

**Sexual Differentiation - BGD Lecture 38 Handout – Dr Mark Hill**  
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**Introduction**

Sexual differentiation begins in the embryo following fertilization and ends 14 to 16 years later! The presence or absence of a Y chromosome following fertilization determines embryo sex and later genital development. In humans, the subsequent sexual development is the conversion of an indifferent (neither male or female) set of organs and features into a system of organs and tubes that have not only reproductive functions, but also endocrine roles in males and females. This hormonal role changes with age and has global roles on other body systems. The complexity of the developmental process means that the reproductive system is also a major contributor to developmental abnormalities.

The other system that develops over an equivalent extended period is the neural system. Interestingly, recent research points to a link between these two systems in how male and female brains may differentially develop under the influence of sex hormones, and perhaps even the sex chromosomes.

**Organs/Tissues**

Gonads, internal genitalia, external genitalia

**Concepts**

Sex chromosomes, germ cells, genital ridge, gonad, embryonic origin, developmental time-course, embryonic/fetal function, postnatal development/ function, abnormalities

**UNSW Embryology**

<http://embryology.med.unsw.edu.au/Medicine/BGDLectureXYXX.htm>

<http://embryology.med.unsw.edu.au/Notes/urogen.htm>

<http://embryology.med.unsw.edu.au/Medicine/BGDLabXYXX.htm>

**3 stages of Genital System Development**

1. Differentiation of gonad (Sex determination)
2. Differentiation of internal genital organs
3. Differentiation of external genital organs

Both 2nd and 3rd stages dependent on presence of endocrine gonad

Long Maturation Time course- embryo, puberty, ageing

**Sex Chromosomes**

Y Chromosome - 200+ genes, 50 million base pairs, SRY

X Chromosome - 1400+ genes, 150 million base pairs, DAX1

One of the X chromosomes in females is randomly inactivated (Barr body)

**Sex Determination**

Humans (week 5-6), Primordial germ cells migrate into gonadal (genital) ridge  
 Gonads (male/female) identical at this stage, indifferent  
 Gonad development dependent on sex chromosome (Y testes, No Y ovary)

**DNA with SRY Protein**

SRY protein binds DNA, Testes determining factor (TDF), transcription factor

**Internal Genital Organs**

All embryos form 3 paired duct systems: Nephric duct (kidney), Mesonephric duct (male), Paramesonephric duct (female)

**Week 5-** Bilateral bulges form urogenital ridge, germ cells migrate into this region.

**Week 7-** Invagination of coelomic epithelium, Cord grows and terminates on urogenital sinus

Male Gonad (testes) secretes Mullerian duct inhibitory factor (MDIF), causes regression of paramesonephric duct Testosterone retains mesonephric duct (female – opposite)

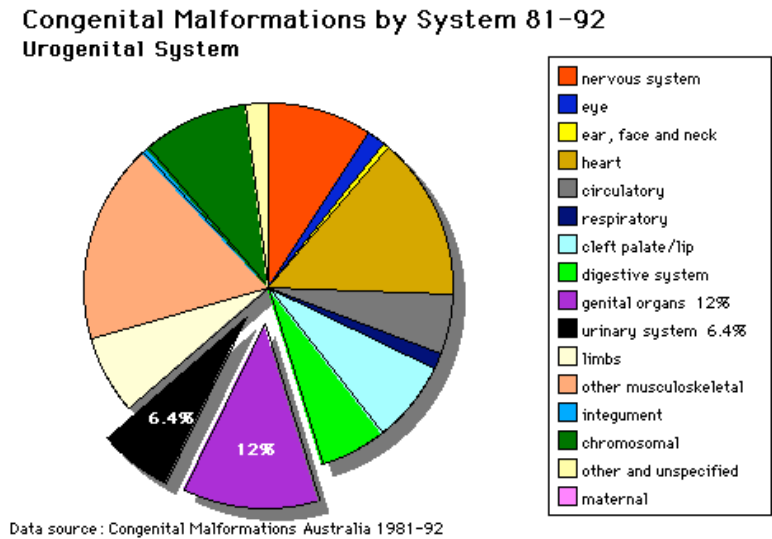
Male (week 7) differentiates before female (week 10-12)

**External Genital Organs**

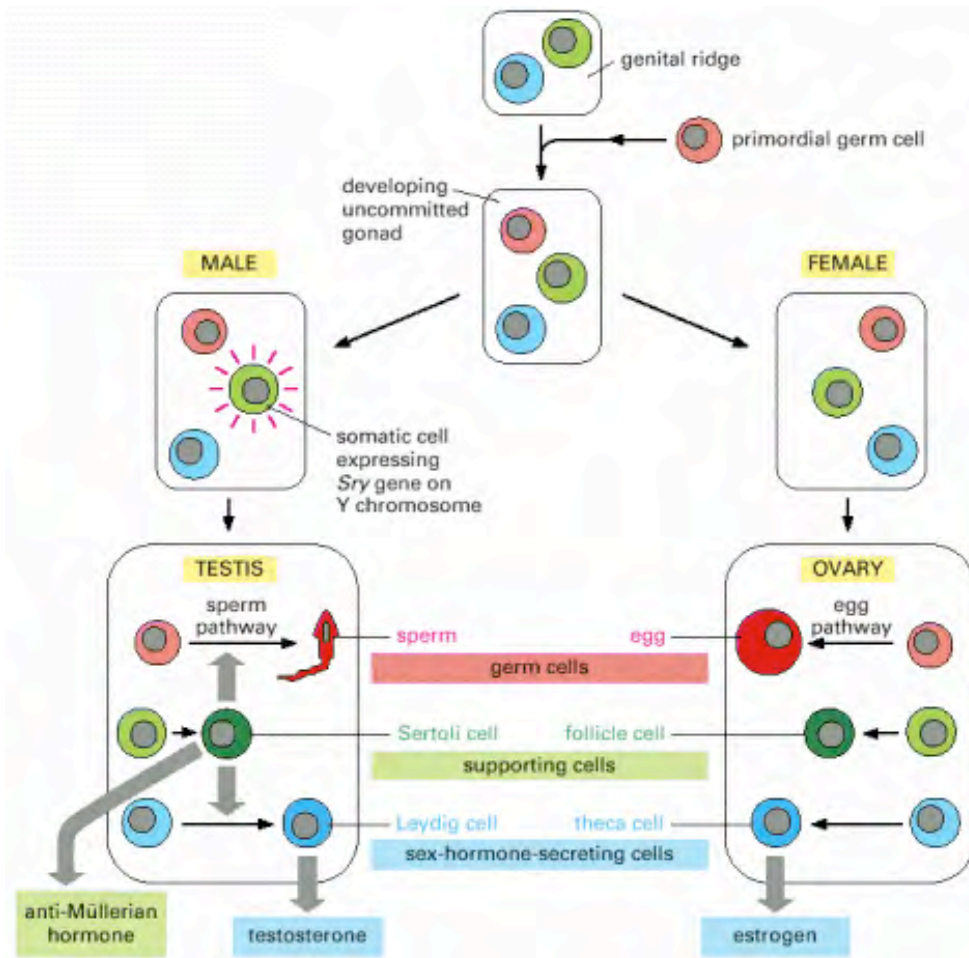
All embryos initially same (indifferent), testosterone differentiates male

**Genital Abnormalities**

Chromosomal, Hermaphroditism, Gonadal Dysfunction, Tract Abnormalities, External Genitalia, **Gonadal Descent** – cryptorchidism, one (unilateral) or both (bilateral) testes fail to descend into scrotum, 1:30 live male births, more frequent in premature babies, may be associated with other abnormalities



Summary of Gonad Development



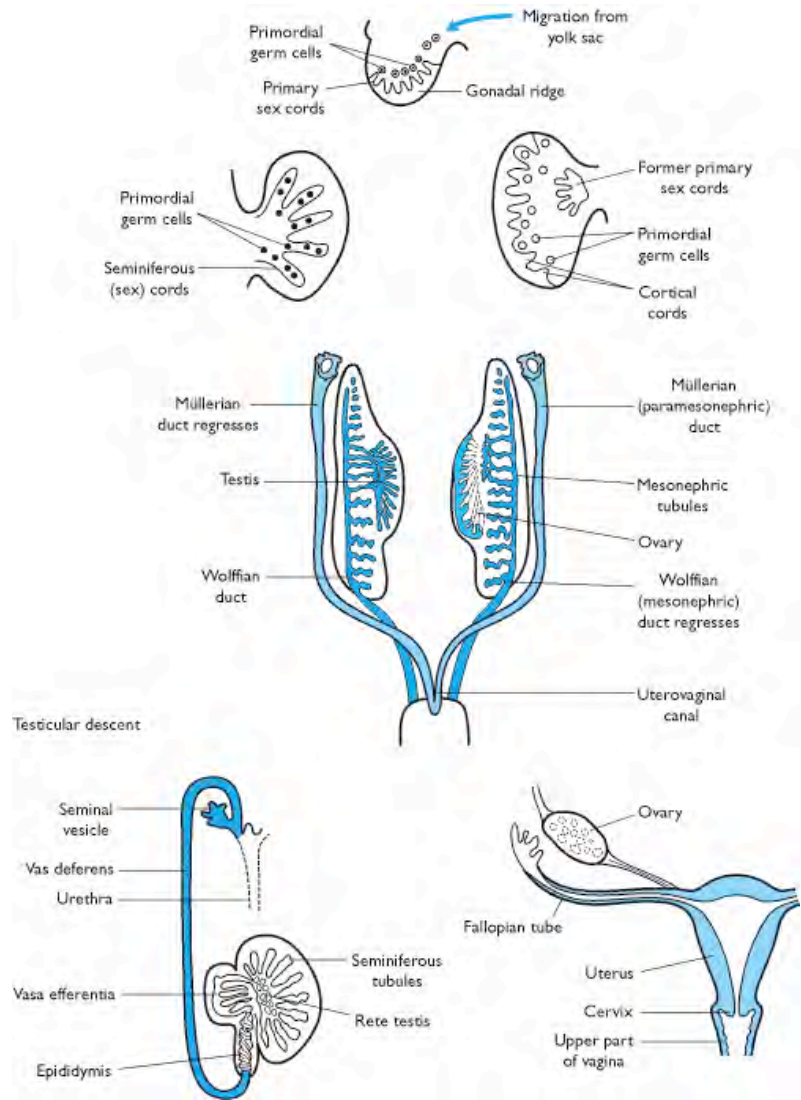
**Figure 20-18. Influence of *Sry* on gonad development.** The germ line cells are shaded in *red*, and the somatic cells are shaded in *green* and *blue*. The change from light to darker color indicates that the cell has matured or differentiated. The *Sry* gene acts in a subpopulation of somatic cells in the developing gonad to direct them to differentiate into Sertoli cells instead of into follicle cells. The Sertoli cells then induce primordial germ cells to commit to sperm development. They also secrete anti-Müllerian hormone, which causes the Müllerian duct to regress, and they help to induce other somatic cells to differentiate into Leydig cells, which secrete testosterone (see Figure 20-28). In the absence of *Sry*, the primordial germ cells commit to egg development, and the somatic cells develop into either follicle cells, which support egg development, or theca cells, which secrete estrogen. Whereas Leydig cells begin secreting testosterone in the fetus, theca cells do not begin secreting estrogen until puberty.

Image & Text: **Molecular Biology of the Cell**. 4th ed. Alberts, Bruce; Johnson, Alexander; Lewis, Julian; Raff, Martin; Roberts, Keith; Walter, Peter. New York: Garland Publishing; 2002.

<http://www.ncbi.nlm.nih.gov:80/books/bv.fcgi?db=Books&rid=mboc4.figgrp.3716>

# Sexual Differentiation Notes

## Internal Genitalia Development



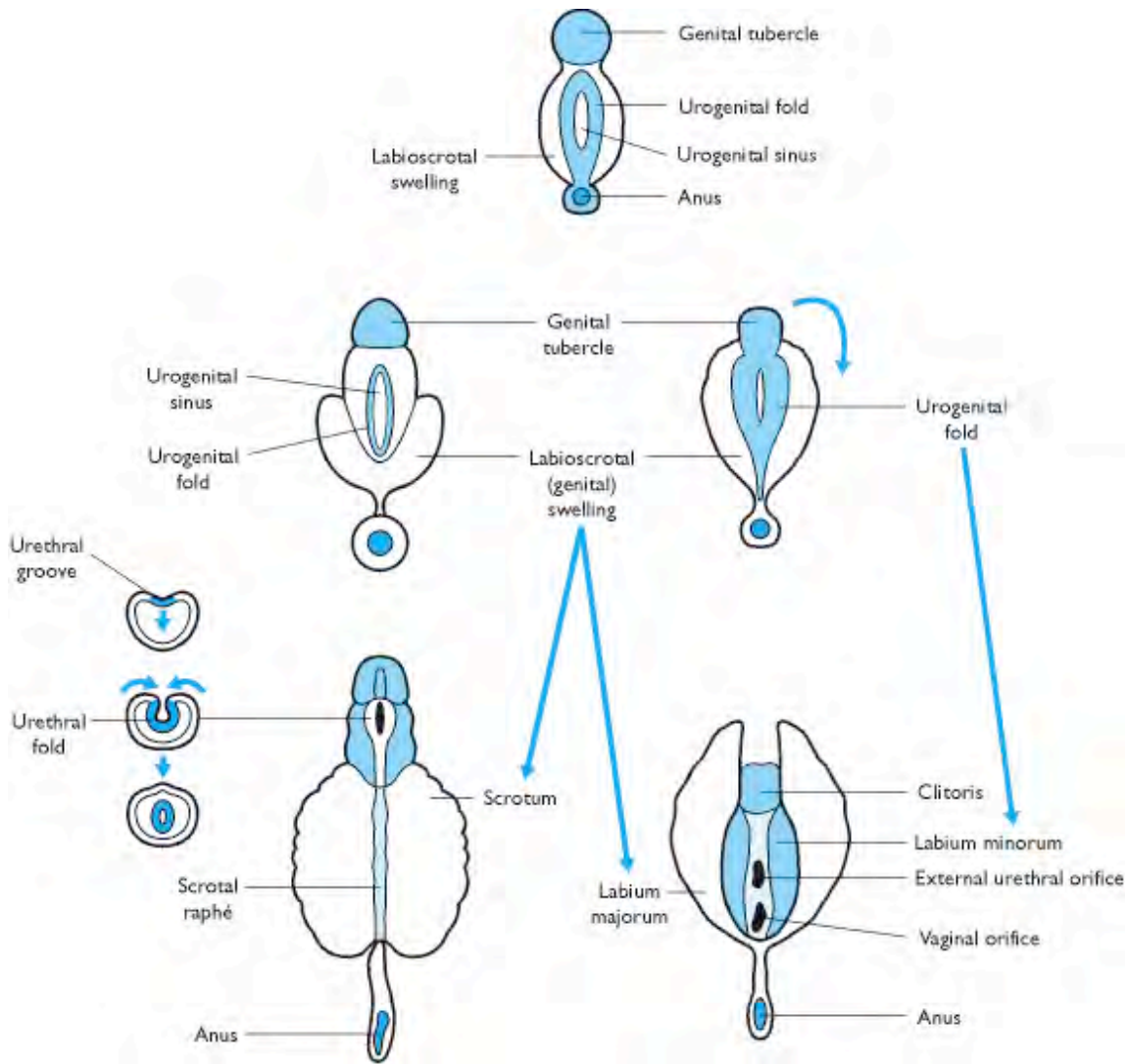
Schematic overview of the differentiation of the internal male and female reproductive tracts from the Wolffian (mesonephric) and Müllerian (paramesonephric) ducts.

Image & Text: **Endocrinology: An Integrated Approach.** Nussey, S.S. and Whitehead, S.A. Oxford, UK: BIOS Scientific Publishers, Ltd; 2001

<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=endocrin.section.1022>

# Sexual Differentiation Notes

## External Genitalia Development



The genital tubercle elongates and forms the shaft and glans of the penis. The urogenital sinus becomes continuous with a groove that develops on the caudal face of the genital tubercle and this groove closes to become the penile part of the urethra while the fused urogenital folds enclosing the sinus becomes the prostate part of the urethra. In the most distal part of the penis, invagination of a cord of epithelial cells covering the glans meets the penile urethra and when this cord canalizes the formation of the urethra is complete. The line of fusion along the urethra and scrotum is called the raphé. The labioscrotal folds form the scrotum.

In females, the genital tubercle bends inferiorly to form the clitoris, the urogenital folds, that do not fuse, form the labia minora and the genital swellings develop into the labia majora. The vagina and the urethra open into the vestibule of the urogenital sinus.

Image & Text: **Endocrinology: An Integrated Approach.** Nussey, S.S. and Whitehead, S.A. Oxford, UK: BIOS Scientific Publishers, Ltd; 2001

<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=endocrin.section.1024>