**Maldevelopment of female genital tract:**

****

**Prof Dr Ban Hadi \F.I.B.O.G. 2022**

**LEARNING OBJECTIVES:**

**Fifth year students should be able to:**

1. Describe the types of genital tract developmental abnormalities
2. Summarize the important points in history, examination and investigations to reach the diagnosis
3. Predict the management option for different case scenarios according to their presentation and type of abnormality.

**Sexual differentiation of the fetus and development of sexual organs:**

* The gonadal rudiments appear as the ‘**genital ridge’** overlying the embryonic kidney in the intermediate mesoderm during the fourth week of embryonic life, and they remain sexually indifferent until the seventh week
* The undifferentiated gonad has the potential to become either a testis or an ovary, and hence is termed **bipotential**, and the chromosomal complement of the zygote determines whether the gonad becomes a testis or an ovary.
* The development of either the testis or ovary is an active gene-directed process. In the male the activity of the **SRY gene** (sex-determining region of the Y chromosome) causes the gonad to begin development into a testis. In the past, ovarian development was considered a ‘default’ development due solely to the absence of SRY, but in the last 10 years ovarian-determining genes have also been found that actively lead to the development of a female gonad.
* The fetus has two sets of structures called the Müllerian (or paramesonephric) ducts and Wolffian (or mesonephric) ducts, which have the potential to develop into male or female internal and external genitalia respectively.





**Development of the male sexual organs**

As the gonad develops into a testis, it differentiates into two cell types: The Sertoli cells produce anti-Müllerian hormone (AMH) and the Leydig cells produce testosterone.

**AMH** suppresses further development of the Müllerian ducts whereas **testosterone** stimulates the Wolffian ducts to develop into the vas deferens, epididymis and seminal vesicles.

In the external genital skin, testosterone is converted by the enzyme 5-alpha-reductase into dihydrotestosterone (DHT). This acts to virilize the external genitalia. The genital tubercle becomes the penis and the labioscrotal folds fuse to form the scrotum. The urogenital folds fuse along the ventral surface of the penis and enclose the urethra so that it opens at the tip of the penis.

**Development of the female sexual organs**

* In the primitive ovary **granulosa cells**, derived from the proliferating coelomic epithelium, surround the germ cells and form primordial follicles. Each primordial follicle consists of an oocyte within a single layer of granulosa cells.
* **Theca cells** develop from the proliferating coelomic epithelium and are

separated from the granulosa cells by a basal lamina.

* **The maximum number** of primordial follicles is reached at 20 weeks’ gestation when there are six to seven million primordial follicles present. The numbers of these reduce by atresia and at birth only 1–2 million remain. Atresia continues throughout life and by menarche only 300,000–400,000 are present, and by menopause none.

The development of an oocyte within a primordial follicle is arrested at the prophase of its first meiotic division. It remains in that state until it undergoes atresia or enters the meiotic process preceding ovulation.

In the female, **the absence of testicular AMH** allows the Müllerian structures to develop and the female reproductive tract develops from these paired ducts. The proximal two-thirds of the vagina develop from the paired Müllerian ducts, which grow in a caudal and medial direction and fuse in the midline. The midline fusion of these structures produces the uterus, cervix and upper vagina, and the unfused caudal

segments form the Fallopian tubes,

Cells proliferate from the upper portion of the urogenital sinus to form structures called the ‘sinovaginal bulbs’. The caudal extension of the Müllerian ducts projects into the posterior wall of the urogenital sinus as the Müllerian tubercle. The Müllerian tubercles and the urogenital sinus fuse to form the vaginal plate, which extends from the Müllerian ducts to the urogenital sinus. This plate begins to canalize, starting at the hymen and proceeding upwards to the cervix in the sixth embryonic month



**External female genitalia**

* The external genitalia do not virilize in the absence of testosterone. Between the fifth and seventh weeks of life, the cloacal folds, which are a pair of swellings adjacent to the cloacal membrane, fuse anteriorly to become the genital tubercle. This will become the clitoris.
* The perineum develops and divides the cloacal membrane into an anterior urogenital membrane and a posterior anal membrane.
* The cloacal folds anteriorly are called the urethral folds, which form the labia minora. Another pair of folds within the cloacal membrane form the labioscrotal folds that eventually become the labia majora.
* The urogenital sinus becomes the vestibule of the vagina.
* The external genitalia are recognizably female by the end of the twelfth embryonic week.

**Müllerian anomalies**

These are common, occurring in up to 6% of the female population, and may be asymptomatic.

The aetiology is unknown, although associated renal anomalies are present in up to 30%.

Several classifications are used that have relevance to the clinical management.

The classification used in Europe:



* **Müllerian agenesis:**

The most common of this group of disorders is Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome which is characterized by congenital absence of the uterus and

vagina in individuals who are **46XX**.

**Clinical features**:

* primary amenorrhea at the age of 12–16 years
* normal secondary sexual characteristics as the ovaries are normally developed and functional.

The combination of normal secondary sexual characteristics and primary amenorrhea suggests an anatomical cause.

* Difficult intercourse
* Inspection of the vulva will reveal that this is normal but there is a short vagina which is blind‐ending

**Investigations:**

* Ultrasound of the abdomen will define the absence of Müllerian structures.
* karyotype will differentiate 46XX
* the renal tract should be investigated using ultrasound and intravenous urography as some 40% of patients will have renal anomalies, with 15% having an absent kidney.
* laparoscopy
* MRI

**Treatment:**

* **Psychological counselling** of patients
* **Correction of the vaginal anatomy** that could be **non‐surgical** technique OR **operative vaginoplasty**

**Non‐surgical**: the patient is instructed to use graduated glass dilators that are placed against the introitus and the blind vagina and gentle pressure is exerted in a posterior direction for approximately 10–20 min twice a day.

Gradually the dilator distends the space and then increasing sizes of dilators are used until a neovagina is created. In general it takes between 8 and 10 weeks of repeated use to achieve a satisfactory result.

The sexual satisfaction associated with this method is better than surgical correction.

**Operative vaginoplasty** procedure a cavity is created between the bladder and the bowel at the site where the natural vagina would have been and the cavity is then

lined by a split‐thickness skin graft from the thigh and applied to the space on a plastic mould

* **Reproduction**: the pregnancy is impossible, but possibility to have a baby by assessed reproductive technique (ART/IVF/surrogacy)
* **Fusion anomalies**

Fusion anomalies of various kinds are common and may present clinically either in association with pregnancy or not.

**Bicornuate uterus**: the lesser degrees of fusion defects are quite common, the cornual parts of the uterus remaining separate, giving the organ a heart‐shaped

Appearance. There is no evidence that such minor degrees of fusion defect give

rise to clinical signs or symptoms.

**Septate or Subseptate uterus**: the presence of a septum extending down the uterine cavity is likely to give rise to clinical problems. Such a may be of normal external appearance or of bicornuate outline.

**Clinically**, patients may present with recurrent spontaneous miscarriage or malpresentation of the fetus during pregnancy, infertility

In **more extreme forms** of failure of fusion **the clinical features may be less**, rather than more, marked. Two almost separate uterine cavities with one cervix are

probably less likely to be associated with abnormalities than are the lesser degrees of fusion defect.

**Uterus didelphys:** Complete duplication of the uterus and cervix is usually associated with a septate vagina.

**Rudimentary horn**: Rupture of the horn with profound bleeding may

occur as the pregnancy is implanted there and shock may be profound, dysmenorrhoea and pelvic pain if there is any obstruction to communication between the horn and the main uterine cavity or the vagina.

Surgical removal of this rudimentary horn is then indicated



**Investigations:**

* **Pelvic ultrasound**:
* **Pelvic magnetic resonance imaging** (MRI), the ‘gold standard’
* **Hysterosalpingography**.
* **Hysteroscopy**:
* **Vaginoscopy**:
* **Laparoscopy**:
* **Laboratory** investigations: *Hormonal assay*: usually show normal follicle-stimulating hormone and luteinizing hormone levels. Testosterone levels . *Chromosomal* studies

**Treatment:** is dependent on the type and extent of the exact structural abnormalities**:**

Bicornuate uterus Strassman's metroplasty can be recommended either open surgery or laparoscopically, with good results and a 90% rate of full pregnancy

Septate uterus the treatment is relatively easy. The chosen treatment is hysteroscopic metroplasty

Patients with a non-obstructed uterus didelphys should undergo a Strassman metroplasty procedure, in which the 2 uterine cavities are unified and the cervix is left intact.

Patients with an obstructed duplicate uterus should undergo a full excision of the vaginal septum in addition to a hemi hysterectomy

* **Transverse vaginal septum/imperforate hymen**

An imperforate membrane may exist at the lower end of the vagina, which is loosely referred to as imperforate hymen, although the hymen can usually be distinguished

separately.

**Clinical features**:

-These abnormalities of vertical fusion are seldom recognized clinically until puberty

when retention of menstrual flow gives rise to the clinical features of **haematocolpos**, - rarely they may present in the newborn as **hydrocolpos**.

The features of haematocolpos are:

* predominantly abdominal pain,
* primary amenorrhoea
* occasionally interference with micturition.

The patient is usually 14–15 years old but may be older, and a clear history may be given of regular cyclical lower abdominal pain for several months previously.

The patient may also present as an acute emergency if urinary obstruction develops.

**Examination:** reveals a lower abdominal swelling, and per rectum a large bulging mass in the vagina may be appreciated. Vulval inspection may reveal the imperforate

membrane, which may or may not be bluish in colour depending on its thickness. Diagnosis may be more difficult if the vagina is imperforate over some distance

in its lower part or if there is obstruction in one‐half of a septate vagina.

**Imaging:** ultrasound or MRI,

**Treatment**: may be relatively simple or rather complex.

If the membrane is thin, then simple excision of the membrane and release of the retained blood

Examination a few weeks later is desirable to ensure that no pelvic mass remains that might also suggest haematosalpinx and Haematometra

When the obstruction is more extensive Resection of the absent segment and reconstruction of the vagina may be done by an end‐to‐end anastomosis of the vagina or by a partial vaginoplasty.





* **Longitudinal vaginal septum**

A vaginal septum extending throughout all or part of a vagina is common; such a septum lies in the sagittal plain in the midline, although if one side of the vagina has been used for coitus the septum may be displaced laterally to such an extent that it may not be obvious at the time of examination.

The condition is found in association with a completely double uterus and cervix or with a single uterus and double cervix.

**Clinically:** asymptomatic, or may cause dyspareunia and difficult tampon insertion, In obstetrics this septum may have some importance if vaginal delivery is to be attempted as the narrow hemivagina may be inadequate to allow passage of the fetus and serious tears may occur

Occasionally, a double vagina may exist in which one side is not patent, and a haematometra and haematocolpos may occur in a single side

**Treatment:** surgical excision of the septum

END OF LECTURE