**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**

- Testis Determining Factor (SRY gene product)
  - Testes develop
  - Sertoli cells secrete anti-mullerian hormone (AMH)
  - AMH causes degeneration of Mullerian duct
  - Deletion of Mullerian duct becomes the epididymis, vas deferens, seminal vesicles, and part of the prostatic urethra

- Without TDF
  - Ovaries develop
  - No anti-Mullerian hormone
  - Mullerian ducts degenerate
  - Development of female duct system

**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

Rapid growth of gubernaculum
- Spermatic Artery
- Visceral Growth
- Peritoneum
- Visceral Growth
- Testis
- Inguinal Ring
- Parietal Tunica Vaginalis
- Visceral Tunica Vaginalis

Testis is pulled down to the inguinal ring.
**Failure or Problems With Testicular Descent**

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

**Normal Dog Seminiferous Tubule**

**Cryptorchid Dog Seminiferous Tubule**

**Inguinal Hernia**
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
    - testosteron
    - anti-mullerian hormone
- Animals are chimeric (WBC from other twin)
  - TDF (SRY) expressed in both individuals

Freemartin

Normal

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

**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

**Testicular Feminization**

**Guevedoces Development**

Normal tissue dependent upon testosterone is shown in black.