Sex differentiation is a complex process that involves many genes, including some that are autosomal. The key to sexual dimorphism is the Y chromosome, which contains the testis determining gene called the SRY (sex-determining region on Y) gene.

**SRY gene**

- under its influence, male development occurs;
- in its absence, female development is established.

**Gonads**

The sex of the embryo is determined genetically at the time of fertilization. The gonads do not acquire male or female morphological characteristics until the seventh week of development.

**The genital or gonadal ridges**

Gonads appear initially as a pair of longitudinal ridges, the genital or gonadal ridges. They are formed by proliferation of the epithelium and a condensation of underlying mesenchyme. Germ cells do not appear in the genital ridges until the sixth week of development.

**Primordial germ cells**

Primordial germ cells originate in the epiblast, migrate through the primitive streak, and by the 3rd week reside among endoderm cells in the wall of the yolk sac close to the allantois. During the 4th week, they migrate by ameboid movement along the dorsal mesentery of the hindgut, arriving at the primitive gonads at the beginning of the fifth week and invading the genital ridges in the sixth week. If they fail to reach the ridges, the gonads do not develop. Hence, the primordial germ cells have an inductive influence on development of the gonad into ovary or testis.

**Indifferent gonad**

Shortly before and during arrival of primordial germ cells, the epithelial cells of the genital ridge proliferates, and penetrate the underlying mesenchyme and they form a number of irregularly shaped cords called the primitive sex cords. In both male and female embryos, these cords are connected to surface epithelium, and it is impossible to differentiate between the male and female gonad. Hence, the gonad is known as the indifferent gonad.

**Testis**

Under influence of SRY gene on the Y chromosome, the primitive sex cords continue to proliferate and penetrate deep into the medulla to form the medullary or testis cords. Toward the hilum of the gland, the cords break up into a network of tiny cell strands, that later give rise to tubules of the rete testis. During further development, a dense layer of fibrous connective tissue, the tunica albuginea separates the testis cords from the surface epithelium.

**Interstitial cells of Leydig**

derived from the original mesenchyme of the gonadal ridge, lie between the testis cords.
They begin development shortly after onset of differentiation of these cords. By the **eighth week of gestation**, Leydig cells begin **production of testosterone**, and the testis is able to influence sexual differentiation of the genital ducts and external genitalia.

In the fourth month, the testis cords **become horseshoe shaped**, and their extremities are continuous with those of the rete testis. They are composed of primitive germ cells and sustentacular cells of Sertoli derived from the surface epithelium of the gland. **Testis cords remain solid until puberty**, when they acquire a lumen, thus forming the seminiferous tubules. Once the seminiferous tubules are canalized, they join the rete testis tubules, which in turn enter the ductuli efferentes.

**Ovary**

**Ovary at the 7th week**

In female embryos with an XX sex chromosome complement and no Y chromosome, primitive sex cords **dissociate into irregular cell clusters**. These clusters, containing groups of primitive germ cells, occupy the **medullary part of the ovary**. Later, they disappear and are replaced by a **vascular stroma** that forms the ovarian medulla. The surface epithelium of the female gonad, unlike that of the male, continues to proliferate. In the seventh week, it gives rise to a **second generation of cords, cortical cords**, which penetrate the underlying mesenchyme but remain close to the surface.

**Ovary at 4th month**

Cortical cords split into isolated cell clusters, with each surrounding one or more primitive germ cells. Germ cells subsequently develop into oogonia, and the surrounding epithelial cells, descendants of the surface epithelium, form follicular cells.

**Genital Ducts**

**Indifferent Stage**

Initially, both male and female embryos have two pairs of genital ducts **mesonephric (wolfian) ducts and paramesonephric (müllerian) ducts**. The paramesonephric duct arises as a longitudinal invagination of the epithelium on the anterolateral surface of the urogenital ridge. Cranially, the duct opens into the abdominal cavity with a funnel-like structure. Caudally, it first runs lateral to the mesonephric duct, then crosses it ventrally to grow caudomedially. In the midline, the paramesonephric duct comes in close contact with the paramesonephric duct from the opposite side. The two ducts are initially separated by a septum but later fuse to form the uterine canal. The caudal tip of the combined ducts projects into the posterior wall of the urogenital sinus, where it causes a small swelling, the paramesonephric or müllerian tubercle. The mesonephric ducts open into the urogenital sinus on either side of the müllerian tubercle.

**Genital Ducts in the Male**

As the mesonephros regresses, a few excretory tubules, the **epigenital tubules**, establish contact with cords of the rete testis and finally form the Efferent ductules of the testis.
Excretory tubules along the caudal pole of the testis, the **paragenital tubules**, do not join the cords of the rete testis. Their vestiges are collectively known as the paradidymis. Except for the most cranial portion, the **appendix epididymis**, the mesonephric ducts persist and become highly convoluted, forming the **(ductus) epididymis**. From the tail of the epididymis to the outbudding of the seminal vesicle, the mesonephric ducts obtain a thick muscular coat and form the **ductus deferens**. The region of the ducts beyond the seminal vesicles is the **ejaculatory duct** and form the main genital ducts. Immediately below the entrance of the efferent ductules, the mesonephric ducts elongate

**Prostate**

Multiple endodermal outgrowths arise from the prostatic part of the urethra and grow into the surrounding mesenchyme. The glandular epithelium of the prostate differentiates from these endodermal cells, and the associated mesenchyme differentiates into the dense stroma and smooth muscle of the prostate

### Genital Ducts in the Female

The paramesonephric ducts develop into the main genital ducts of the female.

Initially, three parts can be recognized in each duct

- a **cranial vertical portion** that opens into the abdominal cavity
- a **horizontal part** that crosses the mesonephric duct, and
- a **caudal vertical part** that fuses with its partner from the opposite side.

With descent of the ovary, the first two parts develop into the uterine tube and the caudal parts fuse to form the uterine canal.

When the second part of the paramesonephric ducts moves mediocaudally, the urogenital ridges gradually come to lie in a transverse plane.

After the ducts fuse in the midline, a broad transverse pelvic fold (**broad ligament of the uterus**) is established. This fold extends from the lateral sides of the fused paramesonephric ducts toward the wall of the pelvis. The uterine tube lies in its upper border, and the ovary lies on its posterior surface.

The uterus and broad ligaments divide the pelvic cavity into the uterovesical pouch and the uterorectal pouch

The fused paramesonephric ducts give rise to the corpus and cervix of the uterus. They are surrounded by a layer of mesenchyme that forms the muscular coat of the uterus, the myometrium and its peritoneal covering the perimetrium.

**Vagina**
Shortly after the solid tip of the paramesonephric ducts reaches the urogenital sinus, two solid evaginations grow out from the pelvic part of the sinus. These evaginations, the sinovaginal bulbs, proliferate and form a solid vaginal plate. Proliferation continues at the cranial end of the plate, increasing the distance between the uterus and the urogenital sinus.

By the fifth month, the vaginal outgrowth is entirely canalized. The wing-like expansions of the vagina around the end of the uterus, the vaginal fornices, are of paramesonephric origin.

Thus, the vagina has a dual origin, with the upper portion derived from the uterine canal and the lower portion derived from the urogenital sinus.

**The hymen**

The lumen of the vagina remains separated from that of the urogenital sinus by a thin tissue plate, the hymen, which consists of the epithelial lining of the sinus and a thin layer of vaginal cells. It usually develops a small opening during perinatal life.

**Clinical Correlates**

**Uterine and Vaginal Defects**

Duplications of the uterus result from lack of fusion of the paramesonephric ducts in a local area or throughout their normal line of fusion.

In patients with complete or partial atresia of one of the paramesonephric ducts, the rudimentary part lies as an appendage to the well-developed side.

If the atresia involves both sides, an atresia of the cervix may result.

If the sinovaginal bulbs fail to fuse a double vagina results.

If the sinovaginal bulbs do not develop at all, atresia of the vagina, results.

**Vestigial Structures Derived from Embryonic Genital Ducts**

**Mesonephric Duct Remnants in Males**

The cranial end of the mesonephric duct may persist as an appendix of the epididymis, which is usually attached to the head of the epididymis.

Caudal to the efferent ductules, some mesonephric tubules may persist as a small body, the paradidymis.

**Mesonephric Duct Remnants in Females**

The cranial end of the mesonephric duct may persist as an appendix vesiculosa.
A few blind tubules and a duct, the *epoophoron*, correspond to the efferent ductules and duct of the epididymis in the male. The epoophoron may persist in the mesovarium between the ovary and uterine tube. Closer to the uterus, some rudimentary tubules may persist as the *paroophoron*.

Parts of the mesonephric duct, corresponding to the ductus deferens and ejaculatory duct, may persist as *Gartner’s duct cysts* between the layers of the broad ligament along the lateral wall of the uterus and in the wall of the vagina.

### Paramesonephric Duct Remnants in Males

The cranial end of the paramesonephric duct may persist as a *vesicular appendix of the testis*, which is attached to the superior pole of the testis.

The *prostatic utricle*, a small saclike structure that opens into the prostatic urethra, is homologous to the vagina.

The *seminal colliculus*, a small elevation in the posterior wall of the prostatic urethra, is the adult derivative of the sinus tubercle. It is homologous to the hymen in the female.

Thank you

Next lecture: External Genitalia