Testicular Descent and Sexual Development
Testicular Descent

- Sexual dev and testicular descent occurs simultaneously
- does not begin until testicular differentiation is initiated in the 7th week of gestation by SRY gene
- Hormones produced by the fetal testes initiate and sustain male dev, absence results in female sexual differentiation
- The hormones that play a role in testicular descent are testicular androgens (Testosterone, DHT) produced by Leydig cells and Mullerian inhibiting substances produced by Sertoli cells
Formation of testis and cords

- Androgens mediate differentiation of the paired Wolffian (mesonephric) ducts into seminal vesicles, epididymis, vas deferens and ejaculatory ducts.
- 4-6 wk – genital ridge organise forms the testes (proliferation of caelomic epithelium and condensation of mesoderm), primordial germ cells (indifferentiate) migrate to genital ridges.
- 7th week – Sertoli cells which are derived from cells migrated from mesonephros develops.
- Germ cells differentiate into gonocytes on entering the testicular cords become fetal spermatogenia by 15 weeks of gestation.
- Gonocytes and Sertoli cells form testicular cords within the testes and canalize to form semineferous tubules.
- Rete testes forms at end of testicular cords and connect to efferent ductules.
Fixation of testes

- 8th week- fetal testes begins to secrete testosterone and MIS independent of pituitary hormonal regulation
- Leydig cells secrete testosterone -> DHT and this induces the wolffian duct to diff to epididymis and vas deferens
- MIS by Sertoli cells causes degeneration of mullerian structures
- 7th week, the gubernaculum appears as a condensation of mesenchymal tissue on either side of the vertebra btw the ext and int oblique muscle
- Cranial aspect of gubernaculum envelopes the cauda epididymis and lower pole tunica albugenia and extends caudally into the inguinal canal
Fixation of testes

- Before descent, testes lies on top of the gubernaculum and covered by peritoneum except on the posterior.
- Just before descent, the gubernaculum undergoes an increase in length and rapid enlargement.
- Its enlargement facilitates lengthening of the testicular vasculature and vas deferens.
- Gubernaculum has an important role in fixing the testes into the inguinal canal before descent.
Undecended testes

- Normal testicular descent is defined as a testes that remains stationary within the dependent portion of the scrotum.
- Cryptorchidism is a development defect in which the testes fails to descend completely into the scrotum.
- Cryptorchid testicular position can be intraabdominal, intracanalicular, extracanalicular, or etopic (superficial pouch, transverse scrotal, femoral, perineal, prepenile)
Formation of inguinal canal

- Its role is to convey the testes into the developing scrotum
- 6th week – the anterior abdominal wall develops
- 8th week – the inguinal canal begin developing as a caudal evagination of the abd wall that forms in conjunction with caudal evagination of the processus vaginalis forming the internal, cremasteric and external spermatic fascia
Testicular Descent

- The testes lies dormant within the abdomen until about 23rd week, during which the processus vaginalis continues its elongation into the scrotum.
- The testis, epididymis, and gubernaculum then descend en mass through the inguinal canal posterior to the patent processus vaginalis.
- Testicular descent occurs in 10% at 24 weeks, 50% at 27 weeks, 75% at 28 weeks and 80% in 34 weeks.
- Complete descent from external ring to the bottom of the scrotum may take more than 3 to 4 weeks.
Theories of descent

- 3 phases
- 1. Transabdominal – controlled by MIS : CSL (cranial susp lig) regression and gubernaculum swelling. (MIS and androgen)
  Gubernaculum fixes the testes
  - differential growth of the lumbar vertebra and pelvis
  - near kidney at 8\textsuperscript{th} week, migrates at 23 week
- 2. Transinguinal – few days
  - mediated by androgen
- 3. Extrainguinal cananicular migration – occurs after 28 weeks, mediated by androgen
Theories of maldescent

1. Abnormal hypothalamic pit gonadal axis- defects in gonadotrophin production, androgen biosynthesis or androgen action. FSH and LH

2. Androgens testosterone and DHT deficiency – impaired function of GnRH or LH receptors, errors in testosterone biosynthesis include 17-a-hydroxylase def, 3 beta hydroxysteroid deH type2 def,

3. MIS – surge in first year of life, peak at 4 to 12 months then decline with age
   - MIS deficiency may have resulted from Sertoli cell dysfx
   - Persistent Mullerian Duct syndrome, dt mutations in MIS receptors gene
Sexual Differentiation

- In sexual development, 3 steps must occur
- 1. establishment of chromosomal sex at fertilisation which determines the dev of different gonads into testes and ovaries
- 2. differentiation of internal ducts and external genitalia
- 3. endocrine functions associated with the type of gonad present
Chromosomal Sex

- In human, initially the Y chromosome gene was termed the testes determining factor.
- Then in 1990, Sinclair and colleagues discovered the testis determining factor (TDF) was a single copy male specific sequence that was termed SRY (sex determining region Y gene).
Gonadal stage of differentiation

- During first 6 weeks of development, the gonadal ridge, germ cells, internal ducts and external genitalia are bipotential in both XX and XY.
- SRY initiates that induce a cascade of genes directing the indifferent gonad towards testicular organogenesis.
- 6-7th week: The differentiation of Sertoli cells is associated with production of MIS.
- In absence of SRY gene, ovarian organogenesis results.
- The testes function as a fetal endocrine organ.
- The ovary undergoes intense mitotic phase prenatally by 20 weeks.
Sexual development in Males

- The initial endocrine function of the fetal testes is secretion of MIS by Sertoli cells at 7-8 weeks.
- 9 weeks, the testes secrete testosterone by Leydig cells.
- Testosterone is essential for development of Wolffian duct structures, the urogenital sinus, and genital tubercle.
- 10 weeks: degeneration of Mullerian ducts are complete and Wolffian ducts becomes prominent.
- Adjacent to testes, Wolffian ducts forms epididymis, ejac ducts, vas deferens.
- Wolffian ducts of epididymis joins the rete testes.
- Distally, ducts join urogenital sinus to form seminal vesicles.
- DHT is produced in the urogenital sinus and is active in tissues who has 5 alpha reductase e.g. prostate, urogenital sinus and external genitalia.
Sexual Differentiation

- 10 weeks: The genital tubercle elongates and becomes the penis
- The urethral folds fuse to form the urethral groove
- Urogenital swellings forms the scrotum
- 12-13 weeks: the genitalia for male is complete
Sexual Differentiation

- Estrogen synthesis is detectable in fetal embryo at 8 weeks
- Estrogens are not required for female differentiation but it can interfere with male differentiation
- Estrogens block the effect of MIS on Mullerian Ducts
- In female testosterone is not secreted, so Wolffian ducts regress, Mullerian ducts are maintained
- Mullerian ducts develop into female reproductive tract which is the fallopian tubes, lumen of vagina and vagina proper
- In female: the genital tubercle forms the clitoris
- The genital swellings forms the labia majora
- Urethral folds forms the labia minora
- Between the labia minora will dev the vaginal intriotus and urethral meatus
THANK YOU