Lectures of Human Embryology

Gonads, External Genitalia

By

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**Introduction**

The gonads in both sexes are derived from 3 sources, as follows: (g.e.m.)

i. Primordial germ cells (that are found at the early stage of development in the wall of yolk sac).

ii. Coelomic (germinal) epithelium of the genital ridge.

iii. Underlying mesenchyme.

At the early stage called indifferent stage, it s not possible to differentiate between male and female gonads, except genetically where it is determined at the time of fertilization.

**Development of Gonads**

The gonad passes through 3 stages:

I. Indifferent stage,

II. Differentiation,

III. Descent.

**I. Indifferent Stage:**

1. The coelomic epithelium between the dorsal mesentery and mesonephros proliferates and its underlying mesenchyme condenses. This results in the formation of a longitudinal ridge called genital ridge.

2. Then, the genital ridge epithelium sends finger-like projections into the underlying mesenchyme, called sex cords.

   N.B.: Until the 6th week of development, no germ cells appear in the genital ridge.

3. Then, the sex cords surround the migrating primordial germ cells, that reach the genital ridge through the dorsal mesentery from the wall of gut.

   N.B.: Primordial germ cells that originate in the wall of the yolk sac, migrate to the wall of gut, then pass to reach the genital ridge.

4. With further growth, the gonad gradually invaginate the dorsal aspect of coelomic cavity (peritoneal cavity) forming a narrow mesentery.

**II. Stage of Differentiation**

A. Development of Testis:

1. The underlying mesenchyme (beneath the coelomic epithelium) proliferates and condenses to form a thick fibrous layer, called
tunica albuginea, separating the sex cords from coelomic epithelium.

2. The tunica albuginea sends fibrous septa to divide the testis into 200-300 compartments. Each compartment contains 2-3 sex cords.

3. The sex cords form solid, U-shaped ducts, converging towards the hilum (mesentery) of testis.

4. The free ends of these solid ducts communicate together at the hilum of testis, forming rete testis.

5. The rete testis becomes canalized and then join the remnants of mesonephric tubules (efferent ductules).

6. The sex cords remain solid till puberty, when they become canalized to form seminiferous tubules that join the rete testis.

   Each tubule has 2 types of cells:
   - Spermatogonia: derived from the primordial germ cells.
   - Sertoli cells: derived from the sex cord cells.

   In-between the tubules, the interstitial cells of Leydig (that secrete testosterone) are derived from the mesenchyme of the genital ridge.

7. The part of genital ridge above the developing testis is fibrosed to form the suspensory ligament of testis, that disappears later on. While the lower part (from the lower pole of testis to the genital swelling) acquires some muscle fibers from the surrounding mesenchyme forming the gubernaculum.

B. Development of ovary:

1. The sex cords of the genital ridge become separated from the coelomic epithelium by a thin tunica albuginea (not thick as that of testis).

2. Then, these cords undergo the following:
   - In the medulla: the cords degenerate and become replaced by vascular fibrous tissue.
   - In the cortex: the cords splits into cell groups, surrounding the primordial germ cells.

3. The primordial germ cells develop to form the oogonia. By the 3rd month, the oogonia undergo mitotic divisions to form the 1ry oocytes.
4. Each 1ry oocyte, surrounded by a layer of granulosa cells (derived from sex cords) form a structure, called 1ry follicle.

5. The genital ridge cranial to the ovary forms the **suspensory ligament of ovary**, while that caudal to it forms the **ovarian ligament and round ligament of uterus**.

N.B.: **Unlike the testis, the ovary does not join the adjacent mesonephric tubules.**

III. **Descent of Gonads:**

The gonads are formed at the upper part of posterior abdominal wall, opposite L1.

Then, they descend as follows:

**A. Descent of testis:**

The testis descends as follows:

- By the 2nd month, it starts descent.
- By the 3rd month, it reaches the iliac fossa.
- By the 4th-6th month, it reaches the deep inguinal ring.
- By the 7th month, it reaches the inguinal canal.
- By the 8th month, it reaches the superficial inguinal ring.
- By the 9th month, it reaches the scrotum.

**Developmental results:** As the testis descends, it takes with it a fold of peritoneum, called *processus vaginalis*. The part of the *processus vaginalis* inside the inguinal canal is obliterated, to form *vestige of processus vaginalis*. While the part reaching the scrotum remains unobliterated forming *tunica vaginalis*. This tunical vaginalis surrounds the testis from all aspects, except posteriorly where the testis is related to epididymis.

* **Factors causing (affecting) descent of testis** include:

1. **Mechanical factor:** through contraction of muscle fibers of the gubernaculum.
2. **Hormonal factor:** especially human chorionic gonadotrophin (HCG). Therefore, injection of HCG in some cases of undescended testis may lead to its descent to the normal site.
3. **Peritoneal factor:** through gliding effect of the *processus vaginalis*.
4. **Relative elongation of the upper half of body:** gives a relative descent for the testis.
B. Descent of Ovary:

* The ovary descends only to pelvis.

* Due to attachment of gubernaculum to the cornu of the developing uterus, it is divided into 2 parts:
  - **Round ligament of uterus** connects the cornu of uterus to labium majus (genital swelling), passing through the inguinal canal.
  - **Ovarian ligament** connects the cornu of uterus to the ovary.

N.B.: The process of oogenesis, unlike the spermatogenesis, does not need temperature lower than that of abdominal cavity.

**Factors causing its descent**, include:
1. Contraction of gubernaculum.
2. Relative elongation of the upper half of body.
1. **Agenesis of testis**: Absence of testis is caused by failure of formation or migration of primordial germ cells. Presence of only one testis in scrotum is called **monorchidism**. N.B.: Primordial germ cells have the inductive effect for development of gonads either into ovary or testis.

2. **Polyorchidism**: Duplication of testis in one side of scrotum.

3. **Cryptorchidism**: Imperfect (or incomplete) descent of testis. The testis fails to reach the scrotum. It may be found in:
   - abdomen (lumbar region or iliac fossa).
   - inguinal canal.
   - superficial inguinal ring.

   - **Results of un-descended testes**:
     - Infertility (Spermatogenesis does not occur in un-descended testis).
     - Increased incidence of testicular neoplasm: (malignancy).
     - Increased incidence of inguinal hernia.

     *Therefore it should be surgically positioned in the scrotum as early as possible after birth. Otherwise if it is detected later on, it must be excised to avoid the possible malignant transformation.*

4. **Ectopic (maldescended) testis**: The testis descends to abnormal site, out of the normal pathway of descent. Cause may be splitting of gubernaculum. It may be found in:
   - the front of abdominal wall.
   - the front of thigh.
   - the perineum, behind the scrotum.

5. **Abnormalities of processus vaginalis** include:
   a. **Congenital inguinal hernia**: due to failure of the normal obliteration of processus vaginalis inside the inguinal canal and
within spermatic cord. Intestine may be herniated through this defect to reach the scrotum.

b. **Congenital hydrocele**: due accumulation of fluid in persistent sac.

c. **Encysted hydrocele of spermatic cord**: due to failure of obliteration of a part of processus vaginalis and then accumulation of fluid in it.

![Image](image.png)

*Normal and congenital anomalies of processus vaginalis; A) Normal case, B) Congenital inguinal hernia, C) Encysted hydrocele of spermatic cord*

**Congenital Anomalies of Ovary**:

1. **Agenesis of ovary**: Absence of ovary is caused by failure of formation or migration of primordial germ cells.

2. **Ectopic ovary**: Ovary may descend to the inguinal canal or even the labium majus. This occurs due to failure of attachment of gubernaculum to the uterus.

3. **Ovo-testes (true hermaphrodites)**: Individuals have both ovarian and testicular tissues combined together. Most of these cases are raised as females. External genitalia are ambiguous or female in appearance.

**Development of External Genitalia**

External genital organs pass into 2 stages, as follows:

I. **Indifferent stage**:
   - Early in development (during the 3\textsuperscript{rd} week of intrauterine life), the mesenchyme of the primitive streak proliferates and migrates caudally to surround the cloaca.
Proliferation of mesenchyme of the primitive streak and its migration caudally to surround the cloaca

- It then raises the surface ectoderm to form 2 lateral swellings, one on each side of cloaca called **cloacal folds**.
- Extension of the uro-rectal septum caudally divides the cloacal membrane into 2 parts;
  - anterior part called **urethral (genital) fold** &
  - posterior part called **anal fold**.
Also, it raises the ectoderm between the previous folds to form the **perineal body**.
- The 2 urethral folds join cranially to form the genital tubercle.
- At the same time, another pair of swellings appears, lateral to the urethral folds called **genital swellings**.

N.B.: At the end of the 6th week, it is not possible to distinguish the sex of embryo externally.

**In summary**, The indifferent stage is characterized by appearance of 5 mesodermal swellings covered by ectoderm. These are:

- Two inner folds, called "urethral folds".
- Two outer folds, called "genital swellings".
- One median swelling called "genital tubercle".
II. **Stage of differentiation**:

A. **External genital organs in male**:

1. The phallus (or genital tubercle) enlarges and elongates rapidly to form the penis.
   
   As the phallus elongates, it pulls the 2 urethral folds on its ventral surface, forming urethral groove.
   
   The urethral groove is bounded by the 2 urethral folds and floored by urethral plate (endodermal plate extending from the urogenital sinus).
   
   *N.B.: The urethral plate is formed after rupture of urogenital membrane. Then proliferation and extension of endoderm of urogenital sinus occurs out into the root of the developing penis.*

2. The 2 urethral folds fuse together forming endodermal penile urethra. This part extends throughout the whole length of penis, except part in the glans penis (where the ectodermal part of penile urethra arises).

3. The ectodermal penile urethra arises as a solid cord of ectodermal ingrowth from the tip of glans penis. Then, this part is canalized and joins the other "endodermal" part.

4. The 2 genital swellings fuse together in the mid-line to form the scrotum.
   
   *N.B.: The line of fusion is indicated on the outer surface as a median raphe.*

5. The erectile tissue develops from the mesenchyme within the core of the developing penis. Also, the prepuce (foreskin) arises as a skin fold appearing at the base of glans penis.

B. **External genital organs in female (vulva):**

These organs arise by growth in situ.

1. The phallus (genital tubercle) elongates but remains smaller than that in male to from the *clitoris*.

2. The 2 urethral folds remain separated and develop to form the *labia minora*.

3. The 2 genital swellings remain separated and enlarge to form the *labia majora*. 
4. The urogenital membrane ruptures so that the urogenital groove becomes opened and communicated with the exterior to form the **vestibule**.

*N.B.: At early stages of development, the phallus in females is usually larger than that in males. Therefore, defining the sex of the foetus during the 3rd or 4th month of gestation through ultrasound examination of phallus only may carry mistakes.*

**Development of External Genitalia**

**Congenital Anomalies of External Genitalia:**

I. **In male:**

1. **Agenesis of penis:**
   Absence of penis results from failure of development of the genital tubercle.

2. **Micropenis:**
   It results from deficiency of testosterone and usually is associated with hypopituitarism.

3. **Bifid (or double) penis:**
   This occurs in cases of bifurcation of the genital tubercle.

4. **Hypospadias:**
   This is abnormal urethral orifice on the ventral surface of penis. It occurs as a result of incomplete fusion of the 2 urethral folds.
5. **Epispadias:**
   This is a very rare anomaly in which urethral orifice is found on the dorsum of penis. In this case, the genital tubercle arises caudal to the urogenital membrane. It is commonly associated with ectopia vesicae.
   N.B.: Incidence of hypospadias is about 3/1000 of births, while that of epispadias is about 1/30000 of births.

6. **Urethral atresia:**
   This occurs due to failure of canalization of the developing "solid" part of urethra.

   ![Diagram of male urethra anomalies](image)

   *Congenital Anomalies of Male Urethra*

   **II. In female:**
   **Congenital hypertrophy** of clitoris, labia minora and/or labia majora. This may be the result of stimulation of their growth by maternal hormones (e.g. oestrogen) or from foetal suprarenal cortex.