Reproductive Tract Structure and Function

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Relevant Terms

Adrenarche—initiation of increased adrenal androgens
Ampulla—wider end of the fallopian tube
Atresia—degeneration and absorption of immature follicles
Bartholin glands—pea sized bilateral vulvar glands that secrete fluid to lubricate the vagina
Cervix—lower portion of the uterus
Chadwick’s sign—bluish color to the cervix, vagina and labia due to increased blood flow in pregnancy, can be seen as early as 6-8 weeks gestation
Clitoris—erogenous organ with erectile tissue covered by labia minora
Cornua—both sides of the upper outer area of the uterus where the fallopian tubes join the uterus
Ectropion—visible columnar cells at the cervical os
Endocervical canal—passageway within the cervix to the inner uterus
Endometrium—lining of the uterus
Escutcheon—pubic hair
Fimbriae—fingerlike projections that move the egg toward and into the fallopian tube
First polar body—other half of the product of division of the primary oocyte
Fornix (fornices)—spaces around the cervix in the vagina
Fourchette—area immediately below the introitus
Gonadarche—period when ovaries begin to secrete sex hormones
Gonadotropin—gonadotropin-releasing hormone pulse generator
Granulosa cells—cells lining an ovarian follicle that become luteal cells after ovulation
Ground substance—mucopolysaccharide between smooth muscle and collagen of the cervix
Hart’s line—line of change where skin transitions to smoother, moist skin
Hegar’s sign—softening and compressibility of the uterine isthmus
Hymen—membranous ring of tissue at the introitus
Introitus—opening to the vagina
Isthmus—uterine “neck” between cervix and body
Labia majora—two rounded folds of adipose tissue covered with pubic hair
Labia minora—folds of tissue between the labia majora
Lactobacilli—normal bacterial flora of the vagina
Leptin—hormone secreted by fat cells that plays a key role in appetite and metabolism
Meatus—opening of the urethra
Menarche—initiation of menses
Metaplasia—normal replacement of one cell type with another
Mittelschmerz—pain upon ovulation
Myometrium—middle, muscular layer of the uterus
Mucin—glycosylated proteins that form mucus that acts as lubricant and protectant
Nulliparous—a woman who has never had a child
Oogenesis—transformation of oogonia into oocytes
Oogonia—primordial female germ cells
Os—opening of the cervix
Parous—woman who has had a child
Peritoneum—thin membrane around abdominal organs that covers the bladder, uterus, and rectum
Rectouterine pouch—fold of peritoneum between the uterus and the rectum
Rectovaginal septum—tissue between the rectum and vagina
Rugae—thin ridges of tissue like an accordion that allow for expansion in the vagina
Squamocolumnar junction (SCJ)—where squamous cells and columnar cells meet on the cervix
Skene glands—small bilateral vulvar glands that secrete fluid to lubricate the urethra
Thelarche—breast development
Vasovagal response—bradycardia and syncope caused by stretching the cervical canal
Vesicouterine pouch—fold of peritoneum between the bladder and the uterus
Vesicovaginal septum—tissue between the bladder and the vagina
Vestibule—area inside the labia minora where openings of the urethra and the vagina are found
Zona pellucida—membrane surrounding the plasma membrane of the oocyte
Anatomy of the Female Reproductive System

An understanding of the anatomy of the female reproductive system is essential in caring for women. It is important to be able to recognize normal structures and to appreciate that there is a wide variation of normal among women.

External Genitalia

The vulva is a term designated for the external genitalia of the female. The vulva includes the mons pubis, labia majora and minora, clitoris, vestibule, hymen, urinary meatus, and Skene and Bartholin glands. Figure 1.1 and Figure 1.2 illustrate the external genitalia and its development from embryonic structures.

The mons pubis is the cushion-like area over the pubic bone. In adult woman, the mons is covered with curly, coarse pubic hair called the escutcheon. The pubic hair distribution is usually triangular but may extend up toward the umbilicus in a diamond shape in women who have higher levels of serum androgens.

The labia majora consist of two rounded folds of adipose tissue covered with pubic hair that extend from the mons to the perineum on either side of the vaginal opening. The labia minora, found between the majora, are thinner, pinkish in color, and hairless (Bickley & Szilagyi, 2013). The labia majora have the same position and general structure as the male scrotum and arise from the same tissues during embryonic development.

The labia minora have two folds above where they divide to descend on either side of the vestibule, ending at the fourchette just below the introitus, or the opening to the vagina. The upper fold forms the prepuce over the clitoris and the lower fold is the frenulum of the clitoris. The clitoris is an erogenous organ with erectile tissue. The clitoris is exquisitely sensitive in most women and is the primary source of sexual pleasure.

The vestibule is that area inside the labia minora where the openings to the urethra, vagina, and Skene and Bartholin gland ducts are found. The urethra is just above the vaginal opening and below the pubic arch. The vaginal introitus is rimmed with the hymen or its tags. Bartholin glands are located at either side of the lower portion of the introitus. The ducts for these glands open near the hymenal ring at 5 o'clock and 7 o'clock. Skene glands and ducts are found near the urethral meatus.

Figure 1.1. External female genitalia. From Tortora & Derrickson (2017). Used with permission.
Hart's line is the line of change in the vestibule where vulvar skin transitions to smoother, moister skin around the urethral meatus and the introitus.

Below the vulva is the perineal body and anal opening. These structures are examined as part of the external genitalia examination. Underlying these structures are the superficial muscles of the perineum and anal sphincter. The superficial muscles most often affected by childbirth include the bulbocavernous muscle, the superficial transverse perineal muscle, and the external and internal.
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anal sphincters. These structures, with the exception of the internal anal sphincter, converge on the central tendon of the perineum found between the introitus and the anus. The central tendon is part of the perineal body that may tear or be cut by episiotomy during birth (Figure 1.3).

**Internal Genitalia**

The vagina is a musculomembranous tube that gives access to the cervix for coitus and serves as the birth canal. The lower third of the vagina is supported and fixed by the pubococcygeus muscles of the levator ani group. The upper portion of the vagina and the cervix are supported by the cardinal and uterosacral ligaments. This portion of the vagina is capable of amazing expansion to accommodate birth. Vaginal rugae allow for elasticity and expansion. Vaginal length varies with genetics, parity, age, and estrogen effect. On average, the length of the vagina is about 6–8 cm anteriorly and 7–10 cm along the posterior wall (Cunningham et al., 2014). The elastic vagina elongates during intercourse and stretches widely during birth. The spaces around the cervix within the vagina are called the anterior, posterior, and lateral fornices.

The rectum supports the middle of the posterior vaginal wall. The anterior vaginal wall offers some support to the bladder (Phillippi, Latendresse, McCance, 2014). The principle innervations for the vagina are the pudendal nerve and the inferior hypogastric plexus, both of which derive from sacral nerve (S) 2–4. Lymph drainage for the vagina is to the para-aortic nodes.

The vagina is lubricated by an epithelial glycoprotein coat and transudate, cervical mucus from the endocervical columnar epithelium, and fluids from the Bartholin and Skene glands (Tufts et al., 2014). The milieu of the vagina is acidic and presents a barrier to many bacteria. The pH is normally between 4.0 and 4.5 in women of childbearing age and is maintained by the estrogen effect on the epithelial glycoprotein coat and lactobacilli (normal bacterial flora of the vagina). Vaginal secretions increase during pregnancy due to increased vascularity.

The lower portion of the vagina is separated from the urinary bladder by the vesicovaginal septum, and is separated from the rectum by the rectovaginal septum. The rectovaginal septum is at risk for lacerations and tears in the event of an operative birth. The upper vagina, around the cervix, is separated from the rectum via a fold of the peritoneum (thin membrane around abdominal organs that covers the uterus, bladder, and rectum) called the rectouterine pouch or pouch of Douglas. There is a similar, smaller pouch in front of the cervix and behind the bladder called the vesicouterine pouch. This area must be incised and the bladder brought forward during cesarean birth (Cunningham et al., 2014).
The cervix is the lower, narrow part of the pear-shaped uterus that protrudes into the vagina (Figure 1.4). About half of the cervix is within the vaginal canal. This part of the cervix has an external os followed by a passageway to the uterus called the endocervical canal. The canal ends at the internal os that opens into the uterine cavity. The size and shape of the cervix varies with parity, age, and the amount of estrogen and progesterone available. The cervix of a nulliparous woman is smaller and the external os is smaller and more circular than the cervix of a parous woman, which is wider and the external os is slit-like and more open. The length of the cervix plays a role in cervical integrity during pregnancy.

The blood supply to the cervix arrives via the uterine arteries that derive from the internal iliac arteries. The cervical branches of the uterine arteries are located at 3 o’clock and 9 o’clock to the cervical os. Venous blood drains to the hypogastric venous plexus.

The cardinal and uterosacral ligaments support the cervix and upper vagina. The cardinal ligament to attaches either side of the cervix and extends laterally to attach to connective tissue called the parametrium. The uterosacral ligament attaches to the posterior cervix and extends posteriorly to attach to the fascia of the sacrum. The main nerve supply to the cervix derives from the hypogastric plexus and follows the uterosacral ligament to the posterior cervix. Since there are sensory, sympathetic, and parasympathetic nerve fibers within the endocervical canal, any instrumentation through the cervical os has the potential for causing a vasovagal response in some women. Conversely, the external cervix has fewer sensory nerve endings, making small external biopsies less painful for women.

The structure of the cervix is complex. It is composed of collagenous connective tissue (smooth muscle and elastic tissue) and ground substance, a mucopolysaccharide. There is a much smaller percentage of smooth muscle in the cervix than in the uterine fundus. The cervix during pregnancy is extraordinarily strong and remains closed as the uterine contents increase in size and volume. Near the end of the pregnancy, the cervix softens and becomes distensible, allowing the fetus to be expelled. This dramatic change requires enzyme activity, an increase in cervical water content, hormonal changes, and an increase in

Figure 1.4. The uterus and associated structures. From Tortora & Derrickson (2017). Used with permission.
prostaglandins (Blackburn, 2013). After birth, the dilated cervix will shorten and become firmer, so that by 1 week postpartum, the os is dilated to only 1 cm.

Histologically, the cervix has two cell types: the columnar cells that line the endocervical canal and the opening of the cervix, and the squamous epithelium that covers the outside of the cervix. Most lower genital tract cancers occur where these two cell layers meet at the squamocolumnar junction (SCJ) (Phillippi, et al., 2014).

Columnar cells secrete mucin (a glycosylated protein that forms mucus that acts as lubricant and protectant) and have a reddened papillary appearance. The squamous epithelium is smooth and pink. At menarche, higher levels of estrogen cause glycogenation and other changes in the squamous epithelium. These changes and the increasing acidity in the vagina cause the squamous cells to migrate and cover the columnar cells. Metaplasia of the squamous and columnar cells occurs at the SCJ. This makes this area highly susceptible to invasion by human papilloma virus, hyperplasia, and dysplasia. Metaplasia occurs throughout a woman’s childbearing years; over time, the SCJ will migrate into the endocervical canal. The SCJ is the most important area for collection of cell samples for the Pap test.

Columnar cells are visible at the cervical os during adolescence, pregnancy, and when women use oral contraceptive pills because of the higher levels of estrogen during these events. This is often referred to as ectropion. Columnar cells produce cervical mucus that changes according to the hormones secreted during the menstrual cycle. During the late follicular phase and ovulation, when estrogen levels are highest, the mucus is clear, stretchy, slick, thin, and abundant. These characteristics of the mucus facilitate sperm passage from the vagina, through the cervix, and into the uterus. Under the influence of progesterone during the luteal phase, the mucus becomes scant, thick, pasty, and opaque. One of the important effects of progestin-only contraceptives is the thickening of the cervical mucus that serves as a barrier to sperm (Lewis et al., 2010).

Mucus from the columnar cells of the endocervical canal becomes thick and forms a mucous plug during pregnancy. This plug helps to prevent the passage of bacteria into the uterus. Increased vascularity and swelling of the cervix during early pregnancy will cause a bluish coloring called Chadwick’s sign.

The uterine cervix is connected to the body of the uterus by the isthmus. This segment of the uterus will soften and become compressible during early pregnancy, a feature specific to pregnancy known as Hegar’s sign.

The body or corpus of the uterus (Figure 1.4) is the most dynamic portion of the uterus. Here, the innermost lining, or endometrium, responds to ovarian hormones every month, building in preparation for implantation, then sloughing as menses if pregnancy does not occur (Behera, 2016). This is also where implantation and gestation take place and where the powerful forces of labor are generated. An adult woman’s uterus is about 3–4 inches long before any pregnancies have occurred. After pregnancy and postpartum involution, the range is 4.5–5 inches. The weight of the nonpregnant uterus is about 60 grams if never pregnant, heavier depending numbers of pregnancies (Cunningham et al., 2014). During pregnancy, the muscles of the uterus hypertrophy and the weight will increase to about 38.8 oz by 40 weeks’ gestation. This hypertrophy does not extend to the cervix, which contains much less muscle tissue.

Attached to both sides of the upper, outer portion of the uterus, known as the cornua, are the fallopian tubes, round ligaments, and ovarian ligaments. The body of the uterus, unlike the cervix, is mostly muscle tissue. Inside the uterus, the anterior and posterior walls lie very close to each other, forming a slit-like space (Cunningham et al., 2014). Within this space is the very active endometrium, the first of three layers within the uterine corpus (Behera, 2016). The endometrial cyclic response to hormones is explained later in this chapter.

The middle layer of the uterus is the myometrium. This layer is composed of smooth muscle united by connective tissue and makes up most of the uterine bulk. The outermost layer is the perimetrium, a thin layer of epithelial cells. The myometrium contains four layers of muscles with blood vessels coursing through each layer. The inner layer of muscle fibers is composed of spirals on the long axis of the uterus. The middle layers of muscle fibers have interlacing fibers that form a figure eight around the many blood vessels. When the placenta is expelled after birth, the empty uterus contracts and the muscles of this layer become “living ligatures” that help halt the blood flow. The outer two layers of muscle fibers are smooth muscle in bundles of 10 to 50 overlapping cells interspersed with connective tissue and ground substance that transmit contractions during labor (Blackburn, 2013, p. 115). Interestingly, the layers of the myometrium arise from different embryonic locations, so they respond to uterine stimuli in different ways. The result is a rhythmic contractile force that propels the fetus toward the cervical opening regardless of the fetal presentation.

The uterine blood supply comes to the uterus from the internal iliac artery via the ovarian and uterine arteries. These arteries feed the arcuate, radial, basal, and spiral arteries. The spiral arteries of the endometrium change during the menstrual cycle. If pregnancy does not occur during the cycle, the spiral arteries constrict, the endometrial matrix breaks down, and menses occurs. There is extensive collateral circulation that is
enhanced during pregnancy. This arterial system is very efficient in supplying nutrients and oxygen to the growing uteroplacental unit and fetus, but if hemorrhage occurs, this interconnected system of vessels makes control of the bleeding difficult.

There are two sets of lymphatics within the uterine body. One set drains into the internal iliac nodes and the other ends in the para-aortic lymph chain (Cunningham et al., 2014). The nerve supply to the uterus is derived mostly from the sympathetic nervous system and partly from the parasympathetic system. The parasympathetic system fibers derive from sacral nerves 2, 3, and 4. The sympathetic system ultimately comes from the aortic plexus just below the sacral promontory. Sensory fibers from the uterus derive from the 11th and 12th thoracic nerve root and carry the pain signals from contractions of labor to the central nervous system. The sensory nerves from the cervix and upper vagina move through the pelvic nerves to sacral nerves 2, 3, and 4. The primary nerve of the lower vagina is the pudendal nerve.

The fallopian tubes (Figure 1.4) extend from the upper sides the uterus. These oviducts vary from 8–14 cm in length. There are three parts: the fimbria, ampulla, and the isthmus. The fimbria opens into the abdominal cavity and have finger-like, ciliated projections, with one longer projection that reaches closer to or touches the ovary, which capture the ovum from the surface of the ovary. The ampulla is the widest section of the uterine tubes. The smooth muscle and ciliated cells within the tubes contract rhythmically all the time. At ovulation, these contractions become stronger and more frequent in order to move the ovum toward the uterine lining. Fertilization, if it occurs, will typically occurs in the ampulla (Blackburn, 2013). The isthmus is the narrowest section of the tubes, connecting the ampulla to the uterine cavity.

The ovaries reside on either side of the uterus and are attached to the ovarian ligament that extends to and attaches to the cornua. Other ligaments help support the ovaries and serve as conduits for vessels and nerves. The top layer of the ovary contains oocytes and developing follicles. The core of the ovary is composed of connective tissue, blood vessels, and smooth muscle. Ovaries vary in size but typically are approximately 2.5–5 cm long and 1.5–3 cm wide, giving them an almond shape. Ovaries are sometimes palpable during the bimanual examination of the adnexa during pelvic examination (Bickley & Szilagyi, 2013).

**Menstrual Cycle Physiology**

The menstrual cycle occurs regularly in most women from menarche to menopause with some expected irregularity during the first year after menarche and the years of perimenopause. It is regulated by complex interactions between the hypothalamus, the pituitary gland, the ovaries, and the uterus. This section will highlight the hormonal changes and how these changes affect the ovary and the uterine lining.

**Beginnings**

The gender of an embryo is determined at the time of fertilization. The male contribution of an X chromosome combined with the female-contributed X chromosome produce the basis for a unique female human. Before the seventh week of gestation, the gonads of male and female embryos look the same. It is not until the sixteenth week after fertilization that primordial germ cells called **oogonia** can be detected along the genital ridge in females (Moore, Persaud, & Torchia, 2016). By 7 months of gestation, all of the oogonia have been transformed into primary oocytes and no new oogonia are formed. At birth, a female newborn will have an average of 200,000–400,000 follicles on the two ovaries. Each follicle contains a primary oocyte that has already begun the first meiotic division (Moore et al., 2016). At puberty, only about 10%, or 40,000, of these early follicles will remain due to atresia. Of these, only about 400–500 will develop into a primary and secondary follicles.

**Oogenesis** is the sequence of events that transforms the oogonia into an oocyte ready to be fertilized. In early fetal life, oogonia divide via mitosis to form primary oocytes. By birth, the primary oocytes have begun the first meiotic division but the process is arrested and remains that way until just before ovulation, when the first meiotic division is completed. At this division, a secondary oocyte receives the bulk of the cytoplasm and the **first polar body** is formed. At ovulation, the secondary oocyte begins its second meiotic division, but the process halts and does not resume unless the secondary oocyte is fertilized by a sperm (Moore et al., 2016). The process of oogenesis is depicted in Figure 1.5.

At term, the gonadotropin-releasing hormone pulse generator, or **gonadostat**, is at work in the fetus. The gonadostat responds to high levels of maternal estrogen by releasing small amounts of gonadotropin-releasing hormone. After birth, when maternal estrogens are removed, the gonadotropins follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are released from the newborn’s pituitary gland (Tufts et al., 2014). During infancy and childhood, estrogen levels are very low and gonadotropin secretion is restrained in a positive feedback fashion.

**Onset of Puberty**

When a girl is 8–12 years old, the gonads begin to produce estrogen and puberty begins with **thelarche** (breast development). Estrogen production begins in
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Response to complex interrelated changes involving the central nervous system, hypothalamus, pituitary, and ovary. Onset of these changes is influenced by genetics, general health, nutrition, geographic location, exposure to light, and body weight (Tufts et al., 2014; Silverthorn, 2016). It is thought that increasing body fat and the adipose hormone leptin facilitate maturation, and both are important to the onset of menses. Reproductive maturation involves the central nervous system and the endocrine system in a sequence of changes that will lead to menarche.

The first in the sequence of events that will lead to reproductive maturation is the release of gonadotropin-releasing hormone from the hypothalamus that will cause the release of FSH and LH from the pituitary. These hormones will induce gonadarche and adrenarche, and the hormones from the gonads and adrenal glands stimulate the development of secondary

### Summary of oogenesis and follicular development

<table>
<thead>
<tr>
<th>Age</th>
<th>Oogenesis</th>
<th>Follicular development</th>
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<tbody>
<tr>
<td><strong>Fetal period</strong></td>
<td>Oogonium</td>
<td>Primordial follicle</td>
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<tr>
<td></td>
<td>Mitosis</td>
<td></td>
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<tr>
<td></td>
<td>2n Oogonium</td>
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<tr>
<td></td>
<td>Meiosis in progress</td>
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<tr>
<td></td>
<td>2n Primary oocyte (in prophase I)</td>
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<tr>
<td><strong>Childhood (no development of follicles)</strong></td>
<td>2n Primary oocyte (still in prophase I)</td>
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<tr>
<td></td>
<td>Meiosis I completed by one primary oocyte each month</td>
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<td></td>
<td>First polar body</td>
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<tr>
<td></td>
<td>Meiosis II of first polar body may or may not occur</td>
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<tr>
<td></td>
<td>All polar bodies degenerate</td>
<td></td>
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<tr>
<td><strong>Puberty to menopause each month</strong></td>
<td>2n Primary oocyte</td>
<td></td>
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<tr>
<td></td>
<td>Meiosis I completed by one primary oocyte each month</td>
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<td>First polar body</td>
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<td></td>
<td>Meiosis II of first polar body may or may not occur</td>
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<tr>
<td></td>
<td>All polar bodies degenerate</td>
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*Figure 1.5.* Oogenesis. From Tortora & Derrickson (2017). Used with permission.
sexual characteristics such as breast growth, pubic and axillary hair growth, and changes in the vagina (Bickley & Szilagyi, 2013; Tufts et al., 2014). These changes also set the stage for the first ovulation and first ovulatory menstrual period. Figure 1.6 illustrates the sequence for the beginning of hormonal stimulation of the ovary and the beginning negative and positive feedback loops.

The average age for menarche in the United States varies according to population, race, socioeconomic conditions, and nutrition. Among well-nourished white females, the average age at menarche is 12.43 (ACOG, 2015). Black females begin about 5 or 6 months earlier. Table 1.1 describes the characteristics of the normal menstrual cycle.

Once menarche and ovulatory cycles are established, puberty is complete and the female is able to reproduce physiologically; however, social and cultural norms influence reproductive behaviors and
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Throughout the childbearing years, the hypothalamic–pituitary–ovarian (HPO) axis and the uterus go through cycles in production of hormones and changes in the endometrial lining.

The Hypothalamic–Pituitary–Ovarian Axis

Once established, the menstrual cycle continues based on feedback mechanisms between the hypothalamus, pituitary, and the ovary. The hypothalamus is a pearl-sized organ at the base of the brain near the optic chiasm. The cells of the hypothalamus synthesize and secrete many releasing hormones that act on the pituitary and other endocrine glands. It is responsible for regulating thirst, sleep, hunger, libido, and many endocrine functions (Tufts et al., 2014). The hypothalamus responds to lower serum levels of estrogen near the end of a cycle by secreting an FSH-releasing factor that will travel to the nearby pituitary gland and stimulate the release of FSH. FSH will stimulate the growth of follicles on the ovary, with one follicle becoming dominant for each cycle. Later, when the follicle releases enough estrogen, the hypothalamus will secrete an LH-releasing hormone that will travel to the pituitary and stimulate the release of LH.

The pituitary gland is located in the sella turcica, below the hypothalamus and optic chiasm. It has a stalk connecting it to the hypothalamus and two lobes, anterior and posterior. The anterior lobe synthesizes and secretes FSH, LH, and many other hormones that affect specific target organs. Figure 1.6, depicts the early HPO axis with feedback loops.

The ovaries are the target organs for the gonadotropins secreted by the anterior pituitary. They are located on either side of the uterus, suspended by the ovarian ligament. They are covered in follicles, each with the potential for growing and releasing an ovum. Figure 1.7 shows the ovarian surface and the stages of the follicle.

The functioning of the HPO axis is dependent on feedback loop control. The most common form of feedback control is negative feedback. This occurs when rising hormone serum levels cause a decrease in another hormone. The other form of feedback control is positive feedback, where rising levels of one hormone causes a rise in another. These feedback mechanisms help to keep the hormones within normal ranges.

The hormones involved in the menstrual cycle include the gonadotropin-releasing hormones from the hypothalamus, the gonadotropin-stimulating hormones from the pituitary, and the ovarian hormones from the ovary (Table 1.2).

Menstrual Cycle Phases

There are two parts to the menstrual cycle that occur simultaneously. To help clarify what is happening in each part, this section will separate the ovarian cycle and the endometrial cycle.

Ovarian cycle

There are three phases of the ovarian cycle: the follicular phase, ovulation, and the luteal phase. The follicular phase begins on the first day of menses and is more variable in length than the luteal phase. It may last anywhere from 10 to 21 days (Silverthorn, 2016). The luteal phase is the most predictable in length because of the life span of the corpus luteum. It lasts 13–15 days unless pregnancy occurs and the life of the corpus luteum continues (Shulman, 2011).

The follicular phase actually begins during the last days of the previous cycle when decreasing estrogen and inhibin deliver a negative feedback signal to the hypothalamus and pituitary. This signal stimulates the hypothalamus to release an FSH-releasing factor that stimulates the anterior pituitary to release FSH. The primordial follicles on the ovary each contain an oocyte and a layer of granulosa cells that will respond to the FSH. It is thought that there is at least a 3-month period of stimulation to recruit a dominant follicle for one ovulation (Blackburn, 2013). It is this one primed follicle that responds to the FSH first and begins to grow before

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Table 1.1 Normal menstrual cycle characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
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<tbody>
<tr>
<td>Menarche (average age)</td>
<td>White: 12.43 years, Black: ~11.5 years</td>
</tr>
<tr>
<td>Menstrual cycle length</td>
<td>First year of menses: 32.2 days (range 20–60 days)</td>
</tr>
<tr>
<td></td>
<td>Typical menstrual cycle length during the years between menarche and menopause: 21–45 days (9%–15% are 28 days in length)</td>
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<tr>
<td></td>
<td>Flow length</td>
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<tr>
<td></td>
<td>First year</td>
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<tr>
<td></td>
<td>Typical length</td>
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<tr>
<td></td>
<td>Flow amount</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Flow length</td>
<td></td>
</tr>
<tr>
<td>First year</td>
<td>2–7 days</td>
</tr>
<tr>
<td>Typical length</td>
<td>4–6 days (less than 2 or more than 8 considered abnormal)</td>
</tr>
<tr>
<td>Flow amount</td>
<td>20–80 mL (second day heaviest)</td>
</tr>
</tbody>
</table>

other follicles on the ovaries that may respond. This follicle takes in more FSH than the others and grows more rapidly. Within this dominant or primary follicle, the oocyte begins to grow and the zona pellucida is formed and grows between the oocyte and the granulosa cells (Tufts et al., 2014). Just before ovulation, the corona radiata will form around the zona pellucida. As these changes progress, some of the follicles that had started to respond to FSH but did not fully mature undergo atresia (Shulman, 2011).

During the follicular phase, the ovary and the primary follicle are secreting both estrogen and progesterone, with estrogen being produced in higher amounts. FSH stimulates the granulosa cells of the dominant follicle to produce much higher levels of estrogen and to upregulate LH receptors within the follicle cells (Tufts et al., 2014). The higher levels of estrogen cause positive feedback stimulation of the hypothalamus and pituitary that result in a rise in LH. Near the end of the follicular phase, estrogen will peak, causing LH to surge and reach its highest
level about 12–24 hours before ovulation (Blackburn, 2013). The higher levels of LH are a very reliable signal of impending ovulation. LH detection kits are available to help couples determine when ovulation occurs (US Food and Drug Administration (FDA), 2014).

LH has other functions. It stimulates ovarian tissue in a way that increases androgen levels and enhances the libido (Shulman, 2011). It stimulates the remaining granulosa cells of the ruptured follicle to become lutein cells so that the corpus luteum is formed. LH is also responsible for stimulating the oocyte to resume meiosis (Silverthorn, 2016).

Ovulation occurs after a surge and peak level of LH, but there are several factors that facilitate the extrusion of the ovum from the follicle. As the follicle and oocyte have grown, the oocyte has shifted to one side of the follicle. When estrogen begins to decrease, the follicle swells and prostaglandins, proteolytic enzymes, and smooth muscle contractions cause the follicular wall to burst open and the ovum is extruded (Blackburn, 2013). The phenomenon of mittelschmerz or pain upon ovulation is thought to be due to the rupture of the follicle and the release of the ovum and surrounding fluid that can irritate the abdominal lining.

After ovulation, the remaining cells of the follicle are re-vascularized and transformed into the corpus luteum by taking up hormones and lutein pigment that gives it a yellow color (Shulman, 2011). The corpus luteum continues to secrete estrogen and progesterone, but now progesterone is produced in higher amounts. Progesterone will cause changes in the endometrium and suppress new follicular growth. It will peak between 7 and 8 days after the rapid increase of LH. This highest level of progesterone corresponds with the time of implantation, if fertilization has occurred. If implantation occurs, the corpus luteum is maintained by the human chorionic gonadotropin secreted by the conceptus so that progesterone levels are maintained.

If fertilization has not occurred, the corpus luteum begins involution and estrogen, progesterone, and inhibin levels will fall. Cellular changes during involution will result in a small scar on the ovary called the corpus albicans (Silverthorn, 2016). The decrease in the ovarian hormones causes a negative feedback stimulation of the hypothalamus and pituitary and the process begins all over again.

### Endometrial cycle

The endometrial cycle has three phases: proliferative, secretory, and menstrual. These phases correspond with events occurring in the ovarian cycle. Proliferative changes in the endometrial lining occur under the influence of estrogen during the corresponding follicular phase. During this phase, there is hyperplasia of the endothelial cells and growth of the stroma within the endometrium (Silverthorn, 2016). The endometrial height will reach 0.5–5 mm during this phase.

After ovulation, when the corpus luteum begins producing more progesterone, the secretory phase begins. During this time, the epithelial cells accumulate glycogen, become more tortuous, the spiral arteries coil, and capillary permeability of the stroma increases (Cunningham et al., 2014). If fertilization occurs, the secretory endometrium begins transformation to decidual tissue and will be 5–10 mm deep when implantation begins (Blackburn, 2013).

If fertilization does not occur, then the endometrium degenerates and the menstrual phase begins. The corpus luteum atrophies, estrogen and progesterone production decreases, and prostaglandins are released. Prostaglandins cause vasoconstriction and other changes that lead to ischemia and necrosis of the secretory structures. At the same time, there is the breakdown of proteins within the superficial layer and sloughing. Rupture of capillaries during sloughing leads to bleeding. Bleeding and myometrial contractions help remove the degenerated endometrium (Tufts, et al., 2014).

Menses typically lasts 4–6 days, but may be considered normal if all of a woman’s bleeding is consistently between 2 and 8 days in length. The prostaglandins released will cause contractions, ischemia, and pain in some women. These contractions, along with increasing levels of estrogen, which encourage clot formation, eventually stop the bleeding (Shulman, 2011). Figure 1.8 illustrates the endocrine changes, ovarian cycle, and endometrial cycle in one chart.

The menstrual cycle is a complex and wondrous phenomenon that ensures the continuation of the human

### Table 1.2  Hormones of the menstrual cycle

<table>
<thead>
<tr>
<th>Hypothalamus</th>
<th>Follicle-stimulating hormone releasing factor</th>
<th>Gonadotropin-releasing factor</th>
<th>Luteinizing hormone-releasing factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pituitary</td>
<td>Follicle-stimulating hormone</td>
<td>Luteinizing hormone</td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>Progesterone</td>
<td>Estrogen</td>
<td>Testosterone</td>
</tr>
</tbody>
</table>

Adapted from: Tufts, Rodway, Huether, & Deneris (2014).
Estrogens are the primary ovarian hormones before ovulation; after ovulation, both progesterone and estrogens are secreted by the corpus luteum.

Resources for Women


Resources for Healthcare Providers

Association of Reproductive Health Professionals: http://www.arhp.org/topics/pregnancy

References
