniotic fluid continues to provide some protec tion for the fetus and aid in dilatation of the cervix. In the fi trimester the fluid volume is normally between 5 and 25 mill liters. At term, the volume of amniotic fluid is between 700 and 1000 milliliters. Abnormal amounts of amniotic fluid result from variations in fetal renal function, swallowing, lun fluid production or transchorionic water flow. The fetus itsel helps regulate these functions hormonally.

In the first trimester, the amniotic fluid results from the transudation of fetal plasma across the fetal skin or umbilical cord or maternal plasma through the vascular uterine decidu First trimester fluid is iso-osmotic relative to fetal and matern

plasma. In the second trimester, the fluid production changes. Urine is eliminated into the amniotic cavity beginning about the ninth week of development. From that point, the fetus participates in the regulation of the amniotic fluid volume by producing hypotonic urine to increase volume and swallowing it to reduce volume. The fetal kidneys produce 600-700 ml of hypotonic urine per day. The lungs produce approximately 250 ml of fluid per day. The fetus swallows approximately 500 ml of fluid per day and another 350-450 ml are reabsorbed across the chorioamnion as a result of the osmotic gradient between the amniotic fluid and maternal plasma. These fluid dynamics assist the obstetrician with evaluating fetal development. Oligohydramnios, a small volume of amniotic fluid, suggests renal agenesis or renal obstruction. Polyhydramnios, a large volume of amniotic fluid, suggests anencephaly because of the inability to swallow or esophageal atresia.[2,3,4,5,6,7,8,10,11,13]

Fetal nitrogenous waste is eliminated by maternal urination since the nitrogenous wastes diffuse across the placenta membrane into the maternal blood supply.[8]

MATURE—GROSS ANATOMY

Two kidneys, concave on the medial side, are located in the retroperitoneal space on either side of the vertebral column. In the concavity, a hilum is formed where the renal ureter exits and the blood vessels, lymphatics and nerves enter. The renal sinus is a cavity surrounded by the renal parenchyma. The renal sinus holds the renal pelvis and calyces. The parenchyma itself consists of a dark-colored cortex and lighter medulla. The cortex contains the glomeruli and some portions of the tubules. The medulla is made up of a number of renal pyramids. The pyramids contain the uriniferous tubules and blood vessels. The bases of the renal pyramids contact the cortex, and the apices terminate in the minor calyces. Several of the minor calyces form a major calyx.[8,9]

NEPHRON AND COLLECTING TUBULES

The functional unit of the kidney, the uriniferous tubules, is composed of the nephron and collecting tubules. The nephrons produce urine, and the collecting tubules concentrate and transport it. The proximal portion of each nephron is called the renal corpuscle. It consists of a cup-like structure called Bowman's capsule and a glomerulus. The renal corpuscle has a vascular pole and a urinary pole. Blood vessels enter and exit the glomerulus at the vascular pole. The parietal epithelium of Bowman's capsule continues with the proximal tubule at the urinary pole. The proximal and distal portions of the tubules are convoluted. Between these convoluted sections lies the loop of Henle. The collecting tubules are ducts that collect urine from the distal tubules and transport it to the papillary ducts[8,9] (Figure 2).

SUMMARY

Three separate nephric structures arise during fetal development. The second and third structures produce urine, but only the third remains as a mature and definitive organ in the fetus. The metanephros or third nephric structure plays a significant role in the regulation of amniotic fluid volume. The kidneys, themselves, are critical to the maintenance of a proper environment for cellular metabolism throughout life.

BIBLIOGRAPHY

1. Baker LA, Gomez RA. "Embryonic development of the ureter." *Semin Nephrol*, 1998, Nov; 18(6): 569-84.
2. Birnholz JC, Madanes AE. "Amniotic fluid accumulation in the first trimester." *J Ultrasound Med* 1995 Aug; 14(8):597-602.
3. Dura TT, da Cunha Ferreira RM, Monreal I, Ezcurdia GM, Villa-Elizaga I. "Zinc concentration of amniotic fluid in the course of pregnancy and its relationship to fetal weight and length." *Gynecol Obstet Invest* 1984; 18(3):152-55.
4. Gulbis B, Gervy C, Jauniaux E. "Amniotic fluid biochemistry in second-trimester trisomic pregnancies: relationships to fetal organ maturation and dysfunction." *Early Hum Dev* 1998 Oct; 52(3):211-19.
5. Gulbis B, Jauniaux E, Jurkovic D, Gervy C, Ooms HA. "Biochemical investigation of fetal renal maturation in early pregnancy." *Pediatric Res* 1996 Apr; 39(4 pt 1):731-35.
6. Heikinheimo M, Seppala M, Brock DJ. "Pregnancy specific beta 1-glycoprotein and human chorionic gonadotrophin levels in amniotic fluid and maternal serum in the first half of pregnancy." *Oncodiv Biol Med* 1980 Aug; 1(1):71-6.
7. Jauniaux E, Gulbis B, Hyett J, Nicolaides KH. "Biochemical analyses of mesenchymal fluid in early pregnancy." *Am J Obstet Gynecol* 1998 Apr; 178(4):765-69.
8. Johnson KE. *Human Developmental Anatomy*. National Medical Series. Williams & Wilkins: Baltimore, MD, 1988.
9. McCance KL, Huether SE. *Pathophysiology: The Biologic Basis for Disease in Adults and Children*. The CV Mosby Co: St Louis, MO, 1990.
10. Puolakka J, Ylostalo P, Tuimala R, Haapalahti J, Jarvinen PA. "Amniotic fluid beta-2-microglobulin in normal and Complicated pregnancies. Correlation with gestational age, creatinine concentration and L/S ratio." *Gynecol Obstet Invest* 1982; 13(3):129-34.
11. Snyder JM, Kwun JE, O'Brien JA, Rosenfeld CR, Odom MJ. "The concentration of the 35-kDa surfactant apoprotein in amniotic fluid from normal and diabetic pregnancies." *Pediatr Res* 1988 Dec; 24(6):728-34.
12. Stuart RO, Nigam SK. "Development of the tubular nephron." *Semin Nephrol* 1995 Jul; 15(4):315-26.
13. Szaflik K, Kozarzewski M, Adamczeqski D. "Fetal bladder catheterization in severe obstructive uropathy before the 24th week of pregnancy." *Fetal Diagn Ther* 1998 May-Jun; 13(3):133-35.
14. Wallner EI, Carone FA, Abrahamson DR, Kumar A, Kanwar YS. "Diverse aspects of metanephric development." *Microsc Res Tech* 1997 Nov 1; 39(3): 261-84.

EARN CE CREDIT AT HOME

You will be awarded one continuing education (CE) credit for recertification after reading the designated article and completing the exam with a score of 70% or better.

If you are a current AST member and are certified, credit earned through completion of the CE exam will automatically be recorded in your file—you do not have to submit a CE reporting form. A printout of all the CE credits you have earned, including *Journal* CE credits, will be mailed to you in the first quarter following the end of the calendar year. You may check the status of your CE record with AST at any time.

If you are not an AST member or not certified, you will be notified by mail when *Journal* credits are submitted, but your credits will not be recorded in AST's files.

Detach or photocopy the answer block, include your check or money order ($6 for members or $10 for non-members) made payable to AST and send it to the Accounting Department, AST, 7108-C S Alton Way, Suite 100 Englewood, CO 80112-2106.

Continuing Education Examination (January 1999) **161**
Kidney Development and Function in the Fetus **Category 3**

❑ **Certified Member** ❑ **Certified Nonmember**

Certification No.

Name

Address

City State ZIP

Chapter or At-Large Region Telephone

Mark one box next to each number. Only one correct or best answer can be selected for each question.

	A	B	C	D		A	B	C	D
1.	❑	❑	❑	❑	6.	❑	❑	❑	❑
2.	❑	❑	❑	❑	7.	❑	❑	❑	❑
3.	❑	❑	❑	❑	8.	❑	❑	❑	❑
4.	❑	❑	❑	❑	9	❑	❑	❑	❑
5.	❑	❑	❑	❑	10.	❑	❑	❑	❑

ASSOCIATION OF SURGICAL TECHNOLOGISTS
AEGER PRIMO— THE PATIENT FIRST®

CUT ALONG DASHED LINE

CE EXAM

1. **Which of the following is not one of the three nephric structures to arise during fetal development:**
   a. metanephros
   b. polyhydramnios
   c. mesonephros ✓
   d. pronephros ✓

2. **Which nephric structure forms the two rudiments that make up the complete kidney and ureter?**
   a. metanephros
   b. polyhydramnios
   c. mesonephros
   d. pronephros

3. **Which structure's component parts (cords of tissue or vesicles) can be seen in the fourth week of pregnancy?**
   a. metanephros
   b. polyhydramnios
   c. mesonephros
   d. pronephros

4. **Which structure is not active in urine production?**
   a. metanephros
   b. polyhydramnios
   c. mesonephros
   d. pronephros

5. **Which structure's vesicles form nephrons?**
   a. metanephros
   b. mesonephros
   c. pronephros
   d. a and b

6. **The urogenital sinus will later develop into the _____.**
   a. urinary bladder and urethra
   b. testes
   c. vagina
   d. ureteric bud

7. **The _____ originates from the metanephric blastema and uteric bud.**
   a. metanephros
   b. mesonephros
   c. bladder
   d. uterus

8. **Congenital anomalies of kidney development are due to a failure in:**
   a. the development of the uteric bud
   b. the production of nephrons
   c. the ascent to the lumbar position
   d. all of the above

9. **Amniotic fluid _____.**
   a. protects the fetus
   b. allows space for development
   c. assists in pulmonary development
   d. all of the above

10. **By the ninth week, the fetus participates in regulating amniotic fluid by _____.**
    a. producing hypotonic urine
    b. swallowing hypotonic urine
    c. producing fluid in the lungs
    d. all of the above