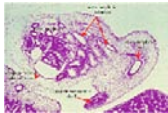



UNSW ANAT2310 Lecture 12

Genital Development

ANAT2310 - Vertebrate Development B Lecture 12



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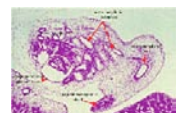
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Lecture Overview

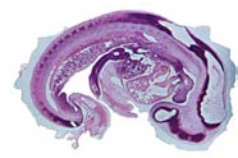
- Gonad
- Reproductive Tract
- External genitalia
 - Development
 - Function
 - Abnormalities



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Background


- ANAT2300 S1
 - Fertilization
 - Week 1
- ANAT2310 S2
 - Kidney
 - Endocrine



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Genital Development



Online References

- UNSW Embryology
 - Gonad Development
 - <http://embryology.med.unsw.edu.au/Notes/urogen.htm>
- NIH Bookshelf
 - Developmental Biology (Gilbert)
 - Chapter 17
 - <http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=dbio.chapter.4101>

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Textbook References

- Human Embryology (2nd ed.) Larson
 - Ch10 p261-306
- The Developing Human (6th ed.) Moore & Persaud
 - Ch13 p303-346
- Before We Are Born (5th ed.) Moore and Persaud
 - Ch14 p289-326
- Essentials of Human Embryology, Larson
 - Ch10 p173-205
- Human Embryology, Fitzgerald and Fitzgerald
 - Ch21-22 p134-152

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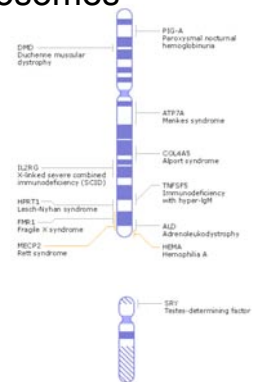
Genital System Development

- 3 stages
 - Differentiation of gonad (Sex determination)
 - Differentiation of internal genital organs
 - Differentiation of external genital organs
 - 2nd and 3rd stages dependent on endocrine gonad
- Long Maturation Timecourse
 - Begins in embryo
 - Finishes in puberty

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Sex Chromosomes

- X Chromosome
 - 1400+ genes
 - 150 million base pairs
 - 95% determined
- Chromosome Y
 - 200+ genes
 - 50 million base pairs
 - 50% determined



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Images: NCBI

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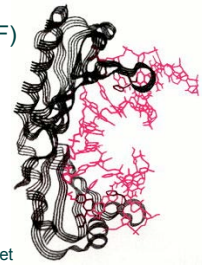
Sex Determination

- Humans (week 5-6)
 - Germ cells migrate into gonadal ridge
 - Gonads (male/female) identical at this stage
 - Indifferent
 - Gonad development dependent on sex chromosome
 - **Y** testes
 - No **Y** ovary

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DNA with SRY Protein

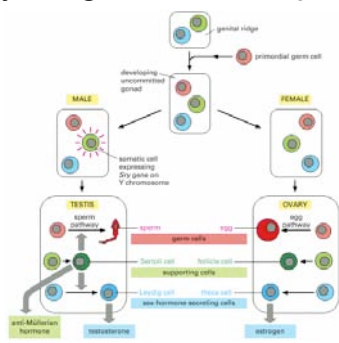
- SRY protein binds DNA
 - Testes determining factor (TDF)
 - Transcription factor
- Bends DNA 70–80 degrees
 - Black
 - SRY protein HMG box
 - Red coil
 - DNA double helix
 - After Haqq et al. 1994 and Werner et al. 1995



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Image: Dev. Biol, Gilbert Fig17.5

Sry on gonad development



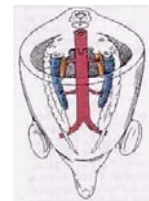
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Image: MBoC4 Fig20.18

Movie: Germ Cells & Gonad



germcell.mov



gonad.mov

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Movies: based on Larsen

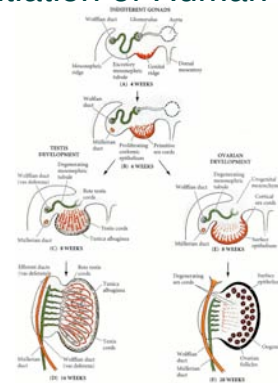
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Internal Genital Organs

- All embryos form paired
 - Mesonephric duct
 - See kidney development
 - Paramesonephric duct
 - Humans 7th week
 - 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

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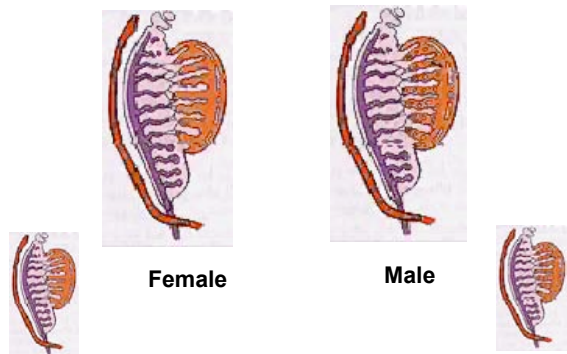
Differentiation of Human Gonads



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Image: Dev. Biol, Gilbert Fig17.3

Movie: Gonad Development



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Movies: based on Larsen

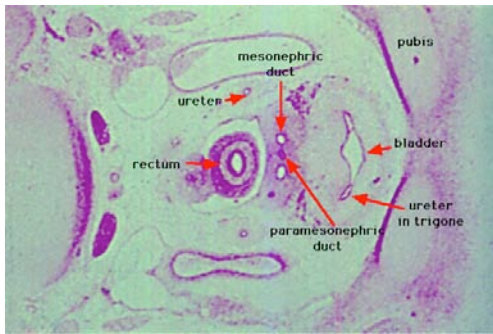
Carnegie stage 13/14



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Genital Development

Male Mesonephric Duct (st22)



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UNSW Embryology

External Genital Organs

- All embryos initially same (indifferent)
- Testosterone
 - Differentiates male



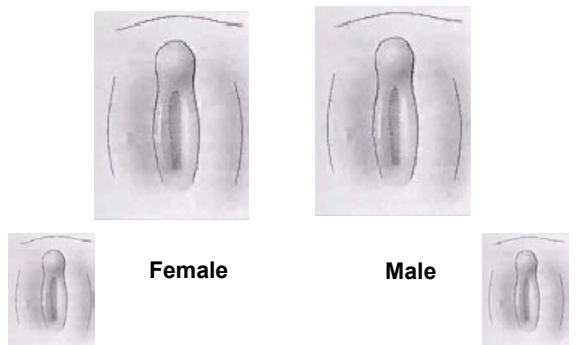
Female



Male

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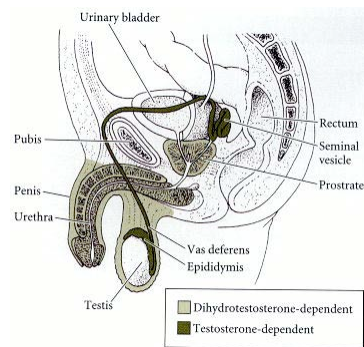
Movie: External Genitalia



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Movies: based on Larsen

Male Hormone dependent anatomy

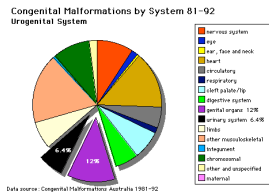


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Image: Dev. Biol, Gilbert Fig17.12

Genital Abnormalities

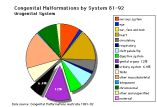
- Chromosomal
- Hermaphroditism
- Gonadal Dysfunction
- Tract Abnormalities
- External Genitalia
- Gonadal Descent



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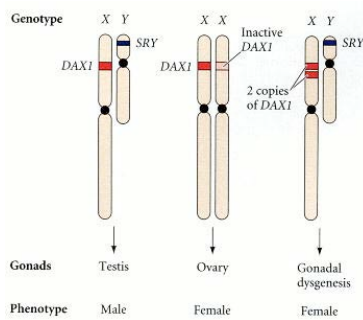
Chromosomal

- Turner's Syndrome
 - Monosomy XO
 - 99% non-viable embryos
 - Fail to sexually mature at puberty
- Klinefelter's Syndrome
 - 47, XXY
 - Begin normal male, become infertile
 - Tall, mental dullness, behaviour problems
- Males
 - 46, XX
 - Develop as male, infertile adults
 - Portion of SRY gene located on one X



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Sex Reversal in Humans

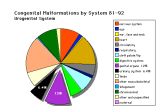


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Image: Dev. Biol, Gilbert Fig17.9

Hermaphroditism

- True
 - Gonads both ovary and teste tissues
 - Ovotestes or ovary and testes
 - 46,XX
- Male Pseudohermaphrodites
 - 46,XY
 - Gonads of one sex, external genitalia of opposite
 - Various causes
- Female Pseudohermaphrodites
 - 46,XX
 - Gonads are ovaries, external genitalia ambiguous
 - Hyperplastic adrenals secrete androgens

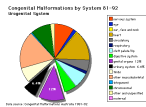


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Gonadal Dysfunction

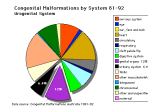
- Gonads fail to develop properly
- Gonadal Dysgenesis
 - Swyer's syndrome
 - 46,XX
- Mixed Gonadal Dysgenesis
 - 45,X/46,XY
- Primary Hypogonadism
 - Affected females 46,XX
- Primary Hypogonadism
 - Defective anterior pituitary production of gonadotropin
 - Lack of gonadotropin-releasing hormone



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Tract Abnormalities

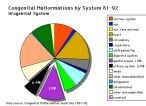
- Many different forms
- Uterine
 - Associated with other anomalies
- Vagina
 - Agenesis, atresia
 - See endocrine lecture DES
- Ductus Deferens
 - Uni- or bilateral absence
 - Failure of mesonephric duct to differentiate



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External Genitalia

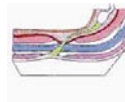
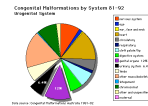
- Multi-factorial
 - Chromosomal, single gene, environmental
 - Developmental arrest gives ambiguous



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Gonadal Descent

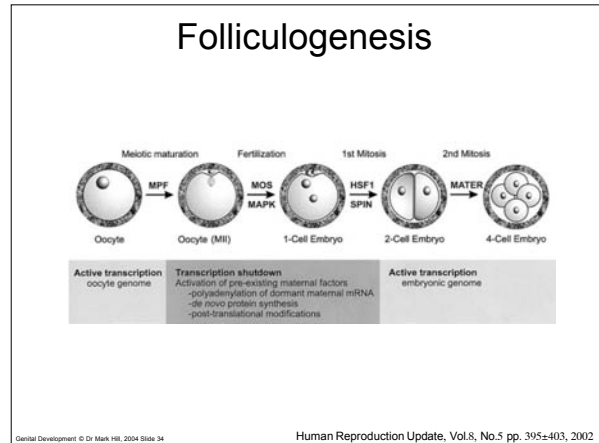
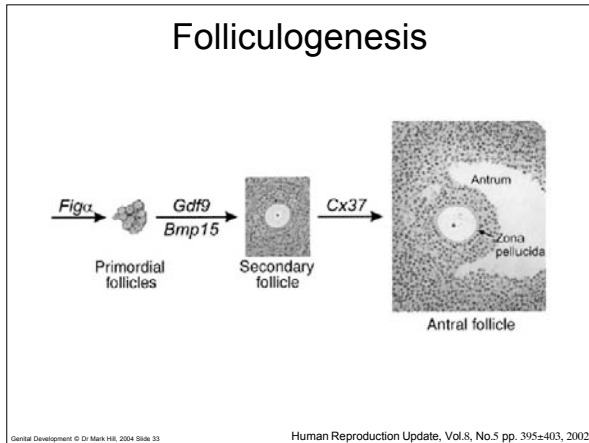
- Cryptorchadism
 - One or both testes fail to descend into scrotum
 - 1:30 live male births
 - May be associated with other abnormalities



Movies: based on Larsen

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Sex Differences in Adult and Developing Brains

- Despite decades of research, we do not know the functional significance of most sex differences in the brain. We are heavily invested in the idea that sex differences in brain structure cause sex differences in behavior. We rarely consider the possibility that sex differences in brain structure may also prevent sex differences in overt functions and behavior, by compensating for sex differences in physiological conditions, e.g. gonadal hormone levels that may generate undesirable sex differences if left unchecked. Such a dual function for sex differences is unlikely to be restricted to adult brains. This review will entertain the possibility that transient sex differences in gene expression in developing brains may cause permanent differences in brain structure but prevent them as well, by compensating for potentially differentiating effects of sex differences in gonadal hormone levels and sex chromosomal gene expression. Consistent application of this dualfunction hypothesis will make the search for the functional significance of sex differences more productive. (*Endocrinology* 145: 1063-1068, 2004)

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Sex Chromosomes and Brain Sexual Differentiation

- The brains of males and females differ, not only in regions specialized for reproduction, but also in other regions (controlling cognition, for example) where sex differences are not necessarily expected. Moreover, males and females are differentially susceptible to neurological and psychiatric disease. What are the origins of these sex differences? Two major sources of sexually dimorphic information could lead to sex differences in brain function. Male and female brain cells carry a different complement of sex chromosome genes and are influenced throughout life by a different mix of gonadal hormones. Until recently all sex differences in the brain have been attributed to the differential action of gonadal hormones. Recent findings, however, suggest that brain cells that differ in their genetic sex are not equivalent, and that difference may contribute to sex differences in brain function. Here we discuss evidence for sex chromosome effects on both neural and nonneural systems, which together provide support for the idea that XX and XY cells differentiate even before they are influenced by gonadal hormones, and even if they are exposed to similar levels of gonadal steroids. Fortunately, new model systems for studying sex chromosome effects have recently been developed, and they should help in testing further the role of sex chromosome genes.
- (*Endocrinology* 145:1057-1062, 2004)

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