Embryogenesis of the Pituitary and Sexual Development: Part B

Significance of DHT

- Androgen receptor has a higher affinity for DHT
- Can get effects with low levels of circulating testosterone
- Secondary sex characteristic tissue in the male expresses 5α-reductase

External Genitalia Differentiation

Testes Determining Factor (SRY gene product)

Testes develop

Sertoli cells secrete anti-mullerian hormone (AMH)

AMH causes mullerian ducts to degenerate

Development of male duct system

Testosterone

Dihydrotestosterone

Development of penis, scrotum, and accessory sex glands

Ovaries develop

No AMH

Regression of wolffian duct

Mullerian ducts become the oviducts, uterus, cervix, and part of the vagina

XX Female

No testosterone

No steroids

No TDF

Male

Testes develop

Sertoli cells secrete anti-mullerian hormone (AMH)

AMH causes mullerian ducts to degenerate

Development of male duct system

Testosterone

Dihydrotestosterone

Development of penis, scrotum, and accessory sex glands

Male

Testis Developing Factor (SRY gene product)
Brain or Behavioral Sex

Brain and Behavioral Sex Differentiation

Genetics

Gonadal Steroid Hormones

Brain Structure

Sexual Behavior

Experience

Brain Sexual Differentiation

- Rat female
  - Give testosterone shortly after birth
    - fail to copulate or cycle like female as adult
- Sexually dimorphic nucleus
- Human male and female differences in behaviors
  - aggression
  - childhood play
  - 3D visual rotation

Descent of the Testis into the Scrotum

Testicular Descent

Fusion of the tunica albuginea and peritoneum to form the visceral tunica vaginalis

Front View

Spermatic Artery

Fusion of Peritoneum and Gubernaculum

Testis

Gubernaculum

Inguinal Ring

Peritoneum
Rapid growth of gubernaculum

Visceral Growth

Spermatic Artery

Peritoneum

Gubernaculum (rapid growth)

Testis is pulled down to the inguinal ring.

Inguinal Ring

Peritoneum

Visceral Tunica Vaginalis

Vaginal Process

Gubernaculum

Continued regression of gubernaculum

Testis pulled deeper into scrotum

Vaginal Process attaches to scrotum

Space between Visceral and Parietal T.V. is continuous with Peritoneum

Gubernaculum (Fully Regressed)

Failure or Problems With Testicular Descent

- Cryptorchid - highly heritable
  - Unilateral or bilateral
    - Germ cells fail to multiply and then die, sertoli cells only in seminiferous tubules
    - High percentage develop testicular cancer
    - Surgical correction possible but does not reduce cancer risk

Normal Dog Seminiferous Tubule

Cryptorchid Dog Seminiferous Tubule

Sertoli Cells
Failure or Problems With Testicular Descent

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- Inguinal Hernia

Abnormalities in Development

- The Freemartin in Cattle
  - Female born twin to a bull
  - Placenta membranes of the 2 fetuses fuse
  - Common blood supply
    - At time of testis formation
    - Before ovarian formation
  - Both fetuses share a common hormone milieu
    - Testosterone
    - Anti-mullerian hormone
  - Animals are chimeric (WBC from other twin)
    - TDF (SRY) expressed in both individuals

Normal

Freemartin
Normal Vs. Freemartin

**Freemartin**
- AMH from bull - blocks Mullerian ducts
  - Posterior vagina, no anterior vagina
- Testosterone from bull
  - Clitoral enlargement
  - Brain changes like that of male
- Ovaries do not grow but are chimeric
  - Ovotestis
    - SRY and therefore AMH and Testosterone
    - Further changes and adult male behavior
- Use as estrus detector
- Abnormalities exist as a continuum

Testicular Feminization in an XY Individual
- No androgen receptor
- Testis
  - No testosterone response so no Wolffian duct development
  - AMH present so mullerian ducts regress
  - External genitalia is female due to lack of androgen

Testicular Feminization

5α Reductase Deficiency in an XY Individual
- Guevedoces (penis at 12)
- Testis
  - AMH present so Mullerian ducts regress
  - Wolffian ducts
  - Pseudovagina and female external genitalia
  - At puberty may differentiate into more of a phenotypic male

Guevedoces Development

Normal tissue dependent upon testosterone is shown in black.
Behavior and Brain Sex *(Puberty Lecture)*

- **Freemartin**
  - T from twin causes brain to develop as male
  - Behavior is male due to brain changes and T expression as adult - Chimera

- **Testicular Feminization**
  - No functional androgen receptor
  - T produced and converted to E in brain to make it male
  - Behavior is male-like

- **5α Reductase Deficiency**
  - No DHT produced but T present
  - T to E in brain and so is male
  - Behavior is male