Gross morphological differences between sexes are Not observed until about the 7th week of gestation.

This early period from 0-7 weeks is called the indifferent stage.

However, differences at the genetic and microscopic levels are already Apparent.

Female nuclei contain a Barr body, which is an inactivated X chromosome.

Male embryos show gene expression of some Y specific proteins such as SRY, testis determining factor, and the H-Y antigen, a minor histo-compatibility antigen.
Sex determination begins at fertilization

Humans have 46 chromosomes
- 22 pairs of autosomes
- 2 sex chromosomes

In general: females are - 46, XX
males are - 46, XY

In mammals, the presence of a Y chromosome determines the male phenotype.
Evidence that SRY is the testis determining factor

SRY is detected in gender reversal:
- XX males who have a translocation of the sry region to an X or another chromosome
- XY females who have a deletion of the SRY region

In transgenic mice, a 14 kb genomic DNA encoding SRY can transform XX females into phenotypic males.

SRY is expressed in male gonads at the time of sex determination.

SRY encodes a DNA binding protein of the HMG class and is thought to function as a master switch for the regulation of testis specific genes.
Migration of primordial germ cells from the posterior extra-embryonic mesoderm through the mesenteries and into the gonadal ridge.
Early stages of sex differentiation, 7 weeks

SRY acts on the indifferent gonad to start the process of male sexual development
Figure 15-10

Figure 15-27
Development of female
External genitalia
Development of male External genitalia

Congenital female abnormalities

A- double uterus & vagina  B- double uterus, single vagina
C- Bicornuate uterus  D- Septate uterus
E- Unicornuate uterus  F- Atresia of the cervix
Congenital male abnormalities

Abnormal testicular decent - cryptorchidism results in sterility if testis have not descended within the first months after birth.

### LE 15-1 Homologies in the Male and Female Urogenital Systems

<table>
<thead>
<tr>
<th>Indifferent structure</th>
<th>Male derivative</th>
<th>Female derivative</th>
</tr>
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<tbody>
<tr>
<td>Genital ridge</td>
<td>Testis</td>
<td>Ovary</td>
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<tr>
<td>Primordial germ cells</td>
<td>Spermatozoa</td>
<td>Ova</td>
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<tr>
<td>Sex cords</td>
<td>Seminiferous tubules (Sertoli cells)</td>
<td>Follicular cells</td>
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<tr>
<td>Mesonephric tubules</td>
<td>Efferent ductules</td>
<td>Eooophoron</td>
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<tr>
<td>Mesonephric (wolfian) ducts</td>
<td>Paradidymis</td>
<td>Paraphoron</td>
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<tr>
<td>Appendix of epididymis</td>
<td>Epididymal duct</td>
<td>Appendix of ovary</td>
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<tr>
<td>Ductus deferens</td>
<td>Ejaculatory duct</td>
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<tr>
<td>Appendix of testis</td>
<td>Prostate utricle</td>
<td>Uterine tubes</td>
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<tr>
<td>Penile urethra</td>
<td>Urinary bladder</td>
<td>Uterus</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>Prostatic urethra</td>
<td>Uterus</td>
</tr>
<tr>
<td>Penis</td>
<td>vaginal vestibule</td>
<td>Vagina</td>
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<tr>
<td>Floor of penile urethra</td>
<td>Prostatic urethra</td>
<td>Urethra</td>
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<tr>
<td>Scrotum</td>
<td>Labia minora</td>
<td>Clitoris</td>
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<tr>
<td>Genital tubercle</td>
<td></td>
<td>Labia majora</td>
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<td>Genital folds</td>
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<tr>
<td>Genital swellings</td>
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</tbody>
</table>
Genetic abnormalities of sex determination

Turner's syndrome - gonadal dysgenesis
45,X0 genotype results in degeneration of the promordial germ cells after reaching the gonadal ridge. Gonads fail to differentiate and do not secrete androgens. External genitalia is female but remains infantile.

True Hermaphroditism - generally 46,XX and appear female but have ovotestis, with both spermatagonia and ovarian follicles (very rare and usually raised as female).

Pseudohermaphroditism - Males are usually 46,XY with insufficient hormone production, phallic hypoplasia, and remnants of the paramesonephric duct present. Females are usually 46,XX but produce too much androgenic hormones by the adrenal cortex and exhibit masculinization of external genitalia.

Testicular Feminization - genetically male, 46XY, but phenotypically female. Individuals have internal testis, produce testosterone but are insensistive to androgens due to a receptor mutation.
Fig. 111-8. — Ambiguous genitalia of a male pseudohermaphrodite showing small phallus with hypospadias and opening of urogenital sinus; 46,XY karyotype.

Figure 8-11 The masculinized external genitalia of a female infant with female pseudohermaphroditism caused by congenital virilizing adrenal hyperplasia. The 17-ketosteroid output was elevated. The virilization was caused by excessive androgens produced by the fetal adrenal glands.
Figure 17-16. Pelvic duplication. A. Normal appearance of the uterus. The upper segment contains a normal
uterus, the lower two uteri are non-maternal (B) and the vault posterior to uterus, (From Beutler
[83]). B. Bilateral pregnancy with normal, non-maternal fetus for the longer of the period. C. Left has a normal
uterus; right has a large, non-maternal uterus, (From Beutler [83]). D. Bilateral pregnancy with normal, non-
fetal uterus, (From Beutler [83]). E. Bilateral pregnancy with normal, non-fetal uterus, (From Beutler
[83]). F. Bilateral pregnancy with normal, non-fetal uterus, (From Beutler [83]).