CHAPTER-6

Embryonic development of the Urogenital System

Objectives

1. Understand the basic principles of the development of the urinary and genital systems.

2. Have a basic understand the three main stages in the development of the kidney

3. To be able to demonstrate knowledge of the main developmental stages of the gonads to ovaries and testes and associated structures

4. Have a basic understanding of the development of the uterus, vagina, penis and scrotum.

Introduction

The urogenital system may be divided into the urinary system and the genital system. This division is purely for functional purposes as their embryological and anatomical development is intimately linked.

In the early stages of the embryonic development the urogenital system is marked with a longitudinal elevation along the dorsal wall of the abdominal cavity, within the intermediate mesoderm.

A portion of the urogenital mesodermal ridge called the nephrotic cord forms the:

a) Pronephros and pronephric duct empty into the cloaca which is the dilated end of the gut. The pronephros degenerates by the 6^{th} week

b) Mesonephros and mesonephric duct degenerates by the 8^{th} week

c) Metanephros and metanephric duct develop at the caudal end near the cloaca. The ureteric bud is attached to the metanephric duct. The latter becomes the ureters.

The pronephrotic system completely regresses in the human. The mesonephros forms the mesonephric duct (wolffian duct). The wolffian duct in the adult becomes the collecting duct of the kidneys. It also forms the Bowman's capsule, glomerulus which form the renal corpuscle.

The metanephros develops from the ureteric bud which is an outgrowth of the mesonephric duct and the metanephric mesoderm. The metanephros eventually becomes the definitive adult kidney and appears by the fifth week. The permanent kidney ascends during development from the sacral region to its adult anatomical location at T12-L3.

The embryonic arteries formed during the ascend may persist as supernumerary arteries in the adult. These arteries are end arteries. This implies that damage to these vessels will result to damage to the tissues they supply.

THE SUPRARENAL GLAND

The cortex of the suprarenal gland forms as a result of two episodes of mesoderm proliferation:

1. The first episode forms the foetal cortex, which regresses by the second postnatal month.

2. The second episode forms the adult cortex which is composed of the zona glomerulosa, zona faciculata and zona reticularis.

The medulla of the suprarenal gland forms from neural crest cells.

12.3 THE URINARY BLADDER

The urinary bladder develops from the upper end of the urogenital sinus, which is continuous with the allantois (see study guide 9). The allantois in the adult degenerates and forms a fibrous cord (median umbilical ligament).

THE GENITAL SYSTEM

Although the genotype of the embryo is established at fertilisation, the female and male embryos are phenotypically (as in appearance) indistinguishable between weeks 1 and 6.

By week 12 some female and male characteristics of the external genitalia can be recognised.

By week 20, the phenotypic differentiation is complete. The components of the different embryo that are remodelled to form the adult female and male reproductive systems are:

a) The gonads
b) The paramesonephric (Mullerian) ducts

c) The mesonephric (Wolffian) ducts
d) The tubules, urogenital sinus, phallus, urogenital folds, and labioscrotal swellings

In the 3rd week of development mesenchymal cells originating from the primitive streak migrate around the cloacal membrane to form a pair of slightly elevated folds known as the cloacal folds. These form the genital tubercle later to become the phallus or clitoris. Caudal to the genital tubercle the genital folds form the future scrotum or labia. Distal to the urethral folds the perineum and anus are formed.

At the distal end of the paramesonephric ducts two solid invaginations grow out of the pelvic part of the sinus call the sinovaginal bulbs which proliferate and form a solid vaginal plate which continues to develop cranially. By the 5th month the vaginal outgrowth is entirely canalised. The lumen of the vaginal remains separated at the distal end by a thin tissue plate known as the hymen.

In the male embryo, the testes connect to the mesonephric duct through a series of tubules which later become the seminipherous tubules. Continued development of the mesonephric ducts produces the efferent ducts, ductus epididymis, ductus (vas) deference, ejaculatory ducts and seminal vesicle. The prostate and bulbourethral glands are of endodermal outgrowths from the urethra. Shortly after the gonads differentiate into testes, the paramesonephric ducts degenerate.

In the female embryo, the gonads develop into ovaries. At about the same time, the distal ends of the paramesonephric ducts fuse to form the uterus and vagina. The unfused portions become the uterine (Fallopian) tubes. The greater (Bartholin's) and lesser vestibular glands develop from endodermal tissue.

Summary of development of reproductive systems:

- The gonads develop near the mesonephric ducts
- The paramesonephric ducts (Muller's), are a second pair of ducts which develop parallel to the mesonephric ducts.
- Differentiation of the gonads for the male depends on a gene on the 'Y' chromosome called testes determination factor (TDF) and subsequent release of testosterone.
- Differentiation to a female gonad depend on the absence of TDF and testosterone.
- In the male the tubules connecting the gonads to the mesonephric duct give rise to the seminiferous tubules.

- In the male the mesonephros gives rise to: efferent ducts, ductus epididymis, ductus (vas) deference, ejaculatory ducts and seminal vesicle. The paramesonephric ducts degenerate in the male without contribution.

- In the female the paramesonephric duct fuse to form the uterus and vagina. The cephalic unfused portion become the fallopian tubes.

- The mesonephric ducts in the female degenerate without contributing to the female reproductive organs.

Development and Descent of the Ovaries and Testes

The ovaries and testes develop within the abdominal cavity but later descend into the pelvis and scrotum respectively.

CLINICAL NOTES

Congenital Cystic Kidney

In the cystic kidney there may be several cysts or a solitary large cyst. The function of the kidney may or may not impaired depending on the extent of the cysts present.

Renal Agenesis

Bilateral or unilateral renal agenesis is thought to be caused by an early degeneration of the ureteric bud. The incidence of unilateral renal agenesis is about 1:1500 and bilateral agenesis is rare and is associated with oligohydramnios.

Horseshoe Kidney

This is essentially caused by fusion of the two kidneys anterior to the aorta. It is relatively common and is found in 1:600 people. Functionally the kidney is normal.

Pelvic Kidney

This is caused by a failure of the kidney to ascend and therefore remains in the pelvis close to the common iliac artery.

Duplication and Atresia of Uterine Canal in the Female

Lack of fusion of the paremesonephric ducts at the distal end may lead to a double uterus and double vagina (uterus didelphys). Other such variations of fusion anomalies are uterus arcuatus (slightly indented in the middle), uterus biconis (two uteri and one vagina, uterus biconis unicollis (one fully formed uterus and one rudimentary uterus).

Atresia of cervix occurs when the cervix fails to unite with the lumen of the uterus. The cervix has not canalised.

Atresia of the vagina occurs due to lack of canalisation of the vaginal especially at the caudal end.

Hypospadias

This occurs when fusion of the urethral folds is incomplete and abnormal openings of the urethra may be found along the inferior aspect of the penis. Most frequently the abnormal orifices are near the glans, along the shaft or near the base of the penis. **Epispadias** is the equivalent anomaly located on the dorsum of the penis and may be associated with bladder anomalies.

Klinefelter's Syndrome

This occurs due to abnormal chromosomal combinations ie **XXY** or **XXXY**. This is the most common major abnormality of sexual differentiation in males (1:500). The patient is infertile with gynaechomastia, varying degrees of impaired of sexual maturation.

Gonadal Dysgenesis (Turner's Syndrome)

The patient has 44 autosomes and 1 **X** chromosome. The female has absence of sexual maturation, webbed neck, broad chest, widely spaced nipples, a short stature, cubitus valgus and often aortic coarctation and are infertile.

Testicular Feminisation Syndrome

These patients have 44 chromosomes and an **XY** chromosome complement but have the external of normal females. The uterine tubes and uterus are absent and the vagina and labia are poorly formed. The testes are frequently found in the inguinal or labial regions. There is no spermatogenesis.

Hermaphroditism and pseudohermaphrodism

A true hermaphrodite is an individual in whom the gonads and external genitalia of both sexes are present.

In pseudohermaphrodites the genotypic sex is masked by a phenotypic appearance that closely resembles the other sex.

📖 Undescended testes
📖 Hydrocele of the testes
📖 Congenital Inguinal hernias

SECTION-A

Anatomy and physiology of the The urinary system

Learning Outcomes:
The student should be able to:

- Identify the components of the urinary tract
- Determine the function of the kidneys
- Describe the anatomy and function of the ureters, urinary bladder and urethra
- Describe the anatomical and histological structures of the kidney.
- Describe the functions of the kidneys
- Describe the flow of blood through the kidneys

The Urinary System is made up of

- 2 retroperitoneal kidneys which filter the blood to form urine.
- 2 ureters which convey the urine from the kidneys to the urinary bladder.
- 1 urinary bladder where urine is temporarily stored.
- 1 urethra through which the urine is discharged to the exterior

The urinary system is made up of:
Two ureters**,** which lead from two kidneys towards the single urinary bladder which, stores the urine, and voids it through a single urethra**.**

The urinary system serves to filter the blood, extract waste metabolic products, and eliminate them as urine. The kidneys do most of the work in this system; the other structures act primarily as passages and storage areas of the resulting urine.

<u>Kidney</u>

Functions of the Kidneys:
Other functions of the kidneys include:

- Regulation of the blood ionic composition.
- Maintenance of the blood osmolarity is achieved by regulating the loss of water and solutes from the blood.
- Blood volume is regulated, which has an effect on the volume of interstitial fluid, and blood pressure.
- Blood pressure is also regulated by the kidneys, through the secretion of renin, which activates the renin-angiotensin pathway – a hormonal system which contributes to the regulation of the blood pressure.
- Release of hormones:
  - **Calcitriol-** the active form of vitamin D, which regulates calcium homeostasis.
  - **Erythropoietin-** stimulates the production of red blood cells.

Thus the kidney is not only part of the urinary system, but also part of the endocrine system.

- Regulation of blood glucose levels – kidneys can deaminate the amino acid glutamine, and use it for gluconeogenisis (production of glucose molecules), and thereby release glucose into the blood stream.
- The pH of the body is partly regulated through the excretion of hydrogen ions by the kidneys. There are other mechanisms, which maintain pH homeostasis, such as respiration, which results in carbon dioxide being eliminated through the lungs.

The location of the kidneys

The kidneys are located retroperitoneally, on either side of the vertebral column, in the right and left hypochondriac regions. The right kidney lies slightly lower than the left, due to the space occupied by the liver. Posteriorly, the 11^{th} and 12^{th} ribs protect the kidneys, and immediately superior to the kidneys, lie the adrenal glands which play a part in diuresis and the endocrine system.

The urinary bladder lies immediately superior to the uterus in the female, and is smaller in the female due to the space occupied by the uterus.

The external anatomy of the kidney

In the adult, a typical kidney is approximately the size of a bar of soap. The kidney is shaped like a bean, with the lateral border being convex in shape and the concave border facing medially. The near the medial border is a vertical fissure called the renal hilus. The renal hilus is the location where the ureters leave the kidney, and the blood vessels, nerves and lymphatic vessels enter and leave the kidney.

The coverings of the kidney

The kidney is surrounded by three layers of tissue:

- The renal capsule is a fibrous membrane, continuous with the outer coat of the ureter. This capsule acts to protect the kidney against trauma, and contributes to the maintenance of the shape of the kidney.
- Intermediately superficial to this layer, is the adipose capsule, which adds further protection to the organ, and holds the kidney in its position within the abdominal cavity.
- The superficial renal fascia anchors the kidney to surrounding structures and the abdominal wall.

The Internal Anatomy of the Kidney:

Deep to the renal capsule, lays an outer area of renal tissue, known as the renal cortex, which forms the peripheral layer of the kidney parenchyma. Portions of the cortex extend between the pyramids, and these are called the renal columns.

Deeper than the renal cortex, lies the renal medulla. This part of the kidney is made up of approximately 8-18 renal pyramids. The apex of these pyramids forms the renal papilla, which extend into the minor and major calyces, and ultimately into the ureter.

These structures convey the urine formed by the functional unit of the kidneys- the nephrons.

The renal pelvis is the expanded upper end of the ureter, and within the renal sinus of the kidney it subdivides to form the major and minor calyces.
The renal sinus is a cavity within the kidney, which houses part of the renal pelvis, the calyces and branches of the renal blood vessels and nerves.
The micro anatomy of the kidney:

The kidney functions to maintain homeostasis through three basic processes:
1) Filtering the blood.
2) Returning useful filtrates to the blood stream.
3) Removing unwanted metabolites from the blood stream and excreting them in the urine.

The nephron is made up of

1) The **renal corpuscle** where blood plasma is filtered.
2) The **renal tubule** which are the structures into which the filtered fluid passes.

Each corpuscle is further divided into 2 components:
1) The glomerulus
2) The glomerular (or Bowman's) capsule – which surrounds the capsule.

The blood is filtered from the glomerulus into the glomerular capsule, and then the filtrate passes into the renal tubule, which is made up of three sections:
1) The proximal convoluted tubule
2) The Loop of Henle
3) The distal convoluted tubule.

The renal corpuscles plus the proximal and distal convoluted tubules lie within the renal cortex, whilst the Loop of Henle, extends into the medulla of the kidney. However, there is a difference:

85% **cortical nephron**- Renal corpuscles in the outer area of the renal cortex
Short loops of Henle, extending superficially into the renal medulla and no thin ascending limb.
Blood supply – peritubular capillaries
15% **Juxtamedullary nephron** Renal corpuscles are deep within the cortex
Long loops of Henle, extending into the deep interior of the medulla, has a thin ascending limb
Blood supply – peritubular capillaries and vasa recta.
The distal convoluted tubule of several nephrons empties into a single collecting duct, several of which converge to the papillary ducts, to minor calyces, major calyces.

The Histology of the Nephron:
The glomerular capsule**:**
Made up of two layers:
1) The outer parietal layer - Simple squamous epithelium.

2) The inner visceral layer - Modified simple squamous epithelium. Podocytes are in contact with the glomerulus.

Between these layers is the capsular space, where the filtered fluid collects.

The filtration membrane (endothelial-capsular membrane)
Made up of three layers:

1) An endothelial cellular layer – A leaky barrier with fenestrations, Contractile mesangial cells, which regulate glomerular filtration.

2) The basal lamina – An acellular matrix of glycoprotein fibrils

3) Podocyte layer –Part of the visceral layer of the Bowman's capsule. A layer of modified simple squamous epithelial cells called podocytes, which wrap around the glomerular capillaries. Pedicels extend from the podocytes, resulting in filtration slits.

Renal Tubule and Collecting Duct
The renal tube is roughly divided into 3 sections:

Proximal Convoluted Tubule:

- This is where most of the glomerular filtrate is reabsorbed back into the bloodstream.
- Made up of simple cuboidal epithelium with a brush border of microvilli, which increase the surface area for reabsorption and secretion.

Descending limb of **the Loop of Henle**, and the thin ascending limb of the Loop of Henle

- Made up of simple squamous epithelial cells.

Thick or final limp of the ascending Loop of Henle:

- Made up of simple cuboidal epithelial cells.
- The macula densa and modified smooth muscle fibres, juxtaglomerular cells form the juxtaglomerular apparatus which produces renin. Renin raises blood pressure through arteriolar constriction.

Distal Convoluted Tubule and Collecting Ducts:

- Made up of simple cuboidal epithelium and few microvilli.
- There are two types cell present:
    1. Principal cells – Receptors for antidiuretic hormone, and aldosterone.
    2. Intercalated cells – Role in homeostasis of blood pH.

Blood supply to the kidney

The kidneys receive their blood supply from the renal artery, which extends out of the abdominal aorta, and are drained by the renal veins into the inferior vena cava.
20-25% of resting cardiac output flows through the renal arteries.

Renal arteries- From the aorta.
Segmental arteries- Several branches enter the parenchyma.
Interlobar arteries- Passing through the renal columns.
Arcuate arteries- Arching between the medulla and cortex. (Bow-like)
Interlobular arteries- Divide in the renal cortex to form-
Afferent arterioles- Each nephron is supplied by 1 arteriole, which forms-

- **Glomerular capillaries-** A ball of capillary network. Unique- between 2 arterioles.

Efferent arterioles- Divide to form:

- **Peritubular capillaries** and/or **vasa recta-** The peritubular capillaries supply the tubules in the cortex, The vasa recta supply the tubules in the medulla

Interlobular veins- Receives blood from the peritubular capillaries and vasa recta**.**
Arcuate veins-
Interlobar veins –Between the renal pyramids
Segmental veins
Renal vein – Blood exits at the renal hilus, joining the inferior vena cava

Ureters

The ureters are tubes, which extend from the hilus of the kidney to the urinary bladder. These tubes function to transport the urine from the kidney to the bladder, through gravity and muscular peristaltic contractions.

The ureters are made up of three coats

- **The inner mucosa-** a mucous membrane of transitional epithelium, making the ureter able to stretch.
- **The muscularis-** an inner longitudinal and outer circular coat of smooth muscle fibres. The distal third of the muscular also contains a third layer of longitudinal fibres.
- Superficially, the ureters are covered in an **adventitia-** a layer of areolar connective tissue, containing blood and lymphatic vessels, and nerves.

Urinary Bladder

The urinary bladder is a pear-shaped muscular bag, which stores the urine before micturition. In the bladder floor is an area referred to as the trigone. The two posterior corners of this triangle are marked by the two ureteral openings, and the internal urethral orifice lies in the anterior corner.

The bladder wall is made up of three layers

- **The mucosa-** transitional epithelium. Rugae (deep folds) are also present, and allow for the stretching of the wall when it fills with urine.
- **The muscularis**. This muscle is known as the detrusor muscle, and is made up of three layers. An outer layer of longitudinal, middle circular and inner longitudinal layer of smooth muscle. Surrounding the urethral opening, the circular layer of smooth muscle forms the internal urethral

sphincter. Inferior to this is the external urethral sphincter of voluntary muscle.
- **The adventitia** is continuous with that of the ureters.

Urethra

The urethra is a tube conveying the urine from the bladder to the external orifice.

It is constructed of the following layers:
- **The mucosa** is lined at the superior end with transitional epithelium continuous with that of the urinary bladder.
- More distally, the urethra is lined with stratified or pseudostratified columnar epithelium changing to stratified squamous epithelium at the distal end.
- **The lamina propria** of the mucosa is composed of loose connective tissues with numerous elastic fibres.
- **The muscularis** is a thin layer of circular smooth muscle with elastic fibres.

The male and female urethras differ considerably:

The female urethra is short- about 4cm long. The urethral orifice is located between the opening of the vagina, and the clitoris. As the urethral orifice is closely adjacent to the vagina and the anus, and is a shorter in length, it becomes more susceptible to pathogenic microbes than the male, which may cause cystitis.

The male urethra is about 20cm long. It is divided into 3 portions.
- The prostatic urethra- adjoins the bladder and is about 3cm in length. It runs through the prostate gland to the pelvic floor, and receives on its posterior wall the numerous ducts of the prostate glands.
- The membranous urethra- 1-2cm penetrates the region of the pelvic floor.
- The spongy urethra- is the longest (15cm).

The male urethra lies within the central tissue body of the penis. The urethral opening is a vertical slit at the distal end of the penis.

The urinary system

SELF ASSESSMENT QUESTIONS

Question 1:
Imagine that you are a potassium ion in the systemic circulation. Describe structures through which you would journey, from the renal artery through the urinary system, until you were eliminated as urine.
In your description, you will name the relevant blood vessels, and structures of the kidney and urinary tract.

Question 2:
a) Which branch of the nervous system innervates the kidneys?
b) How does this nervous stimulation affect the urinary system?

Question 3:
Name the three processes involved in the production of urine.

Question 4:
Where do the following processes occur?
a) Filtration
b) Reabsorption
c) Secretion

Question 5:
The podocytes are part of the glomerular capsule. True or False?

Question 6:
What is the name of the functional unit of the kidney?

Question 7:
Define the following
a) Osmolarity
b) Retroperitoneal

Question 8:
Name four other retroperitoneal organs.

Question 9:
Please list five functions of the urinary system.

Question 10:

Please a simple diagram illustrating the ureter entering the bladder, and how this passage is shut off to prevent reflux of urine back into the kidneys. Include in your illustration, the layers of the bladder wall.

Question 11:

True or false?

a) Urine is excreted through the vagina in females?
b) The adrenal glands form part of the urinary system?
c) Urine is concentrated in the bladder before excretion? 3 marks

Please refer to your labelling supplement handbook and label any images associated with the above chapter.