Atlas of Surgical Correction of Female Genital Malformation

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Editors

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1.1.1 Anatomy of the Female Reproductive System

The female reproductive system is composed of the internal and external genitalia depending on their anatomical positions along the genital tract. The internal genitalia consist of ovaries, fallopian tubes, uterus, and vagina; the external genitalia include the mons pubis, labia majora and minora, clitoris, vestibule, and perineum. The development of these organs prior to puberty is very slow; after puberty, the follicle-stimulating hormone (FSH), luteinizing hormone (LH), and other sex hormones actively promote a rapid development of both internal and external genitalia. The uterus starts to enlarge at the age of 10, and it reaches adult size at the age of 18. The endometrium undergoes cyclical changes and sheds as menstruation under the influence of ovarian hormones. The vagina becomes long and wide and changes to gray in color. The vulva becomes swollen with pubic hairs appearing and undergoes transition to the adult appearance. The labia become hypertrophied and pigmented.

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1.1.1.1 Internal Genitalia

Ovaries

Ovaries are the most important female sex glands. They are white, flat oval bodies of 4×3×1 cm in size, situated on both sides of the uterus. They produce ova and female hormones. They are small and smooth before 8 years old, but they begin to develop at the age of 8–10; thereafter they increase in a linear fashion. At menarche, the weight of an ovary is only 30 % of its adult's weight. It continues to increase in size and is mature at the age of 17–18. There are two aspects of ovarian development: (a) it produces germ cells and then ova, and (b) it produces sex hormones including estrogen and progesterone. Therefore, ovaries are both female reproductive organs and endocrine organs.

Fallopian Tubes

They are a pair of elongated hollow tubes lined with smooth muscles. The medial end communicates with the corner uteri and its lateral end is free lying next to the ovary. The outer end is funnel shaped with many fingerlike projections called tubal fimbria, stretching over the ovary. The fimbria helps to pick up the ovum into the fallopian tube where fertilization takes place when the sperm meets the ovum. The fertilized ovum then travels down into the uterine cavity, and then egg implantation takes place in the uterus.

Uterus

The uterus situates at the center of the pelvic cavity like an inverted pear. It measures about 7–8 cm long, 4–5 cm wide, and 2–3 cm thick. The uterus lay in an anteverted position suspended by its ligaments. Its lower one-third is the narrow cervix, which connects to the vagina. Its upper two-thirds is wider and is the uterine body. The top of the uterine body is the fundus with uterine corners on both sides and connects with a fallopian tube on each side. The cervical canal is a narrow tube-like, leading to the uterine cavity. The uterus is the breeding ground of the fetus, where pregnancy takes place. The uterus composes of three layers of tissues: (1) The inner endometrial layer is rich in glands and blood supply; the endometrium continues to change following each menstrual cycle and the woman's age. During menstruation, the shedding of the endometrium is a major component of the menses; (2) the middle layer is a very thick muscle layer. It can produce strong contractions during labor and at orgasms. It is resilient and can stretch sufficiently to accommodate a mature fetus; (3) the outermost layer is a serosal layer which is a part of the peritoneum.

Vagina

It is a soft elastic hollow tube which tilts backward. It is the female organ of sexual intercourse. It also serves as the passage of menstrual blood and the birth channel. It has a strong stretching property. With advancing age, the vaginal wall gets thinner with reducing vaginal wrinkles and weakened elasticity. Vaginal nerve endings mainly distribute in the outer 1/3 of the vagina, with no nerve endings at the upper 2/3. Therefore, the sex-sensitive area is located at the outer ½ of the vagina.

1.1.1.2 External Genitalia

Female external genitalia consist of the mons pubis, labia, and vaginal opening. All together, they are labeled as the vulva.

Mons Pubis

It is the swelling in front of the pubic symphysis, with the labia majora on adjacent sides. There are pubic hairs on the mons pubis, mostly trapezoid, inverted triangle, or rectangle in distribution. It regulates the local temperature and buffers the body impact of collision. The subcutaneous fat tissue underneath the mons pubis possesses shock-cushioning effect.

Clitoris

The clitoris is homologous to the male penis, both evolved from the same embryonic tissue. It is the only organ without reproductive function in the female genitalia, but it is related to sexual arousal and sexual function in humans. The clitoris is rich in nerve endings, which are very sensitive to touch, and it is the most important sex-sensitive zone.

Labia

There are two pairs of female labia – the labia majora and labia minora. The labia majora are the fat pads on both sides of the vaginal opening, with its skin covering with pubic hairs. Both the labia majora and minora have thin mucosal layers with no pubic hairs on its inner side. The sizes of labia and their thickness vary widely which are not directly related to sexual function. However, the labia are rich in nerve fibers and can have an important role in sexual stimulation and sexual arousal.

Vaginal Vestibule

It is a diamond-shaped area between the two labia minora. Its anterior end has the urethra where urine can pass out; its posterior has the vaginal opening with vestibular bulbs on its sides.

Bartholin Gland

Bartholin glands are located in the lower part of the labia minora as a small pair of glands, with its glandular opening between the labia minora and the hymen. If infected with inflammation, they can be significantly enlarged.

Hymen

Covering the vaginal opening is a layer of thin membrane, called "hymen." The hymen has a central hole, which varies in sizes depending on individuals. Some are too small in size, which will not allow even a finger to pass through, but others may accommodate two fingers through it. The hymen thickness is generally about 2 mm. But individuals may have very thin hymen, which may rupture during strenuous exercise or inadvertent collision to the vulva. It usually tears open at the time of first sexual intercourse and is accompanied by a small amount of bleeding.

1.1.2 The Development of the Female Reproductive System

The genetic sex of an embryo is determined by the sperm type (23X or 23Y) which fertilizes the ovum, but before 6 weeks of life, both male and female embryos have the same undifferentiated gonads, known as the undifferentiated genital phase. At the 7th week, gonads begin to have gender-related morphological changes. In the 8th to 9th weeks, internal genital differentiation begins. The external genital differentiation can only be identified at the 12th week. Therefore, the reproductive system including the gonads, reproductive tract, and external genitalia has an undifferentiated and differentiated phases of development.

1.1.2.1 The Undifferentiated Sex Phase

The Formation of the Undifferentiated Gonads

When the embryo is at 3–4 weeks' gestation, there are many reproductive cells which are larger and more round than the somatic cells lying at the posterior wall of the yolk sac near the allantoic endoderm. These are the primordial germ cells. When the embryo is at the 4th week, the sides of the embryo body start to have fold formation;

the ventral mesoderm gradually moves toward the body separated from intermediate body, forming into the left and right cord-like structure, known as nephrogenic cords. At the end of the 4th week, the volume of the nephrogenic cords continues to increase, and from the posterior wall of the embryo, it bulges to form a body cavity. At this time, at the back of the body cavity, the epithelial hyperplasia of each side of the body forms two longitudinal ridges, known as the urogenital ridges, which are the origins of kidneys, gonads, and primitive reproductive tract. In its further development, a central longitudinal groove forms in this urogenital ridge, dividing it into inner and outer parts. The outer part is longer and thicker and known as the mesonephric ridge; the inner part is shorter and thinner known as the genital ridge. When the embryo is at the 5th week, the genital ridge is covered with a layer of columnar epithelium, also called the germinal epithelium. When the embryo is at the 6th week, the germinal epithelium will hollow down and grow rapidly forming multiple cords with vertical extensions stretching between the gonadal tissues. It is also known as primary sex cord. In a 6-week embryo, primordial germ cells along the hindgut mesentery move to the genital stroma at the 10th thoracic vertebral level. The migration takes 1 week to complete. Some of these sex cord cells will surround each primordial germ cell. The larger primordial germ cells, the smaller primitive sex cord cells and the surrounding stromal tissues will form the undifferentiated gonadal tissue. At this time, whether it is a testis or an ovary cannot be distinguished. Thus, the gonads mainly come from the genital ridge of the coelomic cavity epithelium. But the epithelium, the underneath mesenchymal tissue, and the primordial germ cells are from three different origins.

The Formation of the Primitive Reproductive Tract

The development of the primitive reproductive tract is slightly later than the undifferentiated gonads. At a 6-week embryo, both male and female embryos consist of mesonephric ducts and paramesonephric ducts which are two different reproductive tracts. Both develop from the mesonephric ridge lateral to the genital ridge. One is called the mesonephric duct (also known as Wolffian duct), which originates from the mesonephros of the pronephros and gradually moves downward and ends into the primitive cloaca. This is the primitive male reproductive tract. The other is the paramesonephric duct, also called the Müllerian duct. This is the female primitive reproductive tract which forms at the time of mesonephric duct formation, at the inner aspect of mesonephric duct. It is formed by invagination of the coelomic epithelium. The upper part of the duct is located at the outer aspect of the mesonephric duct, lying parallel to each other. The middle part of the duct turns to the inner aspect and crosses the back of the mesonephric duct and lies in the inner aspect of it. In the lower end, the right and left paramesonephric ducts merge at the midline. The upper part of the paramesonephric duct has a funnel-shaped opening to the coelomic cavity forming the fimbrial end of the fallopian tube. The lower ends are blind ends merging into the sides of the back wall of the urogenital sinus. At the sinus, it forms a protrusion, called sinus tubercle, also known as the Müllerian tubercle or Müllerian nodules.

Embryonic Formation of the External Genitalia

When the embryo is at 9 weeks old, its external genitalia does not show any sex differentiation. At about the 5th week, both sides of the primordial urogenital sinus organize into folds and merge at the cephalic end forming a genital tubercle. A urorectal septum separates the cloacal opening from the primordial urogenital sinus in front and the anus at the back. Lateral to the urogenital fold, a pair of large uplift develops, forming the labia or scrotum. Urogenital fold forms a depression for a urethral groove covered by a urogenital membrane. At the 7th week, the urogenital membrane ruptures.

1.1.2.2 The Differentiated Sex Phase

Differentiation and Descending of the Gonad

The undifferentiated gonad has the potential to differentiate into the testes or ovaries. The sex differentiation depends on whether there is any testis-determining factor – TDF in the Y chromosome. At current knowledge, the Y chromosome sex-determining region Y gene – SRY – is the best candidate gene for TDF. It is situated at the short arm of the Y chromosome near the centromere in the IAIA District (Yp11.32). It contains an exon, is of a non-intron structure, and harbors the histocompatibility Y antigen – H-Y antigen.

If the membranes of body cells and primordial germ cells do not contain the H-Y antigen, the undifferentiated gonad will develop into an ovary. When the embryo is 10 weeks old, the embryonic sex cord will grow deeper, forming an incomplete ovarian network. Later, these embryonic sex cord and ovarian network will degenerate and be replaced by blood vessels and stroma forming the ovarian medulla. Thereafter, the genital surface epithelium (also known as primitive cortical cells) continues to grow thicker. It also penetrates into the deep layer, forming new cell cords, known as secondary sex cord or cortical cord. They are shorter and scatter in the cortex. In a 16th-week human embryo, cortical cord will break into many isolated cell groups that are primitive follicles, also known as primordial follicles. At this time, the ovaries are formed. Each primordial follicle has a primitive germ cell which will differentiate into a cell called oogonium.

The oogonium is surrounded by a layer of cortical cells which differentiate into small and flat follicular cells, also known as granular cells. Between the follicles mesenchymal cells differentiate into ovarian stroma. In the embryonic stage, the oogonium can split, divide, and proliferate into oocytes. There are up to six million oogonia in both ovaries. After the embryo is at the 20th week, these oogonia will no longer divide and a large number of them undergo degradation. Only some grow up and differentiate into primary oocytes. At birth, all oogonia within the ovaries disappeared, leaving about 70–200 million primary oocytes. All cells enter the first meiosis and stop dividing at their early stage. Not until after puberty, they complete their meiotic division before ovulation. Primary oocyte cannot self-replicate. After birth the primary oocytes within the ovary no longer grow, instead many of them gradually degenerate and undergo atresia. At adolescence, there are about four million remaining oocytes. After the embryo reaches 16 weeks, the ovarian cortex and medulla continue to develop. The cortical surface has a layer of connective tissue called the tunica albuginea. Outside the albuginea, it is covered by a layer of cuboidal epithelium arising from the body cavity called the ectodermal epithelia.

The ovary is initially located in the upper part of the posterior coelomic wall between the end of gonadal cord to the labia majora along a cord-like structure called ovarian gubernaculum. With the proliferation and differentiation of the gonadal cord, the gubernaculum gradually rises to the coelomic cavity and position the ovaries in the abdominal cavity. As the embryo gradually grows up, the ligament continues to shorten. The ovaries come down to a pelvic location slightly below the pelvic rim at the 12th week of gestation.

The Evolution of the Internal Genitalia

If the undifferentiated gonads differentiate into ovaries, in the absence of testes to produce androgens and no influence from any Müllerian inhibiting factor (MIF), the mesonephric ducts (Wolffian) will degenerate. The paramesonephric ducts differentiate and develop into the internal female genitalia. It is noteworthy that about 1/4 of the women may have the residual remnant of the mesonephric ducts or tubules. For example, they form the epoophoron and paroophoron in the mesovarium and the Gartner's duct cyst alongside the uterus and vagina.

But in the process of paramesonephric duct differentiation into the internal female genitalia, the mesonephric ducts and ovaries played a leading induction role. The mesonephric ducts induce the fusion and resorption of the bilateral Müllerian ducts. The ovarian tissue attached to the Müllerian duct is composed of muscle fibers from non-Müllerian and mesonephric duct origin and promotes the integration and development of the uterus.

Uterus and Fallopian Tubes

When the fetus is at about the 9th week of gestation, the upper part of the paramesonephric ducts becomes the fallopian tubes. The middle part to the lower part merges at the midline to form the uterus, the cervix, and the vaginal dome. At the beginning of the merger, there is a septum to divide into two ductal cavities. Toward the end of 12 weeks, the septum disappeared into a single cavity to form the uterus and the vaginal tube. The endometrial cavity is lined with columnar epithelium, and in the part of the uterus formed by the paramesonephric duct, the mesenchymal tissue surrounding it will proliferate actively, and the uterine wall will become thickened. The tissue at the uterine cervix will form the vaginal dome. At the 16th week, the muscular and serosal layers of the uterus will form. At the 24th week, glandular buds will form in the endometrial cavity. In the last 12 weeks, by the influence of the placental hormones, there is a rapid development of the uterus, and the endometrium will thicken and be congested with blood. At birth, the development of endometrial glands has been more mature and complete. At birth, the uterus surface is flat. The ratio of the uterine body and uterine cervix is about 1:2, until after puberty, the ratio starts to change. The uterus will further develop and mature.

The Vagina

The vagina comes from two origins. The upper 3/4 to 4/5 of the vagina is from the paramesonephric duct and the lower 1/5 to 1/4 from the urogenital sinus. At the 9th week of gestation, the caudal end of the paramesonephric duct and the back of urogenital sinus will form the paramesonephric duct tubercle (Müllerian tubercle), which is also known as the sinus tubercle. The urogenital sinus epithelial cells and cells at the caudal ends of the paramesonephric duct proliferate together and form a solid sinovaginal bulk and further develop into a vaginal plate. The vaginal plate is initially a solid tubular structure called sinovaginal bulk. It gradually expands and increases the distance between the uterus and the urogenital sinus.

From the 11th week onward, the cells in the central part of the vaginal plate gradually degenerate, forming a cavity. At the 20th week, a vagina is formed, which links the uterus internally and externally with the urogenital sinus, separated by a hymen.

In recent years, many embryologists believe that the whole vagina is from the sinovaginal bulk. The belief is that when the paramesonephric duct reaches the urogenital sinus surface and becomes surrounded by the sinovaginal bulk, the sinovaginal bulk will grow cranially and develop into the vaginal plate, as the prototype of the future vagina. After that, the vaginal plate cavitates from a top-down direction to make the vagina a top-down funnel-shaped cavity. The top forms a vaginal dome, and the bottom separates from the urogenital sinus by a thin tissue. The central part of this thin tissue will be absorbed, and it forms a hole in the vaginal hymen. Although the paramesonephric ducts do not involve in the formation of the vagina, it plays an inducing role in the evolutionary development of the sinovaginal bulk. One side of the paramesonephric duct will induce the vagina formation from the ipsilateral side. However, this belief requires future validation. Another theory is that the mesonephric duct degenerates from top downward; its end at the level of the external cervical opening enlarges to form the sinovaginal bulk and integrates with Müllerian tubercle of the paramesonephric duct. Their further proliferation will form the vaginal plate.

The Development of the External Genitalia

At the 7th to 8th week of fetal development, the external genitalia start to differentiate into male or female. When the gonad is an ovary, the body produces no testosterone. The genital tubercle gradually enlarges slowly and forms the clitoris. The urogenital folds on both sides will not merge and form the labia minora. The right and left labia fuse with the scrotal bulge in the front of the clitoris, forming the mons pubis. The posterior labia fuse together and form the posterior commissure. The rest of the non-fused labia become the labia majora. At this time, the urethral groove expands with the lower end of the urogenital sinus to form the front of the vagina. When the fetus is at the 12th week, the female external genitalia begin to take shape, and they gradually further developed.

1.2 Abnormal Development of Female Reproductive Organs

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The development and differentiation processes of the female reproductive organs are influenced by both endogenous factors (nondisjunction of the germ cell chromosomes, chimera, karyotype abnormalities, etc.) and exogenous factors (use of hormone, drugs, etc.). The differentiation of the primitive gonad, its development and fusions within the reproductive system, and cavity development and formation of the external genitalia may be affected by these factors resulting in a variety of developmental anomalies.

Abnormal development of the female reproductive organs includes the developmental and morphological anomalies in the fallopian tubes, uterus, vagina, and vulva. These anomalies can be associated with abnormal ovaries, kidney, or other organs. Most of the female genital tract anomalies arise from the developmental anomalies of the paramesonephric ducts (Müllerian duct); however, these Müllerian anomalies originate from the abnormal development of the Gartner's duct. Genital tract anomalies have different clinical manifestations. Some do not present with any clinical symptoms, others have different symptoms at different times and different ages, and the impact on fertility is also widely variable. The management of these genital anomalies varies widely from observation to surgery. Therefore, a correct diagnosis within a clear classification of these congenital anomalies is very important.

1.2.1 The Classification of Female Reproductive Tract Anomalies

There are many classifications of female reproductive tract anomalies. The early classification began in 1842; it is based on the embryology and Müllerian duct development, since then there are many other classifications. Before 1950, all classifications are based on embryonic developments: the Müllerian duct fusion and its abnormal developments. After 1950, the classifications take into account many other factors. This chapter describes three types of classifications for reproductive tract anomalies.

1.2.1.1 American Fertility Society (AFS) Classification of Reproductive Tract Anomalies

American Fertility Society (AFS) developed this classification in 1988 [1]. The classification is as follows [6]: (1) Anomaly caused by developmental anomaly of the Müllerian duct including the agenesis of the uterus and vagina and is a defect characterized by no reproductive potential, e.g., in the case of congenital absence of the vagina [7]. (2) Anomaly caused by the developmental anomaly of the genitourinary sinus: The urogenital sinus was not involved in the formation of the lower vagina; it is mainly responsible for the different degrees of vaginal atresia [8]. (3) Anomaly caused by abnormal fusion of the Müllerian ducts. The anomalies are divided into vertical fusion and lateral fusion anomalies. Vertical fusion anomaly presents as transverse vaginal septum and lateral fusion anomaly as longitudinal vaginal septum and oblique vaginal septum syndrome.

AFS classification is mainly based on Müllerian anomalies and their effects on fertility; it includes seven categories (Fig. 1.1): (1) Müllerian agenesis (absent uterus) or hypoplasias, (2) unicornuate uterus (a one-sided uterus), (3) uterus didelphys (double uterus), (4) bicornuate uterus (uterus with two horns), (5) septated uterus (uterine septum or partition), (6) arcuate uterus, and(7) DES uterus as a result of fetal exposure to diethylstilbestrol. This classification is simple and clear; therefore, it has been widely adopted in the past 20 years. This classification defines different levels of uterine anomalies, and its prognosis has a good clinical correlation with the pregnancy outcome. However, this classification has its limitations: Many complex reproductive tract anomalies are not covered. Category 1 includes all patients with dysplasia or congenital absence of the vagina, cervix, uterus, and/or gonads as a single class which would be too vague and generalized.

Figure 1.1 [2]

A type: bilateral developmental anomalies. (1) Vaginal agenesis, complete; (2) vaginal agenesis, partial (upper or lower); (3) cervical aplasia; (4) cervical hypoplasia; (5) tubal aplasia; (6) uterine aplasia; (7) uterine hypoplasia (with or without uterine cavity); (8) combined dysplasia

B type: unilateral developmental anomalies. (1) Unicornuate, no horn; (2) unicornuate, non-fused, non-cavitary horn; (3) unicornuate, fused, non-cavitary horn; (4) unicornuate, cavitary, non-fused horn; (5) unicornuate, cavitary, fused, noncommunicating horn; (6) unicornuate, cavitary, fused, communicating horn.

C type: fusion anomalies. (1) Vaginal septum; (2) arcuate uterus; (3) septate uterus, partial; (4) septate uterus, complete to external os of the cervix; (5) septate uterus, complete, up to internal os of the cervix; (6) complete septate, vagina, and uterus; (7) bicornuate uterus, complete to internal os of cervix; (8) bicornuate uterus, partial; (9) uterus didelphys bicollis; (10) uterus didelphys with the vaginal septum; (11) uterus didelphys with the vaginal septum, with unilateral vaginal obstruction; (12) uterus didelphys with the vaginal septum with bilateral obstructed vagina

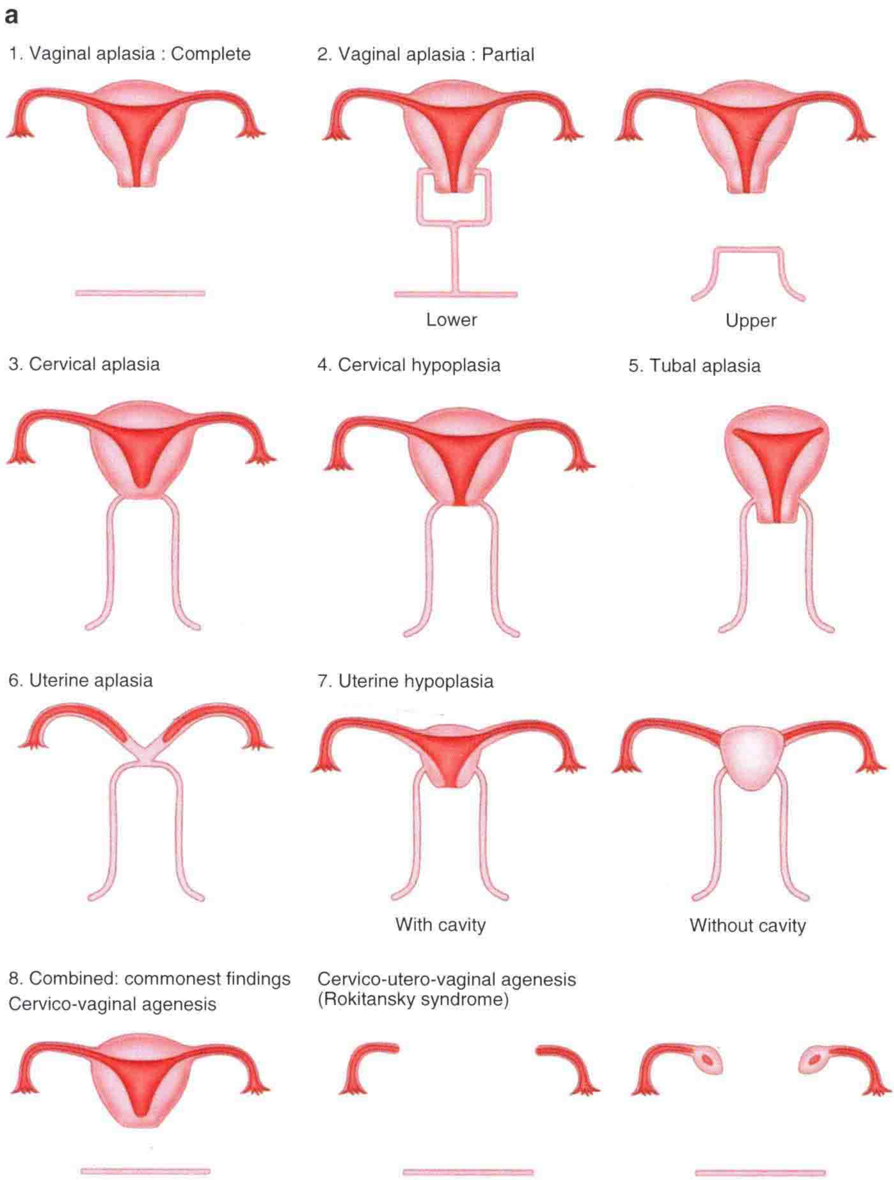

Fig. 1.1 AFS classification based on Müllerian anomalies