Development of Reproductive System
Lecture Objectives

- Describe the development of gonads (indifferent stage) and sex determination.
- Describe the development of testis and ovaries and the related structures.
- Describe the development of the genital ducts.
- Describe the development of male and female glands.
- Describe the development of the male and female external genitalia.
- Discuss the related developmental anomalies.
Development of Urogenital System

- Both the urinary & reproductive systems are closely related (structurally & developmentally)
- Urogenital system develop from the intermediate mesoderm
- Urogenital ridge is a longitudinal elevation of the mesoderm lateral to the dorsal aorta
- Nephrogenic cord (ridge) develop in the urogenital ridge
  - Gives rise to part of the urinary system
- Genital (gonadal) ridge develop close to the nephrogenic cord
  - Gives rise to part of the genital system
Development of Gonads

• Early development of male & female gonads are similar (indifferent stage – indifferent gonads)

• Development of gonads begin in the 5th week

• Source of gonadal development
  • Mesothelium of posterior abdominal wall – lateral somatic mesoderm – cortex
    • Proliferate and form gonadal ridge
    • Primary sex cords
    • In female form ovary
  • Underlying mesenchyme – intermediate mesoderm – medulla
    • In male form testis
  • Primordial germ cells – from the yolk sac
    • Migrate via mesentery & mesenchyme to the primary sex cords (6th week)
Sex Determination

- Y chromosome has SRY gene in the sex determining region for testis determining factor (TDF)
- Presence of TDF determines the differentiation of testis
  - Primary sex cords (in medulla) → seminiferous tubules
  - Absence of Y chromosome & TDF results in ovary formation
- Testosterone from fetal testis determines male characteristics
  - Female characteristics determined without hormonal effect
Development of Testes

- **Primary sex cords** extend into medulla and form **seminiferous cords** (obliterated tubules)
  - Lumen form on puberty
- **Seminiferous cords** Branch & connect to form **rete testis**
- **Rete testis** connect with 15-20 mesonephric tubules → **efferent ductules**
- **Mesonephric duct** becomes **ductus epididymis**
Development of Testes

- The fibrous tunica albuginea form
  - seminiferous cords lose connection with surface epithelium
- Testis enlarge & separate from the abdominal wall leaving a mesentery (mesorchium)
Development of Testes

• Interstitial (leydig) cells form from the mesenchyme between seminiferous cords
  • By 8th week secrete testosterone under influence of hCG
    • Induce differentiation of mesonephric ducts & external genitalia

• Sertoli cells derived from surface epithelium of testis
  • Secrete antimullerian hormone (AMH) at 6-7 week
    • Suppresses development of parmesonephric (mullerian) ducts

• Spermatogonia develop from primordial germ cells
Development of Ovaries

- Primary sex cords → rete ovarii → degenerate
- Secondary sex cords (cortical cords)
  - Extend to underlying mesenchyme at early fetal life
  - Primordial germ cells incorporated in it
  - Disconnect and form primordial follicles
    - Oogonium surrounded by 1 layer of follicular cells
Development of Ovaries

- **Surface epithelium** form 1 layer of **germinal epithelium**
  - Separated from cortex by fibrous **tunica albuginea**
- Ovary separate from the abdominal wall leaving a mesentery (mesovarium)
Development of Genital Ducts

- In the indifferent stage two ducts develop (5th-6th week)
  - Mesonephric (wolffian) ducts from mesonephrone
    - Important in male genital structures
    - Disappear in female
  - Paramesonephric (mullarian) ducts – develop lateral to the gonads & mesonephric ducts
    - Form from longitudinal invagination of the mesothelium
    - Important in female genital structures
    - Disappear in male
Development of Genital Ducts

- **Mesonephric ducts**
  - Proximally – form **epididymis**
  - Distally – form **ductus deferens & ejaculatory duct**
    - Lateral outgrowth give rise to **seminal vesicle**

- **Paramesonephric ducts**
  - Rostrally (with funnel shape opening into the abdomen)
  - Caudally they cross anterior to mesonephric ducts & fuse together forming **uterovaginal primordium**
    - Ends at the posterior wall of the urogenital sinus
    - Results in an elevation called **sinus tubercle**
Formation of the Peritoneal Structures

• The fusion of the distal parts of the paramesonephric ducts extend parts of the peritoneum towards the midline
• The extended peritoneum forms the broad ligament
• Anterior to it forms the vesicouterine pouch
• Posterior to it forms the rectouterine pouch
Development of Male Glands

- **Seminal vesicle** develop from a Lateral outgrowth of the distal part of the mesonephric duct
- **Prostate gland** develop from endodermal outgrowth of the prostatic urethra into the surrounding mesenchyme
- **Bulbourethral glands** develop from outgrowths of the penile urethra
**Development of Female Genital Organs**

- **Uterine tubes** develop from proximal part of **paramesonephric ducts**
- **Uterus** develops from the **uterovaginal primordium**
Development of Female Genital Organs

- **Vagina** develops from the urogenital sinus
  - Sinus tubercle induces the outgrowth of sinovaginal bulbs → vaginal plate → vagina
- Separation between urogenital sinus & vagina → **hymen**
Development of Female Glands

- Urethral & paraurethral glands develop as buds from urethra
- Greater vestibular glands develop from outgrowth of urogenital sinus
Development of External Genitalia
Indifferent Stage (4th-7th weeks)

- **Genital tubercle** formed from mesenchymal proliferation at the cranial end of the cloacal membrane
  - **Phallus** is an elongated genital tubercle
- **Urogenital (urethral) & labioscrotal folds** develop on sides of the cloacal membrane
Development of External Genitalia
Indifferent Stage (4th-7th weeks)

- Cloacal membrane separated into urogenital membrane (anteriorly) and anal membrane (posteriorly) by the urorectal septum
- The end of the urorectal septum form the perineal body
- After a week the membranes rupture and form anus & urogenital orifice
Development of Male External Genitalia

- **Phallus** enlarge to form *penis*
- **Penile corpora** formed by *phallus mesenchyme*
- Urogenital folds fuse & close the urethral groove forming *spongy urethra*
  - Site of fusion – *penile raphe*
- **Prepuce** formed by circular ectodermal ingrowth around the glans
- **Scrotum** formed by the fusion of the labioscrotal folds
  - Site of fusion is the *scrotal raphe*
Development of Female External Genitalia

- **Phallus** become the **clitoris**
- **Urogenital folds** form the **labia minora**
  - Fuse posteriorly to form **frenulum of the labia minora**
- **Labioscrotal folds** form the **labia majora**
  - Fuse posteriorly & anteriorly to form **posterior & anterior labial commissures**
Development of Inguinal Canal

• While mesonephric duct degenerates, a ligament (gubernaculum) appears

• **Gubernaculum** connects the gonads with the labioscrotal swellings through the abdominal wall

• Peritoneal evagination (**processus vaginalis**) follow the gubernaculum taking the layers of the abdominal wall in front of it forming the **inguinal canal**

• **Processus vaginalis** guide the descent of testis through inguinal canal

• **Gubernaculum** in females
  • Cranially – ovarian ligament
  • Caudally – round ligament
Female Genital Malformation

- **Double uterus**
  - Failure of fusion of inferior part of paramesonephric ducts
- **Bicornuate uterus**
  - Failure of fusion in the superior part
- **Unicornuate uterus**
  - Failure of development of one paramesonephric duct
Male Genital Malformation

• **Hypospadias**
  • 1/300
  • External urethral orifice in the ventral side of:
    ❖ **Glans (glandular hypospadias)**
      • Failure of canalization of glandular plate
    ❖ **Body of penis (penile hypospadias)**
      • Failure of fusion of urogenital folds

• **Epispadias**
  • Orifice opens dorsally at the root of the penis
  • Dorsal development of genital tubercle
Male Genital Malformation

• Testicular anomalies
  • Cryptorchidism (undescended testes)
    • 3-4% of full term men
    • Found in its path
  • Ectopic testes
    • Deviate from its path
    • Abnormal location of gubernaculum
<table>
<thead>
<tr>
<th>MALE</th>
<th>EMBRYONIC STRUCTURE</th>
<th>FEMALE</th>
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<tbody>
<tr>
<td>Testis</td>
<td>Indifferent gonad</td>
<td>Ovary</td>
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<tr>
<td>Seminiferous tubules</td>
<td>Cortex</td>
<td>Ovarian follicles</td>
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<td>Rete testis</td>
<td>Medulla</td>
<td>Rete ovarii</td>
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<td>Gubernaculum testis</td>
<td>Gubernaculum</td>
<td>Ovarian ligament</td>
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<td>Round ligament of uterus</td>
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<td>Efferent ductules of testis</td>
<td>Mesonephric tubules</td>
<td>Epipophoron</td>
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<td>Paradidymis</td>
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<td>Paroophoron</td>
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<td>Appendix of epididymis</td>
<td>Mesonephric duct</td>
<td>Appendix vesiculosa</td>
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<td>Duct of epididymis</td>
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<td>Duct of epiophoron</td>
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<td>Ductus deferens</td>
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<td>Longitudinal duct (Gartner duct)</td>
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<td>Ejaculatory duct and seminal gland</td>
<td>Stalk of ureteric bud</td>
<td>Ureter, pelvis, calices, and collecting tubules</td>
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<td>Appendix of testis</td>
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<td>Hydatid (of Morgagni)</td>
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<td>Uterine tube</td>
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<td>Urinary bladder</td>
<td>Urogenital sinuses</td>
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<td>Urethra (except navicular fossa)</td>
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<td>Prostatic urethre</td>
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<td>Vagina</td>
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<td>Urethral and paraurethral glands</td>
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<td>Sinus tubercle</td>
<td>Greater vestibular glands</td>
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<tr>
<td>Seminal colliculus</td>
<td>Sinus tubercle</td>
<td>Hymen</td>
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<tr>
<td>Penis</td>
<td>Primordial phallus</td>
<td>Clitoris</td>
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<td>Glans penis</td>
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<td>Corpora cavernosa of penis</td>
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<td>Corpus spongiosum of penis</td>
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<td>Bulb of vestibule</td>
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<td>Ventral aspect of penis</td>
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*Functional derivatives are in italics.*