

## Practical 11: Sexual Differentiation

Principal Teacher: Dr Mark Hill

### Specific Objectives:

1. Brief understanding of early formation of nephric, mesonephric and paramesonephric ducts.
2. Understand the male and female derivatives of mesonephric and paramesonephric ducts.
3. Understand early differentiation of the gonad.
4. Brief understanding of the early differentiation of the urogenital sinus.
5. Understand the differentiation of external male and female genitalia.

### Introduction:

These notes provide an overview and general introduction to prenatal male and female genital development: gonadal, internal and external genitalia formation and differentiation. Only selected embryonic and fetal aspects will be demonstrated in this practical class.



Female fetus (10 week) pelvic region showing urogenital development

### Resources:

**UNSW Embryology** (<http://php.med.unsw.edu.au/embryology>)

This computer-based class will work through a series of **UNSW Embryology** pages (see link below) with links to: histological images, animations, ultrasound, glossary and additional resources. Serial images from selected developmental stages, early embryonic (stage 13), late embryonic (stage 22) and fetal (10 week) will also be used to show key features. Some congenital abnormalities will also be discussed. There is an online Quiz to test your knowledge after completing the practical.

### Practical Class Link:

[http://php.med.unsw.edu.au/embryology/index.php?title=BGDB Practical - Sexual Differentiation](http://php.med.unsw.edu.au/embryology/index.php?title=BGDB%20Practical%20-%20Sexual%20Differentiation)

### Lecture Link:

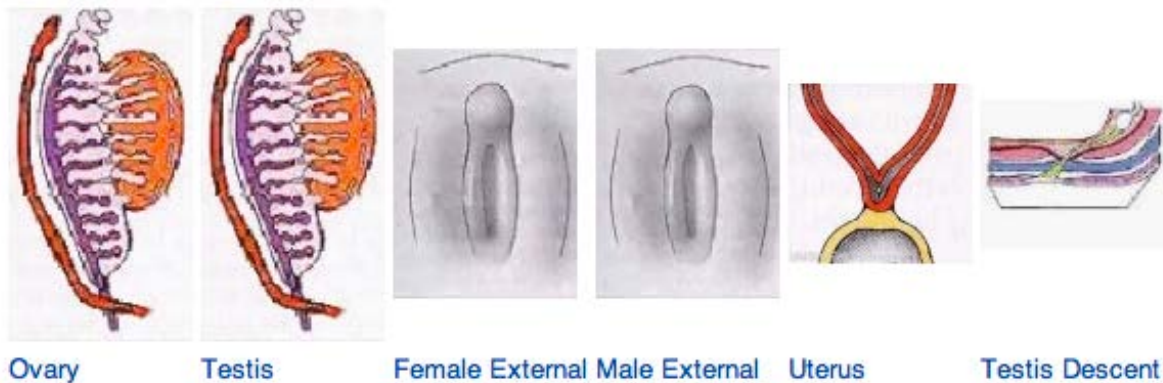
[http://php.med.unsw.edu.au/embryology/index.php?title=BGD Lecture - Sexual Differentiation](http://php.med.unsw.edu.au/embryology/index.php?title=BGD%20Lecture%20-%20Sexual%20Differentiation)

**Textbook:**

There are many good embryology textbooks available, select the one that best suits your studying style. The first two listed below are also available online through the UNSW library and are also linked from your online classes.

(More textbooks [http://php.med.unsw.edu.au/embryology/index.php?title=Embryology\\_Textbooks](http://php.med.unsw.edu.au/embryology/index.php?title=Embryology_Textbooks))

1. **The Developing Human : Clinically Oriented Embryology** (8th ed.) Moore, Keith L; Persaud, T V N; Torchia, Mark G Philadelphia, PA : Saunders/Elsevier, (2008). Chapter 12
2. **Larsen's Human Embryology** (4th ed.) Schoenwolf, Gary C; Larsen, William J, (William James). Philadelphia, PA : Elsevier/Churchill Livingstone (2009). Chapter 15
3. **UNSW Embryology** (12th ed.) Hill, Mark (2012)  
[http://php.med.unsw.edu.au/embryology/index.php?title=Genital\\_System\\_Development](http://php.med.unsw.edu.au/embryology/index.php?title=Genital_System_Development)

**Background Information:****Genital**

There are three key differentiation stages in genital development in the embryo.

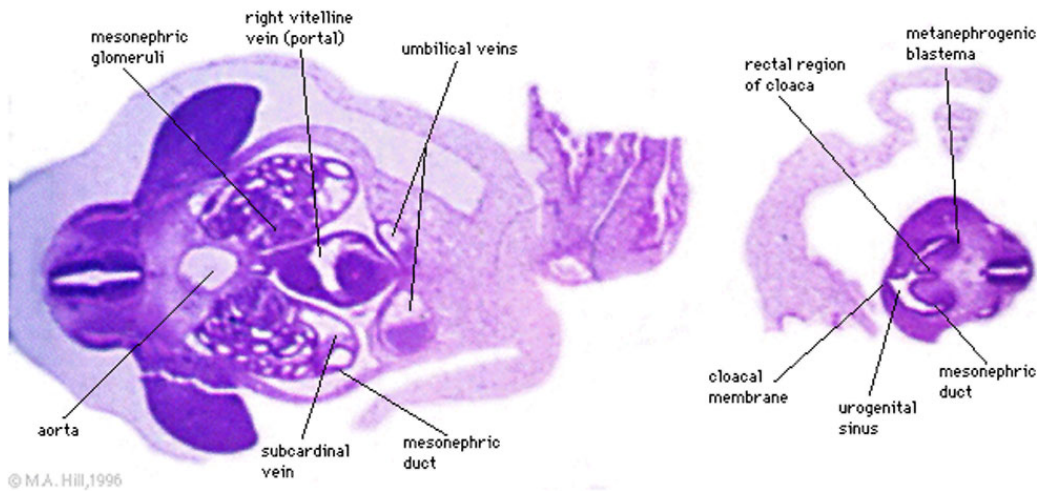
1. Differentiation of indifferent **gonad**
2. Differentiation of ducts, **internal genital organs**
3. Differentiation of **external genitalia**

Stage 2 and 3 are dependent on stage 1, presence of male or female gonad and their endocrine products. The “default” embryo sex is female, in the absence of testes development. Genital development timecourse is long, beginning in embryo and finishing in puberty. Abnormal sex chromosome, either genetic or functional, can impact greatly on this long-term process. While in general sex steroidal hormone function in genital development is understood, much has yet to be determined for the overall impact on other organs, for example in the brain.

**1. Differentiation of indifferent gonad**

Week 5 – gonad development begins

Week 6 – germ cells migrate into gonadal ridge (female XX and male XY gonads are identical at this stage). Further development dependent on sex chromosome: Y Chromosome – testes, No Y chromosome – ovaries.



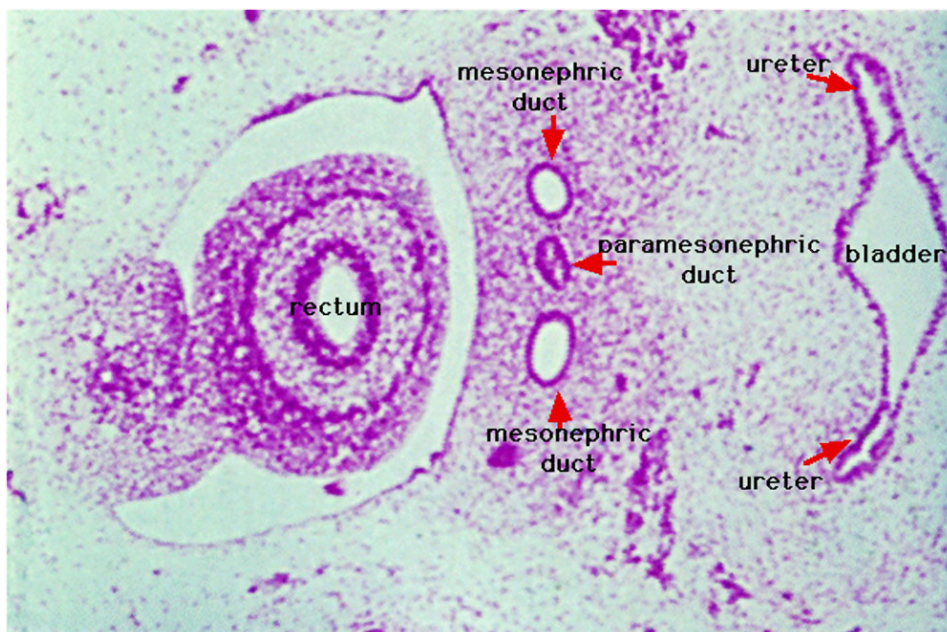
Carnegie stage 13 genital ridge and urogenital sinus.

### Sex Chromosomes

- Y Chromosome – over 200 genes, over 50 million base pairs. **SRY** gene is the Y-linked testis-determining gene in mammals.
- X Chromosome – over 1400 genes, over 150 million base pairs.

### 2. Differentiation of indifferent ducts, internal genital organs

- Week 7 – duct regression or preservation begins



Carnegie stage 22 (male) genital ducts, urinary and rectal relationships.

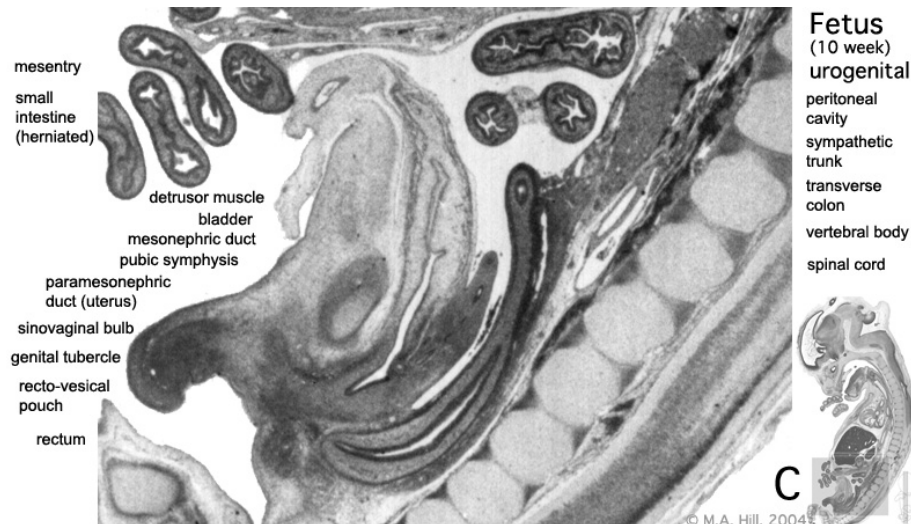
All embryos initially form 2 paired indifferent duct systems:

1. **Mesonephric ducts** (also called the Wolffian ducts)
2. **Paramesonephric ducts** (also called the Mullerian ducts)

Testes secretions- **Mullerian duct inhibitory factor** (MDIF) causes regression of paramesonephric ducts and **testosterone** retains mesonephric ducts.

No Testes- Paramesonephric ducts retained and mesonephric duct regresses.

### 3. Differentiation of indifferent external genitalia (fetal period)



**Fetus (10 week) female, section from midline urogenital region.**

The external genitalia are initially identical and undergo male and female differentiation under the influence or absence of modified steroidal sex hormone.

**Indifferent stage** - cloaca divided by proliferating mesenchyme forming urorectal septum, ventral urethral, dorsal anal pit.

**Difference stage** - locally in this region the presence or absence of **dihydroxytestosterone** (DHT), generated from testosterone, determines male/female development.

- Presence of DHT, locally in this region leads to **genital tubercle** growth, maintenance and fusion of genital folds and external male genitalia.
- Absence of DHT, **genital tubercle** remains small, bends caudally to form the clitoris. Genital folds persist, do not fuse, and form **labia minora**. The open urogenital sinus forms a cleft into which urethra and vagina open. The labioscrotal swellings become the **labia majora**.

#### Gonad Descent

Both kidney and gonads develop retroperitoneally, with the gonads moving into the abdomen or eventually into the scrotal sacs. During fetal development the **gubernaculum** and fetal growth in both male and female, changes the gonads' relative positions finally reaching their adult locations. These positional changes are not covered in detail in this current class.

Testes - two anatomical phases in descent, **transabdominal** and **transinguinal**, under the influence of the shortening gubernaculum.

Ovaries - undergo caudal and lateral shifts to be suspended in the broad ligament of the uterus, gubernaculum does not shorten, attaches to paramesonephric ducts, causing medial movement into the pelvis.

**Questions:**

1. What are the 3 duct systems that develop in the embryo?
2. What are the key differences in male and female gonad development?
3. Why does internal and external genital development rely on successful gonad development?
4. What are the key differences in male and female gonad development?
5. From what embryonic structure is the uterus derived?
6. What does the genital tubercle form in the male and female embryo?
7. What are cryptorchidism and hypospadias and how common are these disorders?