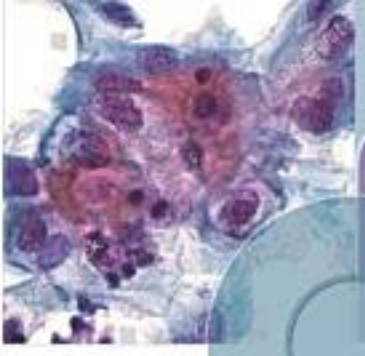

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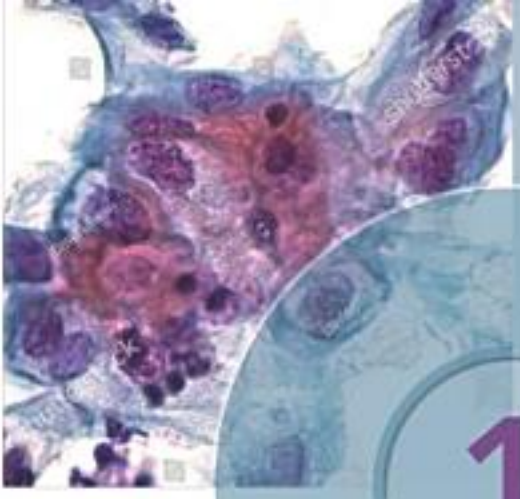

1 Development and anatomy of the female sexual organs and pelvis

YING CHEONG

Learning Objectives

- Understand that sexual differentiation and development begin in early embryonic life.
- Understand the embryonic development and the anatomy of the perineum, vagina, cervix, uterus, ovaries, bladder and ureters.
- Describe the blood supply and lymphatics of the perineum and pelvis.
- Understand the innervation of the perineum and pelvis.
- Understand the vulnerability of certain structures in gynaecological surgery.
- Describe the structural anomalies resulting from Müllerian tract disorders.

SEXUAL DIFFERENTIATION OF THE FETUS AND DEVELOPMENT OF SEXUAL ORGANS

There are four main phases of genital development: the indifferent gonadal phase at 4–6 weeks' gestation, the gonadal differentiation phase at about 7 weeks' gestation, ductal differentiation at 9–11 weeks and external genitalia differentiation at 10–12 weeks.

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 (Figure 1.1). 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 its fate. The development of either the testis or the ovary is an active gene-directed process. In the male, the activity of the sex-determining region of the Y chromosome (*SRY*) gene 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*; however, in the last 10 years, ovarian-determining genes have also been found that actively lead to the development of a female gonad.

At ductal differentiation phase, 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 female or male, respectively, internal and external genitalia.

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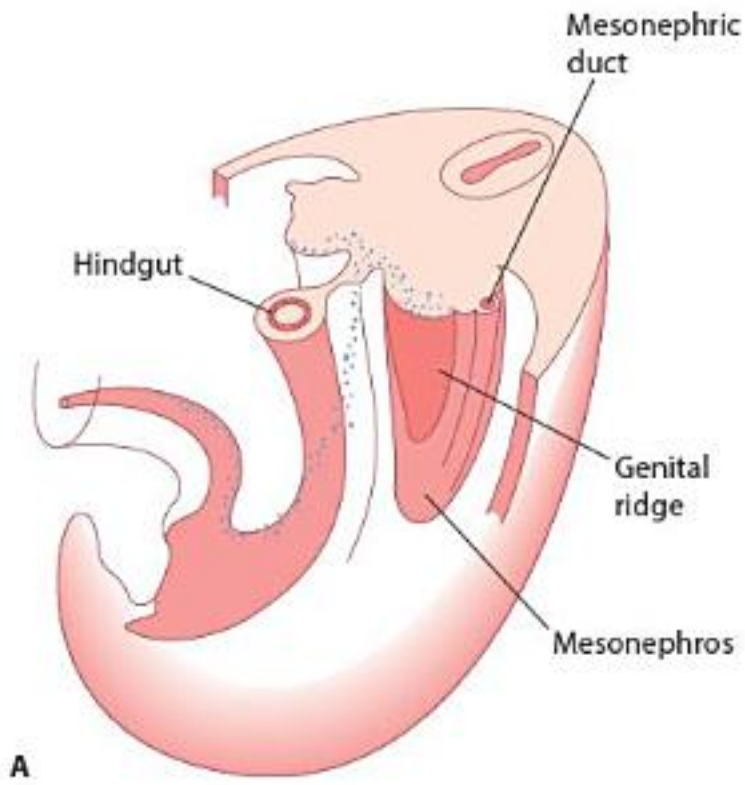

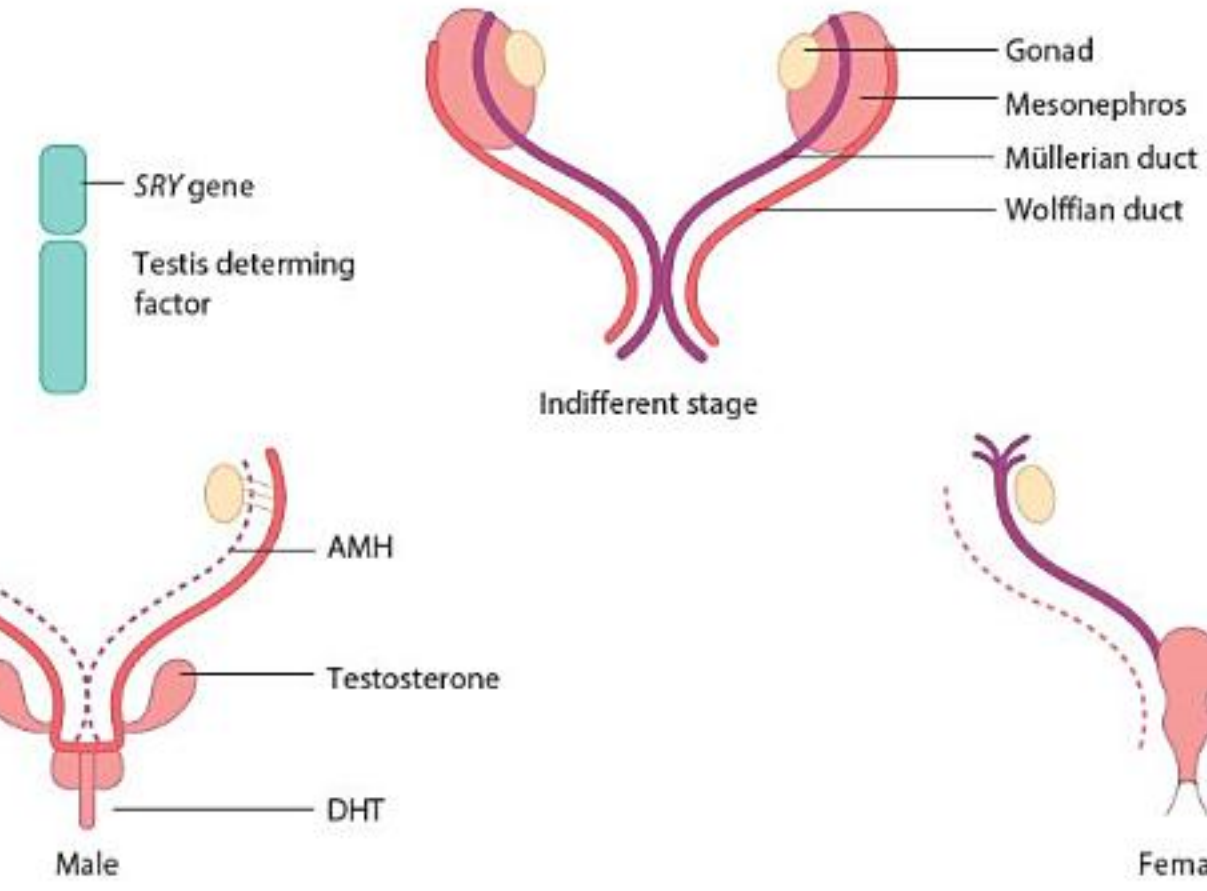

Figure 1.1 (**A**) Cross-section diagram of the posterior abdominal wall showing the genital ridge. (**B**) Diagrammatic representation of the embryological pathways of male and female development. (AMH, anti-Müllerian hormone; DHT, dihydrotestosterone; SRY, sex-determining region of the Y chromosome.)

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 addition, 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 one to two million remain. Atresia continues throughout life and, by menarche, only 300,000–400,000 are present and, by the menopause, there are 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 derives from these paired ducts. At 9–11 weeks, 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 (formation of septum). The midline fusion of these structures produces the uterus, cervix and upper two-thirds of the vagina, and the unfused caudal segments form the fallopian tubes, as shown in Figure 1.2.

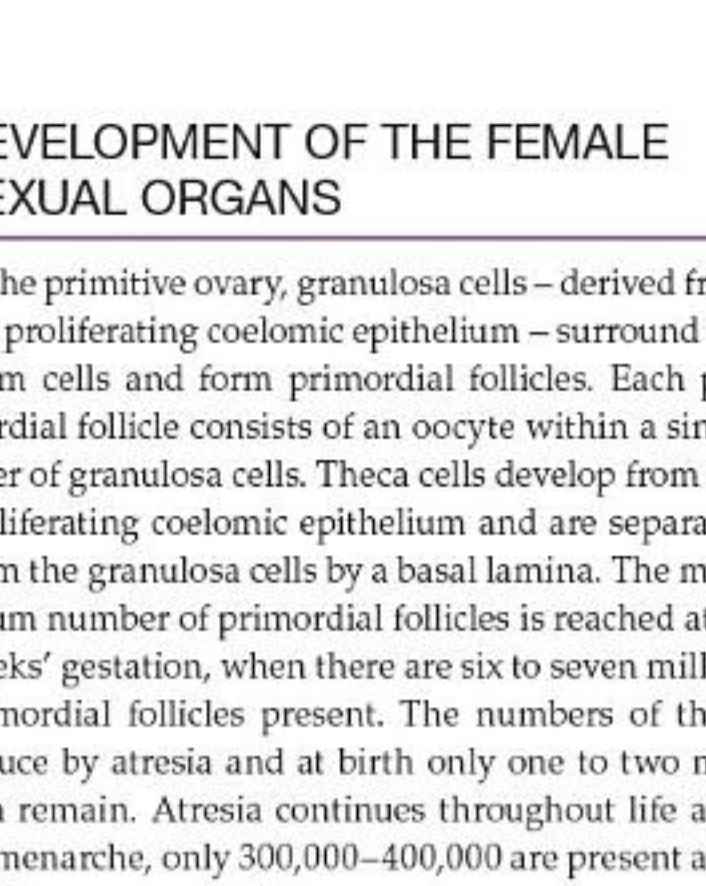

Figure 1.2 Caudal parts of the paramesonephric ducts (top) fuse to form the uterus and fallopian tubes.

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. At 5 months, Müllerian organogenesis is complete with uterine septal resorption/canalization.

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 12th embryonic week.

FEMALE ANATOMY

EXTERNAL GENITALIA

The external genitalia are commonly called the vulva and include the mons pubis, the labia majora and minora, the vaginal vestibule, the clitoris and

KEY LEARNING POINTS

- The primitive gonad is first evident at 5 weeks of embryonic life and forms on the medial aspect of the mesonephric ridge.
- The undifferentiated gonad has the potential to become either a testis or an ovary.
- The paramesonephric duct, which later forms the Müllerian system, is the precursor of female genital development.
- The lower end of the Müllerian ducts fuse in the midline to form the uterus and upper vagina.
- Most of the upper vagina is of Müllerian origin, while the lower vagina forms from the sinovaginal bulbs.
- Primordial follicles contain an oocyte arrested in prophase surrounded by granulosa cells separated by a basement membrane from Theca cells.
- The maximum number of primordial follicles is reached at 20 weeks' gestation. These reduce by atresia throughout childhood and adult life.

the greater vestibular glands (Figure 1.3). The mons pubis is a fibro-fatty pad covered by hair-bearing skin that covers the bony pubic ramus.

The labia majora are two folds of skin with underlying adipose tissue lying either side of the vaginal opening. They contain sebaceous and sweat glands and a few specialized apocrine glands. In the deepest part of each labium is a core of fatty tissue continuous with that of the inguinal canal and the fibres of the round ligament, which terminate here.

The labia minora are two thin folds of skin that lie between the labia majora. These vary in size and may protrude beyond the labia majora where they are visible, but may also be concealed by the labia majora. Anteriorly, they divide in two to form the prepuce and frenulum of the clitoris (clitoral hood). Posteriorly, they divide to form a fold of skin called the fourchette at the back of the vaginal introitus. They contain sebaceous glands, but have no adipose tissue. They are not well developed before puberty and they atrophy after the menopause. Both the labia minora and the labia majora become engorged during sexual arousal.

The clitoris is an erectile structure measuring approximately 0.5–3.5 cm in length. The body of the clitoris is the main part of the visible clitoris and is made up of paired columns of erectile tissue and vascular tissue called the corpora cavernosa. These become the crura at the bottom of the clitoris and run deeper and laterally. The vestibule is the cleft between the labia minora. It contains openings of the urethra, the Bartholin's glands and the vagina. The vagina is surrounded by two bulbs of erectile and vascular tissue that are extensive and almost completely cover the distal vaginal wall. These have traditionally been named the bulb of the vaginal vestibule, although recent work on both dissection and magnetic resonance imaging (MRI) suggests that they may be part of the clitoris and should be

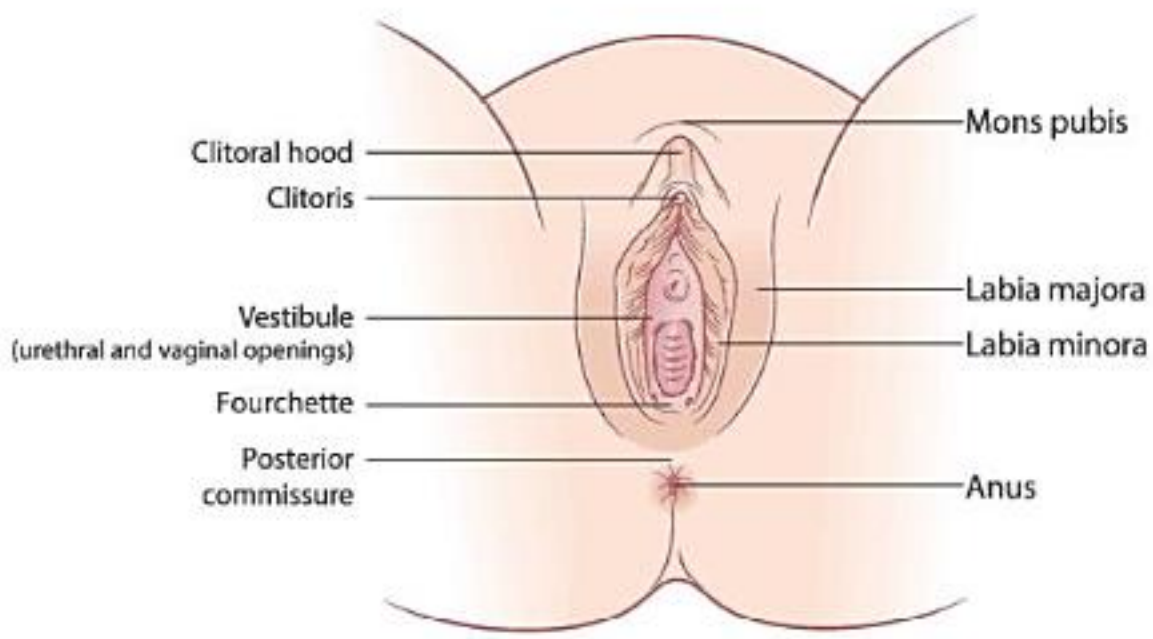

Figure 1.3 Anatomy of the external genitalia.

renamed 'clitoral bulbs'. Their function is unknown but they probably add support to the distal vaginal wall to enhance its rigidity during penetration.

The Bartholin's glands are bilateral and about the size of a pea. They open via a 2 cm duct into the vestibule below the hymen and contribute to lubrication during intercourse.

The hymen is a thin covering of mucous membrane across the entrance to the vagina. It is usually perforated, which allows menstruation. The hymen is ruptured during intercourse and any remaining tags are called carunculae myrtiformes.

FEMALE INTERNAL REPRODUCTIVE ORGANS

VAGINA

The vagina is a fibromuscular canal lined with stratified squamous epithelium that leads from the uterus to the vulva. It is longer in the posterior wall (approximately 9 cm) than in the anterior wall (approximately 7 cm). The vaginal walls are normally in apposition, except at the vault where they are separated by the cervix. The vault of the vagina is divided into four fornices: posterior, anterior and two lateral (Figure 1.4).

The mid-vagina is a transverse slit while the lower vagina is an H-shape in transverse section. The vaginal walls are lined with transverse folds. The vagina has no glands and is kept moist by secretions from the uterine and cervical glands and by transudation from its epithelial lining. The epithelium is thick and rich in glycogen, which increases in the post-ovulatory phase of the cycle. However, before puberty and after the menopause, the vagina is devoid of glycogen due to the lack of oestrogen. Doderlein's bacillus is a normal commensal of the vaginal flora and breaks down glycogen to form lactic acid, producing a pH of around 4.5. This plays a protective role for the vagina in decreasing the growth of pathogenic bacteria.

The upper posterior wall forms the anterior peritoneal reflection of the pouch of Douglas. The

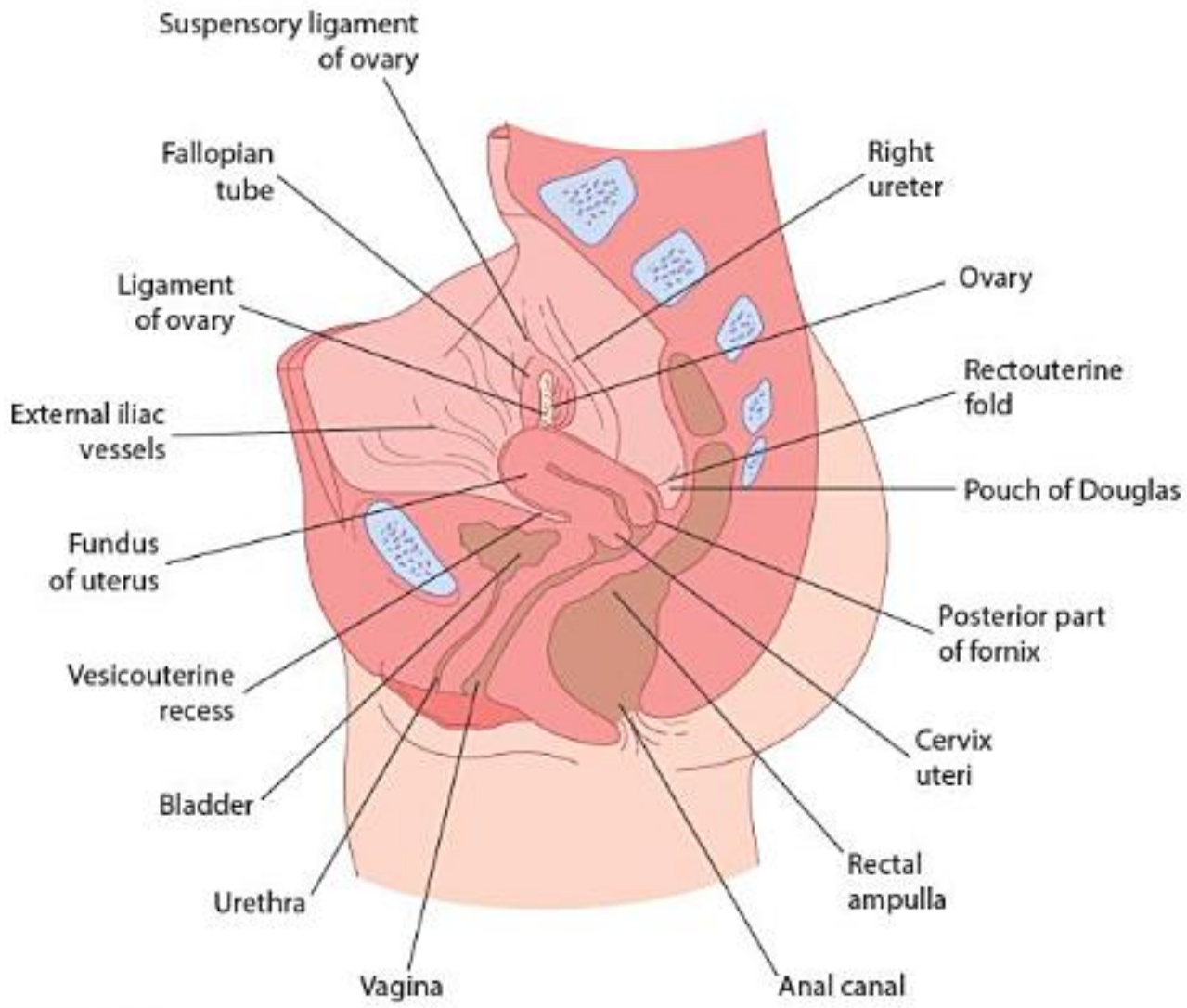

Figure 1.4 Sagittal section of the female pelvis.

middle third is separated from the rectum by the pelvic fascia and the lower third abuts the perineal body. Anteriorly, the vagina is in direct contact with the base of the bladder, while the urethra runs down the lower half in the midline to open into the vestibule. Its muscles fuse with the anterior vagina wall. Laterally, at the fornices, the vagina is related to the cardinal ligaments. Below this are the levator ani muscles and the ischiorectal fossae. The cardinal ligaments and the uterosacral ligaments, which form posteriorly from the parametrium, support the upper part of the vagina.

At birth, the vagina is under the influence of maternal oestrogens, so the epithelium is well developed. After a couple of weeks, the effects of the oestrogen disappear, and the pH rises to 7 and the epithelium atrophies. At puberty, the reverse occurs and, finally, at the menopause, the vagina tends to shrink and the epithelium atrophies once again.

UTERUS

The uterus is shaped like an inverted pear tapering inferiorly to the cervix and in its non-pregnant state is situated entirely within the pelvis. It is hollow and has thick, muscular walls. Its maximum external dimensions are approximately 7.5 cm long, 5 cm wide and 3 cm thick. An adult uterus weighs approximately 70 g. In the upper part, the uterus is termed the body or corpus. The area of insertion of each fallopian tube is termed the cornu, and that part of the body above the cornu is called the fundus. The uterus tapers to a small constricted area (the isthmus) and below this is the cervix, which projects obliquely into the vagina. The longitudinal axis of the uterus is approximately at right angles to the vagina and normally tilts forwards. This is called anteversion. In addition, the long axis of the cervix is rarely the same as the long axis of the uterus. The uterus is also usually flexed forwards on itself at the isthmus, called antiflexion. However, in around 20% of cases, the uterus is tilted backwards, or retroverted and retroflexed. This has no pathological significance, although retroversion that is fixed and immobile may be associated with endometriosis. This has relevance in gynaecological surgery and is referred to again in **Chapter 2**.

The cavity of the uterus is the shape of an inverted triangle and when sectioned coronally the fallopian tubes open at lateral angles. The constriction at the isthmus where the corpus joins the cervix is the anatomical os. Seen microscopically, the site of the histological internal os is where the mucous membrane of the isthmus becomes that of the cervix.

The uterus consists of three layers: the outer serous layer (peritoneum), the middle muscular layer (myometrium) and the inner mucous layer (endometrium). The peritoneum covers the body of the uterus and posteriorly it covers the supravaginal part of the cervix. The peritoneum is intimately attached to a subserous fibrous layer, except laterally where it spreads out to form the leaves of the broad ligament.

The muscular myometrium forms the main bulk of the uterus and is made up of interlacing smooth muscle fibres intermingling with areolar tissue, blood vessels, nerves and lymphatics. Externally, the muscle fibres are mostly longitudinal, but the thicker intermediate layer has interlacing longitudinal, oblique and transverse fibres. Internally, they are mainly longitudinal and circular.

The inner endometrial layer has tubular glands that dip into the myometrium. The endometrial layer is covered by a single layer of columnar epithelium. The luminal and glandular epithelia are ciliated. The mechanistic function of the cilia is largely unknown, although recent studies have indicated a role in implantation and reproduction. The endometrium undergoes cyclical changes during menstruation, as described in **Chapter 3**, and varies in thickness.

CERVIX

The cervix is narrower than the body of the uterus and is approximately 2.5 cm in length. Lateral to the cervix lies cellular connective tissue called the parametrium. The ureter runs about 1 cm laterally to the supravaginal cervix within the parametrium. The posterior aspect of the cervix is covered by the peritoneum of the pouch of Douglas.

The upper part of the cervix mostly consists of involuntary muscle, whereas the lower part is mainly fibrous connective tissue. The mucous membrane of the cervical canal (endocervix) has anterior and posterior columns from which folds radiate out – these are the arbour vitae. The mucous membrane has numerous deep glandular follicles that secrete clear alkaline mucus, the main component of physiological

vaginal discharge. The epithelium of the endocervix is columnar and is also ciliated in its upper two-thirds. This changes to stratified squamous epithelium around the region of the external os and the junction of these two types of epithelium is called the squamocolumnar junction.

Age changes to anatomy

The disappearance of maternal oestrogens from the circulation after birth causes the uterus to decrease in length by around one-third and in weight by around one-half. The cervix is then twice the length of the uterus. During childhood, the uterus grows slowly in length, in parallel with height and age. The average longitudinal diameter ranges from 2.5 cm at the age of 2 years to 3.5 cm at 10 years. After the onset of puberty, the anteroposterior and transverse diameters of the uterus start to increase, leading to a sharper rise in the volume of the uterus. The increase in uterine volume continues well after menarche, and the uterus reaches its adult size and configuration by the late teenage years. After the menopause, the uterus atrophies, the mucosa becomes very thin, the glands almost disappear and the wall becomes relatively less muscular.

FALLOPIAN TUBES

The fallopian tube extends outwards from the uterine cornu to end near the ovary. At the abdominal ostium, the tube opens into the peritoneal cavity, which is therefore in communication with the exterior of the body via the uterus and the vagina. This is essential to allow the sperm and egg to meet. The fallopian tubes convey the ovum from the ovary towards the uterus and promote oxygenation and nutrition for the sperm, ovum and zygote should fertilization occur.

The fallopian tube runs in the upper margin of the broad ligament, known as the mesosalpinx, which encloses the tube so that it is completely covered with peritoneum except for a narrow strip along this inferior aspect. Each tube is about 10 cm long and is described in four parts:

1. the interstitial portion
2. the isthmus
3. the ampulla
4. the infundibulum or fimbrial portion

The interstitial portion lies within the wall of the uterus, while the isthmus is the narrow portion adjoining the uterus. This passes into the widest and longest portion, the ampulla. This, in turn, terminates in the extremity known as the infundibulum. The opening of the tube into the peritoneal cavity is surrounded by finger-like processes, known as fimbria, into which the muscle coat does not extend. The inner surfaces of the fimbriae are covered by ciliated epithelium that is similar to the lining of the fallopian tube itself. One of these fimbria is longer than the others and extends to, and partially embraces, the ovary. The muscular fibres of the wall of the tube are arranged in an inner circular layer and an outer longitudinal layer.

The tubal epithelium forms a number of branched folds or plicae that run longitudinally; the lumen of the ampulla is almost filled with these folds. The folds have a cellular stroma, but at their bases the epithelium is separated from the muscle by only a very scanty amount of stroma. There is no submucosa and there are no glands. The epithelium of the fallopian tubes contains two functioning cell types: the ciliated cells, which act to produce a constant current of fluid in the direction of the uterus, and the secretory cells, which contribute to the volume of tubal fluid. Changes occur under the influence of the menstrual cycle, but there is no cell shedding during menstruation.

OVARIES

The size and appearance of the ovaries depend on both age and stage of the menstrual cycle. In a child, the ovaries are small structures approximately 1.5 cm long; however, they increase to adult size in puberty due to proliferation of stromal cells and commencing maturation of the ovarian follicles. In the young adult, they are almond-shaped and measure approximately 3 cm long, 1.5 cm wide and 1 cm thick. After the menopause, no active follicles are present and the ovary becomes smaller with a wrinkled surface. The ovary is the only intra-abdominal structure not to be covered by peritoneum. Each ovary is attached to the cornu of the uterus by the ovarian ligament and at the hilum to the broad ligament by the mesovarium, which contains its supply of nerves and blood vessels. The ovary has a dual blood supply, namely from