1. Development of the urogenital system

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The development of the urinary and reproductive organs as a part of the prenatal development, concerns the urinary system that includes kidneys, ureter, bladder and urethra, and the genital system, male and female, that can be divided into the gonads, the internal duct system and the external genitalia.

The urinary and reproductive organs are developed for the most part from intermediate mesoderma and they are preceded by a set of structures, which disappear almost entirely before the end of fetal life, except the ducts. These embryonic structures are the pronephros, the mesonephros and the metanephros for the development of the urinary system, and the Wolffian and Müllerian ducts for the development of the reproductive organs. Concerning the genital system, initially there is the indifferent stage, where the two sexes develop in an identical fashion. Subsequent to six weeks, the two sexes develop differently.

Finally, there is an important number of abnormalities and malformations that can be seen in the urinary and reproductive system and it is important to be reported.

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Development of the urinary system

Development of the kidneys

In the embryo there are three different kidneys (pronephros, mesonephros, metanephros) that are developed in a sequence with only the last one persisting and being the permanent and definitive kidney of the adult.

In the outer part of the intermediate mesoderm, immediately under the ectoderm, in the region from the fifth cervical segment to the third thoracic segment, a series of short evaginations from each segment grows dorsally and extends caudally, fusing successively from before backward to form the pronephric duct. This continues to grow caudally until it opens into the ventral part of the cloaca; beyond the pronephros it is termed the Wolffian duct. Thus, the Wolffian duct is what remains of the pronephric duct after the atrophy of the pronephros. In humans, the pronephros begins to regress around the end of the fourth week. It develops a duct system and in the course of each duct a glomerulus also is developed, but it never becomes functional. It undergoes rapid atrophy and it disappears.

As the pronephros is regressing, the mesonephros is developed and arises caudal to the pronephros at 4 weeks. The mesonephric vesicle, a collection of mesoderm, elongates to become a tubule. The medial end receives an invagination of capillaries, creating a Bowman's capsule while the lateral end of the tubule drains into the mesonephric duct. This maturation of the mesonephric vesicles progresses in a cranio-caudal fashion. The caudal end of the mesonephric duct is connected with the urogenital sinus. This junction will be important later in the developing male genital structures. The mesonephric duct is also known as the Wolfian duct. The mesonephros atrophies and for the most part, it disappears rapidly as the metanephros develops beginning during the 6th or 7th week, so that by the beginning of the 5th month, only the ducts and a few of the tubules of the mesonephros remain.

The metanephros is the definitive and permanent but immature kidney. It arises from two closely related structures, the ureteric bud and the metanephrogenic blastema. The ureteric bud starts close to where the Wolfian duct opens into the cloaca, invades the center of the metanephros and grows along the posterior abdominal wall. The ureteric bud forms the collecting ducts and tubules of the pyramids, the calyces, the renal pelvis and the ureter. The renal tubules, on the other hand, are developed from the metanephrogenic blastema and rapidly elongate to form the parts of the nephron: the proximal tubules, the loops of Henle and the distal convoluted tubules. These last join and establish communications with the collecting duct system derived from the ultimate ramifications of the ureteric bud. In
the other end, the renal tubules give rise to Bowman's capsules and glomeruli.

The ureteric bud and the nephrogenic blastema having joined, the future kidney begins its ascent and rotation. As the kidney move into the lumbar region, it takes new arterial supply from the aorta and new venous drainage into the vena cava and it undergoes a rotation of 90 degrees during the 7th and 8th week, so that the renal parenchyma lies lateral to the pelvis, as the kidney face ventrally at first (Fig 1).

### Development of the urinary bladder and the urethra

In contrast to the kidneys and the ureter which are of mesodermal origin, the structures of the lower urinary tract are formed from endoderm.

During the 6th week, the ventral cloaca elongates and forms four segments: an expanded distal portion, the urogenital sinus; a tubular portion, the primitive urethra; an upper dilation, the future bladder; and a tubular portion, the urachus, which is continuous with the extraembryonic allantoic stalk.

The urinary bladder is formed partly from the entodermal cloaca and partly from the ends of the Wolffian ducts. In other words, the allantois takes no share in its formation. When the urorectal septum is separated, it gives the anal canal and the urogenital sinus.

The upper part of the urogenital sinus becomes the urinary bladder. The allantois is connected here and degenerates to give the urachus, the median umbiligal ligament of the adult. The middle part of the urogenital sinus gives males their prostatic and membranous urethra, and the lower, phallic part gives some urethra.

The mesonephric ducts and ureters enter the bladder. As the metanephric kidney ascends, the ureters migrate superiorly on the bladder. The mesonephric ducts migrate inferiorly and become the ejaculatory ducts in males.

The trigone is the triangle located between the entrances of the mesonephric ducts and the ureters. Its mucosa is of mesodermal origin. The rest is endoderm. Eventually the mesoderm of the trigone is replaced by endoderm.

In the male, the prostatic and membranous part of the urethra are formed by the pelvic or the tubular part of the urogenital sinus. In the female, the entire urethra and the paraurethral glands are formed by the cranial part (vesicourethral part) of the endodermal origin. However, in the female, the caudal ends of the mesonephric ducts disappear, whereas in the male, each seminal vesicle is formed from a lateral outgrowth of the caudal end of the mesonephric duct. Each ejaculatory duct is also of mesonephric origin and it is formed by the part which is located between the urethra and the duct. The
muscular layer is mesodermal in origin. The distal part of the male urethra is ectoderm from the gland penis. The mucosa of the urethra is endoderm in the female and in the proximal part of the males. By 13 weeks, the urethra is almost complete.

**Development of the genital system**

**Development of the testis and the ovary**

Although the sex of an individual human normally is determined at conception by the sex chromosomes, the developing gonad shows no morphologic sex differentiation until the 7th week. During this period, the future ovary or testis is in the indifferent stage and can only be termed a gonad.

The gonads develop from the primary germ cells, which migrate into the genital ridge, the mesenchyme of the ventromedial aspects of the mesonephros adjacent to the root of the mesentery, and the celomic epithelium overlying this mesenchyme. The gonads begin to develop as an undifferentiated genital ridge medial to the metanephric kidney.

At 4 weeks, the primordial germ cells develop in the endodermal yolk sac and at 5 weeks, the germ cells migrate to the mesodermal endothelium on both sides of the hindgut. These structures induce the genital ridge just medial to the developing mesonephros. At 6 weeks, the cells from the mesonephros and celomic genital ridge form the primitive sex cords which invest the germ cells.

**Testis**

The Y chromosome causes Testis determining Factor (TDF) to induce the formation of the seminiferous tubules. They then separate from the epithelium and a fibrous thick capsule is formed around the cords, which is called Tunica albuginea. As the testis enlarge, it is separated from the degenerating mesonephros and it becomes suspended from its mesentery, the mesorchium. Seminiferous tubules have spermatogonia and supporting cells. The supporting cells include Sertoli cells and Leydig cells. By the 8th week, the interstitial cells of Leydig develop and produce testosterone that induces the masculine differentiation. Sertoli cells secrete the Mullerian Inhibiting Factor (MIF), which suppresses the development of the paramesonephric ducts.

The MIF causes the paramesonephric ducts to regress, while the testosterone causes the mesonephric ducts to persist and to develop into the ductus deferens, the seminal vesicle and the ejaculatory duct. The prostate arises from the urethral endodermal outgrowths and the bulbourethral glands arise from the spongy tissue of the urethra just inferior to the prostate.
Ovary

The absence of the TDF causes gonads to develop into ovaries. The primary or medullary sex cords degenerate, disappear and become a vascular stroma. During the 10-12 weeks, the secondary or cortical sex cords develop and extend into the medullary mesenchyme. By the 16th week, the cortical cords break into isolated cell cultures called primordial follicles. The developing ovary separates from the regressing mesonephros and becomes suspended by mesentery, the mesovarium.

Figure 1. (By Surgical Anatomy, Anson-Mcvay, Saunders –Sixth edition).
Due to the lack of testosterone, the mesonephric ducts regress, while due to the lack of MIF, the paramesonephric ducts develop. The cranial parts of the paramesonephric duct become the uterine tube and the inferior part forms the uterovaginal primordium, a Y shaped structure that will give the uterus and the superior vagina in females.

The superior part of the unfused paramesonephric ducts forms the fallopian tubes; the superior openings become the infundibula. The fusion of the uterovaginal primordium with the urogenital sinus forms the broad ligament of the uterus. Two outgrowths come from the uterovaginal primordium called the sinovaginal bulbs. They fuse to form the vaginal plate. It is joined by cells of the uterovaginal sinus, which canalize to give the vagina. The superior third part of the vagina is developed from the paramesonephric ducts and the inferior two-thirds from the urogenital sinus. The central vaginal cells eventually break down, forming the vaginal cavity; a thin mucus membrane (hymen) persists at the inferior end of the vagina. The urethral and the paraurethral glands are developed from the urethra, while the vestibular glands are developed as outgrowths from the urogenital sinus.

**Descent of the testes**

The retroperitoneal testis descends through the deep inguinal ring and the inguinal canal, and enters the scrotum with the ductus deferens and the testicular vesicles. There are three phases of the descent of the testis:

1) Initial movement is caused by the enlargement of the testis and the degeneration of the mesonephric kidney.
2) Regression of the paramesonephric ducts help guide the kidney to the level of the external inguinal ring.
3) The gubernaculum guides the testis into the scrotum. It is not known if the gubernaculum actually pulls them down or it holds them in place and all the other structures enlarge around them.

This path is the explanation for the posterior abdominal wall origin or the neurovascular supply of the testis.

**Descent of the ovaries**

The ovaries descend from their retroperitoneal position to just below the pelvic brim. The gubernaculum becomes both the ovarian ligament and the round ligament of the uterus.
Development of the urogenital system

**External genitalia**

The external genitalia is undifferentiated until the 7th week, they can be distinguished by the 9th week and they are fully developed by the 12th week. The mesenchyme cells produce a genital tubercle at the cranial end of the urogenital membrane by the 4th week and they form the phallus. The urogenital membrane divides down the middle to give two urogenital folds and the labioscrotal swellings.

In the male, under the influence of testosterone, the phallus elongates, enlarges and becomes the penis. The labioscrotal swellings enlarge to fuse and form the scrotum. The line of this fusion is called scrotal raphe.

The urogenital folds form the urethral groove along the ventral surface of the penis. They fuse to form the spongy urethra, which is enclosed by the penile raphe. The ectodermal glandular plate is formed at the tip of penis and grows caudally until it meets the spongy urethra, and then, it is canalized. A circular ingrowth of the ectoderm occurs at the periphery of the glans during the 12th week, which breaks down and forms the prepuce.

In the female, the phallic growth ceases and it becomes the clitoris. The urogenital folds grow but they do not fuse, except for a small portion that forms the frenulum of the labia minora. The unfused urogenital folds form the labia minora. The unfused labioscrotal folds enlarge to form the labia majora. The urogenital sinus gives the vestibular of the vagina.

**References**